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About the Journal

Bagcilar Medical Bulletin (Bağcılar Tıp Bülteni) (BMB) is periodical scientific publishing of Health Sciences University Turkey, İstanbul Bağcılar Training and Research Hospital. This editorially independent, unbiased, international journal periodically publishes peer-reviewed work in the all medical fields on an international scientific basis. Publication language is English for full text and Turkish and English for abstracts. The journal is published in English since December issue of 2016 as an e-journal.

The journal is published quarterly in March, June, September and December.

Original clinical and experimental articles,interesting case studies, and literature reviews made from relevant authors in their branches will be accepted for evaluation in BMB.

The editorial policies are based on the "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations)" by the International Committee of Medical Journal Editors (2017, archived at http://www.icmje.org/) rules.

Bagcilar Medical Bulletin is indexed in **TÜBİTAK/ULAKBİM, Türk Medline, Türkiye Atıf Dizini, Index Copernicus, ProQuest, J-Gate, EuroPub** and **ScopeMed**.

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Bağcılar Tıp Bülteni/Bagcilar Medical Bulletin, (BTB) Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesinin süreli bilimsel yayınıdır. Uluslararası, hakem değerlendirmeli, İngilizce ve açık erişim olarak yılda 4 sayı(Mart, Haziran, Eylül, Aralık) olarak yayınlanan bilimsel bir dergi olup, tıbbın tüm alanlarındaki bilgi birikiminin uluslararası bilimsel platformda yayılabilmesini amaçlamaktadır. Bu amaçla tıbbın her alanında yapılmış orijinal klinik ve deneysel çalışmalar ve ilginç olgu sunumları ile konusunda uzman yazarların yaptığı literatür derlemeleri yayın için değerlendirmeye alınır.

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Yayın politikaları "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations)" (2016, http://www.icmje.org/) temel alınarak hazırlanmıştır.

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T.C.Sağlık Bakanlığı Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesi adına Hastane Yöneticisi Ahmet Yaser Müslümanoğlu, Prof. M.D (Türkiye Cumhuriyeti Sağlık Bakanlığı Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesi, Üroloji Kliniği, İstanbul, Türkiye).

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Description

Bagcilar Medical Bulletin is a peer reviewed English journal aiming to publish original research, current review articles, case reports and letters related to all medical fields. The journal is currently published quarterly as online publication. The articles will become freely available to all readers in pdf format as soon as they have been accepted after peer review. Accepted articles will immediately appear as a part of the issue belonging to that publication period. The journal is currently published by Galenos Publishing House. The journal is using online manuscript submission, review and tracking systems.

Editorial Policies and Review Process

Publication Policy

Bagcilar Medical Bulletin considers for publication papers in the following categories:

- Original researches,
- Brief researches,
- Case reports,
- Reviews,
- Letters to the editor

The journal gives high priority to original studies in publication because of aiming to add the findings of searches in Turkey to international scientific knowledge, to share them within the international science milieu and to constitute the introduction of Turkish scientists. The review articles to be published in the journal are authorized by the editor to the relevant authors working on the subject.

General Principles

Papers that have not been published before or under evaluation by other publications are accepted for evaluation by the journal, if approved by each of the author. Publication board may amend manuscripts upon informed consent of authors. Editors and redactors are fully empowered to correct mistakes related to orthography, citation as given in National Library of Medicine MEDLINE/PubMed Resources.

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Bagcilar Medical Bulletin is committed to upholding the highest standards of publication ethics and observes the following principles of Publication Ethics and Malpractice Statement which is based on the recommendations and guidelines for journal editors developed by the Committee on Publication Ethics (COPE), Council of Science Editors (CSE), World Association of Medical Editors (WAME) and the International Committee of Medical Journal Editors (ICMJE).

All submissions must be original, unpublished (including as full text in conference proceedings), and not under the review of any other publication synchronously. Each manuscript is reviewed by one of the editors and at least two referees under double-blind peer review process. We reserve the right to use plagiarism detecting software to screen submitted papers at all times. We check for plagiary and fraudulent data; falsification (fabrication or manipulation of research data, tables, or images) and improper use of humans or animals in research. All manuscripts not in accordance with these standards will be removed from the publication. This also contains any possible malpractice discovered after the publication. In accordance with the code of conduct we will report any cases of suspected plagiarism or duplicate publishing.

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Biomedical Research-revised in 2006 http://www.wma.net/en/30publications/10policies/a18/

For this reason, regarding the subjects of clinical experiments, it should be indicated in the submitted manuscripts definitely that the above mentioned codes of conduct were applied. Besides approvals, from national or local ethical committees should be sent together with the papers as well. Manuscripts that report the results of experimental investigation with human subjects must include a statement that informed consent was obtained after the procedure(s) had been fully explained. In the case of children and those under wardship or with confirmed insanity, authors are asked to include information about whether the legal custodian's assent was obtained. And a letter of affirmation signed by all authors, confirming the collection of informed consents has to be sent to the journal.

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The language of the Bagcilar Medical Bulletin is American English. In addition, abstracts of the articles are published in both English and Turkish, and abstracts in both languages are requested from the authour(s).

Manuscript Organization And Format

All correspondence will be sent to the first-named author unless otherwise specified. Papers should be accompanied by a cover letter indicating that the paper is intended for publication and specifying for which section of the Journal it is being submitted (i.e., original research article,brief research article, review article, case report or letter to the editor). In addition, a Copyright Transfer Form, Author Contribution Form and ICJME Form for Disclosure of Potential Conflicts of Interest must be submitted. Authors will be notified of the receipt of their paper and the number assigned to it. The number should be included in all further correspondence. All parts of the manuscript, including case reports, quotations, references, and tables, must be double-spaced throughout. All four margins must be at least 2.5 cm. The manuscript should be arranged in the following order, with each item beginning a new page: 1) title page, 2) abstract, 3) text, 4) acknowledgement 5) references, and 6) tables and/or figures. All pages must be numbered consecutively.

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On the title page, include full names of authors, academic or professional affiliations, and complete address with phone, fax number(s) and e-mail address (es) of the corresponding author. Acknowledgments for personal and technical assistance should be indicated on the title page.

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Title of the manuscript in English should be written in English abstract, and a Turkish title must be for Turkish abstract.. All articles should include abstract and keywords. For abstracts are most distinct parts of an article and take place on the electronic

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Manuscript Types

Original Research

Original research articles report substantial and original scientific results within the journal scope. Original research articles comprised of Abstract, Key Words, Introduction, Material and Methods, Results, Discussion, Conclusion, References and Table/Figures. The abstract should be structured as the following.

Abstract

The abstract should be no longer than 500 words and structured as follows: objective, method, results, and conclusions. Objective -the primary purpose of the article; Material and Method(s) -data sources, design of the study, patients or participants, interventions, and main outcome measures; Results -key findings; Conclusions -including direct clinical applications.

Key Words

Up to 3-10 key words in English and in Turkish should be in accordance with National Library of Medicine's Medical Subjects Subheadings (MeSH).

Introduction

This section should contain a clear statement of the general and specific objectives as well as the hypotheses which the work is designed to test. It should also give a brief account of the reported literature. The last sentence should clearly state the primary and secondary purposes of the article. Only, the actual references related with the issues have to be indicated and data or findings related with the current study must not be included in this section.

Material and Methods

This section should contain explicit, concise descriptions of all procedures, materials and methods used in the investigation to enable the reader to judge their accuracy, reproducibility, etc. This section should include the known findings at the beginning of the study and the findings during the study must be reported in results section. Ethics Committee Approval of the research and written Informed Consent obtained from the participants should be indicated.

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The methods, apparatus (the manufacturer's name and address in parentheses), and procedures in sufficient detail must be defined to allow others to reproduce the results. References to established methods, including statistical methods (see below) must be given and brief descriptions for methods that have been published but are not well-known must be provided; new or substantially modified methods must be described, the reasons for using them must be given, and their limitations of the methods must be evaluated. The all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration must be identified. Authors submitting review manuscripts should include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.

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The results should be presented in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. The all the data in the tables or illustrations should not be repeated in the text; only the most important observations must be emphasized or summarized. Extra or supplementary materials and technical detail can be placed in an appendix where they will be accessible but will not interrupt the flow of the text, or they can be published solely in the electronic version of the journal.

Discussion

The findings of the study, the findings and results which support or do not support the hypothesis of the study should

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Conclusions derived from the study should be stated. For experimental studies, it is useful to begin the discussion by summarizing briefly the main findings, then explore possible mechanisms or explanations for these findings, compare and contrast the results with other relevant studies, state the limitations of the study, and explore the implications of the findings for future research and for clinical practice. The conclusions should be linked with the goals of the study but unqualified statements and conclusions not adequately supported by the data should be avoided. New hypotheses should be stated when warranted, but should be labeled clearly as such.

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Tables, graphics and illustrations should be numbered in Arabic numerals in the text. The places of the illustrations should be signed in the text. Detailed information is under the related heading in below.

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Brief researches are similar to original research in that they follow the same format and guidelines, but they consider small-scale research or research that is in early stages of development. These may include preliminary studies that has a simple research design or a small sample size and that have produced limited pilot data and initial findings that indicate need for further investigation. Brief researches are much shorter than manuscripts associated with a more advanced, larger-scale research project. They are not meant to be used for a short version of an article about research that would otherwise qualify for a full original research manuscript or for publishing material on research that lacks significance, is not rigorous or, if expanded, would not qualify for a full article or for research.

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Case reports consider new, interesting and intriguing case studies in detail. They should be unique and present methods to overcome any health challenge by use of novel tools and techniques and provide a learning source for the readers. Case reports comprise of: Abstract (unstructured summary), Key-words, Introduction, Case Report, Discussion, Reference, Tables and Figures. Written informed consent of the patient should be obtained and indicated in the manuscript.

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Review articles are written by individuals who have done substantial work on the subject or are considered experts in the field. The Journal invites authors to write articles describing, evaluating and discussing the current level of knowledge regarding a specific subject in the clinical practice.

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Original papers and reviews have no specific word limitation. A case report must be strictly limited to 1000 words excluding abstract and have minimal figures, tables, and references. Letters to the Editor (maximum of 500 words, including references; no tables or figures) will be considered if they include the notation "for publication." A letter must be signed by all of its authors. Letters critical of an article published in the journal must be received within 12 weeks.

Preparation of Manuscripts

The "Bagcilar Medical Bulletin'' follows the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" (International Committee of Medical Journal Editors - http://www.icmje.org/). Upon submission of the manuscript, authors are to indicate the type of trial/research and provide the checklist of the following guidelines when appropriate:

CONSORT statement for randomized controlled trials (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel group randomized trials. JAMA 2001; 285: 1987-91) (http://www.consort-statement.org /),

PRISMA for preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.) (http://www.prisma-statement.org /),

STARD checklist for the reporting of studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al, for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4.) (http://www.stard-statement.org /),

INSTRUCTIONS TO AUTHORS

STROBE statement-checklist of items that should be included in reports of observational studies (http://www.strobe-statement.org /),

MOOSE guidelines for meta-analysis and systemic reviews of observational studies (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis of observational Studies in Epidemiology (MOOSE) group. JAMA 2000; 283: 2008-12).

CARE guidelines are designed to increase the accuracy, transparency, and usefulness of case reports. (Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; the CARE Group. The CARE Guidelines: Consensus-based Clinical Case Reporting Guideline Development.) (http://www.care-statement.org /

References

Although references to review articles can be an efficient way to guide readers to a body of literature, review articles do not always reflect original work accurately. Readers should therefore be provided with direct references to original research sources whenever possible. On the other hand, extensive lists of references to original work on a topic can use excessive space on the printed page. Small numbers of references to key original papers often serve as well as more exhaustive lists, particularly since references can now be added to the electronic version of published papers, and since electronic literature searching allows readers to retrieve published literature efficiently. Using abstracts as references should be avoided.

References to papers accepted but not yet published should be designated as “in press” or “forthcoming”; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication. Information from manuscripts submitted but not accepted should be cited in the text as “unpublished observations” with written permission from the source. Citing a “personal communication” should be avoided unless it provides essential information not available from a public source, in which case the name of the person and date of communication should be cited in parentheses in the text. For scientific articles, written permission and confirmation of accuracy from the source of a personal communication must be obtained.

Reference Style and Format

The Uniform Requirements style for references is based largely on an American National Standards Institute style adapted by the National Library of Medicine for its databases. Authors should consult NLM’s Citing Medicine (http://www.nlm.nih.gov/bsd/uniform_requirements.html) for information on its recommended formats for a variety of reference types. References should be numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by Arabic numerals in parentheses. References cited only in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure. The titles of journals should be abbreviated according to the style used in the list of Journals in National Library of Medicine sources. In addition the list should be obtained in the web address of http://www.nlm.nih.gov. Accuracy of citation is the author’s responsibility. All references should be cited in text. Type references in the style shown below. If there are more than 6 authors, list them followed by et al. Abbreviations of journal names should conform to the style used in National Library of Medicine. If a journal is not indexed in National Library of Medicine’s MEDLINE/PubMed, it should not be abbreviated.

Examples for References:

1. For articles in journals:

For the published article from the journal which placed and abbreviated in MEDLINE:

Crow SJ, Peterson CB, Swanson SA, Raymond NC, Specker S, Eckert ED, et al. Increased mortality in bulimia nervosa and other eating disorders. Am J Psychiatry 2009;166(12):1342-1346.

For the published article from the journal which is not placed and is not abbreviated in MEDLINE:

Sevinçer GM, Konuk N. Emotional eating. Journal of Mood Disorders 2013;3(4):171-178.

2. For the supplement:

For the published article from the journal which placed and abbreviated in MEDLINE:

Sharan P, Sundar AS. Eating disorders in women. Indian J Psychiatry 2015:57(Suppl 2):286-295.

For the published article from the journal which is not placed and is not abbreviated in MEDLINE:

Maner F. Yeme bozukluklarının tedavisi. Anadolu Psikiyatri Dergisi 2009;10(Ek 1):55-56.

3. For articles in press:

Cossrow N, Pawaskar M, Witt EA, Ming EE, Victor TW, Herman BK, et al. Estimating the prevalence of binge eating disorder in a community sample from the United States: comparing DSM-IV-TR and DSM-5 criteria. J Clin Psychiatry, 2016. (in press).

4. For the citations from books:

Books edited by one editor:

McKnight TL. Obesity Management in Family Practice. 1st ed., NewYork: Springer, 2005:47-51.

INSTRUCTIONS TO AUTHORS

For the citation from a section of book edited by editor(s):

Jebb S, Wells J. Measuring body composition in adults and children. In Clinical Obesity in Adults and Children, Copelman P, Caterson I, Dietz W (editors). 1st ed., London: Blackwell Publishing, 2005:12-18.

If the authors of the cited section are the editors of the book:

Eckel RH (editor). Treatment of obesity with drugs in the new millennium. In Obesity Mechanisms and Clinical Management. First ed., Philadelphia: Lippincott Williams & Wilkins, 2003:449-476.

For the citation from a translated book:

McGuffin P, Owen MJ, Gottsman II. Psikiyatri Genetiği ve Genomiği. Abay E, Görgülü Y (Çevirenler) 1st ed., Istanbul: Nobel Tıp Kitabevleri, 2009:303-341.

5. For the citation from thesis:

Keçeli F. Yeme bozukluğu hastalarında obsesif kompulsif bozukluk ve kişilik bozukluğu. Thesis, T.C. Sağlık Bakanlığı Bakırköy Prof. Dr. Mazhar Osman Ruh Sağlığı ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi, Istanbul:2006.

6. For the citation from posters:

Akbaş Öncel D, Akdemir A. Üniversite öğrencilerinde diyet, beden algısı ve kendilik algısı arasındaki ilişkiler. 47. Ulusal Psikiyatri Kongresi Özet Kitabı, 26-30 Ekim 2011, Antalya, 2011:102.

7. Online Article:

Kaul S, Diamond GA. Good enough: a primer on the analysis and interpretation of noninferiority trials. Ann Intern Med [Internet]. 2006 Jul 4 [cited 2007 Jan 4];145(1):62-9. Available from:http://www.annals.org/cgi/reprint/145/1/62.pdf

SUBMISSION TO JOURNAL

All new manuscripts must be submitted through the Bagcilar Medical Bulletin online manuscript submission and peer review system. Complete instructions are available at the website (). A cover letter should accompany with manuscripts, including the knowledge of:

•The findings of previous same studies should be informed and should be cited. The copies of previous same studies should be sent with manuscripts that might help to the editor in the decision process.

•The knowledge of "all authors have read and accepted the study in its form, all authors meet the criteria for being in authorship" should be stated.

•All helpful things for editorial ship should be stated: The comments of previous editor/reviewers and the response of authors should be added if the manuscript has been sent to another journal for consideration, previously. The editor requested this information to accelerate the publication process.

SUBMISSION CHECKLIST

It is hoped that this list will be useful during the final checking of an article prior to sending it to the journal's editor for review. Please consult this Guide for Authors, for further details of any item.

Ensure that the following items are present:

- Cover letter to the editor
- The category of the manuscript
- Acknowledgement of "the paper is not under consideration for publication in another journal"
- Disclosure of any commercial or financial involvement
- Reviewing the statistical design of the research article
- Last control for fluent English
- Copyright Transfer Form
- Author Contribution Form
- ICJME Form for Disclosure of Potential Conflicts of Interest
- Permission of previous published material if used in the present manuscript
- Acknowledgement of the study "in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of in 2000.
- Statement that informed consent was obtained after the procedure(s) had been fully explained.
- Indicating whether the institutional and national guide for the care and use of laboratory animals was followed as in "Guide for the Care and Use of Laboratory Animals".
- Title page
- The title of the manuscript both in Turkish and in English
- All authors and their affiliations
- All authors' e-mail address, full postal address, GSM phone, business telephone and fax numbers
- Abstracts (400-500 words) Both in Turkish and in English
- Key words: 3 to 10 words (in Turkish and in English)
- Body text
- Acknowledgement
- Reference
- All tables (including title, description, footnotes)

YAZARLARA BİLGİ

Derginin Tanımı

Bağcılar Tıp Bülteni (Bagcilar Medical Bulletin), tıbbın her alanında araştırma makalelerini, güncel derleme yazılarını, olgu sunumlarını ve editöre mektupları İngilizce tam metin ve Türkçe özle yayınlayan hakemli bir dergidir. Dergi online olarak yılda 4 sayı yayınlanmaktadır. Tüm makaleler kabul edilir edilmez, online olarak pdf formatında bu web sitesinde, o dönemdeki sayının bir makalesi olarak yer alacaktır. Dergi Galenos Yayınevi tarafından yayımlanmaktadır.

Editoryal Politikalar ve Hakem Süreci

Yayın Politikası

Bağcılar Tıp Bülteni, yayınlanmak üzere gönderilen yazıları aşağıda belirtilen şekillerde kabul eder:

- Orijinal araştırmalar,
- Kısa araştırmalar,
- Olgu sunumları,
- Derlemeler,
- Editöre mektup

Dergi, Türkiye'de yapılan araştırmaların uluslararası bilim arenasına duyurulması, uluslararası bilim çevrelerince paylaşılması ve bu bağlamda Türkiye'nin tanıtılmasına katkıda bulunmayı misyon edindiğinden özellikle orijinal araştırma niteliğindeki yazıları yayınlamaya öncelik vermektedir. Dergide yayınlanacak derleme türündeki yazılar editör tarafından konu ile ilgili çalışan yetkin kişilere hazırlatılmaktadır.

Genel İlkeler

Daha önce yayınlanmamış ya da yayınlanmak üzere başka bir dergide halen değerlendirmede olmayan ve her bir yazar tarafından onaylanan makaleler dergide değerlendirilmek üzere kabul edilir. Yayın kurulu, yazarların iznini alarak yazıda değişiklikler yapabilir. Editör ve dil editörleri dil, imlâ ve kaynakların National Library of Medicine MEDLINE/PubMed Resources'da belirtildiği gibi yazılmasında ve ilgili konularda tam yetkilidir.

Eğer makalede daha önce yayınlanmış alıntı yazı, tablo, resim vs. mevcut ise makale yazarı, yayın hakkı sahibi ve yazarlarından yazılı izin almak ve bunu makalede belirtmek zorundadır. Gerekli izinlerin alınıp alınmadığından yazar(lar) sorumludur.

Bilimsel toplantılarda sunulan özet bildiriler, makalede belirtilmesi koşulu ile kaynak olarak kabul edilir. Editör, dergiye gönderilen makale biçimsel esaslara uygun ise, gelen yazıyı yurtiçinden ve/veya yurtdışından en az iki hakemin değerlendirmesinden geçirtir, hakemler gerek gördüğü takdirde yazıda istenen değişiklikler yazarlar tarafından yapıldıktan sonra yayınlanmasına onay verir. Makale yayınlanmak üzere dergiye gönderildikten sonra yazarlardan hiçbirinin ismi, tüm yazarların yazılı izni olmadan yazar listesinden silinemez ve yeni bir isim yazar olarak eklenemez ve yazar sırası değiştirilemez. Yayına kabul edilmeyen makale, resim ve fotoğraflar yazarlara geri gönderilmez.

Yazarların Sorumluluğu

Makalelerin bilimsel ve etik kurallara uygunluğu yazarların sorumluluğundadır. Yazar makalenin orijinal olduğu, daha önce başka bir yerde yayınlanmadığı ve başka bir yerde, başka bir dilde yayınlanmak üzere değerlendirmede olmadığı konusunda teminat sağlamalıdır. Uygulamadaki telif kanunları ve anlaşmaları gözetilmelidir. Telife bağlı materyaller (örneğin tablolar, şekiller veya büyük alıntılar) gerekli izin ve teşekkürle kullanılmalıdır. Başka yazarların, katkıda bulunanların çalışmaları ya da yararlanılan kaynaklar uygun biçimde kullanılmalı ve referanslarda belirtilmelidir.

Gönderilen makalede tüm yazarların akademik ve bilimsel olarak doğrudan katkısı olmalıdır, bu bağlamda "yazar" yayınlanan bir araştırmanın kavramsallaştırılmasına ve desenine, verilerin elde edilmesine, analizine ya da yorumlanmasına belirgin katkı yapan; yazının yazılması ya da bunun içerik açısından eleştirel biçimde gözden geçirilmesinde görev yapan; yazının yayınlanmak üzere nihai halini onaylayan ve çalışmanın herhangi bir bölümünün doğruluğuna ya da bütünlüğüne ilişkin soruların uygun şekilde soruşturulduğunun ve çözümlendiğinin garantisini vermek amacıyla çalışmanın her yönünden sorumlu olmayı kabul eden kişi olarak görülür. Fon sağlanması, ya da araştırma grubunun genel süpervizyonu tek başına yazarlık hakkı kazandırmaz. Yazar olarak gösterilen tüm bireyler sayılan tüm ölçütleri karşılamalıdır ve yukarıdaki ölçütleri karşılayan her birey yazar olarak gösterilebilir. Çok merkezli çalışmalarda grubun tüm üyelerinin yukarıda belirtilen şartları karşılaması gereklidir. Yazarların isim sıralaması ortak verilen bir karar olmalıdır. Tüm yazarlar yazar sıralamasını Telif Hakkı Devir Formunda imzalı olarak belirtmek zorundadırlar. Yazarların tümünün ismi yazının başlığının altındaki bölümde yer almalıdır.

Yazarlık için yeterli ölçütleri karşılamayan ancak çalışmaya katkısı olan tüm bireyler teşekkür (acknowledgement) kısmında sıralanmalıdır. Bunlara örnek olarak ise sadece teknik destek sağlayan, yazıma yardımcı olan ya da sadece genel bir destek sağlayan kişiler verilebilir. Finansal ve materyal destekleri de belirtilmelidir.

Yazıya materyal olarak destek veren ancak yazarlık için gerekli ölçütleri karşılamayan kişiler "klinik araştırıcılar" ya da "yardımcı araştırıcılar" gibi başlıklar altında toplanmalı ve bunların işlevleri ya da katılımları "bilimsel danışmanlık yaptı", "çalışma önerisini gözden geçirdi", "veri topladı" ya da "çalışma hastalarının bakımını üstlendi" şeklinde belirtilmelidir.

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Teşekkür (acknowledgement) kısmında belirtilen bu ifadeler için bu bireylerden de yazılı izin alınması gerekmektedir.

Bütün yazarlar, araştırmanın sonuçlarını ya da bilimsel değerlendirmeyi etkileyebilme potansiyeli olan finansal ilişkiler, çıkar çatışması ve çıkar rekabetini beyan etmelidirler. Bir yazar kendi yayınlanmış yazısında belirgin bir hata ya da yanlışlık tespit ederse, bu yanlışlıklara ilişkin düzeltme ya da geri çekme için yayın yönetmeni ile hemen temasa geçme ve işbirliği yapma sorumluluğunu taşır. Yazarların katkısını belirten Yazar Katkı Formu ve çıkar çatışması olup olmadığını belirten ICMJE Potansiyel Çıkar Çatışması Beyan Formu makale ile birlikte gönderilmelidir. Yazarların görevleri ve sorumlulukları konusunda aşağıdaki kaynağa bakabilirsiniz; http://www.icmje.org/recommendations/browse/roles-and-responsibilities/

Editör ve Hakem Sorumlulukları ve Değerlendirme Süreci

Editörler, makaleleri, yazarların etnik kökeninden, cinsiyetinden, cinsel yöneliminden, uyruğundan, dini inancından ve siyasi felsefesinden bağımsız olarak değerlendirirler. Yayına gönderilen makalelerin adil bir şekilde çift taraflı kör hakem değerlendirmesinden geçmelerini sağlarlar. Gönderilen makalelere ilişkin tüm bilginin, makale yayınlanana kadar gizli kalacağını garanti ederler. Editörler içerik ve yayının toplam kalitesinden sorumludurlar. Gereğinde hata sayfası yayınlamalı ya da düzeltme yapmalıdırlar.

Genel Yayın Yönetmeni; yazarlar, editörler ve hakemler arasında çıkar çatışmasına izin vermez. Hakem atama konusunda tam yetkiye sahiptir ve Bağcılar Tıp Bülteni'nde yayınlanacak makalelerle ilgili nihai kararı vermekle yükümlüdür. Yayın etiği konusunda COPE kaynağına bakabilirsiniz. https://publicationethics.org/files/u7141/1999pdf13.pdf

Hakemler makaleleri, yazarların etnik kökeninden, cinsiyetinden, cinsel yöneliminden, uyruğundan, dini inancından ve siyasi felsefesinden bağımsız olarak değerlendirirler. Araştırmayla ilgili, yazarlarla ve/veya araştırmanın finansal destekçileriyle çıkar çatışmaları olmamalıdır. Değerlendirmelerinin sonucunda tarafsız bir yargıya varmalıdırlar. Hakemler yazarların atıfta bulunmadığı konuyla ilgili yayınlanmış çalışmaları tespit etmelidirler. Gönderilmiş yazılara ilişkin tüm bilginin gizli tutulmasını sağlamalı ve yazar tarafında herhangi bir telif hakkı ihlali ve intihal fark ederlerse Genel Yayın Yönetmeni'ne raporlamalıdırlar. Hakem, makale konusu hakkında kendini vasıflı hissetmiyor ya da zamanında geri dönüş sağlaması mümkün görünmüyorsa, Genel Yayın Yönetmeni'ne bu durumu bildirmeli ve hakem sürecine kendisini dahil etmemesini istemelidir.

Editör makalelerle ilgili bilgileri (makalenin alınması, içeriği, gözden geçirme sürecinin durumu, hakemlerin eleştirileri ya da varılan sonuç) yazarlar ya da hakemler dışında kimseyle paylaşmaz.

Değerlendirme sürecinde editör hakemlere gözden geçirme için gönderilen makalelerin, yazarların özel mülkü olduğunu ve bunun imtiyazlı bir iletişim olduğunu açıkça belirtir. Hakemler ve yayın kurulu üyeleri topluma açık bir şekilde makaleleri tartışamazlar. Hakemlerin kendileri için makalelerin kopyalarını çıkarmalarına izin verilmez ve editörün izni olmadan makaleleri başkasına veremezler. Hakemler gözden geçirmelerini bitirdikten sonra makalenin kopyalarını yok etmeli ya da editöre göndermelidirler. Dergimiz editörü de reddedilen ya da geri verilen makalelerin kopyalarını imha etmelidir.

Yazarın ve editörün izni olmadan hakemlerin gözden geçirmeleri basılamaz ve açıklanamaz. Hakemlerin kimliğinin gizli kalmasına özen gösterilmelidir. Bazı durumlarda editörün kararıyla, ilgili hakemlerin makaleye ait yorumları aynı makaleyi yorumlayan diğer hakemlere gönderilerek hakemlerin bu süreçte aydınlatılması sağlanabilir. Değerlendirme süreciyle ilgili olarak COPE kaynağına bakabilirsiniz: http://publicationethics.org/files/Peer review guidelines.pdf

Açık Erişim İlkesi

Açık erişimli bir yayın olan Bağcılar Tıp Bülteni dergisinin tüm içeriği okura ya da okurun dahil olduğu kuruma ücretsiz olarak sunulur. Okurlar, yayıncı ya da yazardan izin almadan dergi makalelerinin tam metnini okuyabilir, indirebilir, kopyalayabilir, dağıtabilir, basabilir, arayabilir ve link sağlayabilir.

Yayın Etiği

İlke ve Standartlar

Bağcılar Tıp Bülteni yayın etiğinde en yüksek standartlara bağlıdır ve Committee on Publication Ethics (COPE), Council of Science Editors (CSE), World Association of Medical Editors (WAME) ve International Committee of Medical Journals (ICJME) tarafından geliştirilen yayın etiği ilkelerini ve tavsiyelerini gözetir.

Gönderilen tüm makaleler orijinal, yayınlanmamış (konferans bildirilerindeki tam metinler de dahil) ve başka bir dergide değerlendirme sürecinde olmamalıdır. Her bir makale editörlerden biri ve en az iki hakem tarafından çift kör değerlendirmeden geçirilir. Gönderilen makaleleri intihal yazılımı ile denetleme hakkımız haklıdır. İntihal, veride hile ve tahrif (araştırma verisi, tabloları ya da imajlarının manipülasyonu ve asılsız üretimi), insan ve hayvanların araştırmada uygun olmayan kullanımı konuları denetimden

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geçmektedir. Bu standartlara uygun olmayan tüm makaleler yayından çıkarılır. Buna yayından sonra tespit edilen olası kuraldışı, uygunsuzluklar içeren makaleler de dahildir. Yayın etiği kurallarına bağlı olarak, intihal şüphesini ve duplikasyon durumlarını rapor edeceğimizi belirtiriz. Olası bilimsel hatalı davranışları ve yayın etiği ihlali vakalarını ele alırken COPE Ethics Flowcharts http://publicationethics.org/resources/flowcharts izlenir.

İnsan ve Hayvan Hakları, Bilgilendirilmiş Olur, Çıkar Çatışması

Bağcılar Tıp Bülteni, yayınladığı makalelerin ticarî kaygılardan uzak ve konu ile ilgili en iyi etik ve bilimsel standartlarda olması şartını gözetmektedir. Makalelerin etik kurallara uygunluğu yazarların sorumluluğundadır.

Bağcılar Tıp Bülteni, 1975 Helsinki Deklarasyonu'nun 2004 yılında revize edilen Ethical Principles for Medical Research Involving Human Subjects'e http://www.wma.net/en/30publications/10policies/b3/index.html ve 2006 yılında revize edilen WMA Statement on Animal Use in Biomedical Research'e http://www.wma.net/en/30publications/10policies/a18/uymayı prensip edinmiştir. Bu yüzden dergide yayınlanmak üzere gönderilen yazılarda, klinik deneylere katılan denekler ile ilgili olarak yukarıda belirtilen etik standartlara uyulduğunun mutlaka belirtilmesi gerekmektedir. Ayrıca deneyin türüne göre gerekli olan yerel veya ulusal etik komitelerden alınan onay yazıları yazı ile birlikte gönderilmelidir. Bununla birlikte deneye katılan kişi/hastalardan, hastalar eğer temyiz kudretine sahip değilse vâsilerinden yazılı bilgilendirilmiş onam alındığını belirten bir yazı ile beraber tüm yazarlar tarafından imzalanmış bir belgenin editöre gönderilmesi gerekmektedir.

Hastalardan izin alınmadan mahremiyet bozulamaz. Hastaların ismi, isimlerinin baş harfleri ya da hastane numaraları gibi tanımlayıcı bilgiler, fotoğraflar ve soy ağacı bilgileri vb. bilimsel amaçlar açısından çok gerekli olmadıkça ve hasta (ya da anne-baba, ya da vâsisi) yazılı bilgilendirilmiş onam vermedikçe basılmazlar. Özellikle olgu bildirimlerinde, çok gerekli olmadıkça hasta ile ilgili tanımlayıcı ayrıntılar çıkarılmalıdır. Örneğin, fotoğraflarda göz bölgesinin maskelenmesi kimliğin gizlenmesi için yeterli değildir. Eğer veriler kimliğin gizlenmesi için değiştirildiyse yazarlar bu değişikliklerin bilimsel anlamı etkilemediği konusunda güvence vermelidirler. Olgu sunumlarında yer verilen hastalardan bilgilendirilmiş onam alınmalıdır. Bilgilendirilmiş onam alındığı da makalede belirtilmelidir.

Bu tip çalışmaların varlığında yazarlar, makalenin YÖNTEM(LER) bölümünde bu prensiplere uygun olarak çalışmayı yaptıklarını, kurumlarının etik kurullarından ve çalışmaya katılmış insanlardan "bilgilendirilmiş onam" aldıklarını belirtmek zorundadırlar.

Çalışmada "hayvan" kullanılmış ise yazarlar, makalenin YÖNTEM(LER) bölümünde "Guide for the Care and Use of Laboratory Animals" (www.nap.edu/catalog/5140.html) doğrultusunda çalışmalarında hayvan haklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadırlar. Hayvan deneyleri rapor edilirken yazarlar, laboratuvar hayvanlarının bakımı ve kullanımı ile ilgili kurumsal ve ulusal rehberlere uyup uymadıklarını yazılı olarak bildirmek zorundadırlar.

Editör ve yayıncı, reklâm amacı ile dergide yayınlanan ticari ürünlerin özellikleri ve açıklamaları konusunda hiçbir garanti vermemekte ve sorumluluk kabul etmemektedir. Eğer makalede doğrudan veya dolaylı ticarî bağlantı veya çalışma için maddî destek veren kurum mevcut ise yazarlar; kaynak sayfasında, kullanılan ticarî ürün, ilaç, ilaç firması v.b. ile ticari hiçbir ilişkisinin olmadığını veya varsa nasıl bir ilişkisinin olduğunu (konsültan, diğer anlaşmalar) bildirmek zorundadır. Bağcılar Tıp Bülteni, WAME'nin çıkar çatışması tanımını benimser http://www.wame.org/about/wame-editorial-on-coi

Buna göre, yazar, hakem ya da editör sorumluluklarını aşırı düzeyde ve/veya haksızlığa yol açabilecek düzeyde etkileyebilecek ya da etkileyebileceği olası bir çıkar rekabeti içindeyse, çıkar çatışması söz konusudur ve bunun açıklanması gerekir. Açıklanması öngörülen çıkar çatışması tipleri, finansal bağlar, akademik taahhütler, kişisel ilişkiler, politik ya da dini inançlar, kurumsal bağlantılardır. Çıkar çatışması söz konusuysa bu makalede açıklanmalıdır.

Dil

Bağcılar Tıp Bülteni'nin yayın dili Amerikan İngilizcesi'dir, ayrıca makalelerin özleri hem İngilizce, hem Türkçe yayınlanır. Her iki dildeki özler yazarlardan istenir.

Yazıların Hazırlanması

Aksi belirtilmedikçe gönderilen yazılarla ilgili tüm yazışmalar ilk yazarla yapılacaktır. Gönderilen yazılar, yazının yayınlanmak üzere gönderildiğini ve Bağcılar Tıp Bülteni'nin hangi bölümü (Orijinal Araştırma, Kısa Araştırma, Olgu Sunumu, Derleme, Editöre Mektup) için başvurulduğunu belirten bir mektup, yazının elektronik formunu içeren Microsoft Word 2003 ve üzerindeki versiyonları ile yazılmış elektronik dosya ile tüm yazarların imzaladığı 'Telif Hakkı Devir Formu', Yazar Katkı Formu ve ICMJE Potansiyel Çıkar Çatışması Beyan Formueklenerek gönderilmelidir. Yazıların alınmasının ardından yazarlara makalenin alındığı, bir makale numarası ile bildirilecektir. Tüm yazışmalarda bu makale numarası kullanılacaktır. Makaleler sayfanın her bir kenarından 2,5

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cm kenar boşluğu bırakılarak ve çift satır aralıklı yazılmalıdır. Makalelerde aşağıdaki sıra takip edilmelidir ve her bölüm yeni bir sayfa ile başlamalıdır: 1) başlık sayfası, 2) öz, 3) metin, 4) teşekkür / 5) kaynaklar ve 6) tablo ve/veya şekiller. Tüm sayfalar sırayla numaralandırılmalıdır.

Başlık

Başlık sayfasında, yazarların adları, akademik ünvanları ve yazışılacak yazarın tam adres, telefon ve faks numaraları ile e-mail adresi mutlaka bulunmalıdır. Yazıların Türkçe özlerinde mutlaka Türkçe başlık da yer almalıdır.

Öz ve Anahtar Sözcükler

Makalenin İngilizce başlığı İngilizce özde, Türkçe başlığı da Türkçe özde yer almalıdır. Bütün makaleler öz ve anahtar kelime içermelidir. Özler bir makalenin birçok elektronik veri tabanında yer alan en belirgin kısmı olduğundan, yazarlar özün makalenin içeriğini doğru olarak yansıttığından emin olmalıdır. Öz çalışmanın temeliyle ilgili bilgi vermeli ve çalışmanın amacını, temel prosedürleri (olguların ya da laboratuvar hayvanlarının seçimi, gözlemsel ve analitik yöntemler), ana bulguları (mümkünse özgül etki büyüklüklerini ve istatistiksel anlamlılıklarını vererek) ve temel çıkarımları içermelidir. Çalışmanın ya da gözlemlerin yeni ve önemli yönleri belirtilmelidir. Anahtar sözcükler, her türlü yazıda Türkçe ve İngilizce özlerin altındaki sayfada 3-10 adet verilmelidir. Anahtar sözcük olarak National Library of Medicine'ın Tıbbi Konu Başlıkları'nda (Medical Subject Headings, MeSH) yer alan terimler kullanılmalıdır. MeSH'de yer alan terimlerin Türkçe karşılıklarına Türkiye Bilim Terimleri'nden http://www.bilimterimleri.com erişilebilir.

Makale Türleri

Orijinal Araştırma

Orijinal araştırma makaleleri derginin kapsamına uygun konularda önemli, özgün bilimsel sonuçlar sunan araştırmaları raporlayan yazılardır. Orijinal araştırma makaleleri, Öz, Anahtar Kelimeler, Giriş, Yöntem ve Gereçler, Bulgular, Tartışma, Sonuçlar, Kaynaklar bölümlerinden ve Tablo, Grafik ve Şekillerden oluşur. Öz bölümü araştırma yazılarında aşağıda belirtilen formatta yapılandırılmış olmalıdır.

Öz

Araştırma yazılarında Türkçe ve İngilizce özler en fazla 500 kelime olmalı ve şu şekilde yapılandırılmalıdır: Amaç/Objective: Yazının birincil ve asıl amacı; Yöntem ve Gereçler/Material and Method(s): Veri kaynakları, çalışmanın iskeleti, hastalar ya da çalışmaya katılanlar, görüşme/değerlendirmeler ve temel ölçümler; Bulgular/Results: Ana bulgular; Sonuç(lar)/Conclusion(s):Doğrudan klinik uygulamalar, çıkartılacak sonuçlar belirtilmelidir.

Anahtar Kelimeler

National Library of Medicine'ın Tıbbi Konu Başlıkları'nda (MedicalSubjectHeadings, MeSH) yer alan terimler kullanılmalıdır, en az üç anahtar kelime belirtilmelidir.

Giriş

Giriş/Introduction bölümünde konunun önemi, tarihçe ve bugüne kadar yapılmış çalışmalar, hipotez ve çalışmanın amacından söz edilmelidir. Hem ana hem de ikincil amaçlar açıkça belirtilmelidir. Sadece gerçekten ilişkili kaynaklar gösterilmeli ve çalışmaya ait veri ya da sonuçlardan söz edilmemelidir.

Yöntem ve Gereçler

Yöntem ve Gereçler/Material and Methods bölümünde, veri kaynakları, hastalar ya da çalışmaya katılanlar, ölçekler, görüşme/değerlendirmeler ve temel ölçümler, yapılan işlemler ve istatistiksel yöntemler yer almalıdır. Yöntem bölümü, sadece çalışmanın planı ya da protokolü yazılırken bilinen bilgileri içermelidir; çalışma sırasında elde edilen tüm bilgiler bulgular kısmında verilmelidir. Yöntem ve Gereçler bölümünde olguların seçimi ve tanımlanması hakkında bilgi, teknik bilgi ve istatistik hakkında bilgi yer almalıdır. Araştırmanın Etik Kurul Onayı ve katılımcılardan alınan yazılı Bilgilendirilmiş Onam belirtilmelidir.

Olguların Seçimi ve Tanımlanması

Gözlemsel ya da deneysel çalışmaya katılanların (hastalar, hayvanlar, kontroller) seçimi, kaynak popülasyon, çalışmaya alınma ve çalışmadan dışlanma ölçütleri açıkça tanımlanmalıdır. Yaş ve cinsiyet gibi değişkenlerin çalışmanın amacıyla olan ilişkisi her zaman açık olmadığından yazarlar çalışma raporundaki kullanımlarını açıklamalıdır; örneğin yazarlar niçin sadece belli bir yaş grubunun alındığını ya da neden kadınların çalışma dışında bırakıldığını açıklamalıdır. Çalışmanın niçin ve nasıl belli bir şekilde yapıldığı açık bir şekilde belirtilmelidir. Yazarlar etnisite ya da ırk gibi değişkenler kullandıklarında bu değişkenleri nasıl ölçtüklerini ve geçerliklerini açıklamalıdır.

Teknik Bilgi

Diğer çalışmacıların sonuçları yineleyebilmesi için yöntem ve kullanılan araçlar (üretici firma ve adres paragraf içinde belirtilerek) ayrıntılı bir şekilde belirtilmelidir. Önceden kullanılan bilinen yöntemler için (istatistiksel yöntemler dahildir) kaynak gösterilmeli, basılmış ama iyi bilinmeyen bir yöntem için kaynak verilmeli ve yöntem açıklanmalıdır. Aynı şekilde yeni ya da belirgin olarak modifiye edilmiş yöntemler tanımlanmalı ve kullanılma nedenleri belirtilip kısıtlılıkları değerlendirilmelidir. Kullanılan tüm ilaç ve kimyasallar doğru olarak tanımlanıp jenerik isimleri, dozları ve kullanım biçimleri

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belirtilmelidir. Gözden geçirme yazısı gönderen yazarlar veriyi bulma, seçme, ayırma ve sentezleme yöntemlerini belirtmelidir. Bu yöntemler aynı zamanda özde de yer almalıdır.

İstatistik

İstatistiksel yöntem, orijinal veriye erişebilecek bilgili bir okuyucunun rapor edilen sonuçları onaylayabileceği bir ayrıntıda belirtilmelidir. Mümkünse, bulgular niceliksel hale getirilmeli ve hata ölçümleri (güvenlik aralıkları gibi) sunulmalıdır. Etki büyüklüğünü vermeyen, p değerlerinin kullanımı gibi, salt istatistiksel hipotez sınamasına dayanılmamalıdır. Çalışma deseni ve istatistiksel yönteme dair kaynaklar sayfalar belirtilerek mümkün olduğu sürece standart kaynaklar olmalıdır. İstatistiksel terimler, kısaltmalar ve semboller tanımlanmalıdır. Kullanılan bilgisayar programı belirtilmelidir.

Bulgular

Ana bulgular istatistiksel verilerle desteklenmiş olarak eksiksiz verilmeli ve bu bulgular uygun tablo, grafik ve şekillerle görsel olarak da belirtilmelidir. Bulgular yazıda, tablolarda ve şekillerde mantıklı bir sırayla önce en önemli sonuçlar olacak şekilde verilmelidir. Tablo ve şekillerdeki tüm veriyi yazıda vermemeli, sadece önemli noktaları vurgulanmalıdır. Ekstra materyal ve teknik bilgi ek kısmında verilerek yazının akışının bozulmaması sağlanmalı, alternatif olarak bunlar sadece elektronik versiyonda yer almalıdır.

Tartışma

Tartışma/Discussion bölümünde o çalışmadan elde edilen veriler, kurulan hipotez doğrultusunda hipotezi destekleyen ve desteklemeyen bulgular ve sonuçlar irdelenmeli ve bu bulgu ve sonuçlar literatürde bulunan benzeri çalışmalarla kıyaslanmalı, farklılıklar varsa açıklanmalıdır. Çalışmanın yeni ve önemli yanları ve bunlardan çıkan sonuçları vurgulanmalıdır. Giriş ya da sonuçlar kısmında verilen bilgi ve veriler tekrarlanmamalıdır.

Sonuçlar

Sonuçlar/Conclusions bölümünde çalışmadan çıkarılan sonuçlar sıralanmalıdır. Deneysel çalışmalar için tartışmaya sonuçları kısaca özetleyerek başlamak, daha sonra olası mekanizmaları ya da açıklamaları incelemek ve bulguları önceki çalışmalarla karşılaştırmak, çalışmanın kısıtlılıklarını özetlemek, gelecekteki çalışmalar ve klinik pratik için uygulamalarını belirtmek faydalıdır. Varılan sonuçlar çalışmanın amacıyla karşılaştırılmalı, ancak elde edilen bulgular tarafından yeterince desteklenmeyen çıkarımlardan kaçınılmalıdır. Yazarlar, eğer elde ettikleri veriler ekonomik veri ve analizler içermiyorsa, ekonomik çıkar ya da faydalarla ilgili yorumlardan özellikle kaçınılmalıdır. Gerektiğinde yeni hipotezler ortaya konmalı, ancak bunların yeni hipotezler olduğu belirtilmelidir.

Tablo, Grafik ve Şekiller

Yazı içindeki grafik, şekil ve tablolar Arap sayıları ile numaralandırılmalıdır. Şekillerin metin içindeki yerleri belirtilmelidir. Ayrıntılı bilgi aşağıda ilgili başlık altında yer almaktadır.

Kısa Araştırma

Kısa Araştırma makaleleri tarz ve format açısından Orijinal Araştırma makaleleri gibidir; ancak daha küçük ölçekli araştırmaları ya da geliştirme çalışmasının erken aşamalarında olan araştırmaları ele alır. Basit araştırma tasarımı kullanan ön çalışmalar, sınırlı pilot veri sağlayan küçük örnek kitle ile yapılan çalışmalar, ileri araştırma gereksinimine işaret eden başlangıç bulguları bu tür araştırmalar kapsamında sayılabilir. Kısa Araştırma makaleleri, büyük ölçekli gelişkin araştırma projelerini konu alan Orijinal Araştırma makalelerinden daha kısadır. Ancak Kısa Araştırma, Orijinal Araştırma makalesi olabilecek kalitede bir araştırma makalesinin kısa versiyonu olarak anlaşılmamalıdır; önem derecesi düşük, titizlikle yapılmamış bir araştırma hakkında bir yayın malzemesi hazırlamak için kullanılmamalıdır ya da genişletildiğinde Orijinal Araştırma makalesi ya da araştırma niteliği kazanmayacak bir içeriği değerlendirecek bir makale türü olarak anlaşılmamalıdır.

Olgu Sunumu

Olgu sunumu makaleleri özgün vakaları rapor eden yazılardır. Derginin kapsamına giren konulara ilişkin bir problemin üstesinden gelen tedaviyle ilgili, yeni araçlar, teknikler ve metotlar göstererek okuyucular için bilgilendirme sağlamalıdır. Olgu sunumu yazıları Öz (özün araştırma makalesinde olduğu gibi belli bir formatta yapılandırılmış olması gerekmiyor), Anahtar Kelimeler, Giriş, Olgu Sunumu, Tartışma, Referanslar, gerekirse Tablo ve açıklayıcı bilgilerden oluşur. Olgu sunumunda yazılı bilgilendirilmiş onam alınmalı ve makalede belirtilmelidir.

Derleme

Derleme makaleleri alanında zengin birikime ve atıf alan çalışmalara sahip uzman kişilerce yazılan yazılardır. Klinik pratiğe ilişkin bir konuda mevcut bilgiyi tanımlayan, değerlendiren ve tartışan; geleceğe ilişkin çalışmalara yol gösteren derleme yazıları yazmaları için dergi belirlediği yazarlara davet gönderir. Derleme makaleleri, Öz (özün, araştırma makalesinde olduğu gibi belli bir formatta yapılandırılmış olması gerekmiyor), Anahtar Kelimeler, Giriş, Sonuç bölümlerinden oluşur. Derleme makale gönderen yazarların, makalede kullandıkları verinin seçimi, alınması, sentezi için kullandıkları yöntemleri tanımlayan bir bölüme de makalede yer vermeleri gerekir. Bu yöntemler Öz bölümünde de belirtilmelidir.

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Editöre Mektup

Editöre Mektup, kısa ve net görüş bildiren yazılardır. Dergide daha önce yayınlanmış olan makalelerle ilgili olarak ya da dergide ifade edilmiş görüşlerle ilgili olarak yazılmış olması tercih edilir. Editöre Mektup yazıları, daha sonra yeni bir yazı ile geçerlilik ispatı gerektirebilecek ön görüş bildiren yazılar olmamalıdır.

Tablolar

Tablolar bilgileri etkin bir şekilde gösterir ve ayrıca bilginin istenen tüm ayrıntı seviyelerinde verilmesini sağlar. Bilgileri metin yerine tablolarda vermek genelde metnin uzunluğunu kısaltır.

Her tablo ayrı bir sayfaya çift aralıklı olarak basılmalıdır. Tablolar metindeki sıralarına göre numaralanıp, her birine kısa bir başlık verilmelidir. MS Word 2003 ve üstü versiyonlarında otomatik tablo seçeneğinde "tablo klasik 1" ya da "tablo basit 1" seçeneklerine göre tablolar hazırlanmalıdır. Başlık satırı ve tablo alt üst satırları dışında tablonun içinde başka dikey ve yatay çizgiler kullanılmamalıdır. Her sütuna bir başlık verilmelidir. Yazarlar açıklamaları başlıkta değil, dipnotlarda yapmalıdır. Dipnotlarda standart olmayan tüm kısaltmalar açıklanmalıdır. Dipnotlar için sırasıyla şu semboller kullanılmalıdır: (*,†,‡,§,ǁ,¶,**,††,‡‡).

Varyasyonun standart sapma ya da standart hata gibi istatistiksel ölçümleri belirtilmelidir. Metin içinde her tabloya atıfta bulunulduğuna emin olunmalıdır. Eğer yayınlanmış ya da yayınlanmamış herhangi başka bir kaynaktan veri kullanılıyorsa izin alınmalı ve onlar tam olarak bilgilendirilmelidir. Çok fazla veri içeren tablolar, çok yer tutar ve sadece elektronik yayınlar için uygun olabilir ya da okuyuculara yazarlar tarafından doğrudan sağlanabilir. Böyle bir durumda uygun bir ifade metne eklenmelidir. Bu tip tablolar, hakem değerlendirmesinden geçmesi için makaleyle beraber gönderilmelidir.

Şekiller

Şekiller ya profesyonel olarak çizilmeli ve fotoğraflanmalı ya da fotoğraf kalitesinde dijital olarak gönderilmelidir. Şekillerin basıma uygun versiyonlarının yanı sıra JPEG ya da GIF gibi elektronik versiyonlarda yüksek çözünürlükte görüntü oluşturacak biçimlerde elektronik dosyaları gönderilmeli ve yazarlar göndermeden önce bu dosyaların görüntü kalitelerini bilgisayar ekranında kontrol etmelidir.

Röntgen, CT, MRI filmleri ve diğer tanısal görüntülemeler yüksek kalitede basılmış olarak gönderilmelidir. Bu nedenle şekillerin üzerindeki harfler, sayılar ve semboller açık ve tüm makalede eşit ve yayın için küçültüldüklerinde bile okunabilecek boyutlarda olmalıdır. Şekiller mümkün olduğunca tek başlarına anlaşılabilir olmalıdır. Fotomikrografik patoloji preparatları iç ölçekler içermelidir. Semboller, oklar ya da harfler fonla kontrast oluşturmalıdır. Eğer insan fotoğrafı kullanılacaksa, ya bu kişiler fotoğraftan tanınmamalıdır ya da yazılı izin alınmalıdır (Etik bölümüne bakınız).

Şekiller metinde geçiş sıralarına göre numaralandırılmalıdır. Eğer önceden yayınlanmış bir şekil kullanılacaksa, yayın hakkını elinde bulunduran bireyden izin alınmalıdır. Toplum alanındaki belgeler hariç yazarlığa ve yayıncıya bakılmadan bu izin gereklidir. Basılacak bölgeyi gösteren ek çizimler editörün işini kolaylaştırır. Renkli şekiller editör gerekli gördüğünde ya da sadece yazar ek masrafı karşılarsa basılır.

Şekillerin Dipnotları

Ayrı bir sayfadan başlayarak şekiller için tablo başlıkları ve dipnotları tek aralıklı olarak ve Arap sayıları ile hangi şekle karşı geldikleri belirtilerek yazılmalıdır. Semboller, oklar, sayılar ya da harfler şeklin parçalarını belirtmek için kullanıldığında, dipnotlarda her biri açıkça tanımlanmalıdır. Fotomikrografik patoloji preparatlarında iç ölçek ve boyama tekniği açıklanmalıdır.

Ölçüm Birimleri

Uzunluk, ağırlık ve hacim birimleri metrik (metre, kilogram, litre) sistemde ve bunların onlu katları şeklinde rapor edilmelidir. Sıcaklıklar Celsius derecesi, kan basıncı milimetre civa cinsinden olmalıdır. Ölçü birimlerinde hem lokal hem de Uluslararası Birim Sistemleri (International System of Units, SI) kullanılmalıdır. İlaç konsantrasyonları ya SI ya da kütle birimi olarak verilir, alternatif olarak parantez içinde de verilebilir.

Kısaltmalar ve sembollerde sadece standart kısaltmalar kullanılmalıdır, standart olmayan kısaltmalar okuyucu için çok kafa karıştırıcı olabilir. Başlıkta kısaltmadan kaçınılmalıdır. Standart bir ölçüm birimi olmadıkça kısaltmaların uzun hali ilk kullanılışlarında açık, kısaltılmış hali parantez içinde verilmelidir.

Teşekkür(ler)

Yazının sonunda kaynaklardan önce yer verilir. Bu bölümde kişisel, teknik ve materyal yardımı gibi nedenlerle yapılacak teşekkür ifadeleri yer alır.

Kelime Sayısı Sınırlandırması

Türkçe ve İngilizce özler en fazla 500 kelime olmalıdır. Orijinal makaleler ve derleme yazılarında özel bir kelime sayısı sınırlandırması yoktur. Olgu Sunumları Öz hariç 1000 kelime ile sınırlandırılmalı ve en az sayıda şekil, tablo ve kaynak içermelidir. Editöre mektuplar (en fazla 1000 kelime, tablosuz ve şekilsiz) olmalı ve mektup, tüm yazarlar tarafından imzalanmış olmalıdır. Bağcılar Tıp Bülteni'nde yayınlanmış olan bir yazı ile ilgili eleştiri ya da değerlendirme niteliğindeki mektuplar

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sözü edilen yazının yayınlanmasından sonraki 12 hafta içinde alınmış olmalıdır.

Makale Hazırlığı :

"Bağcılar Tıp Bülteni", Tıp Dergilerinde Bilimsel Çalışmaların Yürütülmesi, Raporlanması, Düzenlenmesi ve Yayınlanmasına İlişkin yönergeleri takip eder "(Uluslararası Tıp Dergisi Editörleri Komitesi - http://www.icmje.org/). Makalenin sunulması üzerine, yazarlar deneme/araştırma türünü belirtmeli ve uygun olduğunda aşağıdaki kuralların kontrol listesini sağlamalıdır:

Randomize çalışmalar için CONSORT açıklaması (CONSORT Grubu için Moher D, Schultz KF, Altman D. CONSORT beyanı paralel grup randomize çalışmaların raporlarının kalitesini iyileştirmek için önerileri gözden geçirdi. JAMA 2001; 285: 1987-91) (http: //www.consort-statement.org /),

Sistematik gözden geçirmeler ve meta-analizler için tercih edilen raporlama maddeleri için PRISMA (Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Grubu. Sistematik İncelemeler ve Meta-Analizler için Tercih Edilen Raporlama Maddeleri: PRISMA Beyanı. PLoS Med 2009; 6 (7): e1000097.) (Http://www.prisma-statement.org /),

Tanısal doğruluk çalışmalarının raporlanması için STARD kontrol listesi (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, vd, STARD Grubu için. Teşhis doğruluğu çalışmalarının eksiksiz ve doğru raporlanmasına yönelik: STARD girişimi, Ann Intern Med 2003; 138: 40-4.) (http://www.stard-statement.org /),

STROBE gözlemsel çalışma raporlarında yer alması gereken maddelerin kontrol listesi (http://www.strobe-statement.org /),

Gözlemsel çalışmaların meta-analizi ve sistemik incelemeleri için MOOSE yönergeleri (Stroup DF, Berlin JA, Morton SC, vd.) Epidemiyolojideki gözlemsel çalışmaların meta-analizi: Epidemiyoloji (MOOSE) grubundaki gözlemsel çalışmaların Meta-analizini bildirme önerisi JAMA 2000; 283: 2008-12).

CARE kuralları, vaka raporlarının doğruluğunu, şeffaflığını ve kullanışlılığını artırmak için tasarlanmıştır. (Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; CARE Grubu. CARE Yönergeleri: Konsensüs Tabanlı Klinik Vaka Raporlama Rehberinin Geliştirilmesi.) (Http://www.care-statement.org /

Kaynaklar

Kaynaklarla İlgili Genel Konular

Gözden geçirme yazıları okuyucular için bir konudaki kaynaklara ulaşmayı kolaylaştıran bir araç olsa da, her zaman orijinal çalışmayı doğru olarak yansıtmaz. Bu yüzden mümkün olduğunca yazarlar orijinal çalışmaları kaynak göstermelidir. Öte yandan, bir konuda çok fazla sayıda orijinal çalışmanın kaynak gösterilmesi yer israfına neden olabilir. Birkaç anahtar orijinal çalışmanın kaynak gösterilmesi genelde uzun listelerle aynı işi görür. Ayrıca günümüzde kaynaklar elektronik versiyonlara eklenebilmekte ve okuyucular elektronik literatür taramalarıyla yayınlara kolaylıkla ulaşabilmektedir.

Özler kaynak olarak gösterilmemelidir. Kabul edilmiş ancak yayınlanmamış makalelere atıflar "basımda" ya da "çıkacak" şeklinde verilmelidir; yazarlar bu makaleleri kaynak gösterebilmek için yazılı izin almalıdır ve makalelerin basımda olduğunu ispat edebilmelidir. Gönderilmiş ancak yayına kabul edilmemiş makaleler, "yayınlanmamış gözlemler" olarak gösterilmeli ve kaynak yazılı izinle kullanılmalıdır. Genel bir kaynaktan elde edilemeyecek temel bir konu olmadıkça "kişisel iletişimlere" atıfta bulunulmamalıdır. Eğer atıfta bulunulursa parantez içinde iletişim kurulan kişinin adı ve iletişimin tarihi belirtilmelidir. Bilimsel makaleler için yazarlar bu kaynaktan yazılı izin ve iletişimin doğruluğunu gösterir belge almalıdır.

Referans Stili ve Formatı

Tek tip kurallar esas olarak National Library of Medicine, tarafından uyarlanmış olan bir ANSI standart stilini kabul etmiştir. Kaynak atıfta bulunma örnekleri için yazarlar www.nlm.nih.gov/bsd/uniform_requirements.html sitesine başvurabilirler. Dergi isimleri National Library of Medicine kaynağında yer alan şekilleriyle kısaltılmalıdır.

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Kaynakların doğruluğundan yazar(lar) sorumludur. Tüm kaynaklar metinde belirtilmelidir. Kaynaklar aşağıdaki örneklerdeki gibi gösterilmelidir. Altı yazardan fazla yazarı olan çalışmalarda ilk altı yazar belirtilmeli, sonrasında "ve ark." ya da "et al." ibaresi kullanılmalıdır. Kaynak dergi adlarının kısaltılması National Library of Medicine'de belirtilen kısaltmalara (https://www.ncbi.nlm.nih.gov/nlmcatalog/journals) uygun olmalıdır. National Library of Medicine'da indekslenmeyen bir dergi kısaltılmadan yazılmalıdır.

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MEDLINE'da yer alan ve kısaltması MEDLINE'a göre yapılan dergi makalesi için: Crow SJ, Peterson CB, Swanson SA, Raymond NC, Specker S, Eckert ED, et al. Increased mortality in bulimia nervosa and other eating disorders. Am J Psychiatry 2009;166(12):1342-1346.

MEDLINE'da yer almayan ve kısaltması olmayan dergi makalesi için: Sevinçer GM, Konuk N. Emotional eating. Journal of Mood Disorders 2013;3(4):171-178.

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2. Ek sayı için:

MEDLINE'da yer alan ve kısaltması MEDLINE'a göre yapılan dergi makalesi için: Sharan P, Sundar AS. Eating disorders in women. Indian J Psychiatry 2015:57(Suppl 2):286-295.

MEDLINE'da yer almayan ve kısaltması olmayan dergi makalesi için: Maner F. Yeme bozukluklarının tedavisi. Anadolu Psikiyatri Dergisi 2009;10(Ek 1):55-56.

3. Baskıdaki makale için:

Cossrow N, Pawaskar M, Witt EA, Ming EE, Victor TW, Herman BK, et al. Estimating the prevalence of binge eating disorder in a community sample from the United States: comparing DSM-IV-TR and DSM-5 criteria. J Clin Psychiatry, 2016. (in press).

4. Kitaptan alıntılar:

Tek yazarlı kitaptan alıntı için:

McKnight TL. Obesity Management in Family Practice. 1st ed., New York:Springer, 2005:47-51.

Kitaptan bir bölüm için, editör(ler) varsa:

Jebb S, Wells J. Measuring body composition in adults and children. In Clinical Obesity in Adults and Children, Copelman P, Caterson I, Dietz W (editors). 1st ed., London: Blackwell Publishing, 2005:12-18.

Editörler aynı zamanda kitabın içindeki metin ya da metinlerin yazarı ise: Önce alınan metin ve takiben kitabın ismi yine kelimeler büyük harfle başlatılarak yazılır.

Eckel RH (editor). Treatment of obesity with drugs in the new millennium. In Obesity Mechanisms and Clinical Management. 1st ed., Philadelphia: Lippincott Williams & Wilkins, 2003:449-476.

Çeviri Kitaptan Alıntı için:

McGuffin P, Owen MJ, Gottsman II. Psikiyatri Genetiği ve Genomiği. Abay E, Görgülü Y (translation editors) 1st ed., Istanbul: Nobel Tıp Kitabevleri, 2009:303-341.

5. Tezden alıntı için:

Keçeli F. Yeme bozukluğu hastalarında obsesif kompulsif bozukluk ve kişilik bozukluğu. Thesis, T.C. Sağlık Bakanlığı Bakırköy Prof. Dr. Mazhar Osman Ruh Sağlığı ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi, Istanbul:2006.

6. Kongre bildirileri için:

Akbaş Öncel D, Akdemir A. Üniversite öğrencilerinde diyet, beden algısı ve kendilik algısı arasındaki ilişkiler. 47. Ulusal Psikiyatri Kongresi Özet Kitabı, 26-30 Ekim 2011, Antalya, 2011:102.

7. Online Makale:

Kaul S, Diamond GA. Good enough: a primer on the analysis and interpretation of noninferiority trials. Ann Intern Med [Internet]. 4 Temmuz 2006 [Atıf tarihi:4 Ocak 2007];145(1):62-9. Erişim adresi:http://www.annals.org/cgi/reprint/145/1/62.pdf

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Yazarların makalelerini göndermeden önce bir eksiklik olmadığından emin olmalarını sağlamak için bir kontrol listesi bulunmaktadır. Yazarlar derginin kontrol listesini kullanıp gönderilerini kontrol etmeli ve makaleleri ile birlikte bu formu göndermelidirler.

SON KONTROL LİSTESİ

- Editöre sunum sayfası
- Makalenin kategorisi
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- ICMJE Potansiyel Çıkar Çatışması Beyan Formu
- Daha önce basılmış materyal (yazı-resim-tablo) kullanılmış ise izin belgesi

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• İnsan öğesi bulunan çalışmalarda "gereç ve yöntemler" bölümünde Helsinki Deklarasyonu prensiplerine uygunluk, kendi kurumlarından alınan etik kurul onayının ve hastalardan "bilgilendirilmiş olur (rıza)" alındığının belirtilmesi

• Hayvan öğesi kullanılmış ise "gereç ve yöntemler" bölümünde "Guide for the Care and Use of Laboratory Animals" prensiplerine uygunluğunun belirtilmesi

• Kapak sayfası

- Makalenin Türkçe ve İngilizce başlığı (tercihen birer satır)
- Yazarlar ve kurumları
- Tüm yazarların yazışma adresi, iş telefonu, faks numarası, GSM, e-posta adresleri

• Özler (400-500 kelime) (Türkçe ve İngilizce)

• Anahtar Kelimeler: 3-10 arası (Türkçe ve İngilizce)

• Tam metin makale

• Teşekkür

• Kaynaklar

• Tablolar-Resimler, Şekiller

BAGCILAR MEDICAL BULLETIN
Bağcılar Tıp Bülteni

CONTENTS / İÇİNDEKİLER

ORIGINAL RESEARCH

Bagcilar Med Bull 2020;5(2):24-27
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Retrospective Analysis of Cases with Premature Thelarche

Prematür Telarş Tespit Edilen Kız Olguların Geriye Dönük Analizi

Hasan Serdar Kıhtır[1], Teoman Akçay[2]

[1]University of Health Sciences Antalya Training and Research Hospital, Clinic of Pediatric Intensive Care Unit, Antalya, Turkey
[2]İstinye University Medical Park Gaziosmanpaşa Hospital, Clinic of Pediatric Endocrinology and Metabolism, İstanbul, Turkey

Abstract

Objective: Premature thelarche is defined as breast enlargement in females (younger than eight years) without other signs of secondary gender character development. Although it is common in the first two years of life, it can be seen in any age group before the age of eight. In this study, girls who presented to pediatric endocrinology outpatient clinic due to early breast development were retrospectively analyzed.

Method: Patient data were analyzed retrospectively between 01.01.2011 and 31.12.2011 (one year) from pediatric endocrinology outpatient clinic files. Patients under two years of age and cases with precocious puberty were excluded from the study.

Results: Twenty-six patients with the mean age of 6.87±1.07 years were included in the study. Premature pubarche was also present in 12 (46%) of the cases. Height and weight standard deviations were 0.92±1 and 1.09±0.75, respectively. The standard deviations of body mass index were over 1 in 61.5% of the cases (16 cases). There was no correlation between the age of onset of thelarche and the age of first permanent tooth eruption and birth weight.

Conclusion: Although the etiology of premature thelarche is still unclear, there is increasing evidence that it may be associated with an increase in body fat mass.

Keywords: Obesity, premature thelarche, pubarche

Öz

Amaç: Prematür telarş 8 yaş öncesi kız çocuklarında cinsel gelişimin diğer bulguları olmaksızın görülen meme büyümesini tanımlar. İlk iki yaş arasında sık görülse de sekiz yaşına kadar her yaş grubunda görülebilir. Çalışmamızda erken meme gelişimi nedeniyle çocuk endokrinoloji polikliniğine başvuran kız olgular geriye dönük olarak incelendi.

Yöntem: Hasta verileri çocuk endokrinoloji polikliniğinin 01.01.2011 ve 31.12.2011 tarihleri arasındaki (bir yıl) dosya kayıtlarından geriye dönük olarak derlendi. İki yaş altı olgular ve puberte prekoks tespit edilen olgular çalışma dışı bırakıldı.

Bulgular: Ortalama yaşları 6,87±1,07 yıl olan 26 olgu çalışmaya dahil edildi. Olguların 12'sinde (%46) prematür pubarş da eşlik ediyordu. Olguların boy ve kilo standart sapmaları sırasıyla 0,92±1 ve 1,09±0,75 olarak tespit edildi. Olguların %61,5'inde (16 olgu) vücut kitle indeksi standart sapması 1'in üzerinde saptandı. Telarş başlama yaşıyla ilk kalıcı diş sürme yaşı ve doğum tartısı arasında korelasyon gözlenmedi.

Sonuç: Prematür telarş etyolojisi halen net olmamakla birlikte obeziteyle ilişkili olabileceği yönünde kanıtlar artmaktadır.

Anahtar kelimeler: Obezite, prematür telarş, pubarş

Introduction

The secular trend describes the change in the physical and developmental characteristics of people over time (1). The changes in height and weight of people in the last century can also be seen in starting age of puberty in children. In a 2009 study comparing the onset of puberty, it was observed that the age of onset of puberty was shifted back, even over a 10-year period. However, there was no significant change in basal luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels, but even basal estradiol (E2) levels were shown to decrease (2). Environmental factors are thought to be the largest part of this change.

Address for Correspondence: Hasan Serdar Kıhtır, University of Health Sciences Antalya Training and Research Hospital, Clinic of Pediatric Intensive Care Unit , Antalya, Turkey
E-mail: serdar.kihtir@gmail.com **ORCID:** orcid.org/0000-0003-0120-8711 **Received:** 09.03.2020 **Accepted:** 06.04.2020

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Isolated breast development is the most common complaint among pediatric endocrinology outpatient admissions. The definition of premature thelarche was first described by Wilkins (3) in 1957 as isolated breast development in girls before eight years of age without other physical and laboratory findings of puberty. Although it is described as a benign condition, it requires a close follow-up due to its potential to progress to early puberty. In this study, we aimed to define the general characteristics and personal risk factors of cases diagnosed with premature thelarche in our endocrinology outpatient clinic.

Materials and Methods

Girls who were admitted to the pediatric endocrinology outpatient clinic of Bakırköy Dr. Sadi Konuk Tranining and Research Hospital with early breast development (before eight years old) between 01.01.2011 and 31.12.2011 (one year) were investigated retrospectively. Anthropometric data, birth weight, age of first deciduous tooth, age of first permanent tooth eruption, activity status, laboratory [basal LH, FSH, E2, 17- hydroxyprogesterone, total testosterone, dehydroepiandrosterone sulfate (DHEAS)] and radiological results (bone age, uterine and ovarian measurements) were retrospectively reviewed from the endocrinology outpatient files. Cases with breast development before the age of eight years were examined for precocious puberty. Precocious puberty was considered with basal and evoked LH and FSH values, ultrasonography of uterine with long diameter greater than 35 mm, each ovarian volume greater than 1 mL, bone age that is two years older than calendar age or bigger than height age. Cases without precocious puberty were accepted as premature thelarche and were followed up for three-month periods without treatment. In cases with pubic or axillary hair, adrenal pathologies were excluded by DHEAS, 17-hydroxyprogesterone, total testosterone levels, and ultrasonographic evaluation of adrenal glands. Male cases, precocious puberty cases and cases under 2 years of age were not included in the study.

Ethical approval was obtained from the ethics committee of the Bakırköy Dr. Sadi Konuk Tranining and Research Hospital with the protocol number 2012/06/01 for the study. The waiver of consent was not required by the ethics committee due to the retrospective design of the study.

Statistical Analysis

Categorical data were presented as n (%) and continuous data were presented as mean ± standard deviation. The Pearson correlation analysis was used for correlation analysis. The chi-square test was used to compare categorical data. A p value of <0.05 was accepted for statistical significance. The Student's t-test was used to compare the difference of means and the results were expressed as the difference of means and confidence interval (CI). Statistical package for social sciences 23.0 for Windows and Medcalc 14.8.1 for Windows were used for calculations.

Results

Twenty-six cases with early breast development under the age of eight years were defined as premature thelarche (Table 1). The mean age of the patients was 6.87±1.07 years. Standard deviations for body mass index (BMI) were found to be over 1 in 6 cases (61.5%) and between the range of -1 and 1 in 10 cases (38.5%). Correlation analysis was performed in all cases in relation to the age of thelarche with birth weight, age of first deciduous tooth and age of first permanent tooth eruption. There was a weak but positive correlation between the age of thelarche and the age of first deciduous tooth eruption (r=0.239, p=0.018). There was no correlation of first permanent tooth eruption age and birth weight (r=-0.027 p=0.788, r=-0.007 p=0.949 respectively) with thelarche age (birth weight: mean 3253.1±384.3 g; first deciduous tooth eruption age: 6.5±1.2 months). Pubic hair development (Tanner pubic stage 2) was also observed in 12 (46%) of the cases. There was no statistically significant relationship between BMI standard deviation score and presence of pubic hair development (p=0.26). In patients with pubic hair, DHEAS levels were 77.85±36.38 pmol/L,

Table 1. Anthropometric, laboratory and radiological data of the subjects

Premature thelarche cases n=26	Mean ± Standard deviation
The age of presentation (year)	6.87±1.07
Height (standard deviation)	0.92±1
Weight (standard deviation)	1.09±0.75
Body mass index (standard deviation)	1.13±0.97
Weight for height (%)	118.33±17.06
Bone age - calendar age	0.32±1.02
Basal LH[1] (IU/L)	0.06±0.07
Basal FSH[2] (IU/L)	1.24±0.90
Basal E2[3] (pg/mL)	9.17±5.77
Uterus volume (cm^3)	1.2±0.64
Uterus height (mm)	22.97±4.1
Total ovarian volume (cm^3)	1.66±1.52

[1]LH: Luteinizing hormone, [2]FSH: Follicle stimulating hormone, [3]E2: Estradiol

17-hydroxyprogesterone levels were 0.88±1.07 ng/mL and total testosterone levels were 0.15±0.12 ng/mL. No adrenal pathology was detected in ultrasonographic imaging.

Discussion

The average onset of breast development (Tanner stage 2) in girls as described by Marshall and Tanner (4) is expected to be around 11.15±1.1 years of age. Premature thelarche is defined as the isolated breast development in girls before eight years of age, without other findings of secondary sexual characteristics (5). It is most commonly (2.2% - 4.7%) seen but rarely associated with true precocious puberty before two years of age. The prevalence of premature thelarche under the age of eight in Turkey is estimated at 8.9% (6). It has been reported that 9-14% of premature thelarche cases can progress to precocious puberty (7). Although endocrine disruptive environmental factors, obesity and prematurity are frequently blamed for the development of premature thelarche, definitive factors have not been identified (8). In a study presented by Selver Eklioğlu et al. (9) in 2016, it was reported that 14 of 96 girls who were followed up for early puberty symptoms were diagnosed with premature thelarche. The age distribution of these cases was determined as mean 5.89±2.18 years and in our study, the mean age of the cases was determined as 6.87±1.07 years (difference of the means: -0.98, 95% CI: -2.01-0.05). In the study of Atay et al. (6), the prevalence of premature thelarche was reported to be 8.3% in Istanbul, whereas BMI standard deviation score was shown as the most important risk factor for the development of premature thelarche. It was reported that 56% of premature thelarche cases had a BMI standard deviation score above 1 and 46% had a range between 1 and -1, and only 1.4% of cases had a BMI standard deviation score below -1. In our study, BMI standard deviation scores were above 1 in 61.5% of the cases and 2 and above in 23% of the cases. The BMI standard deviation score was not less than -1 in any case in our study. In the same study, it was stated that there was no correlation between the age of first permanent tooth eruption, prematurity, socioeconomic status and maternal menarche age with premature thelarche age. Similarly, in our study, no correlation was found between the age of first permanent tooth eruption (6.1±0.6 years) and birth weight (3253.1±384.3 g) and age of premature thelarche. In our study, however, a weak but significant correlation was observed between the age of the first deciduous tooth eruption and the age of premature thelarche. The role of obesity in the development of early puberty has been observed in different studies. In a meta-analysis, the risk of developing early puberty was 2.44 times higher (95% CI: 1.32-4.52) in obese girls than in non-obese subjects. In the subgroup analysis of same study, the risk of early breast development was found to be 2.03 times higher (95% CI 1.65-2.5) in obese subjects than in non-obese subjects, but no direct correlation was found between menarche age and obesity (Relative risk: 1.38, 95% CI: 0.76-2.49) (10).

Premature pubarche is defined as pubic or axillary hair without other signs of puberty. Although the most common cause is premature adrenarche, adrenal androgen levels can be normal. It is thought that there may be increased receptor sensitivity to normal androgen level in these cases (11). In our study, similar to the study of Atay et al. (6), there was no relationship between BMI standard deviation score and pubic hair development in premature thelarche cases.

In early-onset thelarche cases, central or peripheral early puberty should be differentiated by appropriate laboratory and radiological examinations, and cases diagnosed with premature thelarche should be followed up regularly for possible progress to early puberty (5). Although the etiologic factors are not definite in premature thelarche cases, obesity seems to be a risk factor for premature thelarche in cases under eight years of age. Therefore, studies to reduce obesity in this age group may also reduce premature thelarche cases. Although it is accepted as a benign condition, we believe that extensive research on the etiology of premature thelarche may reveal the possible causes more precisely because of its potential to progress to early puberty.

The retrospective design of the study, the small number of cases and the fact that the long-term data of the cases could not be followed are among the limitations of our study. However, it was found that the relationship between the primary tooth eruption age and premature thelarche was not studied in national and international publications. For this purpose, it is important to support the relationship with advanced, multicenter studies in terms of cause and effect and follow-up of pediatric cases.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the ethics committee of the Dr. Sadi Konuk Training and Resarch Hospital with the protocol number 2012/06/01 for the study.

Informed Consent: Patient consent could not be obtained because it was a retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.S.K., T.A., Design: H.S.K., T.A., Data Collection or Processing: H.S.K., T.A., Analysis or Interpretation: H.S.K., T.A., Literature Search: H.S.K., T.A., Writing: H.S.K., T.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Özer BK. Secular Changes in Height and Leg Length Among Turkish Children During the last century. Ankara Üniversitesi Dil ve Tarih-Coğrafya Fakültesi Derg 2007;47(1):95-113.
2. Aksglaede L, Sørensen K, Petersen JH, Skakkebaek NE, Juul A. Recent decline in age at breast development: the Copenhagen Puberty Study. Pediatrics 2009;123(5):e932-e939.
3. Wilkins L. The Diagnosis and Treatment of Endocrine Disorders of Childhood and Adolescence. Arch Dis Child 1958;33(168):184.
4. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Arch Dis Child 1969;44(235):291-303.
5. Khokhar A, Mojica A. Premature Thelarche. Pediatr Ann 2018;47(1):e12-e15.
6. Atay Z, Turan S, Guran T, Furman A, Bereket A. The prevalence and risk factors of premature thelarche and pubarche in 4- to 8-year-old girls. Acta Paediatr 2012;101(2):e71-e75.
7. Pasquino AM, Pucarelli I, Passeri F, Segni M, Mancini MA, Municchi G. Progression of premature thelarche to central precocious puberty. J Pediatr 1995;126(1):11-14.
8. Chiabotto P, Costante L, de Sanctis C. Premature thelarche and environmental pollutants. Minerva Med 2006;97(3):277-285.
9. Selver Eklioğlu B, Atabek ME, Akyürek N, Sarikaya E. The Etiologic Distribution and Clinical Features of Cases Presenting with the Findings of Puberty to the Pediatric Endocrinology Clinic. Turkish J Pediatr Dis 2016;10(4)-233-236.
10. Li W, Liu Q, Deng X, Chen Y, Liu S, Story M. Association between Obesity and Puberty Timing: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health 2017;14(10):1266.
11. Vottero A, Capelletti M, Giuliodori S, Viani I, Ziveri M, Neri TM, et al. Decreased androgen receptor gene methylation inpremature pubarche: a novel pathogenetic mechanism? J Clin Endocrinol Metab 2006;91(3):968-972.

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Effect of the Seasonal Changes on Renal Function in Patients with Acute Ischemic Stroke

Akut İskemik İnmeli Hastalarda Mevsim Değişikliklerinin Böbrek Fonksiyonu Üzerindeki Etkileri

Güleser Akpınar[1], Mustafa Boğan[1], Kaan Yusufoğlu[2], Miray Korkmaz[3], Emine Gül Baldane[4], Erdem Çevik[5]

[1]Düzce University Faculty of Medicine, Department of Emergency Medicine, Düzce, Turkey
[2]Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey
[3]Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Neurology, İstanbul, Turkey
[4]Konya Training and Research Hospital, Clinic of Neurology, İstanbul, Turkey
[5]İstanbul Sultan 2.Abdulhamid Han Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey

Abstract

Objective: This study aimed to define seasonality trends of acute renal dysfunction in the patients with ischemic stroke.

Method: This study was conducted retrospectively. Data were obtained from digital records of Şişli Hamidiye Etfal Training and Research Emergency Medicine Clinical Statistic Office.

Results: One hundred ninety-nine patients with ischemic stroke were included in the study. Patients were divided into two groups according to their renal functions. Group 1 (patients with abnormal renal function) included 70 patients. In this group, the mean urea value was 67.3±26.9 mg/dL, the mean creatinine value was 1.4±1.1 mg/dL, the mean age was 77.0±6.5 years, 34 patients were male (48.6%). Group 2 (patients with normal renal function) included 129 patients. In this group, the mean urea value was 37.9±9.9 mg/dL, the mean creatinine value was 0.9±0.2 mg/dL, the mean age was 76.6±7.3 years, 74 patients were male (57.4%). Season distribution, age and gender distribution, affected area of the brain, and platelet count did not show significant differences between the groups (p>0.05).

Conclusion: There is not a significant relationship between seasonal changes and renal dysfunction in the patients with ischemic stroke.

Keywords: Emergency medicine, ischemic stroke, renal function, season

Öz

Amaç: Bu çalışma iskemik inmeli hastalarda akut böbrek fonksiyon bozukluğunun mevsimsellik eğilimlerini tanımlamayı amaçlamıştır.

Yöntem: Bu çalışma geriye dönük olarak yapılmıştır. Veriler Şişli Hamidiye Etfal Eğitim ve Araştırma Acil Tıp Klinik İstatistik Ofisi dijital kayıtlarından elde edilmiştir.

Bulgular: Çalışmaya 199 iskemik inme hastası dahil edilmiştir. Hastalar böbrek fonksiyonlarına göre iki gruba ayrılmıştır. Grup 1'e (anormal böbrek fonksiyonu olan hastalar) 70 hasta dahil edilmiştir. Bu grupta, ortalama üre 67,3±26,9 mg/dL, ortalama kreatinin 1,4±1,1 mg/dL, ortalama yaş 77,0±6,5 olup, hastaların 34'ü erkekti (%48,6). Grup 2'ye (normal böbrek fonksiyonu olan hastalar) 129 hasta alınmıştır. Bu grupta, ortalama üre 37,9±9,9 mg/dL, ortalama kreatinin 0,9±0,2 mg/dL, ortalama yaş 76,6±7,3 olup, 74 hasta erkekti (%57,4). Mevsim dağılımı, yaş ve cinsiyet dağılımı, beynin etkilenen bölgesi ve platelet sayısı gruplar arasında anlamlı farklılık göstermemiştir (p>0,05).

Sonuç: İskemik inmeli hastalarda mevsimsel değişiklikler ile böbrek fonksiyon bozukluğu arasında anlamlı bir ilişki yoktur.

Anahtar kelimeler: Acil tıp, böbrek fonksiyonu, iskemik inme, mevsim

Introduction

Stroke cases are caused by ischemic reasons at the rate of 80-85% and by hemorrhagic reasons at the rate of 15-20% (1). Acute stroke is the third most common cause of death and cause of morbidity and mortality around the world and in Turkey (2,3). Even though there are many studies about stroke, risk factors are still not fully understood and have some contradictory elements (4).

Address for Correspondence: Mustafa Boğan, Düzce University Faculty of Medicine, Department of Emergency Medicine, Düzce, Turkey
E-mail: mustafabogan@hotmail.com **ORCID:** orcid.org/0000-0002-3238-1827 **Received:** 25.02.2020 **Accepted:** 23.04.2020

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Many factors such as seasonal changes affect ischemic stroke. Results of the studies on the seasonality of stroke occurrence are not clear. Some of the studies have reported that stroke peaks in winter, spring or autumn, but some of the studies have reported no significant relationship between seasonal changes and stroke (5). In this study, we aimed to define the seasonality trends of acute renal dysfunction in the patients with ischemic stroke.

Materials and Methods

This study was conducted retrospectively. Patients who were diagnosed with acute ischemic stroke between the dates 01.01.2013 and 31.12.2014 at Şişli Hamidiye Etfal Training and Research Training and Research Hospital were included in the study. During this period, 305.300 patients presented into Şişli Hamidiye Etfal Training and Research Hospital. Data were obtained from digital records of Şişli Hamidiye Etfal Training and Research Emergency Medicine Clinical Statistic Office.

Inclusion criteria: Patients who

- were diagnosed with acute ischemic stroke on radiological imaging and clinical diagnosis,
- were ≥65 years old,

Exclusion criteria: Patients who

- were <65 years old,
- were diagnosed with hemorrhagic stroke,
- had known chronical renal functional disorders.

Measurements

-Descriptive statistics of patients (gender, age, presentation dates, comorbidity (hypertension, diabetes mellitus, coronary artery disease and chronic obstructive lung disease, etc), situation of renal function (urea, creatinine), platelet counts (PC), mean platelet volume (MPV), computerized cranial tomography and diffusion magnetic resonance records).

-Patients were divided into two groups, Group 1 (patients with abnormal renal function = creatinin level >1.2 mg/dL and urea level >45 mg/dL) and Group 2 (patients with normal renal function).

Statistical Analysis

In data's descriptive statistics, average, standard deviation, the highest and the lowest median, frequency and rate values were used. Range of the variables was measured by the Kolmogorov-Smirnov test. In the analysis of quantitative data, the Kruskal-Wallis test, Mann-Whitney U test and independent sample t-test were used. In the analysis of qualitative data, the chi-square test was used. For analyzing, SPSS 22.0 program was used.

Results

One hundred ninety-nine patients with ischemic stroke were included in the study. 54.3% (n=108) of the patients were male and the mean age of the patients was calculated to be 76.74±7.02 years. One hundred ninety-nine (59.8%) patients had a comorbid disease. Forty nine of the patients had new high-levels of urea and creatinine. Considering the presentation days of the patients, it was seen that 29.1% (n=58) of the presentations were for autumn (Table 1).

Patients were divided into two groups according to their renal functions.

Group 1 (patients with abnormal renal function) included 70 patients. In this group, the mean urea value was 67.3±26.9, the mean creatinine value was 1.4±1.1, the mean age was 77.0±6.5 years, 34 patients were male (48.6%).

Group 2 (of the patients with normal renal function) included 129 patients. In this group, the mean urea value was 37.9±9.9, the mean creatinine value was 0.9±0.2, the mean age was 76.6±7.3 years, 74 patients were male (57.4%).

Season distribution, age and gender distribution, affected area of the brain, and PC did not show significant differences between the groups ($p>0.05$). (Table 1). 59.8% of the patients had at least one comorbid chronical disease, 65.8% of the patients in Group 1 had a comorbid chronical disease and it was remarkably higher than in Group 2 ($p<0.05$). MPV, urea, creatinine, and urea/creatinine levels were remarkably higher in Group 1 ($p<0.05$).

In Group 1, there was no correlation between age and renal functions (urea, creatinine, ure/creatinine) ($p>0.05$). Creatinine and urea/creatinine levels were higher in men in this group ($p<0.05$). There were no significant differences between renal functions (urea, creatinine, ure/creatinine) and variables of the patients (chronic disease, affected area of brain, and presented season) ($p>0.05$) (Table 2).

Discussion

The previous studies reported inconsistent results about the relationship between seasonal difference and ischemic stroke. In a prospective study conducted by Toyoda et al. (6), they analyzed 2.965 acute ischemic stroke patients and they did not find any significant difference between observing

Table 1. Descriptive statistics and comparison of the groups

Parameter	Total	Group 1	Group 2	p
n (%)	199 (100%)	70 (35.2%)	129 (64.8%)	-
Gender	Male: 108 (54.3%) Female: 71 (45.7%)	Male: 34 (48.6%) Female: 36 (51.4%)	Male: 74 (57.4%) Female: 55 (42.6%)	0.234
Age	76.74±7.02	77.0±6.5	76.6±7.3	0.656
Comorbidity	119 (59.8%)	46 (65.7%)	70 (54.3%)	0.031*
Season	Winter: 47 (23.6%) Spring: 40 (20.1%) Summer: 56 (28.1%) Autumn: 58 (28.2%)	Winter: 13 (18.6%) Spring: 14 (20%) Summer: 24 (34.3%) Autumn: 19 (27.1%)	Winter: 34 (26.4%) Spring: 24 (18.6%) Summer: 32 (24.8%) Autumn: 39 (30.2%)	0.422
Affected area of brain	Left anterior: 85 (42.7%) Left posterior: 10 (5%) Right anterior: 87 (43.7%) Right posterior: 16 (8.6%)	Left anterior: 31 (44.3%) Left posterior: 6 (8.55%) Right anterior: 27 (38.6%) Right posterior: 6 (8.55%)	Left anterior: 54 (41.9%) Left posterior: 4 (3%) Right anterior: 61 (47.3%) Right posterior: 10 (7.8%)	0.209
Urea	52.6±18.4	67.3±26.9	37.9±9.9	0.000*
Creatinine	1.15±0.7	1.4 ±1.1	0.9±0.2	0.000*
Urea/Creatinine	53.55±30.6	60.1±29.3	47.0±31.8	0.000*
PC	242±69	240±64	244±73	0.693
MPV	10.2±1	10.5±0.9	9.9±1.1	0.003*

*: Significant level p<0.05, PC: Platelet counts, MPV: Mean platelet volume

Table 2. Variable parameters in the patients of group 1

		Urea	Creatinine	Urea/ Creatinine
Gender	**Male**	66.3±28.7	1.7±1.4	52.2±28.9
	Female	68.4±25.2	1.1±0.3	68.4±27.8
	p	0.304	0.028*	0.006*
Chronic Disease	**Yes**	70.7±29.0	1.4±1.2	63.8±30.9
	No	59.3±19.6	1.3±0.7	51.5±23.7
	p	0.270	0.394	0.196
Affected Area of the Brain	**Anterior**	66.3±25.5	1.3±0.7	62.3±30.6
	Posterior	72.1±34.0	2.0±2.2	49.2±19.5
	p	0.839	0.268	0.230

*: Significant level p<0.05

stroke and seasons. However, they found that severe neurological deficits and one year mortality were frequent in the winter (6). Anlar et al. (7) reported that ischemic stroke was observed more frequently in males in hot seasons. In a meta-analysis, ischemic stroke rate peaked in cold seasons and it decreased in hot seasons (8). Karagiannis et al. (9) reported that ischemic stroke incidence peaked in the spring and reduced in the summer. It was reported that the, renal function was an important factor on long-term mortality in the patients with acute ischemic stroke (10). The incidence of acute renal dysfunction was found to be 8-21% in the patients with ischemic stroke (11). Wang et al. (12) reported that high rate of acute renal dysfunction was observed in the patients with ischemic stroke. It seems that renal function is a remarkable factor on the mortality and the morbidity of ischemic stroke. When we have investigated the studies on seasonal variation of the acute renal dysfunction, we have found that there are many studies but it is not clear like seasonal ischemic stroke variation. Iwagami et al. (13) found that acute renal dysfunction was seen higher in the winter and lower in the summer. Lim et al. (14) reported that acute renal dysfunction increased in hot and warm seasons because of increasing ambient temperature. Phillips et al. (15) found that acute cases with renal dysfunction increased in the first three months of the year, and decreased in the last three months of the year.

Although evidences are not clear about acute renal dysfunction and ischemic stroke, in this study, we aimed to define seasonality trends of acute renal dysfunction in the patients with ischemic stroke. We found that there was no significant relationship between seasons and renal dysfunction in the patients with ischemic stroke. This may be because that the population was small and the study was conducted in a single center. The records about seasonal variation of stroke in the literature vary, which may be because of the difference of geographical situation. Also, total population of the studies could affect the results.

Additionally, ischemic stroke is a result of many etiological factors such atrial fibrillation, hypercoagulable state (oral

contraceptives, antiphospholipid antibodies, protein S and C deficiencies, sickle cell anemia), atherosclerosis, vasculitis, polycythemia etc.

If studies analyze the subgroups according to etiological factors, differences may be observed among the parameters.

Study Limitations

The study was conducted retrospectively and in a single center. It included a small population. Also, the study included only patients with ischemic stroke. The population of the study could not project all people that were affected by the seasonal changes.

Conclusion

There is not a significant relationship between seasonal changes and renal dysfunction in the patients with ischemic stroke.

Ethics

Ethics Committee Approval: The study was approved by Ethics Committee of Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Turkey (decision no: 2204, date: 08/01/2019).

Informed Consent: Not required.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: G.A., Design: G.A., Data Collection or Processing: G.A., M.K., Analysis or Interpretation: M.B., E.G.B., Literature Search: G.A., K.Y., Writing: G.A., M.B., E.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Sacco PL. Vascular diseases. In: Merrit, Rowland LP, editors. Merrit's neurology. 10th ed. Hagerstown: Williams&Wilkins; 2000. p.177-185.
2. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. The Lancet 2006;367(9524):747-1757.
3. Onat A, Keleş İ, Çetinkaya A. On yıllık TEKHARF çalışması verilerine göre Türk erişkinlerinde koroner kökenli ölüm ve olayların prevalansı yüksek. Türk Kardiyoloji Derneği Arşivi 2001;29(1):8-19.
4. Feigin VL, Wiebers DO, Nikitin YP, O'Fallon WM, Whisnant JP. Risk factors for ischemic stroke in a Russian Community: A population-based case control study. Stroke 1998;29(1):34-39.
5. Skajaa N, Horváth Puhó E, Sundbøll J, Adelborg K, Rothman KJ, Sørensen HT. Forty-year seasonality trends in occurrence of myocardial infarction, ischemic stroke, and hemorrhagic stroke. Epidemiology 2018;29(6):777-783.
6. Toyoda K, Koga M, Yamagami H, Yokota C, Sato S, Inoue M, et al. Seasonal Variations in Neurological Severity and Outcomes of Ischemic Stroke -5-Year Single-Center Observational Study.- Circulation Journal 2018;82(5):1443-1450.
7. Anlar O, Tombul T, Unal O, Kayan M. Seasonal and environmental temperature variation in the occurrence of ischemic strokes and intracerebral hemorrhages in a Turkish adult population. Int J Neurosci 2002;112(8):959-963.
8. Li Y, Zhou Z, Chen N, He L, Zhou M. Seasonal variation in the occurrence of ischemic stroke: A meta-analysis. Environ Geochem Health 2019;41(5):2113-2130.
9. Karagiannis A, Tziomalos K, Mikhailidis DP, Semertzidis P, Kountana E, Kakafika AI, et al. Seasonal variation in the occurrence of stroke in Northern Greece: a 10 year study in 8204 patients. Neurological research 2010;32(3):326-331.
10. Tsagalis G, Akrivos T, Alevizaki M, Manios E, Stamatellopoulos K, Laggouranis A, et al. Renal dysfunction in acute stroke: an independent predictor of long-term all combined vascular events and overall mortality. Nephrology Dialysis Transplantation 2008;24(1):94-200.
11. Fiaccadori E, Delsante M, Fani F, Regolisti G. Acute kidney injury and stroke: unresolved issues. Internal and Emergency Medicine 2017;13(1):13-15.
12. Wang D, Guo Y, Zhang Y, Li Z, Li A, Luo Y. Epidemiology of acute kidney injury in patients with stroke: a retrospective analysis from the neurology ICU. Internal and emergency medicine 2018;13(1):17-25.
13. Iwagami M, Moriya H, Doi K, Yasunaga H, Isshiki R, Sato I, et al. Seasonality of acute kidney injury incidence and mortality among hospitalized patients. Nephrology Dialysis Transplantation 2018;33(8):1354-1362.
14. Lim YH, So R, Lee C, Hong YC, Park M, Kim L, et al. Ambient temperature and hospital admissions for acute kidney injury: A time-series analysis. Science of The Total Environment 2018;616(617):1134-1138.
15. Phillips D, Young O, Holmes J, Allen LA, Roberts G, Geen J, et al. Seasonal pattern of incidence and outcome of Acute Kidney Injury: A national study of Welsh AKI electronic alerts. International journal of clinical practice 2017;71(9):e13000.

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The Evaluation of the Use of Traditional and Complementary Medicine in Children and the Level of Knowledge of Families in Bağcılar Region of Istanbul

İstanbul Bağcılar Bölgesinde Çocuklarda Geleneksel ve Tamamlayıcı Tıp Kullanımı ve Ailelerin Bilgi Düzeyinin Değerlendirilmesi

Mustafa Özdemir, Meltem Erol, Özlem Bostan Gayret, Fatih Mete, Abdulrahman Özel, Özgül Yiğit

Health Sciences University Turkey, Bağcılar Training and Research Hospital, Clinic of Pediatrics, İstanbul, Turkey

Abstract

Objective: Nowadays, there are compelling data on the increase in traditional and complementary medicine practices in adults. Although the use of complementary medicine practices in children is frequently observed, studies on children are more limited in this subject. Studies on children mostly include those with chronic diseases. Our study aimed to evaluate the use of traditional and complementary medicine therapies in children without chronic diseases and parents' knowledge.

Method: The study was conducted at Bağcılar Training and Research Hospital Pediatric Clinic between 1 December 2018 and 28 February 2019. In the study, 200 patients in the 0-15 age group without any known chronic diseases were included. A questionnaire form was applied to either mothers or fathers of the patients, and the practices they performed in traditional medicine, their knowledge, and experience, and their socioeconomic-cultural status were questioned.

Results: In our study, which evaluated the use of traditional and complementary medicine methods in children without chronic diseases, 95.5% of the children had a history of the use of at least one complementary medicine method. The use of herbal tea was the most preferred complementary medicine method (68.8%). Other methods were the use of immune boosters, prayers, massage, nutrition-diet, acupuncture, and music. More than half of the patients (56%) had heard or learned about complementary medicine methods from their family elders. The rate of those who had learned about them from the media was determined to be 14%, and the rate of those who had learned from

Öz

Amaç: Günümüzde, yetişkinlerde geleneksel ve tamamlayıcı tıp uygulamalarının artması ile ilgili ilgi çekici veriler mevcuttur. Bu konuda çocuklarda yapılan çalışmalar daha sınırlı olmakla birlikte, tamamlayıcı tıp uygulamalarının çocuklarda kullanımı sıklıkla görülmektedir. Çocuklardaki çalışmalar daha çok kronik hastalığı olanları kapsamaktadır. Çalışmamızda kronik hastalığı olmayan çocuklarda geleneksel ve tamamlayıcı tıp tedavilerinin kullanımı ve ebeveyn bilgilerinin değerlendirilmesi amaçlanmıştır.

Yöntem: Çalışmamız 1 Aralık 2018-28 Şubat 2019 tarihleri arasında Bağcılar Eğitim ve Araştırma Hastanesi Çocuk Kliniğinde yapılmıştır. Çalışmaya, bilinen kronik hastalığı olmayan 0-15 yaş grubunda 200 hasta dahil edilmiştir. Hastaların anne veya babalarına tamamlayıcı ve geleneksel tıp konusunda yaptıkları uygulamaları, bilgi ve deneyimlerini, sosyoekonomik-kültürel durumlarını sorgulayan anket formu uygulanmıştır.

Bulgular: Kronik hastalığı olmayan çocuklarda geleneksel ve tamamlayıcı tıp yöntemleri kullanımının değerlendirildiği çalışmamızda çocukların %95,5'inde en az bir tamamlayıcı tıp yöntemi kullanım öyküsü vardı. Bitki çayı kullanımı en sık (%68,8) tercih edilen tamamlayıcı tıp yöntemiydi. Bağışıklık güçlendirici, dua, masaj, beslenme-diyet, akupunktur ve müzik kullanılan diğer yöntemlerdi. Hastaların yarısından fazlası (%56) tamamlayıcı tıp yöntemini aile büyüklerinden duymuş ya da öğrenmiştir. Yine medyadan öğrenenlerin oranı %14 ve arkadaşından öğrenenlerin oranı %6,5 olarak bulunmuştur. Sadece %3,5 gibi düşük bir oran tamamlayıcı tıp yöntemini sağlık personelinden öğrenmiştir.

Address for Correspondence: Meltem Erol, Health Sciences University Turkey, Bağcılar Training and Research Hospital, Clinic of Pediatrics, İstanbul, Turkey
E-mail: drmeltemerol@yahoo.com **ORCID:** orcid.org/0000-0002-7672-1854 **Received:** 14.02.2020 **Accepted:** 29.04.2020

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Abstract

their friends was found to be 6.5%. The low rate of only 3.5% had learned about the complementary medicine method from healthcare personnel.

Conclusion: It is observed that traditional and complementary medicine practices have been started to be widely used also in children. We think that it would be healthier for families to learn these practices from conscious sources.

Keywords: Children, parents, traditional and complementary medicine

Öz

Sonuç: Geleneksel ve tamamlayıcı tıp uygulamalarının çocuklarda da yaygın olarak kullanılmaya başlandığı görülmektedir. Ailelerin bu uygulamaları bilinçli kaynaklardan öğrenmelerinin daha sağlıklı olacağını düşünmekteyiz.

Anahtar kelimeler: Çocuklar, ebevenyler, geleneksel ve tamamlayıcı tıp

Introduction

In recent years, traditional and complementary medicine practices have been widely used as auxiliary treatment methods for modern medicine (1). Nowadays, there are compelling data on the increase in the use of traditional and complementary medicine in adults. On the other hand, although the use of traditional and complementary medicine practices in children is frequently observed, studies conducted on children are more limited. According to the results of the studies conducted abroad, the use of traditional and complementary medicine in hospitalized children as well as in outpatient children ranges from 1.8% to 84% (2-5). In a paper reviewing the studies conducted in European countries, the use of traditional and complementary medicine in children over the past year was detected to be 56% (6). In the studies conducted in our country, the use of traditional and complementary medicine practices in children ranges from 56.5% to 87% (7-11). As can also be understood from the results of all these studies, the use of traditional and complementary medicine in children is also generally high in our country. It is known that the use of traditional and complementary medicine is common at any age, and this frequency increases in chronic diseases (12,13). In our country, studies on the use of traditional and complementary medicine have generally been conducted on children with chronic diseases (14-16). Herbal remedies, homeopathy, reflexology, and acupuncture are among the most popular therapies used in children (17,18). Discomfort and dissatisfaction with conventional medicine and positive feedback from friends and families are among the reasons for the prevalence of the use of traditional and complementary medicine (19,20).

Complementary and alternative medicine methods are also frequently applied to children without chronic diseases. However, there are no studies in an adequate number and of an adequate quality (21). Providing high-quality data on the use of traditional and complementary medicine methods in children will ensure that all healthcare professionals dealing with child health inform patients and their families about useful traditional and complementary medicine methods. In this study, in order to increase the sensitivity of parents, educators, and healthcare personnel with regard to this issue and to shed light on other studies to be conducted, the evaluation of the use of complementary and alternative therapies in children without chronic diseases and parental knowledge was aimed.

Materials and Methods

The study was carried out at Bağcılar Training and Research Hospital Pediatric Clinic between 1 December 2018 and 28 February 2019. Two hundred patients, who were in the 0-15 age group and did not have any known chronic diseases (chronic kidney disease, diabetes, muscle, heart, asthma, neurological, or genetic disease), were included in the study. A questionnaire form consisting of 25 questions was applied to the mothers or fathers of the patients. In this form, the age of the child, mother, and father, the occupation of the mother and father, their socioeconomic and sociocultural level, whether there was any traditional and complementary medicine method they used, from whom they learned about this, when (before applying to the health institution, after applying, concurrent with treatment) and why they chose a traditional and complementary medicine method (the difficulty in accessing health services, abstaining from drug side effects), and whether they needed more knowledge about traditional and complementary medicine were questioned.

For the study, written and verbal consent was obtained from the families. Ethics committee approval was obtained from the local ethics committee of our hospital (ethics committee approval no: 2019.01.2.02.106.rl.006).

Statistical Analysis

Whether the variables were normally distributed or not was examined with histogram graphs and the Kolmogorov-Smirnov test. While presenting descriptive analyses, mean,

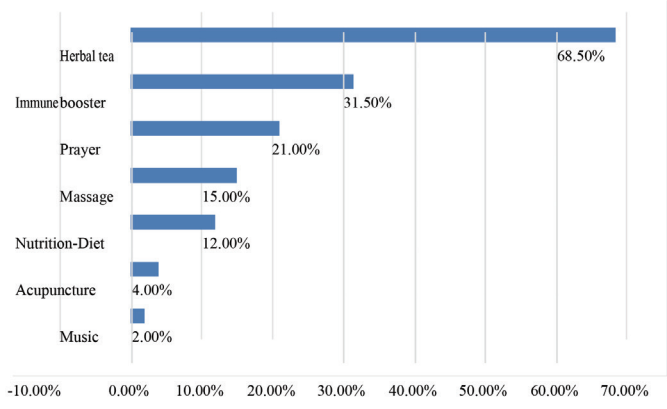
standard deviation, median, and minimum-maximum values were used. It was compared with the Pearson's chi-square and Fisher's exact tests in 2x2 tables. The independent samples t-test was used when the normally distributed (parametric) variables were evaluated between the groups, and the Manny-Whitney U test was used when the non-normally distributed (non-parametric) variables were evaluated between the groups. Results with a p-value below 0.05 were evaluated as statistically significant results.

Results

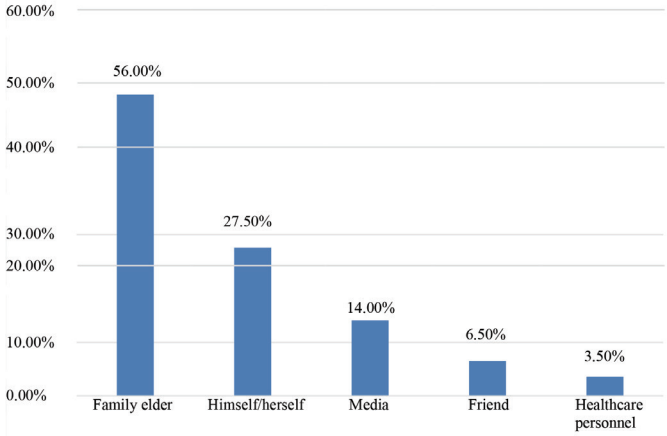
A total of 200 children, including 104 males (52%) and 96 females (48%), were included in the study. The demographic data of the study participants were summarized in Table 1. The mean age of the children participating in the study was 6.97±4.19 years, the mean age of the mothers was 34.23±7.25 years, and the mean age of the fathers was 37.37±7.20 years. As a traditional or complementary medicine method, acupuncture was used in 8 children (4%), herbal tea in 137 children (68.50%), nutrition-diet in 24 children (12%), massage in 30 children (15%), immune boosters in 63 children (31.50%), music in 4 children (2%), and prayers in 42 children (21%) (Graph 1). It was determined that there were 112 people (56%) who had learned traditional or complementary medicine methods from their family elders, 28 people (14%) who had learned them from the media, 13 people (6.50%) who had learned them from their friends, and 7 people (3.50%) who had learned them from healthcare personnel (Graph 2). Demographic data were compared according to the use of traditional or complementary medicine methods. Those who did not use traditional or complementary medicine methods had low monthly income (p=0.039). The rate of being married among parents who used traditional or complementary medicine methods was higher compared to those who did not use them (p=0.015). The rate of wanting to receive counseling was higher among those who used traditional or complementary medicine methods than those who did not use them (p=0.012) (Table 2).

Table 1. The demographic characteristics of the study participants

		n	%
Gender	Male	104	(52.00)
	Female	96	(48.00)
Monthly income	Low	30	(15.00)
	Medium	124	(62.00)
	Good	46	(23.00)
Educational status	Literate	22	(11.00)
	Primary school	46	(23.00)
	High school	70	(35.00)
	University	62	(31.00)
Marital status	Married	197	(98.50)
	Divorced	3	(1.50)
Family structure	Nuclear	127	(63.50)
	Extended	73	(36.50)
Purpose of use	Treatment	22	(11.52)
	Protection	84	(43.98)
	Support	85	(44.50)
When did he/she use it?	Before the medical doctor	164	(82.00)
	After the medical doctor	36	(18.00)
Did he/she benefit from it?	No	28	(14.00)
	Yes	172	(86.00)
Does he/she want to receive counseling?	No	59	(29.50)
	Yes	141	(70.50)



Graph 1. Methods used as traditional or complementary medicine



Graph 2. Sources from which traditional or complementary medicine methods are learned

Demographic data were compared according to the state of benefiting from traditional or complementary medicine methods. Accordingly, the monthly income of those who benefited from them was higher than those who did not benefit (p=0.021). The rate of being a university graduate was high among those who benefited from traditional or complementary medicine methods (p=0.040), and the rate of the nuclear family structure was also high among those who benefited from them (p<0.001) (Table 3).

The rate of benefiting from the methods used is given in Table 4. It was determined that herbal teas were benefited from at most. Demographic data were compared according to the state of wanting to receive counseling. Accordingly, the rate of having a nuclear family structure was significantly higher among those who wanted to receive counseling (p=0.016) (Table 5).

Discussion

Traditional and complementary medicine methods have been increasingly used in recent years. The number of publications on this subject increases in parallel with its widespread clinical use. However, the number of studies evaluating the use of traditional and complementary medicine methods in children is very low compared to the number of studies conducted on adults, and more studies are needed on this subject. According to the results of our study, there was a history of the use of at least one traditional and complementary medicine method in 191 (95.5%) children. At the same time, the use of herbal teas was the most frequently preferred (68.8%) traditional and complementary medicine method. Furthermore, immune boosters, prayers, massage, nutrition-diet, acupuncture, and music were the other methods used. While traditional and complementary medicine methods can be used for therapeutic purposes in chronic diseases, they can also be used to boost the immune system in healthy children

Table 2. Comparison of demographic data according to the use of traditional or complementary medicine methods

		State of use				p
		Does not use		Uses		
		n	%	n	%	
Gender	Male	5	(55.56)	99	(51.83)	0.827
	Female	4	(44.44)	92	(48.17)	
Monthly income	Low	4	(44.44)	26	(13.61)	**0.039**
	Medium	4	(44.44)	120	(62.83)	
	Good	1	(11.11)	45	(23.56)	
Educational status	Literate	1	(11.11)	21	(10.99)	0.878
	Primary school	3	(33.33)	43	(22.51)	
	High school	3	(33.33)	67	(35.08)	
	University	2	(22.22)	60	(31.41)	
Marital status	Married	8	(88.89)	189	(98.95)	**0.015**
	Divorced	1	(11.11)	2	(1.05)	
Family structure	Nuclear	6	(66.67)	121	(63.35)	0.840
	Extended	3	(33.33)	70	(36.65)	
Does he/she want to receive counseling?	No	6	(66.67)	53	(27.75)	**0.012**
	Yes	3	(33.33)	138	(72.25)	

Table 3. Comparison of demographic data according to the state of benefiting from traditional or complementary medicine methods

		Did he/she benefit from them?				p
		No		Yes		
		n	%	n	%	
Gender	Male	12	(60.00)	87	(50.88)	0.440
	Female	8	(40.00)	84	(49.12)	
Monthly income	Low	6	(30.00)	20	(11.70)	**0.021**
	Medium	13	(65.00)	107	(62.57)	
	Good	1	(5.00)	44	(25.73)	
Educational status	Literate	4	(20.00)	17	(9.94)	**0.040**
	Primary school	7	(35.00)	36	(21.05)	
	High school	8	(40.00)	59	(34.50)	
	University	1	(5.00)	59	(34.50)	
Marital status	Married	20	(100.00)	169	(98.83)	0.627
	Divorced	0	(0.00)	2	(1.17)	
Family structure	Nuclear	4	(20.00)	117	(68.42)	**<0.001**
	Extended	16	(80.00)	54	(31.58)	

Table 4. The rate of benefiting according to the methods used

	Did he/she benefit from them?			
	Yes		No	
	n	%	n	%
Acupuncture	7	(87.50)	1	(12.50)
Herbal tea	123	(89.78)	14	(10.22)
Nutrition-diet	20	(83.33)	4	(16.67)
Massage	26	(86.67)	4	(13.33)
Immune booster	57	(90.48)	6	(9.52)
Music	3	(75.00)	1	(25.00)
Prayer	35	(83.33)	7	(16.67)

Table 5. Comparison of demographic data according to the state of wanting to receive counseling

		Does he/she want to receive counseling?				P
		No		Yes		
		n	%	n	%	
Gender	Male	35	(59.32)	69	(48.94)	0.180
	Female	24	(40.68)	72	(51.06)	
Monthly income	Low	12	(20.34)	18	(12.77)	0.146
	Medium	38	(64.41)	86	(60.99)	
	Good	9	(15.25)	37	(26.24)	
Educational status	Literate	7	(11.86)	15	(10.64)	0.308
	Primary school	18	(30.51)	28	(19.86)	
	High school	16	(27.12)	54	(38.30)	
	University	18	(30.51)	44	(31.21)	
Marital status	Married	57	(96.61)	140	(99.29)	0.155
	Divorced	2	(3.39)	1	(0.71)	
Family structure	Nuclear	30	(50.85)	97	(68.79)	**0.016**
	Extended	29	(49.15)	44	(31.21)	

and to support normal growth and development (1). In the literature, most of the studies were conducted on children with asthma, attention deficit and hyperactivity disorder, cancer, pediatric rheumatological disease, neurological disease such as cerebral palsy or other chronic diseases/deficiencies (2-6). In our study, children without any chronic disease were included.

Studies on the frequency and prevalence of the use of traditional and complementary medicine methods in children have been conducted, and quite different results have been obtained. These differences in the literature have been attributed to different factors, such as the sociocultural structure and economic status of the country and families included, the country's health policy, and the characteristics of children. For example, a study including 300 people reported that 35.6% of families used traditional and complementary medicine methods for their children at least once (7). Again, when the studies conducted on children with chronic diseases were examined, it was determined that at least one traditional and complementary medicine method was used in approximately half of the children with asthma, in 68% of children with attention-deficit and hyperactivity disorder, in 65% of children with cancer, and in 56% of children with cerebral palsy (2-5). In a study conducted in our country, it was detected that approximately half of the children, who were aged between 1 and 16 years and diagnosed with asthma, used at least one traditional and complementary medicine method (8). In our study, children without chronic diseases were included, and the rate of the use of traditional and complementary medicine, which was found to be 95.5%, was higher than that in the literature. We can attribute this situation to the broader handling of the methods that were evaluated as traditional and complementary medicine in our study. Traditional and complementary medical units, polyclinics, and centers have been recently established in many health institutions, and certified seminars, courses, congresses, symposia, and meetings have been started to be organized by the Ministry of Health. It is also observed that traditional and complementary medicine methods are recommended, encouraged, and supported in television programs and social media.

When the traditional and complementary medicine methods used in the children included in our study are examined, the use of herbal teas comes first with a rate of 68.5%. The other traditional and complementary medicine methods used were determined to be immune boosters (31.5%), prayers (21%), massage (15%), nutrition-diet (12%), acupuncture (4%), and music (2%). Of those who preferred traditional and complementary medicine methods, 43.98% stated that they used them for protective purposes, 44.5% for support and only 11.52% used them for therapeutic purposes. When studies on the use of traditional and complementary medicine methods in children were examined in the literature, it was observed that the used methods differed according to populations. For example, prayers are directly related to the ethnic and cultural structure of the society, and in our study, prayers were used approximately in one of every five children.

In the study conducted by Kaya et al. (10), it was found that quail eggs (44.3%) were used most frequently in children with asthma. Carob (41.9%), chestnut honey (29.9%), honey (29.3%), herbal mixture (18.6%), and mulberry molasses (15.6%) were determined as the other traditional and complementary medicine methods used. In a study conducted on children with hereditary metabolic diseases, mind-body medicine (28%) and biological-based therapy (21.4%) were reported as the two most commonly used traditional and complementary medicine methods (11). Furthermore, there are studies evaluating the effectiveness of acupuncture used due to cerebral palsy, asthma, enuresis nocturna, digestive system pathologies, amblyopia, and pain (12). Traditional and complementary medicine methods were evaluated in children with hepato-

gastrointestinal disease, and approximately 71% of them were determined to use herbal products (13).

As is seen, studies on the use of traditional and complementary medicine methods in the literature were mostly conducted in a specific pediatric patient group with chronic disease. The inclusion of mostly specific patient groups could be attributed to the fact that those with chronic diseases are in a search more, and their tendency to traditional and complementary medicine methods is higher. Despite the fact that very advanced treatment methods have been defined in recent years in modern medicine, reasons such as the failure to observe the treatment response expected or hoped by patients, not finding a method that will eliminate the disease completely, dissatisfaction with the medical health services, the inadequate relationship between the healthcare professional and the patient, the high demand for health services, long-term waiting, not allocating enough time to the patient, side effects of medical treatments, despair, and distrust in health institutions were found to be the parameters affecting the orientation of patients and their families toward traditional and complementary medicine methods (1,15).

Although being fewer in number, other studies that evaluate the use of complementary and alternative medicine in children were also published. The rate of the use of traditional and complementary medicine methods in 206 children evaluated by Tuncel et al. (22) was found to be 83%. Carrying an evil eye bead (45%) and reading prayers (35%) were found to be the most frequently used practices in order to protect from the evil eye. Belief-based practices were used in 73% of patients, and herbal practices were used in 57% of them. Akçay et al. (23) evaluated the use of traditional and complementary medicine in 125 children without chronic diseases. Herbal practices and religious beliefs were reported as the two most frequently used methods. In our study, the rate of the use of herbal products and religious beliefs was found to be high, and generally, our results are consistent with the literature. Although patients without chronic diseases were included, one of the limitations of our study is that the exact purpose of the use of traditional and complementary medicine (e.g. sleep, constipation, diarrhea, indigestion, etc) was not specified.

In modern medicine, ‘‘evidence-based medicine’’ is accepted as an undeniable fact (16). For this reason, the interest in complementary and traditional medicine methods and such widespread use of them have also brought about discussions, and it has been emphasized that more systematic, randomized controlled studies are required on this subject (17). In this context, the reasons why people prefer traditional and complementary medicine methods and the sources from which these methods are learned are investigated. In our study, more than half of the patients (56%) had heard or learned these methods from family elders. Again, the rates of those who had learned them from the media and friends were found as 14% and 6.5%, respectively. The low rate of only 3.5% had learned traditional and complementary medicine methods from healthcare personnel. Therefore, we can conclude that healthcare personnel do not sufficiently prefer traditional and complementary medicine methods. Furthermore, in the studies in the literature, it was emphasized that most of the traditional and complementary medicine methods were initiated by parents, and even the families using these methods hid this from healthcare personnel. It is mentioned that most of the healthcare personnel are also not interested in traditional and complementary medicine and do not question this aspect of patients (1,18,19). According to a study conducted on children with cancer in Germany, 71% of patients learned and applied traditional and complementary medicine methods from individuals other than medical doctors (20). According to the results of our study, we believe that the rate of recommending traditional and complementary medicine by healthcare personnel will increase in the following years because the number of traditional and complementary medicine centers is increasing every day due to the health policy and incentives carried out at the moment in Turkey and the trend toward this subject is also gradually increasing. Moreover, according to the results of our study, it is noteworthy that the participants benefited significantly from traditional and complementary medicine methods, and this situation should be evaluated by medical doctors. Preferring traditional and complementary medicine methods unconsciously without a medical doctor’s control, or using them together with chemotherapy or with other medical therapies is also crucial in terms of possible side effects, interactions, and complications (24). Such possible complications and interactions of these methods can only be checked if administered by a medical doctor. When it is considered that the majority of those using traditional and complementary medicine methods (72.25%) want to receive professional counseling according to the results of our study, we believe that this deficiency should be closed by trained healthcare professionals and that traditional and complementary medicine methods should be applied under control. The use of herbal products, in other words, phytotherapy is the most frequently used traditional and

complementary medicine method in our study, and it is also clear that more studies should be conducted in terms of the more controlled and safe use of this method and that the literature should also be supported in this regard.

Although the rates differ in the studies conducted, it has been shown that people from all segments of society prefer traditional and complementary medicine methods for themselves or their children (21). Similarly, in our study, people at different socioeconomic levels preferred traditional and complementary medicine methods. However, they were preferred mostly by those with medium income. Furthermore, the economic status of those who applied traditional and complementary medicine methods was found to be higher compared to those who did not apply traditional and complementary medicine methods. The economic status may have affected the provision of herbal products due to reasons such as their relatively high prices and not being covered by health insurance. When the educational levels in our sample group are examined, it is observed that people with different educational levels and different family structures prefer traditional and complementary medicine methods, although the rate of university and high school graduates is higher. It is noteworthy that the rate of university graduates is higher among those using traditional and complementary medicine in our study. This situation can be interpreted as that university graduates investigate more, they are more sensitive in terms of side effects that can be observed in modern medicine and methods that are natural and have no side effects, and they tend toward traditional and complementary medicine.

Although our study is not a prevalence study, our sample group is of an acceptable size. Furthermore, due to the location of our center in the largest city of our country, our hospital's being a tertiary healthcare institution with an education clinic and, thus, being a center to which patients from all segments of society are accepted in the region, we believe that our study will reflect the general population and will be a guide in traditional and complementary medicine practices in children. However, our results should be supported by multicenter studies that will be conducted on larger sample groups.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from the local ethics committee of our hospital (ethics committee approval no: 2019.01.2.02.106. rl.006).

Informed Consent: For the study, written and verbal consent was obtained from the families.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.Ö., M.E., F.M., Design: M.E., Ö.B.G., Ö.Y., Data Collection or Processing: M.Ö., A.Ö., Analysis or Interpretation: M.Ö., A.Ö., Literature Search: Ö.B.G., F.M., Ö.Y., Writing: Ö.B.G., F.M., Ö.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Defining and describing complementary and alternative medicine: panel consensus following CAM research methodology conference, April 1995. Altern Ther Health Med 1997;3(2):49-57.
2. Davis MP, Darden PM. Use of complementary and alternative medicine by children in the United States. Arch Pediatr Adolesc Med 2003;157(4):393-396.
3. Hanson E, Kalish LA, Bunce E, Curtis C, McDaniel S, Ware J, et al. Use of complementary and alternative medicine among children diagnosed with autism spectrum disorder. J Autism Dev Disord 2007;37(4):628-636.
4. Lim A, Cranswick N, Skull S, South M. Survey of complementary and alternative medicine use at a tertiary children's hospital. Journal of Pediatrics and Child Health 2005;41(8):424-427.
5. Kelly KM, Jacobson JS, Kennedy DD, Braudt SM, Mallick M, Weiner MA. Use of unconventional therapies by children with cancer at an urban medical center. J Pediatr Hematol Oncol 2000;22(5):412-416.
6. Zuzak TJ, Boříková J, Careddu D, Garami M, Hadjipanayis A, Jazbec J, et al. Use of complementary and alternative medicine by children in Europe: published data and expert perspectives. Complement Ther Med 2013;21(1):34-47.
7. Fesharakinia A, Abedini M. Prevalence of using complementary and alternative medicine in children and its related factors in East iran. Iran J Pediatr 2014;24(1):111-114.
8. Orhan F, Sekerel BE, Kocabaş CN, Sackesen C, Adalioglu G, Tuncer A. Complementary and alternative medicine in children with asthma. Annals of Allergy, Asthma & Immunology 2003;90(6):611-615.
9. Taşar MA, Potur ED, Kara N, Bostancı İ, Dallar Y. Düşük Gelir Düzeyine Sahip Ailelerin Çocuklarına Tamamlayıcı veya Alternatif Tıp Uygulamaları. Türkiye Çocuk Hastalıkları Dergisi 2011;5(2):81-88.
10. Kaya Y, Ergüven M, Tekin E, Özdemir M, Hamzah ÖY. Bölgemizde çocuklarda bronşial astım tedavisinde alternatif tedavi yöntemleri kullanımı. Çocuk Dergisi 2009;9(2):84-89.
11. Erdol S, Saglam H. Use of complementary and alternative medicine in patients with inherited metabolic disease. J Pediatr Endocrinol Metab 2018;31(10):1091-1098.

12. Snyder J, Brown P. Complementary and alternative medicine in children: an analysis of the recent literature. Curr Opin Pediatr 2012;24(4):539-546.

13. Gottschling S, Gronwald B, Schmitt S, Schmitt C, Längler A, Leidig E, et al. Use of complementary and alternative medicine in healthy children and children with chronic medical conditions in Germany. Complement Ther Med 2013;21(1):61-69.

14. Babayigit A, Olmez D, Karaman O, Uzuner N. Complementary and alternative medicine use in Turkish children with bronchial asthma. J Altern Complement Med 2008;14(7):797-799.

15. Muslu GK, Öztürk C, Tamamlayıcı ve alternatif tedaviler ve çocuklarda kullanımı [Complementary and alternative therapies and their use in children]. Çocuk Sağlığı ve Hastalıkları Dergisi 2008;51(1):62-67.

16. Bozkaya ÖG, Akgün İ, Birgi E, Çinkoğlu A, Gög K, Karadeniz D. Anne babaların çocuklarında uyguladıkları alternatif tıp yöntemleri. DEÜ Tıp Fakültesi Dergisi 2008;3(22):129-135.

17. Gottschling S, Reindl TK, Meyer S, Berrang J, Henze G, Graeber S, et al. Acupuncture to alleviate chemotherapy-induced nausea and vomiting in pediatric oncology–a randomized multicenter crossover pilot trial. Klin Padiatr 2008;220(6):365-370.

18. Gottschling S, Meyer S, Gribova I, Distler L, Berrang J, Gortner L, et al. Laser acupuncture in children with headache: a double-blind, randomized, bicenter, placebo-controlled trial. Pain 2008;137(2):405-412.

19. Robinson N, Blair M, Lorenc A, Gully N, Fox P, Mitchell K. Complementary medicine use in multi-ethnic paediatric outpatients. Complement Ther Clin Pract 2008;14(1):17-24.

20. Laengler A, Spix C, Seifert G, Gottschling S, Graf N, Kaatsch P. Complementary and alternative treatment methods in children with cancer: A population-based retrospective survey on the prevalence of use in Germany. Eur J Cancer 2008;44(15):2233-2240.

21. Meyer S, Gortner L, Larsen A, Kutschke G, Gottschling S, Gräber S, Schroeder N. Complementary and alternative medicine in pediatrics: a systematic overview/synthesis of Cochrane Collaboration reviews. Swiss Med Wkly 2013;143:w13794.

22. Tuncel T, Şen V, Kelekçi S, Karabel Müsemma, Şahin C, Uluca Ü, et al. Kronik hastalığı olmayan çocuklarda tamamlayıcı ve alternatif tıp kullanımı. Türk Pediatri Ars 2014;49(2):148-153.

23. Akçay D, Yıldırımlar D. Çocuklarda Tamamlayıcı ve Alternatif Tedavi Kullanımı ve Ebeveyn Bilgilerinin Değerlendirilmesi Çocuk Dergisi 2017;17(4):174-181.

24. Buckner CA, Lafrenie RM, Dénommée JA, Caswell JM, Want DA. Complementary and alternative medicine use in patients before and after a cancer diagnosis. Curr Oncol 2018;25(4):e275-e281.

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Retrospective Evaluation of Pediatric Patients with Extremity Pains

Ekstremite Ağrısı ile Çocuk Polikliniğine Başvuran Çocuk Hastaların Retrospektif Değerlendirilmesi

Sezin Naiboğlu[1], Emrah Naiboğlu[2], Özden Aksu Sayman[3], Fatma Gül Demirkan[4]

[1]Esenyurt Necmi Kadıoğlu State Hospital, Clinic of Child Health and Diseases, İstanbul, Turkey
[2]SBÜ İstanbul Bakırköy Training and Research Hospital, Clinic of Child Health and Diseases, İstanbul, Turkey
[3]Ordu University Training and Research Hospital, Clinic of Child Health and Diseases, Ordu, Turkey
[4]SB Kanuni Training and Research Hospital, Clinic of Child Rheumatology Child Health and Diseases, İstanbul, Turkey

Abstract

Objective: Recurrent lower extremity pains (growing pains) are the most common non-inflammatory cause of musculoskeletal pain in children. This study aims to investigate musculoskeletal symptoms that may be associated with vitamin D deficiency. We retrospectively examined the data of the patients who applied to the pediatric outpatient clinic and who had vitamin D levels measurement results.

Method: We retrospectively evaluated the clinical, laboratory, and diagnostic findings of patients aged 3-16 years, who presented to our outpatient clinic with growing pains between January 2019 and December 2019. We excluded patients with chronic diseases, those with joint findings that might be associated with rheumatological or orthopedic diseases, and those who used vitamin D supplements.

Results: There were a total of 103 subjects. Forty-eight subjects were female (46.6%) and 55 (53.4%) were male. The mean age of the subjects was 8.8±4.2 years (3-16). The mean serum 25-hydroxyvitamin D [25(OH) D] level of the subjects was 15.4±6.5 nmol/L. The subjects were categorized according to their 25(OH) D levels. Ten subjects (9.7%) had severe vitamin D deficiency, 25 (23.4%) had vitamin D deficiency, and 42 (40.8%) had vitamin D insufficiency.

Conclusion: Leg pains are common in children, and growing pains are the most common non-inflammatory causes of muscle-joint pain in children. Patients with musculoskeletal pain should be screened for vitamin D deficiency. In this study, we aimed to emphasize the importance of vitamin D level assessment in patients presenting with joint-muscle pains that were primarily evaluated as growing pains.

Keywords: Child, growth pain, vitamin D

Öz

Amaç: Tekrarlayan alt ekstremite ağrıları (büyüme ağrıları) çocuklardaki kas-iskelet sistemi ağrılarının enflamatuvar olmayan en sık sebebidir. Bu araştırmada çocuk polikliniğine kas iskelet sistemi şikayetleriyle başvuran ve D vitamini düzeyi bakılan hastaların verilerini inceledik. Böylece D vitamini eksikliği ile ilişkili olabilecek kas iskelet sistemi semptomlarını araştırmayı amaçladık.

Yöntem: Polikliniğimize Ocak 2019-Aralık 2019 tarihleri arasında eksremite ağrısı ile başvuran 3-16 yaş grubundaki çocukların klinik özellikleri, tetkik sonuçları ve tanılarına ait bilgiler retrospektif olarak incelendi. Kronik hastalığı olan, romatolojik veya ortopedik olabilecek eklem bulgusu olan ve D vitamini kullanan hastalar çalışma dışı bırakıldı.

Bulgular: Çalışmamıza katılan 103 çocuğun 48'i (%46,6) kız, 55'i (%53,4) erkekti. Çocukların yaşları 3-16 yaş aralığında olup, ortalama yaşı 8,8±4,2 idi. Çocukların ortalama serum 25 (OH) D vitamin düzeyi 15,4±6,5 olarak saptandı. Serum 25 (OH) D vitamin düzeyine göre gruplandırılan çocukların 10'unda (%9,7) ağır D vitamini eksikliği, 25'inde (%23,4) D vitamini eksikliği, 42'sinde (% 40,8) D vitamini yetersizliği saptandı.

Sonuç: Çocuklarda bacak ağrısı şikayeti sık karşılaşılan bir durum olup, büyüme ağrıları gibi enflamatuvar olmayan nedenler kas-eklem ağrısının en sık sebebidir. Kas-iskelet ağrısı olan hastaların D vitamini eksikliği açısından mutlaka taranması gerekir. Çalışmamızda eklem-kas ağrısı şikayeti ile başvuran ve büyüme ağrısı düşünülen hastalarda vitamin D düzeyi incelemesinin önemini vurgulamak istedik.

Anahtar kelimeler: Büyüme ağrısı, çocuk, D vitamini

Address for Correspondence: Sezin Naiboğlu, Esenyurt Necmi Kadıoğlu State Hospital, Clinic of Child Health and Diseases, İstanbul, Turkey
E-mail: sezin_ctnol@hotmail.com **ORCID:** orcid.org/0000-0002-9593-1136 **Received:** 24.03.2020 **Accepted:** 29.04.2020

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Introduction

Recurrent lower extremity pains (growth pain) are the most common non-inflammatory cause of musculoskeletal pain in children (1).

The medical history of the child who experiences pain is significant for approaching the diagnosis. When obtaining the medical history, the location of the pain, the occurrence time of the pain, the duration and quality of the pain, the relationship of the pain with exercise, systemic findings accompanying the pain, vaccination status, nutritional habits, psychological state and trauma are the points that require attention (2). A full physical examination to be performed in the child who experiences musculoskeletal pain provides important data to the doctor.

Most frequently, growth pains are observed as the reason for applying to the doctor with a pain complaint in childhood. Growth pains are defined as the pains which may be experienced generally in the legs (in the back of the knee, thigh and calf) in children aged 3-12 years and these pains are less frequently in the arms, together with the legs, appear in the evening and at night, awaken the person, last from a few minutes up to a few hours, and are the cause of which is now known. The relationship between these pains and growth has not been demonstrated, and this reference is commonly used since it is the reason for consultation. In physical examination, no characteristic is detected even in the painful period. However, the symptoms of another disease should be sought carefully before establishing this diagnosis (3).

It has been put forward that the prevalence of low vitamin D in patients with non-specific musculoskeletal pain may be 38-93% (4). Even though vitamin D deficiency primarily causes osteomalacia, the pain can cause nonspecific symptoms such as weakness (4). Besides, vitamin D deficiency is thought to be correlated with various pain syndromes. Vitamin deficiency can lead to severe skeletal pain, low back pain, non-inflammatory arthritis and joint stiffness even in healthy individuals (5).

The normal vitamin D level is defined as the serum vitamin D level, which prevents the development of rickets or osteomalacia, and keeps the parathormone (PTH) level within the normal range by enabling optimal absorption of calcium in the diet. The 25 (OH) vitamin D level, above 32 ng/mL in adults and 20 ng/mL in children, is considered as a normal level (6,7).

Today, it has been realized that the effectiveness of vitamin D is not only limited to regulating calcium-phosphore homeostasis and bone metabolism, but also has pro-apoptotic, anti-inflammatory and immunomodulatory characteristics (8). For this reason, vitamin D deficiency, which is a preventable and treatable condition, is significant for patients experiencing musculoskeletal pain.

In this research, we examined the data of the patients who applied to the pediatric department with musculoskeletal complaints and whose vitamin D levels were examined. Hence, we wanted to research the musculoskeletal symptoms and to emphasize the importance of examining the vitamin D level in patients assumed to have growth pain.

Materials and Methods

The medical history, physical examination and laboratory tests of 103 children in the 3-16 years of age group, who applied to our pediatric outpatient clinic between January 2019 and December 2019 with extremity pain, were examined retrospectively for the differential diagnosis of the disease related to the musculoskeletal system. The demographic information, serum calcium, phosphore, alkaline phosphatase, PTH and 25 (OH) vitamin D levels of the patients were evaluated. As a result of all the evaluations, the patients were diagnosed with growth pain according to the Peterson (3) criteria. Patients whose extremity pain depended on any organic disease and who had definite diagnosis, those with a chronic disease, those with possible rheumatological or orthopedic joint findings and patients who were taking vitamin D were excluded from the study.

According to Pediatric Endocrine Association, serum 25 (OH) vitamin D levels above 20 ng/mL were classified as 'normal', 12-20 ng/mL as 'insufficient', 5-12 ng/mL as ''deficiency'' and <5 ng/mL as ''severe deficiency''. Patients were divided into 3 groups as 3-6 years of age (play age), 7-11 years of age (school period), and 12-18 years of age (adolescence) according to their ages. The age groups and genders of the patients, their 25 (OH) vitamin D levels and the classification of their levels were compared.

Statistical Analysis

Statistical analyses were conducted by means of IBM Statistical Package for Social Sciences 21.0 package program. The categorical data were expressed in frequency (n) and percentage (%) for descriptive analysis, and the continuous data were expressed in mean ± standard deviation and median (25. percentile-75. percentile). Normality distribution was decided with the coefficient of variation, histogram and normality tests. The chi-square

test was used in the analysis of the categorical variables. The Mann-Whitney U test was employed to compare the continuous variables of two independent groups, because normality distribution could not be achieved. The Kruskal-Wallis test was implemented for the comparison of the continuous variables of more than two independent groups as normality conditions could not be fulfilled. The cases when the p value was below 0.05 were considered statistically significant.

Results

Of 103 children who participated in our study, 48 (46.6%) were female and 55 (53.4%) were male. The mean age of the children, whose ages varied between 3 and 16 years, was 8.8±4.2 years. When classified by age, 36 (35%) children were at play age (3-6 years of age), 38 (36.9%) were at school age (7-11 years of age), and 29 (28.1%) were in adolescence. The mean serum 25 (OH) vitamin D level of the children who participated in the study was found as 15.4±6.5. Severe vitamin D deficiency was detected in 10 (9.7%) of the children, who were grouped according to their serum 25 (OH) vitamin D levels, vitamin D deficiency in 25 children (24.3%) and vitamin D insufficiency in 42 children (40.8%). In total, the serum 25 (OH) vitamin D levels of 77 children (74.2%) were below the normal limit (Figure 1).

When the serum 25 (OH) vitamin D levels of children and their genders were compared, the serum 25 (OH) vitamin D levels in males were discovered to be significantly higher than those in females (p=0.04). When the age groups and serum 25 (OH) vitamin D levels were compared, no significant difference was observed (p=0.06) (Table 1).

The serum 25 (OH) vitamin D levels of 40 (83.3%) female children in our study were found below the normal limits. Of the female children, 5 (10.4%) were found to have a serum 25 (OH) vitamin D level at the grade of severe deficiency, 16 (33.3%) at the grade of deficiency, and 19 (39.6%) at the grade of insufficient. Serum 25 (OH) vitamin D levels of 8 (16.7%) female children were within the normal limits. Serum 25 (OH) vitamin D levels of 37 (67.3%) of the male children were below the normal limits. Regarding serum 25 (OH) vitamin D levels, it was observed that 5 (9%) had severe deficiency, 9 (16.4%) had deficiency, and 23 (41.8%) had insufficient levels. Eighteen (32.7%) of the male children had normal limits (Figure 2).

In the classification of serum 25 (OH) vitamin D according to the age groups of the children in our study, the serum 25 (OH) vitamin D levels of 22 (61.1%) children in the play age, 31 (81.5%) children in the school age and 24 (82.7%) children in adolescence were found to be below the normal limits (Figure 3).

Discussion

In children, musculoskeletal complaints are quite common. The incidence ranges between 4% and 30% (9,10). Non-inflammatory muscle joint pain is among the

Table 1. Comparison of vitamin D levels by age and gender

		Serum 25 (OH) D level		
	n (%)	Mean ± SD	Median (25p-75p)	p
Gender				
Girl	48 (46.6)	14.1±6.5	12.8 (9.6-19)	**0.04***
Boy	55 (53.4)	16.5 ±6.4	17 (11.8-21.2)	
Age				
Play age	36 (35)	17.3±6.8	18.4 (11.5-22.9)	-
School period	38 (36.9)	15.2±6.4	14.1 (10.3-19.1)	0.06**
Adolescence	29 (28.1)	13.3±5.8	13.3 (9.6-17.2)	-

*: Mann-Whitney U test, **: Kruskal-Wallis test, SD: Standard deviation

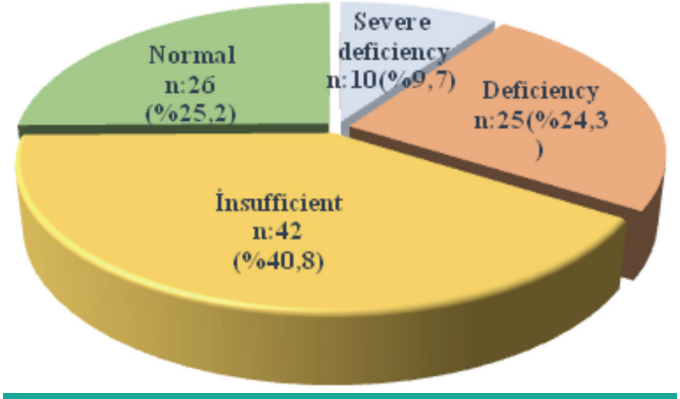

Figure 1. Classification of serum 25 (OH) vitamin D levels of the cases

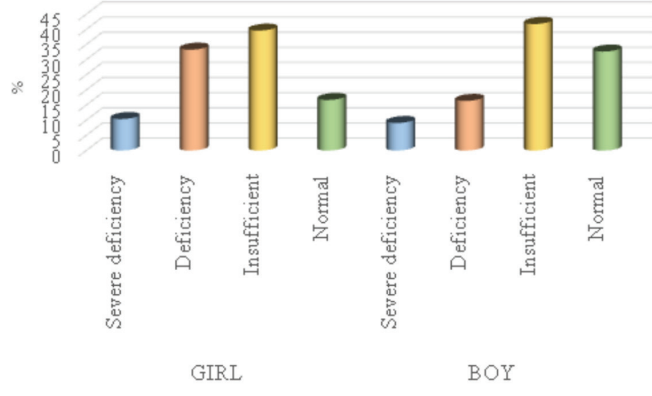

Figure 2. Classification of serum 25 (OH) vitamin D by gender

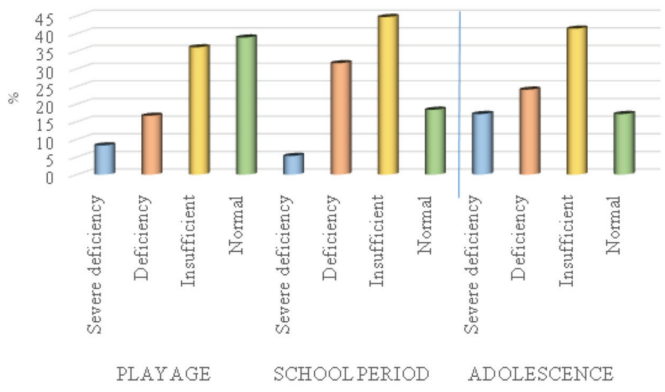

Figure 3. Classification of serum 25 (OH) vitamin D by age group

most common complaints in childhood. However, other causes must definitely be eliminated (11). If there are other findings such as high fever, malaise, weight loss, decrease in joint movements, edema in the joint, unsymmetrical leg pain or joint stiffness in the morning, the diagnoses of growth pain can be established with the Peterson (3) criteria (atypical growth pains) following the elimination of other causes with more laboratory and X-ray studies.

It is often called growth pains because it affects arms and legs, which is the most obvious evidence of growth. It is generally observed after intense physical activity. Although many researchers try to develop diagnostic criteria, the Peterson (12) criteria based on clinical findings are the most useful. They were completed by Russel and Abu-Arafeh (13). The criteria for growth pain are based on the current clinical picture of children and the recurrent pain in the lower extremity. There are no trauma, edema, redness, tenderness that can be localized, or other general and regional findings of inflammation. These pains continue for less than 72 hours, cannot be localized in the bone and do not cause movement restriction in more than one joint. The frequency of growth pains is variable (2.6% - 49.4%) (14). In recent studies, the prevalence was found to be 38.3% in children aged between 4 and 6 years (15). According to the results of our study, there are similar consultations from all age groups.

The biological and physiological mechanisms related to the relationship between vitamin D deficiency and pain and how it causes chronic painful conditions have not been clarified. In in vitro cultures, an inverse relationship has been revealed between vitamin D levels and the growth of sensory neurons (16). It is believed that sufficient vitamin D at the cellular level has a protective effect on cell functions and decreases inflammation (9). As a result, it is thought that low vitamin D increases the pain by increasing inflammation (16). Vitamin D deficiency can disrupt the bone mineralization and cause pain in the joints and muscles related to isolated or prevalent bone pain. In their study conducted on 276 patients, Heidari et al. (17) compared the patients with non-specific musculoskeletal pain and normal healthy individuals, and discovered that vitamin D deficiency especially in female patients was correlated with non-specific musculoskeletal pains.

Even though our country has a geographical location with sunny weather, vitamin D deficiency continues to be a significant problem affecting infants and adolescents (18,19). Worldwide researches conducted to evaluate the vitamin D state of healthy children and the frequency of vitamin D deficiency was found to be between 30% and 80% in children and adults (8,20). In a group of Turkish girls aged 14-18 years, the prevalence of vitamin D insufficiency was reported to vary between 15.6% and 59.4% according to socio-economic status and season (21). In our study, the rate of vitamin D deficiency of children who applied with the complaint of musculoskeletal pain is 74.8%, which is the same with those values.

In some researches on healthy children, vitamin D deficiency was shown to be more frequent in female children (22). In our study, serum 25 (OH) vitamin D levels of males were found to be significantly higher than those of females.

It is known that vitamin D level is affected by making use of the sunlight, sunscreen usage, nutritional status, vitamin D content of the diet, daily physical activity amount, socioeconomic level and clothing style (23). One of the most significant limitations of the research is that these factors could not be evaluated since the research was retrospective. In our study, the vitamin D levels by age group were similar, and deficiency was observed in all the groups. Patients with very low vitamin D levels may be eating poorly or making less use of the sunlight.

We wanted to emphasize that other causes should be investigated before the establishment of the diagnosis of the growth pain. Joint complaints are commonly encountered in children, and non-inflammatory causes are the most common causes of the muscle-joint pain. However, growth pain should be diagnosed after eliminating all the organic causes such as rheumatism, infection and malignancy.

In our study, we aimed to emphasize the importance of vitamin D level assessment in patients who consulted for joint-muscle pain and were thought to have growth pain.

Ethics

Ethics Committee Approval: The study was approved by the ethics committee of Bakırköy Sadi Konuk Training and Research Hospital with decision no: 2020-254/08.06.202.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.N., E.N., Ö.A.S., Design: S.N., E.N., Ö.A.S., Data Collection or Processing: S.N., Analysis or Interpretation: S.N., F.D., Writing: S.N.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Al Khattat A, Campell J. Recurrent limb pain in childhood ("growing pains"). Foot 2000;10(3):117-123.
2. Kasapçopur Ö. Çocukluk çağı romatizmal hastalıklarına tanılandırıcı yaklaşım. İ.Ü. Cerrahpaşa Tıp Fakültesi Sürekli Tıp Etkinlikleri, Sempozyum dizisi 2003;34(4):43-50.
3. Peterson H. Growing pains. Pediatr Clin North Am 1986;33(6):1365-1372.
4. Plotnikoff GA, Quigley JM. Prevalence of severe hypovitaminosis D in patients with persistent, nonspesific musculoskeletal pain. Mayo Clin Pro 2003;78(12):1463-1470.
5. Pfeifer M, Begerow B, Minne HW. Vitamin D and muscle function. Osteoporos Int 2002;13:187-194.
6. Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M, Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. Pediatrics 2008;12(2)2:398-417.
7. Grant WB, Holick MF. Benefits and requirements of vitamin D for optimal health: a review. Altern Med Rev 2005;10(2):94-111.
8. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357(3):266-281.
9. Goodman JE, McGrath PJ. The epidemiology of pain in children and adolescents: a review. Pain 1991:46(3):247-264.
10. Symmons DP, Jones M, Osborne J, Sills J, Southwood TR, Woo P. Pediatric rheumatology in the United Kingdom: data from the British Pediatric Rheumatology Group National Diagnostic Register. J Rheum 1996;23(11):1975-1980.
11. Cassidy JT, Petty RE. Musculoskeletal Pain Syndromes Of Nonrheumatic Origin. In: Pediatric Rheumatology. 3rd ed., Pennsylvania:Saunders Company, 1995:108-132.
12. Petersen HA. Leg aches. Pediatr Clin North Am 1977;24(4):731-736.
13. Abu-Arafeh I, Russell G. Recurrent limb pain in schoolchildren. Arch Dis Child 1996;74(4):336-339.
14. Williams MF. Rheumatic conditions in school children. Lancet 1928;211(2):720-721.
15. Evans AM, Scutter SD. Prevalence of "Growing Pains" in young children. J Pediatr 2004;145(2):255-258.
16. Glover TL, Goodin BR, Horgas AL, Kindler LL, King CD, Sibille KT, et al. Vitamin D, race, and experimental pain sensitivity in older adults with knee osteoarthritis. Arthritis Rheum 2012;64(12):3926-3235.
17. Heidari B, Shirvani JS, Firouzjahi A, Heidari P, Hajian-Tilaki KO. Association between nonspecific skeletal pain and vitamin D deficiency. Int J Rheum Dis 2010;13(4):340-346.
18. Özkan B, Döneray H. D vitamininin iskelet sistemi dışı etkileri. Çocuk Sağlığı ve Hastalıkları Dergisi 2011;54(2):99-119.
19. Hatun Ş, Bereket A, Çalıkoğlu AS, Özkan B. Günümüzde D vitamini yetersizliği ve nütrisyonel rikets. Çocuk Sağlığı ve Hastalıkları Dergisi 2003;46:224-241.
20. Salvo MS, Whiting SJ, Barton CN. Vitamin D intake: a global perspective of current status. J Nutr 2005;135(2):310-316.
21. Olmez D, Bober E, Buyukgebiz A, Cimrin D. The frequency of vitamin D insufficiency in healthy female adolescents. Acta Paediatr 2006;95(10):1266-1269.
22. Pelajo CF, Lopez-Benitez JM, Miller LC. Vitamin D and autoimmune rheumatologic disorders. Autoimmun Rev 2010;9(7):507-510.
23. El-Hajj Fuleihan G, Nabulsi M, Choucair M, Salamoun M, Shahine CH, Kizirian A, et al. Hypovitaminosis D in healthy schoolchildren. Pediatrics 2001;107(4):E53.

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Polycystic Ovary Syndrome in Overweight and Normal Weight Women: The Relationships with Inflammatory Markers

Kilolu ve Normal Kadınlarda Polikistik Over Sendromunun Enflamatuvar Belirteçlerle İlişkisi

Tolga Atakul[1], Özgür Deniz Turan[1], Çiğdem Yenisey[2]

[1]Adnan Menderes University Faculty of Medicine, Department of Obstetrics and Gynecology, Aydın, Turkey
[2]Adnan Menderes University Faculty of Medicine, Department of Medical Biochemistry, Aydın, Turkey

Abstract

Objective: The etiology and pathophysiology of Polycystic Ovary syndrome (PCOS) are not yet clearly explained as the disease has a heterogeneous clinical presentation. Several cytokines produced by the ovary and other tissues contribute to the maintenance of a chronic inflammatory state and metabolic imbalance in PCOS. The present study aims to widen the scientific scope concerning the association between the inflammatory state and PCOS through the measurement and evaluation of several inflammatory markers.

Method: Forty-nine medication-naive PCOS patients and 39 healthy controls were enrolled in this case-control study. Blood samples were obtained for the measurement of inflammatory markers.

Results: Cyclooxygenase-2 (COX-2), IL-12, IL-18, IL-23, Krüppel-like factor-4 (KLF-4), peroxisome proliferator-activated receptor (PPAR)-gamma, sirtuin (SIRT) and toll-like receptor-2 (TLR-2) were found to be significantly higher in the PCOS group compared to the healthy controls. There were no significant differences regarding these inflammatory markers when overweight and normal weight PCOS women were compared (p>0.05). Receiver operating characteristic curve analysis revealed that the following cut-off values had satisfactory sensitivity and specificity for the diagnosis of PCOS: 5.9 ng/mL for COX-2, 22.3 pg/mL for IL-12, 32 pg/mL for IL-18, 57 pg/mL for IL-23, 203 pg/mL for KLF-4, 2.54 ng/mL for PPAR-gamma, 2.9 ng/mL for SIRT, and 2 ng/mL for TLR-2.

Conclusion: Our findings demonstrate that these inflammatory markers might be used to identify patients with PCOS with high sensitivity and specificity. Our results support the consideration that the low-grade inflammation observed in women with PCOS is likely intrinsic to the pathophysiology of the disease.

Keywords: Cyclooxygenase-2, interleukins, krüppel-like factor-4, low-grade inflammation, polycystic ovary syndrome

Öz

Amaç: Polikistik Over sendromunun (PCOS) etiyolojisi ve patofizyolojisi henüz açıklanamamıştır, çünkü hastalık heterojen klinik tabloya sahiptir. Over ve diğer dokular tarafından üretilen birkaç sitokin, PCOS'de kronik bir enflamatuvar durumun ve metabolik dengesizliğin korunmasına katkıda bulunur. Bu çalışma, çeşitli enflamatuvar belirteçlerin ölçümü ve değerlendirilmesi yoluyla enflamatuvar durum ile PCOS arasındaki ilişkiyi ve bilimsel kapsamı genişletmeyi amaçlamaktadır.

Yöntem: Bu olgu-kontrol çalışmasına ilaç kullanmamış 49 PCOS hastası ve 39 sağlıklı kontrol dahil edildi. Enflamatuvar belirteçlerin ölçümü için kan örnekleri alındı. Siklooksijenaz-2 (COX-2), IL-12, IL-18, IL-23, Krüppel benzeri faktör-4, peroxisome proliferator-activated receptor (PPAR)-gama, sirtuin (SIRT) ve geçiş ücreti benzeri reseptör-2 (TLR-2) ölçümleri yapıldı.

Bulgular: PCOS grubunda sağlıklı kontrollere göre COX-2, IL-12, IL-18, IL-23, Krüppel benzeri faktör-4, PPAR-gama, SIRT ve TLR-2 anlamlı olarak daha yüksek bulundu. Aşırı kilolu ve normal kilolu PKOS kadınları karşılaştırıldığında bu enflamatuvar belirteçler açısından anlamlı fark yoktu (p>0,05). Alıcı işletim karakteristiği analizi, aşağıdaki kesme değerlerinin PCOS tanısı için tatmin edici duyarlılığa ve özgüllüğe sahip olduğunu ortaya koymuştur: COX-2 için 5,9 ng/mL, IL-12 için 22,3 pg/mL, IL-18 için 32 pg/mL, 57 IL-23 için pg/mL, Krüppel benzeri faktör-4 için 203 pg/mL, PPAR-gama için 2,54 ng/mL, SIRT için 2,9 ng/mL ve TLR-2 için 2 ng/mL.

Sonuç: Bulgularımız, bu enflamatuvar belirteçlerin PCOS'li hastaları yüksek duyarlılık ve özgüllükte tanımlamak için kullanılabileceğini göstermektedir. Sonuçlarımız PCOS'li kadınlarda gözlenen düşük dereceli enflamasyonun muhtemelen hastalığın patofizyolojisine özgü olduğu düşüncesini desteklemektedir.

Anahtar kelimeler: Düşük dereceli enflamasyon, interlökinler, krüppel benzeri faktör-4, Polikistik Over sendromu, siklooksijenaz-2

Address for Correspondence: Tolga Atakul, Adnan Menderes University Faculty of Medicine, Department of Obstetrics and Gynecology, Aydın, Turkey
E-mail: tolgaatakul@gmail.com **ORCID:** orcid.org/0000-0002-0219-000X **Received:** 05.03.2020 **Accepted:** 14.04.2020

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Introduction

Polycystic Ovary syndrome (PCOS) is the most common and complex endocrine disorder among women of reproductive age with an estimated prevalence ranging between 5% and 15% (1). Given the established associations between PCOS and several diseases including cardiovascular diseases, type 2 diabetes, dyslipidemia, obesity and infertility, PCOS represents a major challenge regarding potential long-term morbidity, mortality and increased health-care costs (2).

The etiology and pathophysiology of PCOS are not yet clearly explained as the disease has a heterogeneous clinical presentation. Several genetic and environmental factors as well as lifestyle are believed to have a role in the development and progression of PCOS. Hyperinsulinism due to insulin resistance and hyperandrogenism are considered to be the primary underlying conditions that lead to the development of this syndrome (3,4). Studies have shown that insulin resistance is present in more than half of the patients with PCOS, irrespective of weight and obesity (5). The overstimulation of the insulin receptors of follicular theca cells by the synergistic action of hyperinsulinism and luteinizing hormone (LH) is likely the major cause of the hyperandrogenism and associated ovulatory dysfunction observed in PCOS women (6). Although the mode of inheritance is still unclear, familial clustering of the cases and higher prevalence of the syndrome in identical twins compared to non-identical twins suggest that genetic susceptibility may also contribute to PCOS development (7).

Recently, several pieces of research have been published investigating the relationship between chronic low-grade inflammation and PCOS. Adipokines and inflammation mediators produced by the adipose tissue have been shown to contribute to the metabolic changes presenting in PCOS (8). Moreover, several cytokines produced by the ovary and other tissues are considered to cause a chronic inflammatory state which maintains the metabolic imbalance(s) observed in the syndrome (9,10). However, current data are available for only a minority of inflammatory markers.

The present study aims to widen the scientific scope concerning the association between the inflammatory state and PCOS through the measurement of several previously unassessed inflammatory markers. This study also aims to address the potential role of inflammatory markers in the diagnosis of PCOS.

Materials and Methods

All consecutive female patients (age, 18 to 40 years) diagnosed with PCOS at the Department of Gynecology, Adnan Menderes University, Aydın, Turkey between June 2015 and July 2016 were enrolled in this cross-sectional study. The diagnosis of PCOS was based on the revised diagnostic criteria by the Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group (11). A group comprised of healthy volunteers was also included in the study as a control group. Those who had any chronic diseases or infectious diseases within 3 months of enrollment, and pregnant patients or those in the initial six weeks of the post-partum period and breastfeeding women were excluded from the study. Written informed consent was obtained from all participants included in the study. The study was approved by the Institutional Ethical Committee and was performed in accordance with the most recent version of the Helsinki Declaration (2017/1131). Age, body mass index (BMI), menstrual cycle (ir) regularity, presence of hirsutism, and the systolic and the diastolic blood pressures of all patients were recorded.

Blood samples following a 12-hour fasting were drawn from all participants for fasting blood glucose, insulin, follicle stimulating hormone (FSH), LH, thyroid stimulating hormone (TSH), estradiol, prolactin, total testosterone, cyclooxygenase-2 (COX-2), interleukin-12, interleukin-18, interleukin-23 (IL6), Krüppel-like factor-4 (KLF-4), peroxisome proliferator-activated receptor (PPAR)-gamma, sirtuin-1 (SIRT1) and toll-like receptor-2 (TLR-2) measurements. After centrifugation (4000 × g for 10 min), 1 to 2 mL serum samples for the measurement of the aforementioned inflammatory markers were stored at -80 °C until being assayed. Enzyme-linked immunosorbent assay was performed to determine the serum levels of these inflammatory markers. Insulin resistance was determined by using the homeostasis model assessment HOMA-IR formula as follows:

(HOMA-IR) formula [HOMA-IR = fasting insulin (mIU/mL) × fasting glucose (mg/dL)/18)/22.5].

The predictive value of the inflammatory markers for identifying PCOS was the primary outcome of the present study.

Statistical Analysis

All analyses were performed on SPSS v21 (IBM, Armonk, USA). For the normality check, the Kolmogorov-Smirnov test was used. Normally distributed variables (height, weight, and blood glucose) were compared with

the independent samples t-test, while non-normally distributed variables were compared with the Mann-Whitney U test. Chi-square test or Fisher's exact test were used to compare the categorical variables. Data were given as mean ± standard deviation or median (minimum - maximum) for continuous variables with regard to normality, and as frequency (percentage) for categorical variables. Diagnostic performance of each variable was assessed by performing receiver operating characteristic (ROC) curve analysis. A p-value <0.05 was accepted to show statistical significance.

Results

A total of 49 medication-naive PCOS patients [median age 21 (18-39)] and 39 healthy controls [median age 22 (19-40)] were enrolled in this cross-sectional study. Patients' average weight was higher in the PCOS group compared to the healthy controls (68.76±13.90 kg vs. 61.38±8.89 kg, p=0.005). However, the number of overweight and obese patients were similar in the two groups. Patients with POCS and controls were similar with regard to systolic and the diastolic blood pressures. Menstrual cycle irregularity and hirsutism were more frequent in PCOS patients compared to controls. FSH, prolactin and TSH levels were similar among groups, while total testosterone, fasting blood glucose and insulin levels, and the HOMA index were higher in PCOS patients. LH and the estradiol levels were also higher in the PCOS group compared to the control group (Table 1).

Inflammatory markers including COX-2, IL-12, IL-18, IL-23, KLF-4, PPAR-gamma, sirtuin (SIRT), and TLR-2 were significantly higher in PCOS patients than the controls. ROC curve analysis revealed that the following cut-off values provided satisfactory sensitivity and specificity for the diagnosis of PCOS:5.9 ng/mL for COX-2, 22.3 pg/mL for IL-12, 32 pg /mL for IL-18, 57 pg /mL for IL-23, 203 pg/mL for KLF-4, 2.54 ng/mL for PPAR-gamma, 2.9 ng/mL for SIRT, and 2 ng/mL for TLR-2 (Table 2, Figure 1).

Discussion

The present study demonstrates that COX-2, IL-12, IL-18, IL-23, KLF-4, PPAR-gamma, SIRT, and TLR-2 are significantly higher in patients with PCOS compared to healthy controls. The blood levels of inflammatory markers were similar in overweight PCOS women and normal weight PCOS women. Our findings also demonstrate that these inflammatory markers might be useful in identifying patients with PCOS with high sensitivity and specificity.

PCOS is a common and complex endocrinopathy which effects 5% to 15% of reproductive-age women. Recent data indicate that adiposity and low-grade inflammatory state are two main factors contributing to the development of PCOS (12). Due to the fact that adipose tissue acts as an endocrine organ by releasing adipokines, cytokines, and several hormones, the increased levels of inflammatory markers in PCOS women were initially suggested to be due to PCOS-related adipocyte hypertrophy. In support of this hypothesis, it is known that adipocytes are vulnerable to hypertrophy when exposed to excessive androgen stimulation, as is the case in women with PCOS. Hyperandrogenism and the hypertrophy of adipocytes lead to stromal vessel compression which further induces adipose tissue hypoperfusion (13). Activation of nuclear factor kappa-B, which is a transcription factor mediating inflammatory processes, by adipose tissue hypoperfusion stimulates the release of various inflammatory cytokines, including interleukins (1β , 6,10, and 18), tumor necrosis factor alfa (TNF-α), interferon gamma, complement factors, transforming growth factor β, monocyte chemotactic protein-1 (MCP-1) and vascular cell adhesion molecule (8). The resultant macrophage recruitment maintains inflammatory state and leads to adipocyte dysfunction. PCOS ovarian tissue has been shown to contain more macrophages and lymphocytes than the ovarian tissues of controls in previous studies (14). Increased blood concentrations of TNF-α, interleukins (IL-6, IL-18, IL-1β, IL-7, IL-17), MCP-1, macrophage inflammatory protein-1α, macrophage migration inhibitory factor, matrix metalloproteinases (MMP) 2 and 9, soluble intercellular adhesion molecule-1 and soluble endothelial leukocyte adhesion molecule-1 have been shown in PCOS (15).

It has also been postulated that low-grade inflammation itself might be a precursor for the development of insulin resistance and the characteristic ovarian dysfunction in patients with PCOS. Nevertheless, whether low-grade inflammation and the altered release of adipokines are intrinsic to PCOS or a consequence of PCOS-related adipocyte hypertrophy and hyperandrogenism, is a matter of debate (16). Previous data demonstrated that white blood cell count and the platelet-to-lymphocyte ratio, a marker of proinflammatory state, were significantly higher in obese PCOS patients compared to normal weight PCOS patients. However, neutrophil-to-lymphocyte ratio and mean platelet volume did not differ in obese and normal-weight PCOS patients, although both were found to be higher than in the healthy controls (17,18). Prior studies have demonstrated significantly higher levels of high-sensitive C-reactive

protein, IL-6, and TNF-α in women with PCOS compared to BMI-matched controls (19). Additionally, these markers are also reported to be increased in lean PCOS women suggesting a special association between inflammatory state and PCOS, regardless of obesity-associated alterations (20). The cytokine elevation in PCOS was initially considered as a consequence of the excessive visceral fat deposition, which is known to be related to increased adipocytokine levels in obese patients (21,22). However, several subsequent studies have failed to demonstrate any significant differences in visceral, abdominal subcutaneous, gluteal subcutaneous, or midfemoral subcutaneous fat (as measured by MRI) of women with or without PCOS (21). We found that COX-2, IL-12, IL-18, IL-23, KLF-4, PPAR-gamma, SIRT and TLR-2 were significantly higher in the PCOS group compared to the healthy controls. However, there were no significant

Table 1. Summary of patients' characteristics regarding groups

	Controls	PCOS	Total	p
n	39	49	88	N.A
Age	21 (18-39)	22 (19-40)	22 (18-40)	0.227
Height (cm)	164.41±6.39	163.51±5.95	163.91±6.13	0.497
Weight (kg)	61.38±8.89	68.76±13.90	65.49±12.44	**0.005**
Overweight (BMI>25)	15 (38.46%)	29 (59.18%)	44 (50.00%)	0.086
Obesity (BMI>30)	2 (5.13%)	8 (16.33%)	10 (11.36%)	0.175
Systolic BP	110 (90-125)	110 (90-152)	110 (90-152)	0.385
Diastolic BP	70 (55-80)	70 (50-90)	70 (50-90)	0.443
Menstrual Cycle				
Irregular	3 (7.69%)	35 (71.43%)	38 (43.18%)	**<0.001**
Regular	36 (92.31%)	14 (28.57%)	50 (56.82%)	
Hirsutism				
Absent	25 (64.10%)	3 (6.12%)	28 (31.82%)	
Mild	14 (35.90%)	15 (30.61%)	29 (32.95%)	**<0.001**
Medium	0 (0.00%)	16 (32.65%)	16 (18.18%)	
Severe	0 (0.00%)	15 (30.61%)	15 (17.05%)	
FSH (mIU/mL)	4.5 (2.82-9.00)	4.47 (1.33-10.60)	4.50 (1.33-10.60)	0.589
LH (mIU/mL)	3.18 (0.70-13.46)	4.13 (0.71-16.40)	3.61 (0.70-16.4)	**0.030**
Estradiol (pg/mL)	29 (15-82)	40 (2-133)	35 (2-133)	**0.004**
Prolactin (ng/mL)	13.08 (1.62-28.00)	14.95 (6.01-52.00)	14.24 (1.62-52.00)	0.058
TSH (mIU/mL)	1.38 (0.54-2.81)	1.78 (0.58-4.69)	1.75 (0.54-4.69)	0.280
Total testesterone (ng/dL)	1.04 (0.71-2.10)	1.33 (0.56-3.50)	1.17 (0.56-3.50)	**0.016**
Blood glucose (mg/dL)	83.12±9.30	89.31±8.64	87.19±9.29	**0.006**
Insulin (μIU/mL)	6.20 (1.42-21.50)	9.35 (3.70-31.20)	8.60 (1.42-31.20)	**0.007**
HOMA-IR	1.39 (0.27-4.28)	2.11 (0.72-7.16)	1.94 (0.27-7.16)	**0.003**
COX-2 (ng/mL)	2.21 (0.30-5.96)	6.58 (3.66-10.80)	5.53 (0.30-10.80)	**<0.001**
IL-12 (pg/mL)	11.29 (6.29-22.18)	32.76 (15.41-133.65)	21.44 (6.29-133.65)	**<0.001**
IL-18 (pg/mL)	19.00 (9.94-58.06)	48.62 (31.75-199.88)	37.06 (9.94-199.88)	**<0.001**
IL-23 (pg/mL)	47.33 (15.67-98.17)	92.33 (53.17-385.67)	64.83 (15.7-385.7)	**<0.001**
KLF-4 (pg/mL)	170.85 (147.8-299.8)	204.26 (147.7-884.3)	196.20 (147.7-884.3)	**<0.001**
PPAR-gamma (ng/mL)	1.15 (0.24-3.44)	4.58 (1.37-9.70)	2.67 (0.24-9.7)	**<0.001**
SIRT (ng/mL)	1.37 (1.29-3.22)	3.42 (3.20-6.97)	3.25 (1.29-6.97)	**<0.001**
TLR-2 (ng/mL)	1.29 (0.38-2.70)	3.62 (1.11-9.64)	2.23 (0.38-9.64)	**<0.001**

Data given as mean ± standard deviation or median (minimum - maximum) for continuous variables regarding normality and frequency (percentage) for categorical variables. N.A: not applicable, PCOS: Polycystic Ovary syndrome, BMI: Body mass index, cm: Centimeter, kg: Kilogram, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, HOMA-IR: Homeostasis Model Assessment of Insulin Resistance, TLR-2: Toll-like receptor-2, PPAR: Peroxisome proliferator-activated receptor, COX-2: Cyclooxygenase-2, TSH: Thyroid stimulating hormone, BP: Blood pressure, SIRT: Sirtuin, KLF-4: Krüppel-like factor-4

differences regarding these inflammatory markers when overweight and normal-weight PCOS women were compared. This indicates an intrinsic pathology of PCOS regarding pro-inflammatory state.

In the current study, we assessed the levels of several inflammatory markers which were not studied previously in PCOS, including COX-2, IL-12, IL-18, IL-23, KLF-4, PPAR-gamma, SIRT and TLR-2, which were found to be significantly higher in patients compared to the controls. These markers are utilized in the evaluation of the different pathways of inflammation and higher concentrations show the presence of a global activation of inflammation in PCOS women. Furthermore, the high sensitivity and specificity for the diagnosis of PCOS with these markers support the evidence derived from previous studies which suggest a significant role for low-grade inflammatory activity in the development of PCOS. When we elucidate the diagnostic predictivity of the parameters we measured in our study, significant results were found in ROC analysis. It was observed that all of the other markers except the KLF-4 results showed high (>0.90) Area under receiver operating characteristic curve values in predicting PCOS diagnosis. These remarkable results demonstrate that these markers can be used in a diagnostic sense; however, it is obvious that more extensive studies are needed. It is also important to note that there are several other studies that have been performed for the evaluation of these markers, but it is evident that the findings of our research are important.

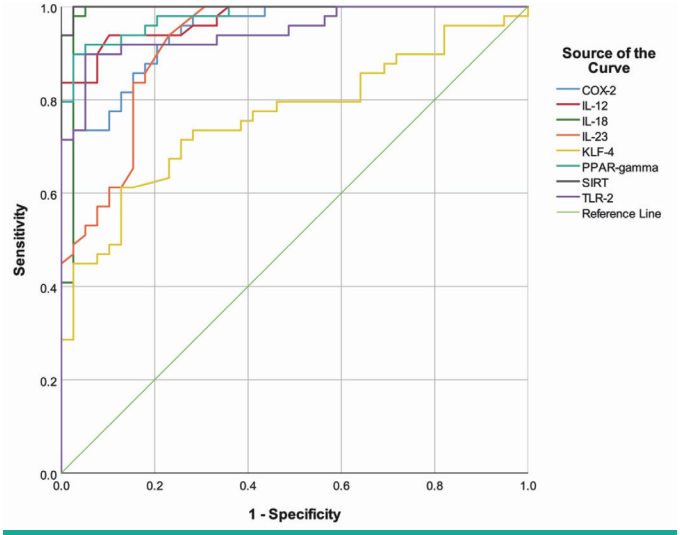

Figure 1. ROC curve demonstrating the diagnostic performance of the inflammatory markers in identifying women with PCOS

PCOS: Polycystic ovary syndrome, COX-2: Cyclooxygenase-2, PPAR: Peroxisome proliferator-activated receptor, TLR-2: Toll-like receptor-2, SIRT: Sirtuin, ROC: Receiver operating characteristic

There is also evidence that the inflammatory state can itself promote androgen production and hyperandrogenemia. An experimental study conducted by Spaczynski and colleagues has shown that TNF-α can stimulate proliferation of ovarian theca cells in murine models (23). In addition, a systematic review including 31 studies, carried out by Escobar-Morreale et al. (24) has revealed that PCOS women exhibit an elevated circulating C-reactive protein, which is independent of obesity. The reduction in serum concentrations of the inflammatory markers with atorvastatin and simvastatin, which have been shown to exert remarkable anti-inflammatory effects, also supports the specific role of inflammation in PCOS (25,26). With these results in mind, we suggest that our findings support the consideration that low-grade inflammation and the altered release of the adipokines are intrinsic to PCOS pathophysiology. However, although only a few, there are also some studies indicating increased visceral fat accumulation in normal-weight PCOS women (27,28). Therefore, one could consider that a patient with PCOS does not

Table 2. Measurements of performance for Polycystic Ovary syndrome diagnosis

	Cut-off	Sensitivity	Specificity	Accuracy	PPV	NPV	AUC	95.0% CI		p
COX-2 (ng/mL)	5.9	71.40%	100.00%	84.09%	100.00%	73.58%	0.947	0.907	0.987	<0.001
IL-12 (pg/mL)	22.3	71.40%	100.00%	84.09%	100.00%	73.58%	0.972	0.945	0.999	<0.001
IL-18 (pg/mL)	32	98.00%	97.40%	97.73%	97.96%	97.44%	0.984	0.954	1,000	<0.001
IL-23 (pg/mL)	57	93.90%	76.90%	86.36%	83.64%	90.91%	0.919	0.862	0.977	<0.001
KLF-4 (pg/mL)	201	61.20%	87.20%	72.73%	85.71%	64.15%	0.763	0.664	0.863	<0.001
PPAR-gamma (ng/mL)	2.54	89.80%	97.40%	93.18%	97.78%	88.37%	0.979	0.956	1.000	<0.001
SIRT (ng/mL)	2.9	100.00%	97.40%	98.86%	98.00%	100.00%	0.998	0.995	1.000	<0.001
TLR-2 (ng/mL)	2	89.80%	94.90%	92.05%	95.65%	88.10%	0.948	0.904	0.992	<0.001

PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under receiver operating characteristic curve, CI: Confidence intervals, COX- 2: Cyclooxygenase-2, PPAR: Peroxisome proliferato-activated receptor, TLR-2: Toll-like receptor, SIRT: Sirtuin

necessarily need to have a high BMI for the development of adipocyte-associated inflammatory activation. This particular finding can be considered as a limitation of the current study, as we did not assess visceral fat deposition. Further research, including the measurement of the visceral fat accumulation, will probably serve additional information concerning the clarification of the role of inflammation and obesity in the pathogenesis of PCOS.

We have to underline the fact that a few previous reports have shown higher accumulation of fat in the viscera of normal-weight PCOS patients. This accumulation may cause insulin resistance, adipocyte dysfunction and low-grade inflammation, even though patients have normal BMI. Although our findings indicate that the low-grade inflammatory state observed in PCOS is irrespective of BMI value, we have not measured the visceral fat accumulation. However, there are also studies that report a lack of difference in visceral fat deposition between patients with PCOS and healthy individuals. The relatively low number of patients included in this study is also another drawback.

Conclusion

The present study shows that inflammatory markers, including COX-2, IL-12, IL-18, IL-23, KLF-4, PPAR-gamma, SIRT and TLR-2, are increased in PCOS regardless of BMI. Our findings also demonstrate that these inflammatory markers might be used to identify patients with PCOS, with high sensitivity and specificity. The lack of any difference in the serum concentrations of the aforementioned inflammatory markers in overweight and normal-weight PCOS patients supports the consideration that the low-grade inflammation shown in women with this syndrome is intrinsic to PCOS.

Ethics

Ethics Committee Approval: The study was approved by the Institutional Ethical Committee and was performed in accordance with the most recent version of the Helsinki Declaration (2017/1131).

Informed Consent: Written informed consent was obtained from all participants included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Consept: T.A., Ö.D.T., Ç.Y., Design: T.A., Data Collection or Processing: T.A., Ç.Y., Analysis or Interpretation: T.A., Ö.D.T., Literature Search: T.A., Ö.D.T., Ç.Y., Writing: T.A., Ö.D.T., Ç.Y.

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References

1. Bozdag G, Mumusoglu S, Zengin D, Karabulut E, Yildiz BO. The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. Human reproduction 2016;31(12):2841-2855.
2. Goldrat O, Delbaere A. PCOS: update and diagnostic approach. Clinical biochemistry 2018;62:24-31.
3. Meier RK. Polycystic Ovary Syndrome. The Nursing clinics of North America 2018;53(3):407-420.
4. Nandi A, Chen Z, Patel R, Poretsky L. Polycystic ovary syndrome. Endocrinology and metabolism clinics of North America 2014;43(1):123-147.
5. Moghetti P. Insulin Resistance and Polycystic Ovary Syndrome. Current pharmaceutical design 2016;22(36):5526-5534.
6. Rosenfield RL, Ehrmann DA. The pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocrine reviews 2016;37(5):467-520.
7. Vink J, Sadrzadeh S, Lambalk C, Boomsma D. Heritability of polycystic ovary syndrome in a Dutch twin-family study. The Journal of Clinical Endocrinology & Metabolism 2006;91(6):2100-2104.
8. Spritzer PM, Lecke SB, Satler F, Morsch DM. Adipose tissue dysfunction, adipokines, and low-grade chronic inflammation in polycystic ovary syndrome. Reproduction 2015;149(5):R219-R227.
9. Çakıroğlu Y, Vural F, Vural B. The inflammatory markers in polycystic ovary syndrome: association with obesity and IVF outcomes. Journal of endocrinological investigation 2016;39(8):899-907.
10. Durmus U, Duran C, Ecirli S. Visceral adiposity index levels in overweight and/or obese, and non-obese patients with polycystic ovary syndrome and its relationship with metabolic and inflammatory parameters. Journal of endocrinological investigation 2017;40(5):487-497.
11. The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertility and sterility 2004;81(1):19-25.
12. Ebejer K, Calleja-Agius J. The role of cytokines in polycystic ovarian syndrome. Gynecological endocrinology 2013;29(6):536-540.
13. Spritzer PM, Lecke SB, Satler F, Morsch DM. Adipose tissue dysfunction, adipokines, and low-grade chronic inflammation in polycystic ovary syndrome. Reproduction 2015;149(5):R219-227.
14. Xiong YL, Liang XY, Yang X, Li Y, Wei LN. Low-grade chronic inflammation in the peripheral blood and ovaries of women with polycystic ovarian syndrome. European Journal of Obstetrics & Gynecology and Reproductive Biology 2011;159(1):148-150.
15. Deligeoroglou E, Vrachnis N, Athanasopoulos N, Iliodromiti Z, Sifakis S, Iliodromiti S, et al. Mediators of chronic inflammation in polycystic ovarian syndrome. Gynecological Endocrinology 2012;28(12):974-978.

16. Shorakae S, Teede H, de Courten B, Lambert G, Boyle J, Moran LJ. The Emerging Role of Chronic Low-Grade Inflammation in the Pathophysiology of Polycystic Ovary Syndrome. Seminars in reproductive medicine 2015;33(4):257-269.

17. Dogan BA, Arduc A, Tuna MM, Karakilic E, Dagdelen I, Tutuncu Y, et al. Association of mean platelet volume with androgens and insulin resistance in nonobese patients with polycystic ovary syndrome. International journal of endocrinology and metabolism 2014;12(4):e18642.

18. Cakiroglu Y, Vural F, Vural B. The inflammatory markers in polycystic ovary syndrome: association with obesity and IVF outcomes. J Endocrinol Invest 2016;39(8):899-907.

19. Ebejer K, Calleja-Agius J. The role of cytokines in polycystic ovarian syndrome. Gynecological Endocrinology 2013;29(6):536-540.

20. Samy N, Hashim M, Sayed M, Said M. Clinical significance of inflammatory markers in polycystic ovary syndrome: their relationship to insulin resistance and body mass index. Disease markers 2009;26(4):163-170.

21. Barber T, Franks S. Adipocyte biology in polycystic ovary syndrome. Molecular and cellular endocrinology 2013;373(1-2):68-76.

22. Zhuang XF, Zhao MM, Weng CL, Sun NL. Adipocytokines: a bridge connecting obesity and insulin resistance. Medical hypotheses 2009;73(6):981-985.

23. Spaczynski RZ, Arici A, Duleba AJ. Tumor necrosis factor-ň stimulates proliferation of rat ovarian theca-interstitial cells. Biology of Reproduction 1999;61(4):993-998.

24. Escobar-Morreale HF, Luque-Ramirez M, Gonzalez F. Circulating inflammatory markers in polycystic ovary syndrome: a systematic review and metaanalysis. Fertil Steril 2011;95(3):1048-1058.

25. Sathyapalan T, Kilpatrick ES, Coady A-M, Atkin SL. The effect of atorvastatin in patients with polycystic ovary syndrome: a randomized double-blind placebo-controlled study. The Journal of Clinical Endocrinology & Metabolism 2009;94(1):103-108.

26. Banaszewska B, Pawelczyk L, Spaczynski RZ, Duleba AJ. Comparison of simvastatin and metformin in treatment of polycystic ovary syndrome: prospective randomized trial. The Journal of Clinical Endocrinology & Metabolism 2009;94(12):4938-4945.

27. Sathyapalan T, Atkin SL. Mediators of inflammation in polycystic ovary syndrome in relation to adiposity. Mediators of inflammation 2010;2010:758656.

28. Kirchengast S, Huber J. Body composition characteristics and body fat distribution in lean women with polycystic ovary syndrome. Human Reproduction 2001;16(6):1255-1260.

ORIGINAL RESEARCH

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Conservative Treatment of Epistaxis: Comparing Oxytetracycline with Sodium Pentaborate Pentahydrate

Tekrarlayan Anterior Epistaksis Tedavisinde Topikal Sodyum Pentaborat Pentahidrat Uygulaması ile Topikal Oksitetrasiklin Uygulamasının Karşılaştırılması

Ayşe Sezim Şafak[1], Fikrettin Şahin[2]

[1]İstanbul Yeniyüzyıl University Faculty of Medicine, Department of Audiometry, İstanbul, Turkey
[2] Yeditepe University Faculty of Medicine, Department of Genetics and Bioengineering, İstanbul, Turkey

Abstract

Objective: In daily practice, the treatment of epistaxis is generally conservative. Surgical options, which are rarely used, also exist. However, a gold standard treatment option - especially one that is easily applied without need for specialist intervention- has not been introduced. Topical agents are easy to apply and are widely used but success is moderate to low, which demonstrates the requirement for new agents. Sodium pentaborate pentahydrate (SPP) is a natural mineral which has drawn attention in the medical field due to its remarkable wound healing properties. Our aim was to compare the results of topical SPP and oxytetracycline in the treatment of anterior epistaxis.

Method: A total of 66 patients with recurrent anterior epistaxis were included in the study which was performed at the Clinic of Otorhinolaryngology Gebze Central Hospital from January 2018 to February 2018. The age, gender, date of application, medications, chronic illnesses, the frequency of epistaxis after treatment (first week) were recorded. Additionally, we recorded the pre- and post-treatment SNOT-22 scores and Kisselbach area measurement results of all patients. Thirty-two patients received topical SPP gel and 34 received topical oxytetracycline treatment. Groups were similar in terms of age and gender.

Results: SPP gel and oxytetracycline treatments mostly showed similar results. However, the frequency of epistaxis during the first week after treatment was significantly lower with SPP gel treatment.

Conclusion: Our results suggest that SPP gel may be used in the treatment of epistaxis with success similar to that of oxytetracycline. Furthermore, the frequency of epistaxis during the first week after treatment was significantly lower in patients treated with SPP, which is an important advantage.

Keywords: Epistaxis, oxytetracycline, SPP, SNOT 22, topical treatment

Öz

Amaç: Kulak burun boğaz pratiğinde epistaksis (burun kanaması) tedavisi genellikle konservatiftir. Cerrahi tedavi seçeneği, nadir durumlarda gerekir. Öte yandan uzman muayenesi gerekmeden altın standart kolay uygulanan bir tedavi seçeneği henüz tanımlanmamıştır. Yaygın kullanılan topikal ajanların kullanımları kolaydır, ancak orta ile düşük düzeyde başarı gösterdikleri için yeni tedavi seçenekleri ve medikal tedavi ajanlarına ihtiyaç vardır. Sodyum pentaborat pentahidrat (SPP) doğal bir mineral olup medikal alanda yara iyileşmesi üzerine belirgin başarısı gözlenmiştir. Biz de çalışmamızda anterior epistaksis tedavisinde hali hazırda yaygın kullanılan topikal oksitetrasiklin ile topikal SPP uygulamasını epistaksis tedavi başarısı olarak karşılaştırmayı hedefledik.

Yöntem: Ocak 2018 ile Şubat 2018 tarihleri arasında Özel Gebze Merkez Hastanesi KBB Kliniği'ne tekrarlayan anterior epistaksis şikayeti ile başvuran toplam 66 hastayı çalışmaya dahil ettik. Hastaların yaş, cinsiyet, başvurma zamanları, kullandıkları ilaçlar, kronik hastalıkları, bir haftalık topikal tedavi sonrasındaki epistaksis sıklığı kaydedildi. Ek olarak tedavi öncesi ve sonrası SNOT-22 skorları ve Kisselbach alanının ölçümleri yapıldı. Otuz iki hastaya topikal SPP jel, 34 hastaya topikal oksitetrasiklin tedavisi uygulandı. Grupların yaş ve cinsiyet aralıkları benzerdi.

Bulgular: Topikal SPP jel ve oksitetrasiklin tedavileri benzer sonuçlar göstermişlerdir. Öte yandan tedavi sonrasındaki ilk haftada görülen epistaksis sıklığı anlamlı olarak SPP jel uygulamasında daha düşük bulunmuştur.

Sonuç: Sonuçlarımız göstermiştir ki, SPP jel epistaksis tedavisinde kullanılabilir, başarısı oksitetrasiklin ile benzerdir. Ayrıca tedavi sonrasındaki ilk haftada epistaksis sıklığının anlamlı derecede az olması da önemli bir avantajdır.

Anahtar kelimeler: Epistaksis, oksitetrasiklin, SPP, SNOT 22, topikal tedavi

Address for Correspondence: Ayşe Sezim Şafak, İstanbul Yeniyüzyıl University Faculty of Medicine, Department of Audiometry, İstanbul, Turkey
E-mail: ayse.sezim@yeniyuzyil.edu.tr **ORCID:** orcid.org/0000-0001-8514-7172 **Received:** 26.11.2019 **Accepted:** 26.05.2020

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Introduction

Although only 10% of patients who suffer from epistaxis apply to hospitals (1), its life-time prevalence of 60% makes epistaxis a substantial health problem (2). While gender distribution of epistaxis is similar, the frequency increases with age. Epistaxis is categorized according to the location of bleeding (anterior, posterior). Anterior epistaxis is much more frequent compared to posterior epistaxis which may be more severe and may require surgical intervention (3). Even though most epistaxis episodes regress without any complications, controlling the bleeding can be difficult with available treatment options in some cases. However, medical treatment for epistaxis is usually both therapeutically and prophylactically effective (4). On a side note, etiological factors such as hypertension and hematological disorders must be identified and corrected during the initial approach. Surgical options for the treatment of epistaxis also exist; however, surgical intervention is rarely performed due to rare but serious complications, including cerebrovascular events, septal perforation, blindness, ulcerations, altered mental status, ophthalmoplegia and tissue necrosis (5-7). Conservative management includes combinations of external pressure, nasal packing, anterior cautery, humidification and topical agents (8).

Sodium pentaborate pentahydrate (SPP), which has been shown to positively affect wound healing and fibroblast activation, is a recent addition to medical literature and promising results have been achieved in the treatment of many diseases (9,10). Although its role in wound healing has been demonstrated, to our knowledge, it is still unused in the treatment of epistaxis in otorhinolaryngology practice. When previous data are considered, SPP seems to be an ideal candidate for epistaxis treatment due to its wound-healing and antimicrobial properties.

The aim of our study was to compare the treatment results of topical SPP and oxytetracycline in patients with anterior epistaxis.

Materials and Methods

The current study was conducted on patients who applied to the Clinic of Otorhinolaryngology Gebze Central Hospital with epistaxis from January 2018 to February 2018. The inclusion criteria were as follows: experiencing at least 3 cases of spontaneous anterior (Kisselbach region) epistaxis and not having a history of recent upper respiratory tract infection. Exclusion criteria were determined as follows: having a diagnosis of hypertension, chronic sinusitis or allergic rhinitis, having an active nasal infection, having recently suffered from nasal trauma, being diagnosed with any type of bleeding disorder, and the use of medications which affect coagulation. We included a total of 66 patients according to these criteria. Ethical approval was obtained from the İstanbul Yeniyüzyıl University Medical Faculty Ethical Committee (decision number: 01.02.2018/003). All steps of the study were designed in accordance with the Helsinki Declaration. Informed consent was obtained from all patients.

Patients were divided into two groups according to treatment type. All patients received daily nasal decongestant treatment, regardless of group. In addition to decongestants, patients in the first group received SPP (Dermobor®, Bi7Tech, Istanbul, Turkey) treatment (three times a day) while patients in the second group received oxytetracycline (three times a day). The suggested volume of both treatments was 0.1 mL; patients were shown the appropriate amount on a cotton ear swab and were told that the size should be close to the size of a single lentil. Both agents were applied topically and directly on the site of bleeding.

The Sinonazal Outcome test (SNOT-22) test was used to evaluate naso-sinusoidal quality of life. The SNOT-22 is known to be a highly accurate tool for determining the effect of interventions in naso-sinusoidal illnesses. The test is comprised of 6-level Likert-type items (0: no problem, 6: worst possible problem) with a total of 22 questions (11). The final score of the scale may range between 0 and 110 points. The Turkish language reliability and validity study of the test was performed by Hanci et al. (12).

After a patient applied with epistaxis, their history of previous epistaxis and illnesses were assessed in addition to complaints and findings regarding the present event. The age, gender, date of application, medications and chronic illnesses of patients were recorded. The vascularization area (mm^2) of the Kisselbach region was measured before and after treatment. Size was measured via manual calipers (Elektron Medikal, Ankara, Turkey) with the help of endoscopic visualization of the area. Pre- and post-treatment SNOT-22 tests were completed by all patients. The frequency of epistaxis during the first week after treatment was recorded and all patients attended follow-up for one month - during which complications were evaluated and treated accordingly.

Statistical Analysis

All analyses were performed with SPSS version 21.0. The Shapiro-Wilk test was used to test for normality of distribution. Continuous data were given as mean ± standard deviation for normally distributed variables and median (minimum - maximum) for non-normally distributed variables. Categorical data were given as frequency (percentage). Age was compared with the independent samples t-test. Bleeding area and SNOT-22 scores before and after treatment were compared with the Wilcoxon Signed Rank tests. For the evaluation of these variables between the groups, we calculated the difference between pre- and post-treatment measurements and compared them with the Mann-Whitney U test (due to non-normal distribution). Bleeding frequency was compared with the Pearson chi-square test. P<0.05 values were accepted to be statistically significant. Power analysis was performed according to a pilot study performed in 5 patients. We found a bleeding area of 10.1±2.7 mm^2 in these patients. Hypothesizing that a reduction of at least 15% was required to consider the treatment was successful, we found that each group required at least 29 patients with a power of 80% and an alpha error of 5%.

Results

A total of 66 patients (33 males and 33 females) with a mean age of 34.4±10.2 years were included in the study. Thirty-two patients (17 males, 15 females) were treated with SPP (group 1) and 34 patients (16 males, 18 females) were treated with oxytetracycline (group 2) (Table 1). There was no significant difference between our groups regarding age and gender. Bleeding area significantly decreased in both groups after treatment (p<0.001 for each group) (Figure 1). In terms of change in bleeding area, there was no significant difference between the groups (p=0.106). Compared to the SPP group, bleeding frequency after treatment was significantly higher for the oxytetracycline group (p=0.011). The SNOT-22 scores of both groups decreased significantly after treatment (p<0.001 for each group). There was no significant difference between the groups regarding the change in SNOT-22 scores (p=0.856) (Figure 2).

Discussion

In the current study, the efficacy of SPP and oxytetracycline in the treatment of anterior epistaxis were compared by

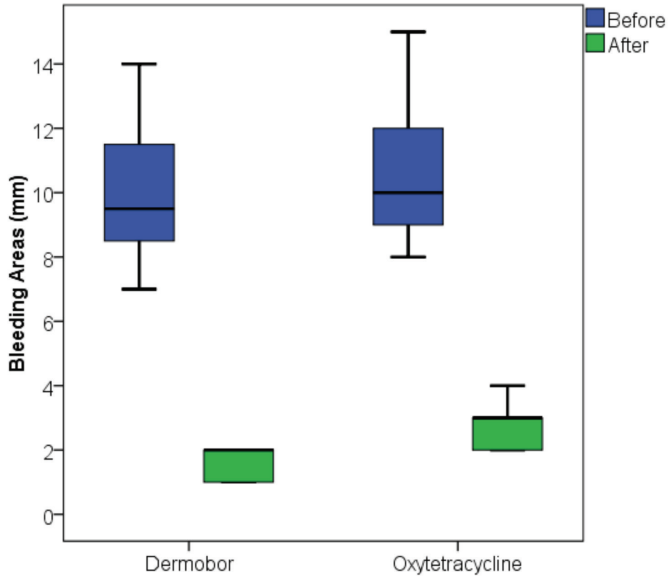

Figure 1. Bleeding area (mm^2) before and after treatment regarding groups
mm: Millimeter

Table 1. Descriptives and statistical analysis results of our variables

	SPP	Oxytetracycline	p
Patient count (n)	32	34	N/A
Age (years)	33.50±10.22	35.15±10.27	0.516
Male	17 (53.1%)	16 (47.1%)	0.805
Bleeding area before treatment (mm^2)	9.5 (7-14)	10 (8-15)	0.106
Bleeding area after treatment (mm^2)	2 (1-2)	3 (2-4)	
Bleeding frequency after treatment (first week)			
0	20 (62.5%)	10 (29.4%)	
1	11 (34.3%)	17 (50.0%)	**0.011**
2	1 (3.1%)	7 (20.6%)	
SNOT-22 score before treatment	12 (7-15)	11.5 (8-16)	0.856
SNOT-22 score after treatment	2 (0-4)	2 (0-4)	

Data given as mean ± standard deviation or median (minimum - maximum) or frequency (percentage), SPP: Sodium pentaborate pentahydrate, mm: Millimeter, SNOT-22: Sinonazal Outcome test

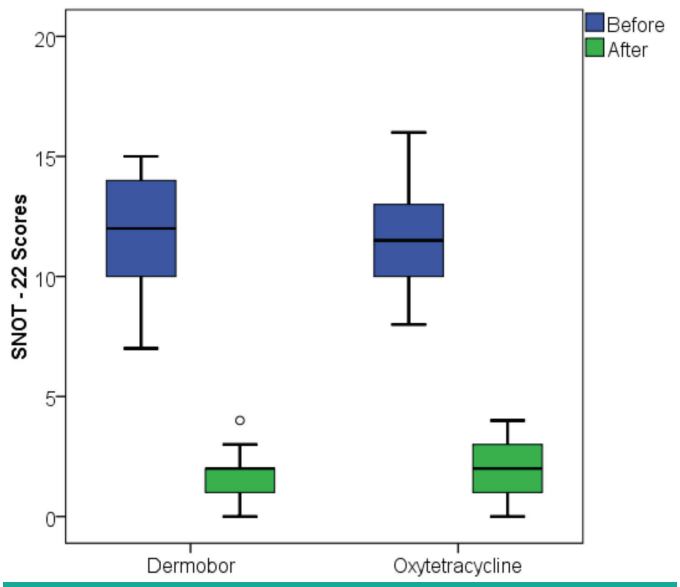

Figure 2. SNOT-22 scores before and after treatment regarding groups

SNOT-22: Sinonasal Outcome test

measuring the changes in bleeding area, the frequency of post-treatment bleeding and SNOT-22 scores. Our results demonstrate that, both SPP and oxytetracycline are effective in treating epistaxis. However, apart from a lower number of recurrent bleeds during the first week after treatment, no major difference was found between these two agents.

Epistaxis is treated with conservative and surgical methods. Conservative treatments include external pressure, nasal packing, anterior cautery, humidification and topical agents (8). Surgical options involve the ligation of maxillary, anterior ethmoid and sphenopalatine artery, and also endoscopic nasal cautery (13). However, in clinical practice, if the bleeding does not sufficiently cease with external pressure and nasal packing, patients are usually informed of surgical options and are directed to otorhinolaryngology clinics (Traboulsi, 2015 #228). Also, the lack of a widely-accepted standardized treatment algorithm - or failure to follow available algorithms - may cause insufficient conservative treatment (Tunkel, 2020 #229). Thus, investigating options for conservative treatment and their success rate is important to increase the number of options in the first-line treatment of epistaxis.

SPP, also named spp., is a rare natural mineral (14) with remarkable wound healing, antimicrobial and fibroblast activation properties (10,15). SPP gel (0.2% chlorhexidine digluconate and 3% SPP) has been used with successful results in various dermatological diseases and wound healing studies (10,16,17). A study on rats by Doğan et al. (18) demonstrated the efficacy of SPP gel in full thickness wounds. The study reported that, while the mechanism of action could not be elucidated, a combination of SPP and pluronics increased the levels of transforming growth factor-ß and vascular endothelial growth factor which were instrumental in wound healing. They concluded that SPP could be used for the treatment of chronic wounds. Other effects of SPP include increases in metalloproteinase activation, extracellular matrix turnover, ion transport and keratinocyte migration. In the current study, a gel containing SPP was found to be similar to oxytetracycline in the treatment of epistaxis; however, post-treatment bleeding frequency was significantly reduced with SPP compared to oxytetracycline, which is a major advantage. Although the mechanism of action could not be determined in the current study, we believe the effects were related to the repair of mucosal damage, especially considering the fact that none of the patients had any chronic conditions that could increase epistaxis frequency (hypertension, bleeding disorder etc).

There are some limitations to our study. Firstly, we used the SNOT-22 scale and bleeding area measurements for the evaluation; however, these are not entirely objective parameters for the evaluation of treatment success. Secondly, we did not assess bleeding frequency during the week prior to treatment, and this is also a limitation; however, most patients could not recall the number of nose bleeds accurately. Therefore, in order to avoid bias, this datum was not included in the study. Other limitations are: the absence of a control group without treatment (due to ethical concerns) and the lack of a gold standard treatment for epistaxis (which would be used to evaluate the efficacy of the agent). However, these limitations were unavoidable and our aim was to compare SPP with the most frequently used and widely-accepted topical treatment option. The strengths of our study include the fact that we report the efficacy of an agent which is very new to medical literature. Additionally, to our knowledge, this is the first clinical study investigating the use of SPP for the treatment of epistaxis.

Conclusion

We have demonstrated that SPP may be used in the clinical treatment of anterior epistaxis. Although we were unable to identify the mechanism of action due to the design of the study, it is feasible to suggest that treatment success was associated with the repair of mucosal damage. We believe that further studies with larger patient groups and

comparisons with different agents may better demonstrate the efficacy of SPP in the treatment of epistaxis.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the İstanbul Yeniyüzyıl University Medical Faculty Ethical Committee (decision number: 01.02.2018/003).

Informed Consent: All patients' informed consent was taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.S.Ş., Design: A.S.Ş., Data Collection or Processing: A.S.Ş., Analysis or Interpretation: A.S.Ş., F.Ş., Writing: A.S.Ş., F.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Villwock JA, K Jones. Recent trends in epistaxis management in the United States: 2008-2010. JAMA Otolaryngol Head Neck Surg 2013;139(12):1279-1284.
2. Kucik CJ, Clenney T. Management of epistaxis. Am Fam Physician 2005;71(2):305-311.
3. Viducich RA, Blanda MP, Gerson LW. Posterior epistaxis: clinical features and acute complications. Ann Emerg Med 1995;25(5):592-596.
4. Fatakia A, Winters R, Amedee RG. Epistaxis: A Common Problem. The Ochsner Journal 2010;10(3):176-178.
5. Kotecha B, Fowler S, Harkness P, Walmsley J, Brown P, Topham J. Management of epistaxis: a national survey. Ann R Coll Surg Engl 1996;78(5):444-446.
6. Neto PS, Nunes LMA, Gregorio LC, Santos RP, Kosugi EM. Surgical treatment of severe epistaxis: an eleven-year experience. Brazilian Journal of Otorhinolaryngology 2013;79(1):59-64.
7. Dubel GJ, Ahn SH, Soares GM. Transcatheter Embolization in the Management of Epistaxis. Seminars in Interventional Radiology 2013;30(3):249-262.
8. Razdan U, Raizada RM, Chaturvedi VN. Efficacy of conservative treatment modalities used in epistaxis. Indian Journal of Otolaryngology and Head and Neck Surgery 2004;56(1):20-22.
9. Aysan E, Idiz UO, Elmas L, Saglam EK, Akgun Z, Yucel SB. Effects of Boron-Based Gel on Radiation-Induced Dermatitis in Breast Cancer: A Double-Blind, Placebo-Controlled Trial. Journal of Investigative Surgery 2017;30(3):187-192.
10. Doğan A, Demirci S, Cağlayan AB, Kılıç E, Günal MY, Uslu U, et al. Sodium pentaborate pentahydrate and pluronic containing hydrogel increases cutaneous wound healing *in vitro* and *in vivo*. Biological trace element research 2014;162(1-3):72-79.
11. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. Clin Otolaryngol 2009;34(5):447-454.
12. Hanci D, Altun H, Şahin E, Altıntoprak N, Cingi C. Turkish translation, cross-cultural adaptation and validation of the SinoNasal Outcome Test (SNOT)-22. ENT Updates 2015;5(2):51-57.
13. Traboulsi H, Alam E, Hadi U. Changing Trends in the Management of Epistaxis. Int J Otolaryngol, 2015;2015:263987.
14. Gong Y, Yatongchai C, Wren AW, Mellott NP. Reintroducing sborgite: Crystallization through exposure of sodium borosilicate glasses to moisture. Materials Letters 2014;136:265-270.
15. Tepedelen BE, Soya E, Korkmaz M. Boric acid reduces the formation of DNA double strand breaks and accelerates wound healing process. Biological trace element research 2016;174(2):309-318.
16. Chen X, Pei Y. Effects of sodium pentaborate pentahydrate exposure on *Chlorella vulgaris* growth, chlorophyll content, and enzyme activities. Ecotoxicology and environmental safety 2016;132:353-359.
17. Büke Ç. Current Treatment of Diabetic Foot Infections and the Effect of Dermobor. Cyprus Journal of Medical Sciences 2017;2(2):29-34.
18. Doğan A, Demirci S, Cağlayan AB, Kılıç E, Günal MY, Uslu U, et al. Sodium Pentaborate Pentahydrate and Pluronic Containing Hydrogel Increases Cutaneous Wound Healing *in vitro* and *in vivo*. Biological Trace Element Research 2014;162(1-3):72-79.

CASE REPORT

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A Rarity, Oncocytoma of the Eyelid

Nadir Bir Durum, Gözkapağı Onkositomu

Perçin Karakol[1], Tevfik Balıkçı[1], Cem Leblebici[2]

[1]Health Science University Turkey, Bağcılar Training and Research Hospital, Clinic of Plastic, Reconstructive and Aesthetic Surgery, İstanbul, Turkey
[2]İstanbul Training and Research Hospital, Clinic of Pathology, İstanbul, Turkey

Abstract

Eyelid tumors are most common in the skin, and lacrimal gland and adnex origin are very rare. Although oxyphilic adenoma (oncocytoma) is generally located in the internal organ, it is one of the rare areas where it can hold around the eyes. Oncocytomas are one of the rare benign tumors that usually appear as cystic lesions around the eyes and can be diagnosed with punctum biopsies. If it is not excised totally, it is one of the tumors that can progress locally and become malignant. Although the cases with periocular, peripunktal and lacrimal glands are located in the literature, eyelid placement is very rare.

Keywords: Eyelid, oncocytoma, oxyphilic adenoma

Öz

Göz kapağı tümörleri en sık deri kaynaklı olup, lacrimal gland ve adnex kaynaklı olanlar oldukça nadirdir. Oksifilik adenom (onkositom) genellikle iç organda olmasına rağmen, göz çevresi de tutabildiği nadir bölgelerden biridir. Onkositomlar genellikle göz çevresindeki kistik lezyonlar olarak görülen ve punktum biyopsileri ile teşhis edilebilen nadir görülen benign tümörlerden biridir. Total olarak eksize edilmezse lokal agresif seyredip malignleşebilen tümörlerdendir. Periokuler, peripunktal ve lakrimal gland yerleşimli olgular literatürde yer almasına rağmen, göz kapağı yerleşimi oldukça nadirdir.

Anahtar kelimeler: Göz kapağı, onkositom, oksifilik adenom

Introduction

Oxyphilic adenomas (oncocytomas) are generally benign, rarely malignant tumors with distant spread. Hamper described it benign adenomatous tumours composed of oncocytes (1). Metastasis often depends on the exact site. These tumors could have been found in several organs including kidneys, liver, breasts, testes, endocrinal glands such as adrenals, thyroid-parathyroid and pituitary glands. Oculer forms are not common and usually examined in benign form. Some of them have orbital involvement, the incidence of ocular oncocytoma has been estimated to be 0.3 per milion/year (2), often considered as malignant. Eyelid forms are very infrequent and surgical excision is the rightful treatment of choice. However, although very rare, recurrence of the eyelid, lacrimal sac and lacrimal gland have been reported (3,4).

Case Report

A 66-year-old man presented in 2014 with a three year of slowly enlarging five lesions with the diameter of 0.2 cm min to 0.4 cm maximum at the left lower eyelid (Image 1). According to the patient, there was no discomfort or pain but only cosmetic problem on the first examination. Lesions were found to be brownish to reddish in colour, round shaped and tended to fluctuate. All of them were completely removed and excision material was sent to pathology department.

Results

The light microscopic examination showed a tumor composed of tubulopapillary structures lined by large cells with eosinophilic granular cytoplasm (Figure 1 and 2). No atypia, mitotic activity, necrosis, or hemorrhage was identified. The histological diagnosis of oncocytoma was

Address for Correspondence: Perçin Karakol, Health Science University Turkey, Bağcılar Training and Research Hospital, Clinic of Plastic, Reconstructive and Aesthetic Surgery, İstanbul, Turkey
E-mail: ppercin@gmail.com **ORCID ID:** orcid.org/0000-0003-0068-2139 **Received:** 07.01.2020 **Accepted:** 03.04.2020

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Image 1. Patient's lower eyelid

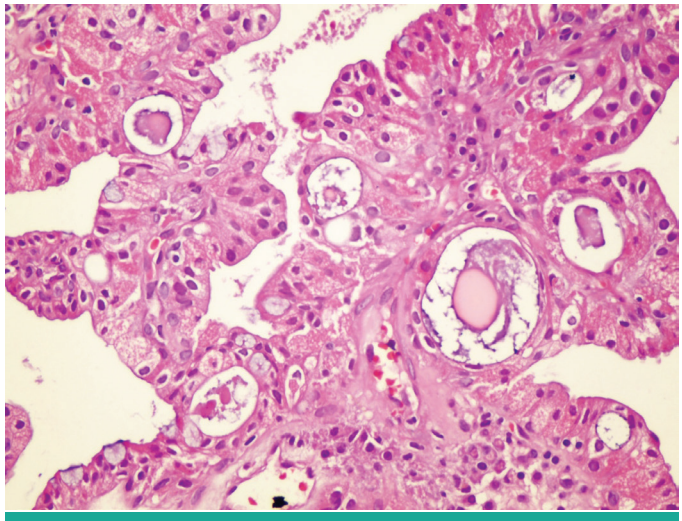

Figure 1. Multiple tubulopapillary proliferations lined by epithelial cells with intensely eosinophilic cytoplasm (HE, x100)

established. By the way, the patient was followed up for one year, week by week prior to the surgery for the first month and once every three months, respectively. Radiotherapy was not a choice of treatment after the operation. There was no sign of recurrence, neither metastatic lesions through this period. Therefore, a complete surgical excision and a closure with advencement flep made from lower lid skin was performed. We complied with all the reconstructional principles of eyelid closure. A comfortable and cosmeticaly satisfactory result was gained with no complaints from the patient who continued being asymptomatic.

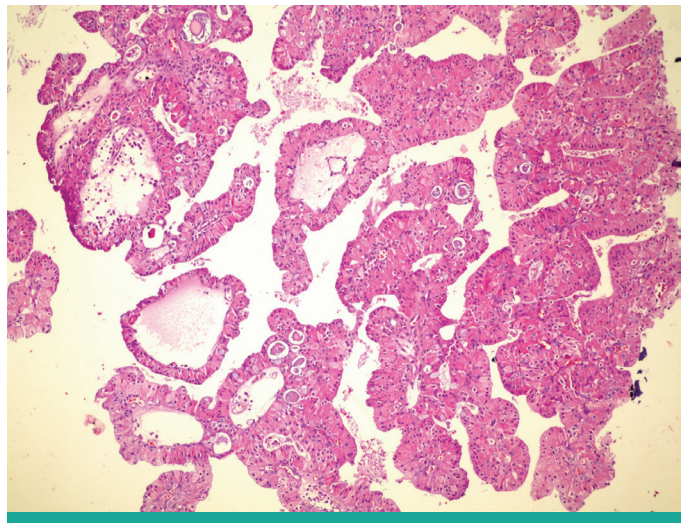

Figure 2. Columnar cells with granular, eosinophilic cytoplasm, indicating an oncocytic lesion (HE, x400)

Discussion

Brick and Schiagenhauffwere mentioned the oncocytes in the ophthalmic regions by noting their presence in the lacrimal glands (5). First case of an oncocytoma of the ocular adnexae was reported by Radnot (6). In the literature, there are limited cases of the upper of lower eyelid with onocytomas. The reason behind this is the rarity of the oncocytomas of ocular appendages. These tumors may develop in the lacrimal glands (7), sac (7-10), and the caruncle (7-9,11-15). Some palpebral oncocytomas like this case originate from the epithelium of Moll's gland or from the epithelium of the lacrimal duct (16-19). In spite of appereance of oncocytes in the lacrimal apparatus, palpebral involvement is a rare site for tumor formation (20). These tumors ordinarily grow slowly and stay asymptomatic. On the other hand, local recurrence can sometimes be seen in malign formations, notably after partial excisions. It was reported by Perlman et al. (21) and Tomic et al. (22) that recurrance could be likely after surgery. So, complete excision, close observation, and routine follow-up are advised. In our case, because the tumors were in a plural-flat form, it was complicated to be sure for deciding whether they were originated from lid or somewhere else. Oncocytomas manifesting themselves in the ocular adnexa region are rare. Regardless of their benign features, developing into a malignant pattern is always possible.

In the current case, we addressed oncocytomas might have gone unnoticed, often been referred as a different skin lesion because of their nevus-like appearance to the naked eye. We need to study and examine these tumors

more precisely for a proper diagnosis, determination, and rightful treatment. This can lead us to find the tumors' exact origin, foresee malignant progression and also describe the clinical-histological factors truely. By reporting a patient having oncocytomas on his lower eyelid, we aimed to emphazise this issue particularly.

Ethics

Informed Consent: All forms of consent are available to share the patient's photos and data after surgery.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: P.K., C.L., Design: P.K., C.L., Data Collection or Processing: P.K., T.B., Analysis or Interpretation: P.K., T.B., Writing: P.K.

Conflict of Interest: The authors declare that there is no conflict of interest with regard to this manuscript.

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References

1. Hamper H. Oncocyten und Geschwülste der Speicheldrüsen. Virchows Arch (Pathol Anat) 1931;282:724-736.
2. Ostergaard J, Prause JU, Heegaard S. Oncocytic lesions of the ophtalmic region: a clinicopathological study with emphasis on cytokeratin expression. Acta ophtalmol 2011;89(3):263-267.
3. Lamping KA, Albert DM, Ni C, Fournier G. Oxyphil cell adenomas. Three case reports. Arch Opthamol 1984;102(2):263-265.
4. Morand B, Bettega G, Bland V, Pinel N, Lebeau J, Raphael B. Oncocytma of the eyelid: an aggressive benign tumor. Opthalmology 1998;105(12):2220-2224.
5. Hamperl H. Oncocyten und Geschwulstc der Spcichcldruscn. Virchows Arch (PatholAnat) 1931;282:724-736.
6. Radnot M. Aus Oncocyten bestchende adenomartigc Hyperplasic in der Tranensackwand. Ophthalmologica 1941;101:95-100
7. Biggs SL, Font RL. Oncocytic lesions of the caruncle and other ocular adnexa. Arch Ophthalmol 1977;95(3):474-478.
8. Domanski H, Ljungberg O, Andersson LO, Schele B. Oxyphil cell adenoma (oncocytoma) of the lacrimal sac. Review of the literature. Acta Ophthalmol 1994;72(3):393-396.
9. Lamping KA, Albert DM, Ni C, Fournier G. Oxyphil cell adenomas: three case reports. Arch Ophthalmol 1984;102(2):263-265.
10. Ni C, D'Amico DJ, Fan CQ, Kuo PK. Tumors of the lacrimal sac: a clinicopathological analysis of 82 cases. Int Ophthalmol Clin 1982;22(1):121-140.
11. Chang WJ, Nowinski TS, Eagle RC Jr. A large oncocytoma of the caruncle. Arch Ophthalmol 1995;113(3):382.
12. Dini M, Soma PF, Comin CE. Oxyphil cell adenoma (oncocytoma) of the lacrimal caruncle: a case report. Tumori 1996;82(3):276-279.
13. Haye C, Chic F, Dhermy P, d'Hermies F. L'oncocytome de la caroncule: a` propos de trois observations. Bull Soc Ophtalmol Fr 1987;87(12):1345-1349.
14. Rennie IG. Oncocytomas (oxyphil adenomas) of the lacrimal caruncle. Br J Ophthalmol 1980;64(12):935-939.
15. Shields CL, Shields JA, Arbizo V, Augsburger JJ. Oncocytoma of the caruncle. Am J Ophthalmol 1986;102(3):315-319.
16. Fukuo Y, Hirata H, Takeda N, Hayami H, Katayama T. A case of oncocytoma in the eyelid. Ophthalmologica 1994;208(1):54-57.
17. Pe'er J, Neufeld M, Ilsar M. Peripunctal eyelid oncocytoma. Am J Ophthalmol 1993;116(3):385-387.
18. Rodgers IR, Jakobiec FA, Krebs W, Hornblass A, Gingold MP. Papillary oncocytoma of the eyelid. A previously undescribed tumor of apocrine gland origin. Ophthalmology 1988;95(8):1071-1076.
19. Thaller VT, Collin JRO, McCartney ACE. Oncocytoma of the eyelid: a case report. Br J Ophthalmol 1987;71(10):753-756.
20. Bock J. Schlagcnhauff K. Uber das Vorkommcn von Onkocytcn in der mcnschlichen Tranendruse. ZAugenheilkd 1938;94(4):244.
21. Perlman JI, Specht CS, McLean IW, Wolfe SA. Oncocytic adenocarcinoma of the lacrimal sac: report of a case with paranasal sinus and orbital extension. Ophthalmic Surg Lasers 1995;26(4):377-379.
22. Tomic S, Warner TF, Brandenburg JH. Malignant oncocytoma of the lacrimal sac: ultrastructure and immunocytochemistry. Ear Nose Throat J 1995;74(10):717-720.

CASE REPORT

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The Clinical Spectrum of Reactions Due to Banana Allergy

Muz Alerjisine Bağlı Olarak Gelişen Reaksiyonların Klinik Spektrumu

Abdullah Dayıoğlu[1], Sena Akgiray[1], Hikmet Tekin Nacaroğlu[1], Semiha Bahçeci Erdem[2]

[1]İstanbul Medipol University Faculty of Medicine, Department of Pediatric Allergy and Immunology, İstanbul, Turkey
[2]Çiğli Regional Training and Research Hospital, Clinic of Pediatric Allergy and Immunology, İzmir, Turkey

Abstract

Allergic reactions to bananas have rarely been reported. The clinic reports mostly moderate local allergic reactions (Oral Allergy syndrome) to bananas, though some reports state reactions reaching anaphylaxis. We report three cases of banana allergy. The first case, immediately after giving a teaspoon of banana to a 7-month-old baby by the mother, he was admitted to the emergency department with the complaints of vomiting, urticaria, swelling of the mouth and eyes. The second case, after some banana yogurt was eaten by a 6.5-month-old baby, she presented with a rash which developed at the 3rd hour. In the third case, a 16-year-old male patient applied with itchy rashes on his body after eating a banana in 1-2 hours. Our cases are presented to emphasize that urticaria and anaphylaxis may occur due to banana allergy.

Keywords: Anaphylaxis, atopic dermatitis, banana allergy

Öz

Muza karşı alerjik reaksiyon nadir olarak raporlanmıştır. Muz alerjisinde klinik genellikle orta derecede lokal semptomlar (Oral Alerji sendromu) şeklinde bildirilmekte, ancak bazı raporlarda anafilaksiye kadar gidebilen şiddetli semptomlar da bildirilmiştir. Bu bildiride muz alerjisi tanısı alan üç olgu sunulmuştur. İlk olgu 7 aylıkken annesinin 1 çay kaşığı muz yedirmesinden hemen sonra fışkırarak kusma, ürtiker, ağız ve gözlerde şişlik şikayetiyle acile başvurdu. İkinci olgu 6,5 aylıkken yediği muzlu yoğurt sonrası 3. saatte gelişen döküntü şikayetiyle bize başvurdu. Üçüncü olgu olan 16 yaşındaki erkek hasta, muz yedikten 1-2 saat sonra vücutta kaşıntılı döküntüler ile başvurdu. Muz alerjisine bağlı ürtiker ve anafilaksi görülebileceğini vurgulamak için olgularımız sunulmuştur.

Anahtar kelimeler: Anafilaksi, atopik dermatit, muz alerjisi

Introduction

Food allergy is defined as an abnormal or exaggerated immune response to food proteins. It has been reported that 4-6% of the world's child population has food allergy (1). Responsible foods differ according to culture and population. While the most common food causing allergies in the United States pediatric population are cow's milk, eggs, peanuts, soy, wheat, fish and shellfish, peanuts, fish and shellfish are more common in adults (1). In a study conducted in the Black Sea region of Turkey, beef (31.8%), cow's milk (18.1%), cocoa (18.1%), eggs (13.6%), and kiwi (13.6%) were found to be among the most common food allergens (2). In another study conducted in Turkey, eggs (57.8%), cow's milk (55.9%), nuts (21.9%), peanuts (11.7%), walnuts (7.6%), lentils (7.0%), wheat (5.7%) and cattle meat (5.7%) were found as other allergens (3).

Allergic reactions to bananas have rarely been reported. It has been shown in studies from different parts of the world that banana allergy is seen between 0.04% and 1.2% in the general population (4). Five allergens causing banana allergy have been identified. Mus a 1 profile, actin binding protein, weighing 14 kilodaltons, found in all eukaryotic cells; causes cross reaction with pollen and plants. Mus a 2 is a member of class 1 chitinase pathogen-associated

Address for Correspondence: Hikmet Tekin Nacaroğlu, İstanbul Medipol University Faculty of Medicine, Department of Pediatric Allergy and Immunology, İstanbul, Turkey
E-mail: tekin212@gmail.com **ORCID ID:** orcid.org/0000-0003-1333-2648 **Received:** 24.04.2020 **Accepted:** 12.05.2020

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protein family 3. It causes skin test positivity in more than 50% of cases with banana allergy. In addition, plant-derived nutrient class 1 chitinase is the most important panallergen causing Latex-fruit syndrome. Mus a 3 (non-specific lipid transfer protein), Mus a 4 (thaumatin like protein) and Mus a 5 (β-1.3 glucanase) have been reported by the IUIS Allergen Nomenclature Sub committee in recent years (5,6).

The clinic reports mostly moderate local allergic reactions (Oral Allergy syndrome) to banana, though some reports state reactions reaching anaphylaxis (7). In this report, three cases with banana allergy with different clinical findings are presented.

Case Reports

The First Case

Seven-month-old patient was admitted to the emergency department with vomiting, widespread urticaria on face, swelling of the mouth and eyes. This was anaphylaxis and aggressive emergency management was done. Diagnostic tests revealed total IgE: 37 kU/L and banana-specific IgE: 8.7 kU/L. The symptoms of our patient, who had no health problem until 4 months of age, had immediately started with the contact with banana peel. Banana specific IgE: 2.4 kU/L was obtained and epidermal prick to prick test revealed 3x3 mm induration. Specific IgE levels for cross-reactive allergens were checked; kiwifruit: 0.165 kU/L, latex: 0.114 kU/L, strawberries: <0.10 kU/L, avacado: <0.10 kU/L. The results of the prick to prick test were as follows: positive control: 5x5 mm, banana: 3x3 mm positive, strawberry: 2x2 mm positive, avocado and latex were negative. No food provocation test was performed. Adrenaline autoinjector was prescribed and the patient was told to continue the elimination diet.

The Second Case

Six and a half month old patient applied to us with a rash developed three hours after eating banana yogurt. There was no drug intake before the onset of his/her complaints. She was the first child of unrelated parents and was born in normal vaginal route at the 40th gestational week, following a smooth pregnancy. She was diagnosed with atopic dermatitis due to a history of rashes starting at 2 months and 10 days of age. Formula milk was started in addition to breast milk because the breast milk was insufficient. At the 4 months of age, skin prick tests and specific IgE levels were all negative for cow's milk, egg and wheat. She was advised to continue moisturizing. It was reported that she had previously consumed yogurt and had no symptoms. Banana prick to prick test was negative and banana specific IgE was 0.194 kU/L. In the food provocation test with banana yogurt, eczematous skin lesions were observed 4 hours later (Figure 1). A banana elimination diet was initiated and the patient was informed about cross reactions. At the last follow-up, the specific IgE results were as follows: banana: 0.597 kU/L, kiwi: <0.10 kU/L, latex: <0.10 kU/L, strawberries: <0.10 kU/L, avacado: <0.10 kU/L.

The Third Case

A 16-year-old male patient applied with itchy rashes on his body that developed after 1-2 hours of eating orange, pear and banana. Four years ago, he had symptoms of rash, facial swelling, dyspnea, cough, difficulty swallowing immediately after eating a cherry. He and his family did not have any history of additional allergic diseases such as asthma, rhinitis or eczema. In the skin prick to prick test, the diameters of induration were: Banana: 15 mm, pear 3 mm, orange 3 mm. (Figure 2). Epidermal prick to prick test was not performed because of the history of anaphylaxis with cherry. Latex and pollen sensitivities were not detected in the epidermal skin test. The patient did not accept oral food challenge test with banana, pear and orange. Due to a history of anaphylaxis with cherry, no food challenge with cherry was performed. Adrenaline autoinjector was prescribed and elimination diet was recommended. They were informed about cross reactions and called for follow-ups.

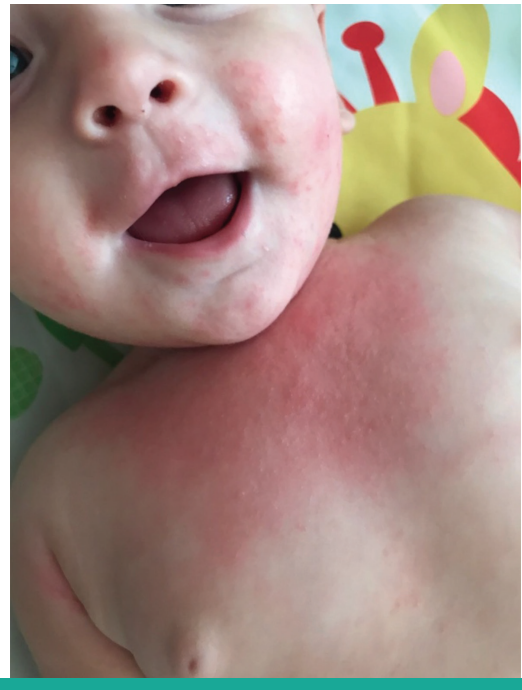

Figure 1. Exacerbation of eczema observed after oral food challenge in our second case

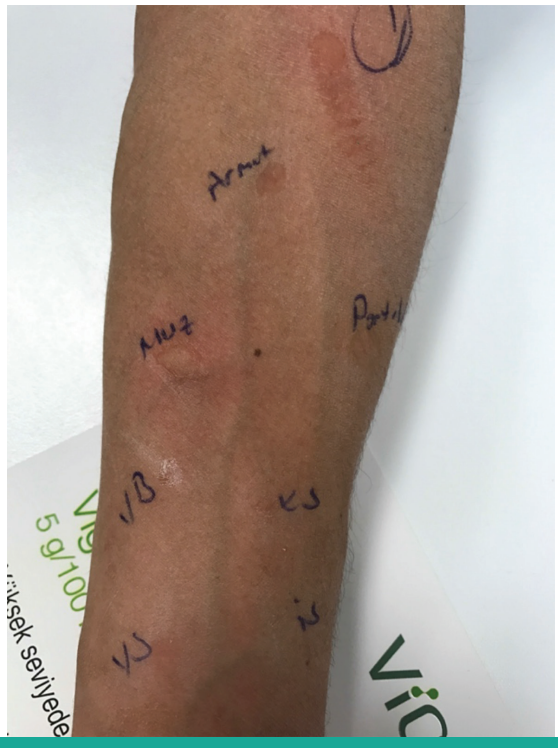

Figure 2. Prick to prick test with food in our third case

Discussion

Cow's milk and egg are the most common cause of food allergy in children in our country (3). Allergic reaction due to banana intake is a very rare food allergy. Banana allergy has been shown to be seen between 0.04% and 1.2% in studies all over the world (4). Rarely, anaphylaxis has been reported in banana allergy with especially oral-cutaneous involvement. Systemic reactions such as skin involvement, hypotension, angioedema, respiratory arrest have been reported as a symptom in patients with anaphylaxis (8-10).

In a male patient with a 4-month history of eczema, banana-related anaphylaxis was diagnosed with vomiting, urticarial and cyanosis symptoms 5 minutes after eating a banana. The authors reported that, in this case, the susceptibility to food antigens may be mediated by many ways, such as through the skin, by inhalation, through the gastrointestinal tract, through direct exposure or directly through breast milk. They also stated that exposure to fresh bananas may have increased the severity of symptoms, given that the major allergens of bananas may have heat sensitivities (9). Hauswirt and Burks (7) reported a case of anaphylaxis after banana ingestion and the patients' skin test was negative. The first case of anaphylaxis after banana ingestion is a 7-month-old patient with a diagnosis of atopic dermatitis and a history of anaphylaxis due to cow's milk. Urticaria, angioedema, vomiting, respiratory symptoms started two hours after banana intake, and there was no history of reactions to latex and other foods that could cross-react with bananas. While the skin test performed with commercial solution was negative, 20x20 mm induration was detected in the prick to prick test with banana and the specific IgE value was 4.70 ku/L. To date, the positive predictive value for banana-specific IgE has not yet been described in the literature. In previously reported cases, specific IgE values of two cases with symptoms after banana intake were found to be 5.21 kU/L and 5.24 kU/L (11).

The specific IgE value of our first case was 8.7 kU/L, and 0.194 kU/L for the second case. The specific IgE test was not taken for the third case. Epidermal prick test was performed in two of our cases and susceptibility to banana was detected. In the second case, the oral food challenge test was positive. This shows us that the specific IgE value or skin tests alone are not significant, and in cases without contraindications, symptoms should be confirmed by oral food challenge tests. However, allergic reactions may occur during these tests. For this reason, they must be performed in experienced centers. In our first case, no food challenge was performed because of the patient's history of anaphylaxis. In our second case, eczema exacerbation was observed within 4 hours after oral provocation test with banana. The third case did not accept the food challenge test because he had already observed the rash every time he ate bananas, pears and oranges. Due to a history of anaphylaxis with cherry, no food challenge test was performed with cherry.

The first step in the management of allergic reactions due to bananas is the elimination of the allergen from the diet. In life threatening conditions such as anaphylaxis, intramuscular adrenaline must be used. Adrenaline auto-injector must be prescribed to the patients with a history of food anaphylaxis. The usage should be taught carefully. Elimination diet was suggested for our patients. Patients with history of anaphylaxis was prescribed adrenaline and the use of autoinjector was taught.

Besides being rarely seen, banana allergy is also known for causing Latex-fruit syndrome. The most common cross-reactivities of the banana allergy are kiwi, avocado, melon, pollen and latex. 20-60% of the patients were identified to have latex allergy, IgE mediated reactions caused by fruits. From oral allergy syndrome to severe anaphylaxis, we come across different presentations. Class 1 enzyme N-terminus hevein, responsible for the cross-reaction, was reported as the major latex allergen (6). In our cases, latex sensibility

was not observed in latex specific immunoglobulin results and epidermal prick tests.

As a result, besides being seen rare, banana allergy leads to both severe systemic reactions and Latex-fruit syndrome. Patients with a history of food anaphylaxis must definitely be prescribed an adrenaline auto injector. The usage must be taught and the families must be informed about how to carry the injector.

Ethics

Informed Consent: Informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.D., H.T.N., Design: A.D., H.T.N., Data Collection or Processing: A.D., H.T.N., S.G., S.B.E., Literature Search: A.D., H.T.N., S.G., S.B.E., Writing: A.D., H.T.N.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Sicherer SH, Munoz-Furlong A, Sampson HA. Prevalence of seafood allergy in the United States determined by a random telephone survey. J Allergy Clin Immunol 2004;114(1):159-165.
2. Orhan F, Karakas T, Cakir M, Aksoy A, Baki A, Gedik Y. Prevalence of immunoglobulin E-mediated food allergy in 6-9-year-old urban schoolchildren in the eastern Black Sea region of Turkey. Clin Exp Allergy 2009;39(7):1027-1035.
3. Yavuz ST, Sahiner UM, Buyuktiryaki B, Soyer OU, Tuncer A, Sekerel BE, et al. Phenotypes of IgE-mediated food allergy in Turkish children. Allergy Asthma Proc 2011;32(6):47-55.
4. El-Sayed ZA, El-Ghoneimy DH, El-Shennawy D, Nasser MW. Evaluation of banana hypersensitivity among a group of atopic egyptian children: relation to parental/self reports. Allergy Asthma Immunol Res 2013;5(3):150-154.
5. Aleksic I, Popovic M, Dimitrijevic R, Andjelkovic U, Vassilopoulou E, Sinaniotis A, et al. Molecular and immunological characterization of Mus a 5 allergen from banana fruit. Mol Nutr Food Res 2012;56(3):446-453.
6. Makinen-Kiljunen S. Banana allergy in patients with immediate-type hypersensitivity to natural rubber latex: characterization of cross-reacting antibodies and allergens. J Allergy Clin Immunol 1994;93(6):990-996.
7. Hauswirth DW, Burks AW. Banana anaphylaxis with a negative commercial skin test. J Allergy Clin Immunol 2005;115(3):632-633.
8. Ito A, Ito K, Morishita M, Sakamoto T. A banana-allergic infant with IgE reactivity to avacoda but no latex. Pediatr Int 2006;48(3):321-323.
9. O'Keefe, Ben-shoshan. A 4 month -old baby boy presenting with anaphylaxis to banana: a case report. J Med Case Rep 2014;8:62.
10. Moreno-Ancillo A, Dominguez-noche C, Gill adrados AC, Cosmes PM. Allergy to banana in a 5 month-old infant. Pediatr Allergy Immunol 2004;15(3):284-285.
11. Grob M, Reindl J, Vieths S, Wuthrich B, Ballmer-Weber BK. Heterogeneity of banana allergy: characterization of allergens in banana-allergic patients. Ann Allergy Asthma Immunol 2002;89(5):513-516.

LETTER TO THE EDITOR

Bagcilar Med Bull 2020;5(2):64-66
DOI: 10.4274/BMB.galenos.2020.02.02

A Practical Method for Purification of Fat Grafts Using Gelatin Sponge

Jelatin Sünger Kullanarak Yağ Greftlerinin Saflaştırılması için Pratik Bir Yöntem

Perçin Karakol[1], Mehmet Bozkurt[1], Emin Kapı[2]

[1]Health Science University Turkey, Bağcılar Training and Research Hospital, Clinic of Plastic, Reconstructive and Aesthetic Surgery, İstanbul, Turkey
[2]Adana Training and Research Hospital, Clinic of Plastic, Reconstructive and Aesthetic Surgery, Adana, Turkey

Dear Editor,

Fat grafting has dramatically become popular during recent years not only in plastic surgery, but also in other medical fields. Processing of fat grafts can be done in different ways, either with filtering, cotton-gauze rolling, or centrifugation methods (1). A major focus was the use of centrifugation or other methods to separate the aqueous and oil components before injection because this stage is the most important part for fat graft survival (2). There is no consensus on the various techniques, neither a gold standard technique for processing stage. In this letter, we aimed to use an alternative method for purification and filtering of fat grafts using gelatin sponge for low quantities of fat grafts.

Our standard tumescent solution is injected into the harvest site. Fat is aspirated by hand using 60 mL syringe and harvesting cannula. In this method, fat lobules are removed through fibrous septas by degrading. For this reason, fat grafts obtained are free of fibrous septa and have a homogenic formation. A gelatin sponge with dimension of 80×50×10 mm is divided transversely into two parts by using no: 10 blades for enlarging the surface area used (Figure 1a and b). The rough surfaces of the gelatin sponge are used as it is more absorbent. The hand-suctioned specimens are divided into lesser parts and poured onto the surface of the sponge. The specimens are rolled with forceps for about 3 minutes until all blood, aqueous and oil components are absorbed and separated (Figure 1c and d). The purified fat grafts area are filled to 2 mL syringes using curettes. The purified and unprocessed fat graft is seen in Figure 2.

The gelatin sponge for purifying fat grafts is a cheap, quick method and it is quite easy to apply. Gelatin sponge (Spongostan®, Ferrosan A/S, Denmark) is an absorbable hemostatic agent derived from pig skin collagen and is widely used in humans for over 60 years (3). It is a material that can be absorbed between 4 and 6 weeks, and it is sponge-like and contains hemostatic gelatin. It has porous formation. It promotes platelet aggregation and increases the matrix formation of fibrin (4). It is cheap (0.30€ per one) and commercially available, it can be found easily almost in every hospital. The surgeon himself can easily perform the technique without any help. Although fat grafting which is performed by closed system has been regarded as ideal, there has not been any kind of evidence that indicates infection is increased through desiccation air oxidation or decreases fat graft viability (1). As far as the study of the Kuran and Tumerdem (5), although the application period is 15-20 minutes, there have been available data showing that air exposure does not increase bacterial growth. In our study, as gelatin sponge has a fast absorbent character,

Address for Correspondence: Perçin Karakol, Health Science University Turkey, Bağcılar Training and Research Hospital, Clinic of Plastic, Reconstructive and Aesthetic Surgery, İstanbul, Turkey
E-mail: ppercin@gmail.com **ORCID ID:** orcid.org/0000-0003-0068-2139 **Received:** 06.02.2020 **Accepted:** 21.04.2020

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execution time is shorter and thus we believe that potential risks are minimized. The common agreed methods for fat processing are the cotton gauze rolling and centrifugation, and also filtration which is less commonly used. According to literature, there are conflicting reports on that one of them has superiority to another (1,6). The filtration method has an advantage to process large volumes efficiently and quickly at the same time. It may be safer for infection and

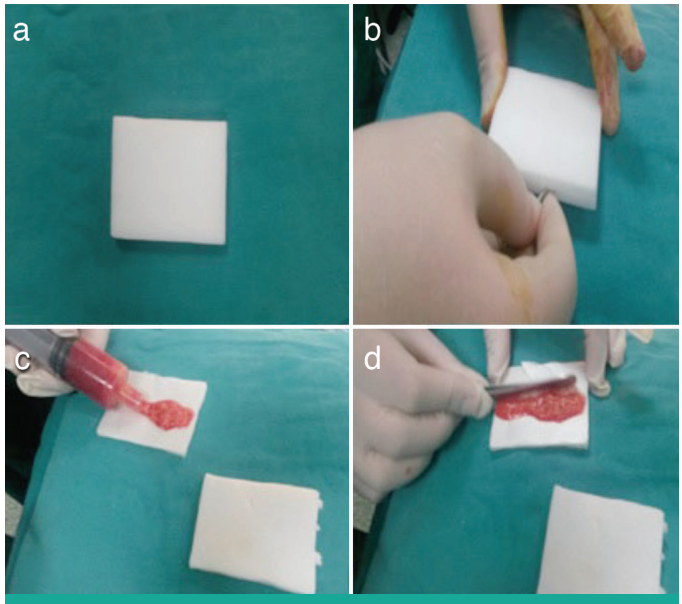

Figure 1. a) View of the gelatin sponge b) View of the division of gelatin sponge c) The appearance of the pouring of the fat grafts d) The appearance of the rolling of the fat grafts with forceps

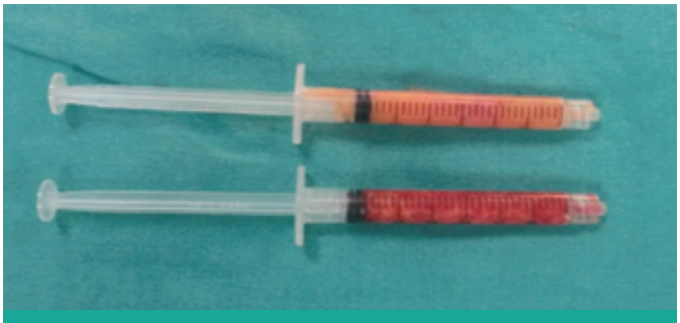

Figure 2. The appearance of the purified fat graft

it increases graft viability but there is not enough evidence for these situations. It is not widely available, not suitable for little volumes; and it is also expensive (1). Kuran and Tumerdem (5) also described a filtration method which was inspired by yogurt concentration methods in Anatolia, that is believed to prevent the adverse affects of centrifugation (5).

The centrifugation and cotton gauze rolling methods are useful for little amounts of fat. The cotton gauze derived technique of Telfa (Covidien, Mansfield, Mass.) is commercially available in local market. It is disposable. It is proven to be the best option for removing oil fraction (1). The centrifugation method (Coleman's technique) is as efficient to purify and to drain fat by gravity as the cotton gauze method. It can be found easily but it requires a centrifugation machine and cannot be performed by the surgeons themselves during the operation.

In the comparison of filtering, centrifugation, cotton gauze rolling and gelatin sponge methods, the processing time, residual oil ratio contained in the graft after processing, removing of aqueous oil degree, the fat grafts volume retention percentile which was observed in 6 weeks after the application were compared (Table 1). According to this, in the cotton gauze sponge and gelatin sponge techniques, it was seen that both period of time was shortened and the most favorable results were obtained in terms of efficacy.

Compared to all groups, in the gelatin sponge group, adipocytes were evaluated by examining the presence of needle-shaped fissure formations, which contain nuclei in terms of viability and the radial distribution formed by dissolving the triglyceride crystals. In terms of this parameter, adipocyte viability was found to be high in fat graft samples. It is noteworthy that fibrotic areas are in narrower areas, and capillary blood vessels are much denser among adipocytes. Minimal necrosis was observed when staining with hematoxylin eosin (Figure 3).

As the processes of cotton gauze and filtration, a drain work is performed by making the fat grafts held or mixed.

Table 1. Comparison of filtering, centrifugation, cotton gauze rolling in gelatin sponge methods

Parameters	Methods			
	Filtering	Centrifugation	Cotton gauze rolling	Gelatin sponge
Processing time (min)	5	3	5	3
Residual oil (%)	1	4	0	0
Removing of aqueous oil	++	++	+++	+++
Fat graft volume retention (%)	58	47	70	75

min: Minimum

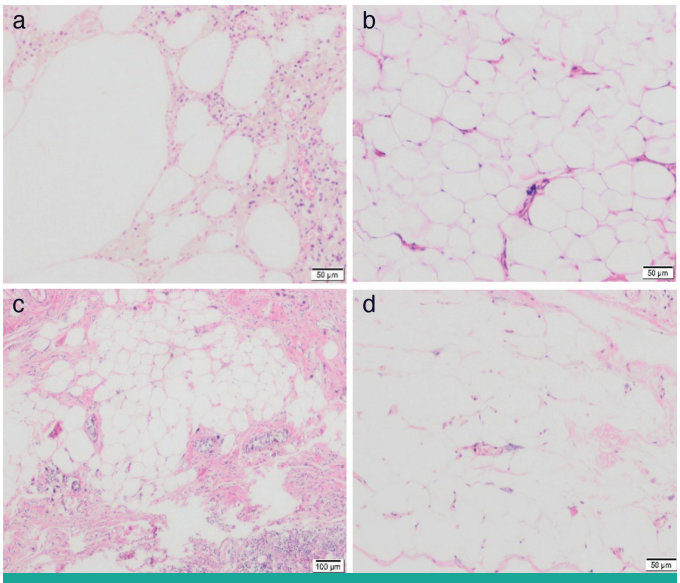

Figure 3. Histological evaluation of new vascularity and adipocyte viability with HE

a) Filtering b) Centrifugation c) Cotton gauze rolling d) Gelatine sponge

In spite of a long holding duration for these works, it can be faced by the situations that the liquid side of the fat is not absorbed efficiently. As the content of gelatin sponge is of the characteristic for rather absorbing and sponge-porous, it absorbs the liquid quickly and it makes fat graft concentrated. In addition to this, the possibility that gauze particles may remain between the fat tissues in cotton gauze method, it brings about the foreign-body reaction risk. Since gelatin sponge is of the kind that melts, we are of the opinion that the tendency of forming foreign-body reaction in the long term period is lower. At the same time, besides mechanical effect over the fat graft application, because of the contribution to fibrin formation, we think that fat grafts increase the penetration into tissue and decreases the melting rate (5).

The most important limitation of this method is that it allows little amounts of fat purification. A single gelatin sponge can purify about 10 mL of fat and about 3-4 mL purified fat graft is obtained. We use purified fat grafts into facial areas especially nasolabial sulcus and malar area and the obtained amounts are usually sufficient. If greater amounts are required, it may not be favorable, because of timely and personal constraints; other purification techniques like filtration may be used. Further studies must be performed for the effectiveness and showing the advantages and disadvantages and short and long term results may be helpful for comparison. For the parameters which are the matters in question, performing experimental work is more convenient. For this issue, a more detailed study has been planned.

Although, the cotton gauze rolling and centrifugation have become established methods for removing unwanted oil and aqueous fluid from the lipo-aspirate to purify the fat before grafting, the presented gelatin sponge method may be kept in mind as an alternative due to its easiness, cheapness especially for small amounts of fat grafts. The manuscript does not contain clinical studies or patient data.

Keywords: Fat graft, sponge, purification

Anahtar kelimeler: Saflaştırma, sünger, yağ grefti

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Ethics

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.B., Concept: P.K., Design: P.K., Data Collection or Processing: P.K., M.B., Analysis or Interpretation: E.K., Writing: P.K., M.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Fisher C, Grahovac TL, Schafer ME. Comparison of harvest and processing techniques for fat grafting and adipose stem cell isolation. Plast Reconstructive Surgery 2013;132(2):351-361.
2. Coleman SR. Structural fat grafts: The ideal filler? Clinic Plastic Surgery 2001;28(1):111–119.
3. Arias-Gallo J, Chamorro-Pons M, Avendano C. Influence of acidic fibroblasts growth factor on bone regeneration in experimental cranial defects using spongostan and bio-oss as protein carriers. Journal of Craniofacial Surgery 2013;24(5):1507-1514.
4. Spotnitz WD, Burks S.Hemostats, sealants, and adhesives: components of the surgical toolbox. Transfusion 2008;48(7):1502-1516.
5. Kuran I, Tumerdem B. A new simple method used to prepare fat for injection. Aesthetic Plastic Surgery 2005;29(1):18-22.
6. Gir P, Brown SA, Oni G. Fat grafting: evidence based review on autologous fat harvesting, processing, reinjection, and storage. Plastic Reconstructive Surgery 2012;130(1):249-258.

LETTER TO THE EDITOR

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Expanding Intensive Care Unit Management for Critically Ill Patients During COVID-19 Pandemic

COVID-19 Pandemisinde Kritik Hastaların Tedavisi için Yoğun Bakım Ünitelerinin Kapasite Artışı

Kerem Erkalp, Mehmet Salih Sevdi, Ali Özalp

Bağcılar Training and Research Hospital, Clinic of Anesthesiology and Reanimation, İstanbul, Turkey

Dear Editor,

The cumulative incidence of coronavirus disease (COVID-19) cases has also been increased in Turkey. In approximately 14% cases, COVID-19 develops into a more severe disease requiring hospitalization, while the remaining 6% of the cases experience critical illness requiring management in intensive care unit (ICU)s (1). Therefore, the demand for ICU beds has increased in İstanbul Bağcılar Training and Research Hospital.

In our hospital, anesthesiology and reanimation department has two ICUs including a level- III ICU with 20 beds (20 ventilators) and a level-II ICU with 11 beds (5 ventilators). In addition, there are only six isolation rooms in there.

In the middle of March, with the onset of the first cases, we started to use the ICU area with six-bed isolation rooms for suspected COVID-19 patients since the number of COVID-19 positive patients was low in the first place (Triage ICU). When the test results of the patients resulted as positive during their stay, we transferred the COVID-19-positive patients to the three-bed isolation rooms in cardiovascular surgery (CVS) ICU in cooperation with the CVS clinic (Cohort ICU). Since patient hospitalization increased dramatically in a short period of time, we started to provide care to suspected COVID-19 patients by transferring the patients in the level III-ICU with 14 beds to the clinics, palliative care center, ICU at the department of general surgery and level II-ICU. Thus, isolated ICU areas were created for 14 COVID-19-suspected (Triage ICU) and nine COVID-19-positive patients (Cohort ICU). In addition, a level-III arena area with 14 beds of CVS-ICU and a level II-arena area with 13 beds ICU were turned into a 50-bed Cohort ICU with the ventilator that was re-supplied as a result of cooperation with the cardiology clinic and general surgery clinics (Figure 1). As in many countries, we might not have enough ICU beds, let alone isolation or single rooms, in the first place. With an executive attitude, all ICU areas were converted to areas that were negatively pressurized with respect to surrounding areas. In this regard, national and regional modeling is crucial for ICUs for patient and employee safety (2).

At the moment, it has been approximately the end of the first month since the pandemic started in Turkey. In the ICUs in our hospital, a total of 48 patients, 20 of which have been receiving non-invasive mechanical ventilation, have been treated. Before the pandemic, our department's ICU beds were 6.2% of the number of hospitalized patients while during these days, it increased to 14.9% thanks to the increase in the capacity. The increase in the bed numbers is not enough to expand the ICU capacity and it should be supported by the increase in the necessary equipment (i.e.

Address for Correspondence: Kerem Erkalp, Bağcılar Training and Research Hospital, Clinic of Anesthesiology and Reanimation, İstanbul, Turkey
E-mail: keremerkalp@hotmail.com **ORCID ID:** orcid.org/0000-0002-4025-7092 **Received:** 16.04.2020 **Accepted:** 22.04.2020

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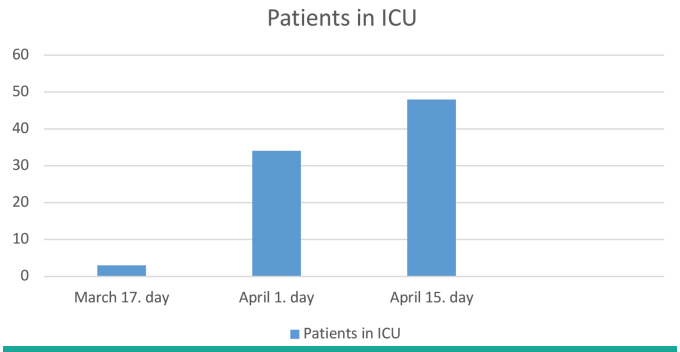

Figure 1. The number of patients in ICU in COVID-19 pandemic's first month period

ICU: Intensive care unit, COVID-19: Coronavirus disease

ventilators), consumables, pharmaceuticals, and staffing. Although focusing on bed numbers without ensuring the availability of necessary equipment is unsafe, such equipment might be in short supply. Even though one can suggest that increased number of beds should not be considered as safe as without being able to have essential equipment, such tools may become scarce. Requirement of use of transport, operating theatre, and military ventilators may arise (3). Moreover, we do not have any issues with the number of beds in the ICU with patients' turn over.

We will share the data regarding patients in the upcoming days.

Keywords: Bed capacity, COVID-19 pandemic, intensive care

Anahtar kelimeler: COVID-19 pandemisi, yatak kapasitesi, yoğun bakım

Ethics

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References

1. Kinross P, Suetens C, Dias JG, Alexakis L, Wijermans A, Colzani E, et al. Rapidly increasing cumulative incidence of coronavirus disease (COVID-19) in the European Union/European Economic Area and the United Kingdom, 1 January to 15 March 2020. Euro Surveill 2020;25(11):2000285.
2. Phua J, Weng L, Ling L, Egi M, Lim CM, Vasishta J, et al. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. Lancet Respir Med 2020;6(20):30161-30162.
3. Xie J, Tong Z, Guan X, Du B, Qiu H, Slutsky AS. Critical care crisis and some recommendations during the COVID-19 epidemic in China. Intensive Care Med 2020;46(5):837-840.