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About the Journal

Bagcilar Medical Bulletin (Bağcılar Tıp Bülteni) (BMB) is periodical scientific publishing of Health Sciences University, 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 brancheswill 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.

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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.

Bağcılar Tıp Bülteni/Bagcilar Medical Bulletin, yazıların İngilizce dilinde, yazıların özetlerinin Türkçe ve İngilizce dillerinde online olarak yayınlandığı bir dergidir.

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Derginin Sahibi

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.

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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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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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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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be discussed, results should be compared and contrasted with findings of other studies in the literature and the different findings from other studies should be explained. The new and important aspects of the study and the conclusions that follow from them should be emphasized. The data or other information given in the Introduction or the Results section should not be repeated in detail.

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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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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 semboller sadece standart kısaltmaları kullanın, 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.

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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. Kaynaklar yazının sonunda (Kaynaklar/References) başlığı altında metindeki geçiş sırasına göre numaralandırılıp dizilmelidir. Metin içinde ise parantez içinde belirtilmelidir. Kaynakların listesiyle metin içinde yer alış sırası arasında bir uyumsuzluk bulunmamalıdır.

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Kaynaklar için örnekler aşağıda belirtilmiştir:

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MEDLINE'da yer alan ve kısaltması MEDLINE'a göre yapılan dergi makalesi için: Crow SJ, Peterson CB, Swanson SA,

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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.

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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• Aynı ya da çok benzer çalışmadan elde edilen raporların daha önce yayına gönderilip gönderilmediği mutlaka belirtilmelidir. Böyle bir çalışmaya özgül olarak atıfta bulunulmalı ve ayrıca yeni makalede de eskisine atıfta bulunulmalıdır. Gönderilen makaleye bu tip materyalin kopyaları da eklenerek editöre karar vermesinde yardımcı olunmalıdır.

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BAGCILAR MEDICAL BULLETIN
Bağcılar Tıp Bülteni

CONTENTS / İÇİNDEKİLER

ORIGINAL RESEARCH

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Management with Guidance of Minimally Invasive Cardiac Output Monitoring (PiCCO®) in Coronary Artery Bypass Surgery and Postoperative Results

Koroner Arter Bypass Cerrahisinde Minimal İnvaziv Kalp Debisi Ölçüm (PICCO®) Kılavuzluğu ile Yönetim ve Postoperatif Sonuçlar

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Abstract

Objective: Our study aimed to assess the correlation between the measured PiCCO® parameters and extubation time and intensive care unit (ICU) length of stay in patients who underwent coronary artery bypass grafting (CABG) surgery and were managed by monitorization of cardiac output and cardiac performance parameters with PiCCO®.

Method: This study was conducted by retrospective analysis data of all 44 patients who underwent CABG surgery during December 2015-March 2016 and were managed through PiCCO® monitorization. The patients' demographic characteristics (age, sex, weight, height, body mass index), American Society of Anesthesiologists physical conditions, comorbidities, ejection fractions, anesthetic management, operative details, hemodynamic data, PiCCO® parameters, extubation times, cardiovascular surgery ICU lengths of stay, requirements for vasoactive agent and blood transfusion, mortality, and morbidity were recorded from patient records and evaluated the correlation between the measured PiCCO® parameters and extubation time and ICU length of stay inpatients.

Results: A significant increase was detected in the parameters of cardiac contractility and performance monitored with PiCCO® in the postoperative period ($p<0.05$). No significant correlation was found between PiCCO® parameters and extubation time and ICU length of stay ($p<0.05$).

Conclusion: Coronary revascularization patients managed with the guidance of PiCCO® showed improved myocardial contractility and cardiac performance and no increase beyond what is anticipated in the extubation time and ICU lengths of stay of the patients. Thus, we believe that optimum volume and hemodynamic targets can be achieved in patients managed through monitorization of cardiac function parameters.

Keywords: Coronary artery bypass surgery, PiCCO®, cardiac output monitoring

Öz

Amaç: Çalışmamızda; koroner arter bypass greftleme cerrahisi (KABG) geçiren ve PİCCO® ile sürekli kalp debisi ve kardiyak performans paremetreleri monitörize edilerek yönetilen hastalarda, ölçülen PİCCO® parametreleri ile ekstübasyon ve yoğun bakım ünitesi (YBÜ) kalış süreleri arasındaki korelasyon değerlendirildi.

Yöntem: Bu çalışma, Aralık 2015-Mart 2016 tarihleri arasında KABG cerrahisi geçiren ve PİCCO® monitorizasyonu ile yönetilen 44 olgunun kayıtlarının retrospektif incelenmesi ile yapıldı. Hastaların demografik özellikleri (yaş, cinsiyet, kilo, boy, vücut kitle indeksi), Amerikan anestezi derneği fiziksel durumları, eşlik eden hastalıklar, ejeksiyon fraksiyonları, anestezi yönetimi, operasyon bilgileri, hemodinamik veriler, PİCCO® paremetreleri, ekstübasyon süreleri, kardiyovasküler cerrahi YBÜ kalış süreleri, vazoaktif ajan ve kan transfüzyonu gereksinimleri, mortalite ve morbidite durumları kaydedildi ve ölçülen PİCCO® parametreleri ile ekstübasyon ve YBÜ kalış süreleri arasındaki korelasyon değerlendirildi.

Bulgular: Postoperatif dönemde PİCCO® ile değerlendirilen kardiyak kontraktilite ve performansı gösteren parametrelerin anlamlı şekilde arttığı tespit edildi ($p<0,05$). PİCCO® parametreleri ile ekstübasyon ve YBÜ kalış süreleri arasında anlamlı korelasyon saptanmadı ($p>0,05$)

Sonuç: PICCO® kılavuzluğu ile yönettiğimiz koroner revaskülarizasyon olgularında, miyokardiyal kontraktilitenin ve kardiyak performansın iyileştiği, hastaların ekstübasyon ve yoğun bakım kalış sürelerinde beklenenin dışında bir uzama olmadığı gösterilmiş olup, kardiyak fonksiyon paremetreleri takip edilerek yönetilen hastalarda optimum volüm ve hemodinamik hedeflerin sağlanabileceğini düşünüyoruz.

Anahtar kelimeler: Koroner arter bypass cerrahisi, PİCCO®, kalp debisi ölçümü

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Introduction

The primary objective in anesthetic management of coronary artery bypass grafting (CABG) surgery is to maintain hemodynamic stability. It has been shown that rates of morbidity and mortality can be decreased in a CABG that is started with hemodynamic stability during induction of anesthesia and ended with stable parameters (1,2,3). It is possible to ensure and maintain hemodynamic stability through targeted treatment. There is strong evidence in Enhanced Recovery After Surgery protocols recommending targeted treatment in CABG (1). The objective in this approach is to ensure that the fluid, blood and vasoactive surgery required for sufficient tissue perfusion is done based on cardiac outflow and associated parameters (1,2).

For target treatment practices today, minimally invasive cardiac outflow monitoring systems (PiCCO®) are used, allowing for assessment of cardiac outflow and cardiac performance parameters based on the principle of transpulmonary thermodilution and pulse contour analysis system (2,3,4).

This retrospective study assessed the correlation between the changes in postoperative PiCCO® parameters and the PiCCO® parameters measured and extubation time and intensive care unit (ICU) length of stay in patients who underwent CABG surgery and were managed by monitorization of cardiac output and cardiac performance parameters with PiCCO®.

Material and Methods

This study was conducted by retrospective analysis of the records of 44 patients who underwent CABG surgery during December 2015-March 2016 and were managed through PiCCO® monitorization, having obtaining approval of the Ethics Board of Health Sciences University, İstanbul Bağcılar Training and Research Hospital (17.03.2016-2016/449).

Patients' preoperative demographic characteristics (age, sex, weight, height, body mass index) as seen from the records, American Society of Anesthesiologists physical conditions, comorbidities as established preoperatively (hypertension, Diabetes Mellitus, hyperlipidemia, previous myocardial infarction, respiratory diseases, cerebrovascular diseases), smoking, ejection fractions, anesthetic management, operative details, hemodynamic data measured, PiCCO® parameters, extubation times, cardiovascular surgery ICU lengths of stay, requirements for vasoactive agent and blood transfusion, mortality, and morbidity were evaluated.

Anesthetic Management

All patients were subjected to anesthetic assessments and submitted informed consent forms. The patients on the operating table underwent routine anesthetic monitorization followed by premedication with 0.5 mg/kg of midazolam (Dormicum®, Roche Ltd, Basel, Switzerland), after which invasive arterial pressure was monitored from the right/left radial artery under local anesthesia. Anesthesia was induced with 0.1 mg/kg^{-1} of midazolam, 5-7 µg/kg^{-1} of fentanyl (Fentanyl® Johnson & Johnson, New Brunswick, NJ, USA) and 0.1 mg/kg^{-1} of vecuronium bromide (Norcuron® Mustafa Nevzat Tıbbi Ürünler Trade Inc., Turkey) and maintained with 1-1.5% Sevoflurane (Sojourn®, Adeka İlaç ve Kimyasal Ürünler San. ve Trade Inc.), 50% O_2-air, and intermittent doses of fentanyl, midazolam, vecuronium and remifentanil (Ultiva®, Glaxo Smith Kline İlaçları San. ve Trade Inc.) 1-1.5 µgkg^{-1} min infusions. After orotracheal intubation, end-tidal CO_2, central venous pressure (CVP-from internal jugular vein), nasopharyngeal temperature and urine flow were monitored; and all patients received 0.3-0.5 µgkg^{-1} min of nitroglycerine infusion.

Five-French sheath was inserted in the femoral artery for cardiac output monitorization, and cardiac function parameters were measured by injecting 15 mL of normal saline at 8°C in the distal lumen of the central venous catheter. The measurements recorded were evaluated at 3 time points, which were immediately after induction of anesthesia (T1), at the end of cardiopulmonary bypass (CPB) (T2), and before transferring the patient to the ICU having closed the sternum (T3). Based on PiCCO® measurements, colloid boluses were administered when volume was needed and vasoactive treatment was performed when necessary. The hemodynamic parameters [heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP)] recorded at the same time points and arterial blood gas analyses were also evaluated. The parameters measured with PiCCO® and the values considered to be the normal range are given in Table 1.

Surgical Management

All patients underwent conventional CABG, and membrane oxygenator (Dideco, Italy) was used for CPB. The pump was primed with 1,000 mL of normal saline, 200 mL of Ringer Lactate, 100 mL of 20% Mannitol, 30 mEq of Sodium Bicarbonate, and 10,000 iu heparin. Moderate systemic

hypothermia (30-32°C), mean blood pressure of 50-70 mmHg and $PaCO_2$ of 30-40 mmHg was maintained with through non-pulsatile flow of 2.0-2.4 L $min^{-1}m^{-2}$ and with by applying alpha-stat strategy for acid-base balance. Myocardial protection was attained with intermittent antegrade or retrograde cold blood cardioplegia or both.

Statistical Analysis

Number Cruncher Statistical System 2007 Statistical Software (Utah, USA) package program was used for statistical analyses. When evaluating the data, in addition to descriptive statistical methods (mean, standard deviation), we used repeated measures analysis of variance for multiple groups, Newman-Keuls multiple comparison test to compare subgroups, independent t-test to compare two groups, and Pearson's correlation test among the variables. The results were evaluated according to significance level of $p<0.05$.

Results

Four patients were excluded from this retrospective study due to missing information on the records kept. Demographic characteristics of the 40 patients evaluated are given in Table 2.

All patients underwent isolated CABG under cardiopulmonary perfusion, and no intra-operative complications were experienced. Whereas 12 patients with hematocrit level of 20-25% and hemoglobin of 7-8 gr/dL required erythrocyte transfusion, no patient required vasoactive agent administration. The operative details of the patients are given in Table 3.

Based on the patients' PiCCO® data recorded at the 3 time points, whereas the mean values of the parameters such as CVP associated with the volume status and right ventricular performance, and CO, CI, Cardiac Function Index (CFI), and global ejection fraction (GEF) indicating cardiac performance and sufficiency were found to be statistically significantly higher at the end of CPB (T2) and before transferring the patient to the ICU having closed the sternum (T3) when compared to immediately after induction of anesthesia (T1) ($p=0.0001$), no significant difference was found between the time points T2 and T3. While no significant difference was revealed by the measurements of the dP_{max}, which is another parameter associated with cardiac contractility and systolic pressure increase, the dP_{max} was found to be higher at the time points T2 and T3 than at T1 (Table 4).

Table 1. Parameters measured and evaluated

CO	3-5 L/min/m^2
CI	3-5 L/min/m^2
CFI	4.5-6.5 L/min
GEF	25-35%
GEDI	680-800 mL/m^2
GEDV	-
EVLW	3-7 mL/kg
EVLWI	-
PVPI	1-3
SVR	1700-2400/dyncm/ H_2O
SVRI	-
SVV	<10%
PPV	<10%
dP_{max}	-

CO: Cardiac output, CI: Cardiac index, CFI: Cardiac function index, GEF: Global ejection fraction, GEDI: Global end-diastolic index, GEDV: Global end-diastolic volüme, EVLW: Extravascular lung water, EVLWI: Extravascular lung water index, PVPI: Pulmonary vascular permeability index, SVR: Systemic vascular resistance, SVRI: Systemic vascular resistance index, SVV: Stroke volume variation, PPV: Pulse pressure variation, dP_{max}: Systolic pressure increase

Table 2. Demographic characteristics and comorbidities of the patients

Parameters	Number of patients n=40 (%)	Mean ± SD (minimum-maximum)
Gender		
Male	30 (75%)	-
Female	10 (25%)	-
Age (year)	-	58.73±10.62 (33-79)
Height (cm)	-	166.9±8.54 (145-183)
Weight (kg)	-	73.85±10.17 (56-96)
BMI (kg/m^2)	-	26.48±3.01 (20.2-33.3)
EF%	-	57.5±5.32 (36-62)
ASA		
II	30 (75%)	-
III	10 (25%)	-
NYHA III	40 (100%)	-
CANADA II	40 (100%)	-
HT	25 (62.5%)	-
COPD	1 (2.5%)	-
DM	23 (57.5%)	-
Stent	7 (17.5%)	-
MI	17 (42.5%)	-
Hypercholesterolemia	15 (37.5%)	-
Smoking	19 (47.5%)	-

EF: Ejection fraction, ASA: American Society of Anesthesiologists, NYHA: New York Heart Association, CANADA: Canadian Cardiovascular Society Grading for Angina Pectoris, HT: Hypertension, COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, MI: Myocardial infraction, BMI: Body mass index, SD: Standard deviation

While Systemic vascular resistance (SVR) and Systemic vascular resistance index (SVRI) associated with afterload were found to be significantly high at the time point T1 compared to T2 and T3 (p=0.0001), no significant difference was found between the time points T2 and T3 (Table 4).

Table 3. Operative details

Parameters	Number of patients n=40 (%)	Mean ± SD (minimum-maximum)
Aortic cross clamp time (min)	-	54.3±18.16 (19-96)
Total pump time (min)	-	94.13±27.45 (40-155)
Pump crystalloid (mL)	-	1,450±349.36 (700-2,000)
Pump colloid (mL)	-	405.56±128.56 (150-500)
Anesthesia crystalloid (mL)	-	1,130±475.82 (400-1,500)
Anesthesia colloid (mL)	-	662.5±237.17 (500-1,000)
Preoperative total fluid (mL)	-	3,265±631.97 (2,400-4,600)
Diuresis (mL)	-	941.75±191.35 (500-1,340)
Pump balance (mL)	-	+723.5±288.49 (140-1,500)
Total balance (mL)	-	+1,255.25±411.87 (400-1,950)
Blood products used		
Erythrocyte suspension	12 (30%)	-
Fresh frozen plasma	0	-
Whole blood/unit	0	-

SD: Standard deviation

No significant difference was found at any of the time points in the measurements of GEDV and GEDI associated with the end-diastolic volume status (p=0.07, p=0.124), and the values measured were within the normal range. Stroke volume variation (SVV) and pulse pressure variation (PPV) values also associated with the volume status was found to be significantly lower at the time point T1 than T2 and T3 (p=0.0001) (Table 4).

Whereas no significant difference was found in all measurements of Extravascular Lung Water Index and extravascular lung water (EVLW) associated with pulmonary edema (p=0.990, p=0.438), pulmonary vascular permeability index (PVPI) measurements indicating pulmonary vascular permeability were within normal range but significantly higher at T2 and T3 than at T1 (p=0.002).

Whereas the other hemodynamic parameters monitored (SAP, DAP and MAP) were found to be significantly higher when measured at the time point T1 compared to T2 and T3, the HR value was found to be lower (Table 5). However, all the values measured were within the normal range.

The hemoglobin and hematocrit levels monitored via arterial blood gas were found to be significantly lower at T2 when compared to time points T1 and T3. No significant difference was observed in the lactate levels in any of the three time points, but an increase was observed at the time points T2 and T3 (Table 5).

Table 4. PiCCO® parameters measured at three time points

Parameters	T1	T2	T3	p*
CO	3.47±0.73*	4.3±1.28	4.37±1.1	**0.0001**
CI	1.9±0.4*	2.37±0.69	2.41±0.57	**0.0001**
CFI	3.56±0.95*	4.22±1.12	4.35±1	**0.0001**
GEF	20.93±3.77*	23.98±4.85	25.13±5.32	**0.0001**
CVP	8.63±3.72*	9.33±3.32	10.53±3.61	**0.0001**
dP_{max}	730.53±413.51	777.6±390.93	789.43±381.5	0.203
SVR	1640.98±608.19*	1220.23±390.09	1235.23±489.33	**0.0001**
SVRI	2965.08±1087.3*	2219.75±681.27	2243.45±850.24	**0.0001**
GEDI	593.7±121.55	545.78±135.71	578±186.6	0.124
GEDV	1053.75±233.87	969.55±222.9	1015.33±239.29	0.07
PVPI	2.25±0.83*	2.57±0.86	2.63±0.83	**0.002**
ELWI	7.75±2.18	7.77±1.61	7.73±2.1	0.990
EVLW	555.43±196.43	548.28±130.83	529±146.01	0.438
PPV	8.63±2.46*	11.08±3.9	11.8±4.69	**0.0001**
SVV	12.05±4.83*	13.8±4.27	15.1±4.77	**0.0001**

CO: Cardiac output, CI: Cardiac index, CFI: Cardiac function index, GEF: Global ejection fraction, GEDI: Global end-diastolic index, GEDV: Global end-diastolic volume, EVLW: Extravascular lung water, EVLWI: Extravascular lung water index, PVPI: Pulmonary vascular permeability index, SVR: Systemic vascular resistance, SVRI: Systemic vascular resistance index, SVV: Stroke volume variation, PPV: Pulse pressure variation, dP_{max}: Systolic pressure increase, CVP: Cardioventricular pacing

While the mean extubation time of patients was found to be 9.6±3.57 (0-21) hours and their mean ICU length of stay was found to be 4±5.86 (2-39) days in the postoperative period, no significant relationship was seen having examined the correlation between the PiCCO® parameters measured, the extubation times and the ICU lengths of stay.

In the postoperative period, we detected morbidities such as pleural effusion in two (5%), pericardial effusion in one (2.5%), pneumonia in one (2.5%), pneumothorax in one (2.5%), bleeding revision in one (2.5%), acute renal failure in one (2.5), and delirium in two (5%) out of 40 patients, as well as mortality in one (2.5%) patient due to multiorgan dysfunction.

Discussion

In cardiac surgery, postoperative sufficient cardiac outflow and performance are targeted. Thus, it is necessary to ensure optimal fluid balance and support the patient with vasoactive treatment when needed. Adverse events include hypovolemia and hypervolemia. However, increased vascular permeability due to non-pulsatile flow and systemic inflammatory response syndrome associated with CPB, decreased sensitivity of certain parameters used to evaluate the volume status such as CVP and pulmonary capillary wedge pressure complicate the management of fluid and vasoactive treatment (5,6). In such cases, there is a fine line between low cardiac output status associated with hypovolemia and diffuse tissue edema due to fluid load. A targeted treatment approach adopted for hemodynamic management provides for optimal use of intravenous fluids and vasoactive support, allowing for optimization of cardiac output and improving postoperative survival (5,6,7).

In a study of hemodynamic management performed with target values of GEDV> 640 mL/m^2, CI> 2.5 mL/min/m^2 and MAP >70 mmHg and based on clinic evaluation criteria in coronary artery surgery patients whose cardiac outflows were measured, it was shown that larger amounts of colloid infusion were administered in the targeted treatment group to attain optimum values, but lower doses and shorter times of inotropic support were required and the mechanical ventilation time and ICU length of stay were shortened (8). In our study, optimal interventions were made targeting optimal values of cardiac volume, contractility and performance indicators such as CVP, GEDV, GEDI, CO, CI, CFI, GEF, and dP_{max} in 40 patients who were monitored only via PiCCO®. It was found out that there was no significant difference in the values of GEDI and GEDV that indicate end-diastolic cardiac volume and volume status across the three measurement time points, and the patients received 662.5±237.17 mL of colloid infusion after CPB for volume support. Cardiac performance parameters such as CO, CI, CFI, GEF and dP_{max} were found to be significantly higher after coronary revascularization (T2 and T3) than before the operation (T1) (Table 4). As such, it could be considered that optimum volume status was achieved and the patients benefited from the coronary revascularization. In addition, good preoperative ventricular function of the patients (ejection fraction 57.5±5.32%) included in our study is an important factor that has an effect on ensuring good postoperative myocardial contractility parameters.

The key parameters to take into consideration when administering volume infusion for sufficient cardiac outflow are EVLW and PVPI. Increased EVLW and PVPI are associated with edema and also known as predictors of mortality (9). EVLW values are important in terms of guiding fluid treatment, providing highly valuable information on preload and lung water. In our study, it was observed that there was no statistically significant difference between the EWLI and EVLW values recorded at the three measurement time points and the values were close to the physiological range. PVPI, which is considered to have an important role when determining the direction to pulmonary edema that indicates pulmonary vascular

Table 5. Hemodynamic data, Hct, Hb and lactate values measured at three time points

Parameters	T1	T2	T3	p
HR	69.85±14.67*	80.13±16.42	81.7±16.37	**0.0001**
SAP	106.78±23.12*	97.4±15.78	99.43±14	**0.008**
DAP	61.65±14.49*	54.85±10.26	56.78±12.71	**0.002**
MAP	77.48±17.68*	69.05±11.04	70.83±13.49	**0.002**
Hct	33.95±4.25	25.78±3.39*	28.55±2.36	**0.0001**
Hb	11.36±1.51	8.51±1.15*	9.47±0.88	**0.0001**
Lactate	1.34±0.57	1.49±0.53	1.6±0.53	0.055

HR: Heart rate, SAP: Systolic arterial pressure, DAP: Diastolic arterial pressure, MAP: Mean arterial pressure, Hct: Hematocrit, Hb: Hemoglobin

permeability, was found to be within the normal range at the time points T2 and T3 but was higher than at T1. It could be considered that such increase was due to the increased vascular permeability as a result of systemic inflammatory response that occurred due to extracorporeal circulation (Table 4). In the fluid infusion management performed by monitoring cardiac function parameters via PiCCO® monitorization, significantly increased values of CO, CFI and GEF compared to preoperative values, in spite of GEDI being a little bit below the normal range, allowed for maintaining MAP at 70 mmg, which is of importance to supplying the heart, and stable hemodynamic conditions were attained by preventing increased EWLW and PVPI that might result in respiratory complications. Furthermore, the lactate concentration, which is considered as an indicator of hypoperfusion, staying below the value of 2 mmol/L throughout the operation and at the end of the operation might indicate that sufficient tissue perfusion was achieved (Table 5).

Inotropic and vasopressor therapy used to improve cardiac functions in cardiovascular surgery are emphasized as the cornerstone of hemodynamic therapy. However, it was shown to increase myocardial oxygen consumption, cause arrythmias and disrupt microcirculation (10,11,12). It is certainly inevitable to use it in case of left ventricular dysfunction and low cardiac output. In our study, inotropic or vasopressor support was not needed as sufficient cardiac function and hemodynamic parameters were achieved.

In our study, the SVR and SVRI values indicating the postoperative vasomotor tonus were found to be significantly lower than preoperative values but within the normal range. It could be considered that such decrease might be attributable to vasodilating effect of anesthesia, infusion of nitroglycerin at 0.3-0.5 µgr/kg/min throughout the clinical routine operation and extracorporeal circulation that result in vasodilatation by activating the systemic inflammatory response. In addition, vasopressor support was not considered since elevated SVR and SVRI values that result in decreased CO by increasing the afterload are an adverse event.

Conventional monitoring parameters SAP, DAP, MAP and HR values were found to be significantly low at the end of the operation and CVP value was found to be high. However, no intervention was made since hemodynamic stability was maintained with such values (Table 5).

In our study, when we analyzed the SVV and PPV values, which are dynamic measurement parameters recently used to evaluate the intravascular volume response in particularly non-cardiac surgeries, we found that the postoperative values were significantly higher than the preoperative values and the targeted normal ranges could not be provided.

However, we believe this increase that reflects a deficit of volume does not affect the hemodynamic parameters as it is minimal. Furthermore, a study conducted by using the PPV target values as a basis in cardiac surgery reported that volume application based on PPV values did not affect the patient results, could be highly limited in improving the results, and transient thermal changes associated with CPB might result in abnormal arterial pressure gradients, decreasing the reliability of PPV and SVV values (13,14).

Several studies showed that targeted fluid and vasoactive therapy protocols conducted on the basis of minimally invasive monitorization shortened the mechanical ventilation time and hospital and ICU lengths of stay as compared to patients managed on the basis of conventional monitoring parameters (15,16,17,18).

In our study, a control group was not created to compare treatment protocols. Evaluation of cardiac function parameters of the patients measured with PiCCO® at three time points, extubation times and ICU lengths of stay did not reveal a statistical relationship. However, there was no increase beyond what was anticipated in the extubation time and ICU lengths of stay of the patients.

During the ICU monitoring, we detected mortality due to multiorgan dysfunction in one out of 40 patients, and morbidity due to pleural effusion in two patients, pericardial effusion in one patient, acute renal failure in one patient, and bleeding revision in patient. As our study evaluated a small homogenous group of patients and lacked a control group, although it is not possible to make a definitive comment on the causes of the mortality and morbidities developed, these are complications that might be anticipated after a cardiovascular surgery.

Conclusion

Intraoperative and postoperative hemodynamic disorders attributable to complex causes in cardiac surgeries render hemodynamic management difficult. Minimally invasive methods that allow for immediate and close monitorization of cardiac function parameters in hemodynamic management and targeted therapy practices are recommended for better patient results. Although it had a limitation, worked on a small number of patients

and lacked a control group, our study on the coronary revascularization patients managed with the guidance of PiCCO® measurement parameters showed improved myocardial contractility and cardiac performance and no increase beyond what was anticipated in the extubation time and ICU lengths of stay of the patients. Therefore, we believe optimum volume and hemodynamic targets can be achieved in the patients managed through monitorization of cardiac function parameters.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from the Ethics Board of Health Sciences University, İstanbul Bağcılar Training and Research Hospital (17.03.2016-2016/449).

Informed Consent: All patients were subjected to anesthetic assessments and submitted informed consent forms.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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ORIGINAL RESEARCH

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Comparison of Vitamin D Levels in Allergic Patients with and Without Asthma

Astım Tanısı Olan ve Olmayan Allerjik Hastalarda Vitamin D Seviyelerinin Karşılaştırılması

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Abstract

Objective: To determine whether serum vitamin D levels had a relationship with pulmonary function test (PFT) results and serum immunoglobulin E (IgE) levels in allergic patients with and without asthma.

Method: The study group was comprised of patients who had positive allergy skin tests with and without asthma (n=31, n=28, respectively) and healthy controls (n=31). The skin allergy test (prick test) and PFT were performed on all of the study groups. Also, the patients' serum vitamin D and IgE levels were determined. Comparisons among these groups and also subgroups of the patients were investigated in addition to correlation analyses for vitamin D, IgE and PFT results.

Results: Seventy percent of the asthma group was found to have abnormal PFT results, while all healthy controls and non-asthmatic patients had normal PFT results (p<0.001). IgE levels were significantly higher in asthma and non-asthma groups compared to the control group (p=0.024). Asthma and non-asthma groups were similar regarding the frequency of multiple allergic factors (p=1.000). In terms of vitamin D levels, the asthma group and the non-asthma group were similar, while the healthy control group was found to have a significantly higher mean vitamin D level than both groups.

Conclusion: The results of our study indicate that vitamin D levels are lowered in patients with allergies; however, no association with asthma was determined. Additionally, we found no correlations between vitamin D, IgE and PFT results. The literature on this topic is highly conflicted and there is a requirement for future studies that evaluate vitamin D levels according to covariates.

Keywords: Vitamin D, asthma, allergy

Öz

Amaç: Astım tanısı olan ve olmayan alerjik hastalarda D vitamini düzeylerinin solunum fonksiyon testi (SFT) sonuçları ve serum immünoglobulin E (IgE) düzeyleri ile ilişkisinin belirlenmesi amaçlandı.

Yöntem: Çalışma grubu, alerjik cilt testi pozitif olan astımı olan ve olmayan hastalardan (sırasıyla n=31, n=28) ve sağlıklı kontrollerden (n=31) oluşuyordu. Tüm çalışma grubuna cilt alerji testi (prick testi) ve SFT uygulandı. Ayrıca, hastaların serum vitamin D ve IgE seviyeleri belirlendi. Vitamin D, IgE ve SFT sonuçları arasındaki korelasyon analizlerine ek olarak bu gruplar ve hasta alt grupları arasında karşılaştırmalar yapıldı.

Bulgular: Astım grubunun %70'inde anormal SFT sonuçları saptanırken, tüm sağlıklı kontroller ve astımlı olmayan hastalar normal SFT sonuçlarına sahipti (p<0,001). IgE düzeyleri astım ve astım olmayan gruplarda kontrol grubuna göre anlamlı derecede yüksekti (p=0,024). Astım ve astım olmayan gruplar, çoklu alerjik faktörlerin sıklığı açısından benzerdi (p=1,000). Vitamin D düzeyleri açısından, astım grubu ve astım olmayan grup benzerdi, sağlıklı kontrol grubunun her iki gruptan anlamlı seviyede yüksek ortalama vitamin D seviyesine sahip olduğu bulundu.

Sonuç: Çalışmamızın sonuçları alerjisi olan hastalarda vitamin D seviyelerinin düştüğünü göstermektedir; ancak, astım ile ilişki tespit edilememiştir. Ek olarak, vitamin D, IgE ve SFT sonuçları arasında korelasyon saptanamamıştır. Bu konuyla ilgili literatür oldukça çelişkilidir ve vitamin D seviyelerini karıştırıcı faktölere göre değerlendiren daha ileri çalışmalara ihtiyaç vardır.

Anahtar kelimeler: D vitamini, astım, allerji

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Introduction

Asthma is a respiratory condition which manifests with episodes of spasms in the bronchi. It is a rather complex disease which originates from a variety of genetic changes and has been associated with various environmental triggers; including allergens, microorganisms and irritants (1). In recent years, the prevalence of asthma has been increasing in parallel with the increase in atopic sensitization, in developed and developing countries alike (2).

Many cell types have been associated with asthma pathogenesis and asthma attacks (3) and some relatively recent studies have associated vitamin D levels with asthma incidence and allergic rhinitis (4,5). Indeed, Vitamin D has some properties which can be associated with the immune system, such as regulation of T-cells, production of cytokines, and decrease in the production of IgE (6,7). Furthermore, some studies have shown that lower 25(OH)D levels are associated with various characteristics of the condition, including worsened disease control, attack frequency and respiratory function in terms of clinical findings; and elevation of inflammatory parameters and decrease in T-cell ratio (Th1/Th2) in terms of laboratory findings (8,9,10,11,12). Vitamin D has been shown to promote the production of the anti-inflammatory cytokine, IL-10; while its biologically active form [1.25(OH)D] is suggested to have anti-inflammatory properties in various tissues, including the lung (11,13). Vitamin D receptors have also been found to be abundant in the epithelium and smooth muscle of the respiratory system (14).

Therefore, Vitamin D levels may have an important role in the respiratory system and the body's allergic response. However, to date there has been no definite association between asthma and parameters of pulmonary function and allergy; largely due to differences in disease mechanism and the allergy levels of patients. To address this problem, we comprised our study group from patients who were confirmed to have allergies by prick test. Our aim was to determine the relationship between serum vitamin D levels and the results of pulmonary function test (PFT) and serum immunoglobulin E (IgE) levels in allergic patients with and without asthma, and to compare results with healthy controls.

Material and Methods

A total of 59 patients who had positive allergy skin tests in our clinic from December 2017 to February 2018, and 31 healthy controls were included in the study. The lowest number of individuals required to complete the study with 95% confidence level (alpha=0.05) and 90% power (beta=0.10) was calculated as 48 for each group. One patient group was comprised of those who were positive for both allergy skin test and asthma [asthma group, n=31 (52.5%)], while the other patient group was comprised of patients who were positive for allergy skin test but did not have asthma [non-asthma group, n=28 (47.5%)]. The control group was comprised of 31 healthy individuals.

The criteria for patient inclusion were as follows: 1) being aged between 18-50, 2) having a medical history and physical examination compatible with allergy, 3) having a positive allergy skin test result, and–for those who were included in the asthma group–having stable asthma without any attacks in the prior month. Exclusion criteria were as follows: 1) Acute or chronic respiratory disease, 2) gestation, 3) having any type of autoimmune disease, 4) having any type of oncologic disease. The control group was comprised of health volunteers.

Patients who accepted to participate the study were included in the study after they completed the questionnaire in full. Ethical approval was obtained from the local Clinical Research Ethical Committee (approval no: 25.12.2017/052). All steps of the study complied with the Helsinki Declaration.

Measurements

1-The skin allergy test (prick test) contained the most common allergens such as house dust, mushrooms and pollens. The negative control solution was serum physiologic and the positive control solution was histamine (Albio skin prick test). The application was made on the inside of the forearm and was interpreted after 20 minutes of waiting. A wheal larger than 3 millimeters in diameter was accepted to show a positive result. Patients were told not to use antihistamines and paracetamol during the 10 days before the test.

2-Pulmonary function test was performed with spirometry (Custo Med, Germany) and the patient was told not to use short-acting beta two agonist medications 8 hours before the test. The measurement was performed by closing the nose with the nasal plug while the patient was in the sitting position. Forced expiratory volume (FEV1) and forced vital capacity (FVC) were measured, from which the FEV1/FVC ratio was calculated.

3-Serum Vitamin D concentrations were measured by ELISA (Enzyme-linked Immunosorbent Assay). It was noted that

the patients had not received vitamin D supplementation in the past year. A result between 30-150 ng/mL was considered normal, 10-30 ng/mL was considered to show insufficiency, and 0-10 ng/mL was defined as deficiency (DIA source 25OH Vitamin D Total Elisa kit lowain-L NEUVE).

4-Serum IgE level was measured by ELISA (Bio-Clin-Inc., USA).

Statistical Analysis

All analyses were performed on SPSS version 21. For the normality check of continuous variables, the Shapiro-Wilk test was used. Data were given as mean ± standard deviation for normally distributed data and median (minimum-maximum) for non-normally distributed data. Categorical variables were given as frequency (percentage). The independent samples t-test and the Mann-Whitney U test were used to compare continuous variables in regard to normality of distribution. Categorical variables were evaluated by the chi-square test with continuity correction. For continuous variables, either the Pearson or the Spearman Correlation Coefficients were calculated according to normality of distribution. Comparison of Vitamin D levels were made by using the Analysis of Covariances (ANCOVA) with age as a covariate because of significant correlation between age and Vitamin D levels. For continuous variables, either the Pearson or the Spearman correlation coefficients were calculated according to normality of distribution. We created subgroups for patients and controls regarding the presence of single or multiple allergic factors and comparison of our subgroups were made by two-way Analysis of Variances (ANOVA). P≤ 0.05 values were accepted as statistically significant.

Results

We included 90 individuals into our study, mean age was 33.51±15.92. Mean age was significantly higher in the healthy group than in the other groups (p<0.001) and male frequency was significantly lower in the healthy group than in the other groups (p=0.048). Seventy percent of the patients with asthma were found to have abnormal PFT results while all individuals in the other groups had normal PFT results (p<0.001). IgE levels were significantly higher in the healthy group than in the other groups (p<0.001). We also evaluated a number of allergic factors and found that there were no significant differences between allergic patients with asthma and without asthma regarding the frequency of single factor or multiple factor allergies (p=1.000).

Vitamin D levels were significantly higher in the females (p=0.027; 21.87±13.57 vs 16.54±8.75) and also individuals with normal PFT results (p=0.002; 21.13±12.31 vs 13.90±7.53). There was a significant negative correlation between IgE and Vitamin D levels (r=-0.286; p=0.007) and a significant positive correlation between age and Vitamin D levels (r=0.488; p=0.001). Due to significant differences between our groups regarding age and gender, we used covariance analysis to compare Vitamin D levels (Table 1).

Table 1. Summary of our variables and analysis results between our groups

	Allergic with asthma (n=31)	Allergic without asthma (n=28)	Healthy individuals (n=31)	p
Age	32.19±14.06[a]	25.86±15.15[a]	41.74±14.86[b]	<0.001
Gender				
Male	17 (54.8%)[a]	14 (50.0%)[a]	8 (25.8%)[b]	0.048
Female	14 (45.2%)[a]	14 (50.0%)[a]	23 (74.2%)[b]	
Allergic factor				
Absent	0 (0.0%)[a]	0 (0.0%)[a]	31 (100.0%)[b]	
Single	23 (74.2%)[a]	20 (71.4%)[a]	0 (0.0%)[b]	<0.001
Multiple	8 (25.8%)[a]	8 (28.6%)[a]	0 (0.0%)[b]	
PFT				
Normal	9 (30.0%)[a]	27 (100.0%)[b]	31 (100.0%)[b]	<0.001
Abnormal	21 (70.0%)[a]	0 (0.0%)[b]	0 (0.0%)[b]	
Ig E	130.5 (18.0-2477.0)[a]	87.5 (23.0-323.0)[a]	21.0 (5.0-40.0)[b]	<0.001
Vitamin D	14.60±8.52[a]	12.40±6.1[a]	30.98±10.47[b]	<0.001[(1)]

Ig E: Immunoglobulin E, PFT: Pulmonary function test

Same letters denote lack of significant difference between groups

[(1)]p value calculated by using Analysis of Covariances with age correction

The analysis showed that age was a significant covariate (p=0.002) while gender was non-significant (p=0.438). After Vitamin D levels were corrected according to age, we found that levels were higher in the healthy group compared to the other groups (p<0.001).

Finally, groups were also compared in subgroups according to the number of allergic factors (single vs multiple). No significant differences were observed between these subgroups (p=0.927).

Discussion

In this study we compared vitamin D levels with IgE and PFT results in allergic patients with and without asthma and healthy controls. We did not find a significant difference in terms of vitamin D levels between the asthma and non-asthma groups after adjusting for age. A study comparing asthmatic patients with healthy volunteers reported that asthmatic patients had lower levels of vitamin D levels than healthy volunteers, but no difference between patients with allergic and nonallergic asthma were determined (5). A large collaborative study by the Childhood Asthma Management Program Research Group found that, asthmatic patients with vitamin D level lower than 30 ng/mL (adjusted for various factors) were at higher risk for hospitalization or emergency department visit (Odds ratio, 1.5; 95% CI, 1.1-1.9; p=0.01) (15). In another study, those with vitamin D levels lower than 20 ng/mL were found to be 50% more likely to have asthma compared to those with a vitamin D level between 20-30 ng/mL (16). Shahin et al. (9) defined vitamin D sufficiency as >25 ng/mL and reported lower vitamin D in asthmatic patients compared to healthy controls (19.88±9.6 ng/mL vs 33.5±6.1 ng/mL). In comparison, the whole of our study group showed significantly lower levels than their patients. While our controls had higher vitamin D levels than allergic patients, compared to other studies, overall vitamin D levels were significantly lower in our study group. There may be various explanations for this, including differences in measurement method, race, and location; each of which may be the cause for remarkably low vitamin D levels in the whole of our study group.

The role of IgE in the pathogenesis of allergic diseases is well established. Despite the fact that the patient groups displayed similar allergic characteristics, mean IgE level in the asthma group was significantly higher than that of the control group. However, no correlations were found between IgE and vitamin D levels. In a study comparing allergic and nonallergic asthmatics, IgE levels were reported to be higher in allergic asthmatics and there was also no correlation between IgE level and vitamin D concentration. In the same study, patients with asthma were divided into three groups (hypersensitivity to one inhaled allergen, to more than one inhaled allergen, and to mixed allergens). After evaluation of the comparisons between these groups, the authors of the study suggested that vitamin D insufficiency could be an important part of asthma pathogenesis in patients with hypersensitivity to more than one inhaled allergen (5). We also divided our patients into subgroups according to the presence of single or multiple allergic factors. However, we found no significant difference between single factor and multiple factor groups in the current study. Recent studies have presented controversial data on the correlation between vitamin D and total IgE, some authors suggest that there is no link, while others put forth various associations (5,17,18,19,20). Further studies are needed to clarify this hypothesis.

In the current study, patients were divided into two groups based on PFT result (normal and abnormal PFT). All patients with abnormal PFT were from the asthma group (allergic asthmatic patients). In other words, there was a strong relationship between allergic asthma and abnormal PFT. However, no statistically significant association was found between vitamin D levels and PFT. Tolppanen et al. (21) found a significant association between FEV1 and 25(OH) D2 but no significant correlation between lung function and 25(OH)D3. In another study, it was reported that there was no correlation between vitamin D levels and lung function (5). There are also studies which report contrasting findings; Shahin et al. (9) reported that they found a positive correlation between 25(OH)D level and FEV1% in asthmatic patients. Similarly, Damera et al. (22) reported that higher serum 25(OH)D concentrations in asthmatic patients were associated with higher FEV1%. They suggested that the inhibition of matrix metalloproteinase formation and fibroblast proliferation by vitamin D (which effects collagen synthesis) may be the underlying cause of this association. They also explained that the tissue remodeling effects of 1.25(OH) vitamin D may have significant influence on lung function.

Study Limitations

There are some limitations in our study. Firstly, our study was single-centered, which can be considered as a limitation. Secondly, the observed low levels of vitamin D in all of our participants may be associated with poor health and nutritional or lifestyle factors in general. Apart from some lifestyle factors, other factors which may have

had an effect on vitamin D levels were not considered in the current study.

Conclusion

The results of our study indicate that vitamin D levels are lowered in patients with allergies; however, there was no difference regarding vitamin D levels between allergic patients with and without asthma. Also, there were no correlations between IgE levels and the results of PFT and vitamin D. We also evaluated whether there were any differences between patients in regard to the number of allergic factors (single vs multiple); however, we found no significant differences. Further studies are required to determine whether vitamin D and IgE levels are effective on the pathophysiologic characteristics of asthma.

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Ethics

Ethics Committee Approval: Ethical approval was obtained from the local Clinical Research Ethical Committee (approval no: 25.12.2017/052).

Informed Consent: Patients who accepted to participate the study were included in the study after they completed the questionnaire in full.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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ORIGINAL RESEARCH

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Mean Platelet Volume Values and Its Effects on Prognosis in Patients with Acute Ischemic Stroke

Akut İskemik İnme Geçiren Hastalarda Ortalama Trombosit Hacmi Değerleri ve Prognoza Etkileri

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Abstract

Objective: Stroke is a rapid onset of focal or global loss of cerebral function and is the most common cause of mortality and morbidity in adulthood cancer and heart disease patients. Although it has been reported that mean platelet volume (MPV) values may be an independent risk factor for the severity and prognosis of stroke, the results of previous studies are inconsistent. The aim of the present study was to determine the MPV values of ischemic stroke patients which reflects the activity and function of platelets and to observe its effect on clinical outcomes.

Method: Sixty-two acute ischemic stroke patients were recruited for the study. Clinical information, MPV, platelet, white blood cell (WBC) and neutrophil, CRP and troponin-T levels were obtained.

Results: The mean ± standard deviation age was 72.4±12.6 years. At the end of the study, 28 patients were discharged and 34 patients passed away. The frequency of bilateral stroke was higher in deceased patients (p=0.005). In addition, platelet counts were significantly higher in discharged patients (p=0.016). At first admission, MPV values were 10.59±1.01 fL in discharged patients and 11.29±1.12 fL in deceased patients (p=0.029). At the end of the study, MPV values were measured as 11.46±1.28 fL in deceased patient sand 10.47±0.74 fL in discharged patients (p<0.001). WBC and neutrophil counts, troponin-T and CRP values were not significantly different between deceased and discharged patients (p>0.05).

Conclusion: Our study indicated that MPV and platelet levels may be associated with mortality in acute ischemic stroke patients and can be used as prognostic markers.

Keywords: Stroke, cerebrovascular diseases, MPV, platelet, prognosis

Öz

Amaç: İnme, ani başlangıçlı, fokal veya global serebral fonksiyon kaybıdır ve yetişkin çağ kanserleri ve kalp hastalıklarından sonra en sık mortalite ve morbidite nedenidir. Ortalama trombosit hacmi (MPV) değerlerinin inmenin şiddeti ve prognozu için bağımsız bir risk faktörü olabileceği bildirilmiş olmasına rağmen, önceki çalışmaların sonuçları tutarsızdır. Bu çalışmanın amacı, iskemik inme hastalarında trombositlerin aktivitesini ve fonksiyonunu yansıtan MPV değerlerini belirlemek ve bunun klinik sonuçlar üzerindeki etkisini gözlemlemektir.

Yöntem: Altmış iki akut iskemik inme hastası çalışmaya alındı. Klinik bilgi, MPV, trombosit, beyaz kan hücresi (WBC) ve nötrofil, C-reaktif protein (CRP) ve troponin-T düzeyleri elde edildi.

Bulgular: Ortalama yaş 72,4±12,6 idi. Çalışmanın sonunda 28 hasta taburcu edildi ve 34 hasta eksitus oldu. Bilateral inme sıklığı ölen hastalarda daha yüksekti (p=0,005). Ayrıca taburcu edilen hastalarda trombosit sayısı anlamlı derecede yüksek bulundu (p=0,016). İlk başvuruda, MPV değerleri taburcu olan hastalarda 10,59±1,01 fL ve ölen hastalarda 11,29±1,12 fL idi (p=0,029). Çalışmanın sonunda ölen hasta gurubunda MPV değerleri 11,46±1,28 fL, taburcu olmuş hastalarda 10,47±0,74 fL olarak ölçülmüştür (p<0,001). WBC ve nötrofil sayısı, troponin-T ve CRP değerleri ölen ve taburcu olan hastalar arasında anlamlı farklılık göstermedi (p>0,05).

Sonuç: Çalışmamız MPV ve trombosit seviyelerinin akut iskemik inme hastalarında mortalite ile ilişkili olabileceğini ve prognostik belirteçler olarak kullanılabileceğini göstermiştir.

Anahtar kelimeler: İnme, serebrovasküler hastalıklar, MPV, trombosit, prognoz

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Introduction

Stroke is a rapid onset of focal or global loss of cerebral function and is the most common cause of mortality and morbidity in adulthood following cancer and heart disease patients (1). The prognosis of stroke varies from complete recovery in a couple of days to death. The incidence and mortality rate of stroke increases with age. The annual incidence of stroke was found to be 1.7-3.6/1000 in people aged between 55-64 years, 4.9-8.9/1000 in people aged between 65-74 years and 13.5-17.9/1000 in people over the age of 75 (2). With an aging population, stroke becomes a leading health problem in Turkey. Stroke is expected to increase exponentially in the coming years due to the progressive aging of population and also increasing prevalence of risk factors for stroke such as hypertension, diabetes, and obesity. Better understanding the effects of stroke-related risk factors on mortality and morbidity may help us to determine diagnosis, treatment, and prognosis of stroke.

Stroke is divided into two categories as ischemic and hemorrhagic. In a previous study conducted in Turkey, the rate of ischemic stroke was found to be 71.2% and the rate of hemorrhagic stroke was found to be 28.8% (3).When blood flow falls below a critical level, substrates such as oxygen and glucose begin to deplete in the brain tissue, and necrosis develops as neuron death occurs. Ischemic stroke develops as a result of atherothrombotic, embolic or hemodynamic processes. The atherothrombotic process, which includes fibrin production, platelet activation and disruption of fibrinolysis, plays an important role in the development of ischemic stroke (4).

Platelets are involved in hemostasis, thrombosis and coagulation processes. Circulating platelets are heterogeneous in size, density, and reactivity, and large platelets are more active metabolically and enzymatically (5). Large platelets produce a greater number of prothrombotic factors such as β-thromboglobulin, thromboxane B2, serotonin, glycoprotein IIIA, and P-selectin, and they are more prone to aggregate. Mean platelet volume (MPV) shows platelet size and it is an indicator of platelet function and activation. MPV levels have been studied in many pro-thrombotic and pro-inflammatory diseases and it has been reported that MPV could be an indicator that can be used to diagnose diseases such as acute cerebral ischemia and transient ischemic attack (6,7). Despite the inconsistent results, previous studies conducted on stroke patients concluded that MPV may be an independent risk factor related to the severity and prognosis of the stroke.

In this study, we aim to determine the MPV values of acute ischemic stroke patients, which are indicative of activation and function of platelets and to examine the effects of MPV on the prognosis of ischemic stroke.

Material And Methods

The present study was designed as retrospective cohort study. Between January 2013 and May 2018, 62 patients who were admitted to the Emergency Clinic of Yeniyüzyıl University Faculty of Medicine, Gaziosmanpaşa Hospital with first or recurrent cerebral acute ischemic stroke and treated in the adult intensive care unit, were included. Systemic and neurological examination findings and the results of computerized brain tomography, electrocardiography, echocardiography (Echo) and carotid vertebral doppler ultrasonography of patients were obtained from patients' files. The results of Trans Esophageal Echo, cranial magnetic resonance imaging and cranial angiography were recorded as necessary in some cases. Demographic information and information about concurrent diseases such as hypertension, diabetes mellitus, chronic obstructive pulmonary disease, coronary artery disease, atrial fibrillation, and chronic renal failure were also recorded. In addition, clinical information such as the affected brain region and length of hospitalization were also obtained from the patients' files.

Patients with a history of acute or chronic infectious disease, hematological disorders (hemoglobin >16.5 g/dL, thrombocytopenia, anemia, myeloproliferative disorder), cancer, autoimmune or metabolic disease, thrombosis, drug use, bone marrow disease, hypersplenism were excluded from the study. Also, pregnant patients and acute ischemic stroke patients whose MPV values were not determined at the time of admission were excluded.

Biochemical Measurements

We collected 5 mL blood samples from patients' antecubital veins at the time of admission and at the time of discharge. For complete blood count, tubes containing EDTA were used. For Troponin-T and C-reactive protein (CRP) measurements, blood samples were collected into tubes containing clot activator gel and were centrifuged for 10 minutes at 4000 rpm for serum separation. Biochemical parameters were measured within 1 hour after blood collection. MPV, platelet count, white blood cell count (WBC) and neutrophil count values were obtained by complete blood count analysis. The results of complete blood counts were obtained by using the same SYSMEX

XN-2000 analyzer which uses the laser flow cytometry scattergram technique and routinely checked. CRP was measured by immunoturbidimetric method using Rochec501 device with the kit of the relevant company. Results greater than 5 mg/dL were considered as high level. Troponin-T levels were measured by using Roche Diagnostic Troponin-T kit according to the sandwich principle (ELISA) in the Roche c601 device.

Statistical Analysis

All statistical analyses were performed by using SPSS (Statistical Package for the Social Sciences) version 21.0 (SPSS Inc., Chicago, IL, USA). The conformance of quantitative data to normal distribution was checked by using the Shapiro-Wilk test. The descriptive statistics of the variables corresponding to the normal distribution were given as mean ± standard deviation, and the other variables were given as median (minimum-maximum value). Descriptive statistics of qualitative variables were given as frequency and percentage. Intergroup comparisons of white cell, platelet and neutrophil variables suitable for normal distribution were performed by using t-test in independent samples. The values of the MPV variable, which were suitable for the normal distribution, were evaluated by two-way ANOVA analysis of variance in repeated measures. Age, length of stay, CRP and troponin variables that were not suitable for normal distribution were analyzed by using Mann-Whitney U test. Chi-square test was used to analyze the categorical data. P values equal to or under 0.05 were considered as statistically significant.

Results

Of those 62 patients, 28 (45.16%) were females and 34 (54.84%) were males. Participants were aged between 43 and 92 years. The mean age of the patients was 72.4±12.6 years. At the end of the study, 28 patients were discharged and 34 patients died. The survival rate was not associated with age and with gender (p>0.05) (Table 1). A concurrent disease was found in 59 patients (26 discharged patients and 33 deceased patients). There was no association between having an additional disease and survival (p=0.585). Twenty-two of 38 hypertension patients were deceased. Survival rates between hypertension patients and non-hypertension patients were not significantly different (p=0.729). Atrial fibrillation was detected in eight patients. Seven of atrial fibrillation patients died. Having atrial fibrillation was found to be not associated with survival in ischemic stroke (p=0.063). Table 1 shows the demographics and concurrent diseases of patients.

Thirteen patients had a right hemiparesis, 26 had a left hemiparesis and 23 had a bilateral stroke. Out of 23 bilateral stroke patients, 18 patients died. Bilateral stroke frequency was statistically significantly higher in deceased patients (p=0.005) (Table 2). Fifty-two (83.87%) of the patients had acute cerebral stroke attacks for the first time and 10 (16.13%) had their second attacks. Survival rates between first-time stroke patients and second-time stroke patients were not significantly different (p=0.097). The duration of hospitalization was 3-216 days in patients who were discharged and 4-839 days in patients who died. There was

Table 1. General characteristics of the patients

	Discharged (n=28)	Deceased (n=34)	Total (n=62)	p
Age	72.5 (44-88)	74 (43-92)	73.5 (43-92)	0.708
Gender				
Female	14 (50.00%)	14 (41.18%)	28 (45.16%)	0.661
Male	14 (50.00%)	20 (58.82%)	34 (54.84%)	-
Concurrent diseases	26 (92.86%)	33 (97.06%)	59 (95.16%)	0.585
Hypertension	16 (57.14%)	22 (64.71%)	38 (61.29%)	0.729
Diabetes Mellitus	10 (35.71%)	13 (38.24%)	23 (37.10%)	1.000
COPD	3 (10.71%)	5 (14.71%)	8 (12.90%)	0.719
Coronary artery disease	13 (46.43%)	15 (44.12%)	28 (45.16%)	1.000
Atrial fibrillation	1 (3.57%)	7 (20.59%)	8 (12.90%)	0.063
Neurological diseases	4 (14.29%)	3 (8.82%)	7 (11.29%)	0.691
Chronic kidney failure	3 (10.71%)	6 (17.65%)	9 (14.52%)	0.494
Other	5 (17.86%)	5 (14.71%)	10 (16.13%)	-

COPD: Chronic obstructive pulmonary disease

Neurological diseases: dementia, Parkinson's disease, Alzheimer's disease, Other: pancreatic cancer, goiter, kidney cancer, lung cancer, vasculitis, asthma, benign prostatic hyperplasia, pulmonary embolism. Data was given for quantitative variables as mean ± standard deviation or median (minimum-maximum value) according to normal distribution suitability, and for qualitative variables as frequency (percentage). P<0.05 was considered as statistically significant

no statistically significant difference between these two groups regarding length of hospital stay (p=0.195).

At the time of hospital admission, platelet counts were 253.64±97.82x10^3/mm^3 in discharged patients and 196.15±84.24x10^3/mm^3 in deceased patients (p=0.016). WBC values were 11.75±4.59x10^3/mm^3 in discharged patients and 11.40±4.57x10^3/mm^3 in deceased patients (p>0.05). In addition, neutrophil values were measured as 8.84±3.92x10^3/mm^3 in discharged patients and 9.57±4.39x10^3/mm^3 in deceased patients (p>0.05). Also, there was no statistically significant difference between discharged and deceased patients regarding Troponin-T and CRP levels (Table 3). The biochemical measurement results were shown in Table 3.

At the time of the first admission, MPV values were 10.59±1.01 fL in discharged patients and 11.29±1.12 fL in deceased patients (p=0.029). At the end of the study, we found that MPV values of deceased patients (11.46±1.28 fL) were significantly higher than discharged patients (10.47±0.74 fL) (p<0.001).

Discussion

The aim of this study was to determine MPV values in acute ischemic stroke patients and to investigate its effect on the prognosis of ischemic stroke. Our study showed that deceased patients had higher MPV values than survived patients. As a consequence, MPV may have an importance in determining the prognosis of acute ischemic stroke.

Epidemiological studies have identified predisposing risk factors for stroke, and have shown that stroke risk can be reduced by treatment and modification of these risk factors (2,8,9,10,11,12,13). It has been shown that the risk of stroke increases with the progression of age, and 70% of people with stroke are older than 65 years (8).

Consistent with the literature, our study was included elderly patients and the mean age of the patients was 72.4±12.7 years. Modifiable risk factors for stroke include diseases such as hypertension, diabetes mellitus, atrial fibrillation, hyperlipidemia, asymptomatic carotid stenosis, and habits like smoking and alcohol use. It has been shown that the decrease in systolic blood pressure

Table 2. Clinical characteristics of the patients

	Discharged (n=28)	Decreased (n=34)	Total (n=62)	p
Affected region				
Right hemisphere	10 (35.71%)	3 (8.82%)	13 (20.97%)	**0.005**
Left hemisphere	13 (46.43%)	13 (38.24%)	26 (41.94%)	
Bilateral	5 (17.86%)	18 (52.94%)	23 (37.10%)	
Number of CVD				
First	26 (92.86%)	26 (76.47%)	52 (83.87%)	0.097
Second	2 (7.14%)	8 (23.53%)	10 (16.13%)	
Length of stay	11.5 (3-216)	15.5 (4-839)	14 (3-839)	0.195

CVD: Cerebrovascular diseases

Data was given for quantitative variables as mean ± standard deviation or median (minimum-maximum value) according to the normal distribution suitability, and for qualitative variables as frequency (percentage). P<0.05 was considered as statistically significant.

Table 3. Biochemical analyses results

	Discharged (n=28)	Deceased (n=34)	Total (n=62)	p
Platelet (x1000)	253.64±97.82	196.15±84.24	222.11±94.37	0.016
White cell (x1000)	11.75±4.59	11.40±4.57	11.56±4.54	0.769
Neutrophile (x1000)	8.84±3.92	9.57±4.39	9.24±4.16	0.500
CRP	27.96 (1.2-336)	64.3 (1.6-257.7)	34.73 (1.2-336)	0.132
Troponin-T	0.042(0.007-0.452)	0.081 (0.014–3.490)	0.073 (0.007-3.490)	0.053
MPV				
First visit	10.59±1.01	11.29±1.12	10.97±1.12	**0.029**
Last	10.47±0.74	11.46±1.28	10.98±1.15	**0.001**

CRP: C-reaktifprotein, MPV: Mean platelet volume

Data was given for quantitative variables as mean ± standard deviation or median (minimum-maximum value) according to the normal distribution suitability, and for qualitative variables as frequency (percentage). P<0.05 was considered as statistically significant

by 10 mmHg and diastolic blood pressure by 5 mmHg reduces the risk of stroke by 30-40% (9). Also consistent with the literature, 95% of our study group had comorbid diseases and 61% of them had hypertension. However, our study showed no association between hypertension and survival in acute ischemic stroke. Patil et al. (7) conducted a hospital-based cross-sectional study in 79 stroke patients (25 diabetics and 54 non-diabetics). They found that MPV values were to be higher in the diabetic group. In a prospective study of 200 diabetic patients conducted by Han et al. (10), it was shown that after 28.4 months of follow-up, 14 patients developed ischemic stroke and eight patients developed coronary artery disease. Further, stroke and coronary artery disease development rates were higher in patients with high MPV values. In the same study, it was proposed that MPV is a predictive factor for stroke and coronary artery disease development, independent of age, gender, hypertension, and HbA1c values. In our study, 23 patients had diabetes mellitus as a concurrent disease. In contrast to Han et al. (10)'s study, we did not observe any effects of diabetes mellitus on survival of acute ischemic stroke patients. An association between stroke and atrial fibrillation as a predisposing factor has been shown in various previous studies (11,12). In a prospective study that followed up 90 paroxysmal atrial fibrillation (PAF) patients, it has been observed that 31 patients developed stroke (11). The same study concluded that MPV levels may help to determine the increased risk of developing acute or transient ischemic attacks in patients with PAF. In a study comparing 63 stroke-atrial fibrillation patients and 77 non-stroke atrial fibrillation patients, it was determined that MPV values bigger than 9.4 were associated with stroke development. The aforementioned study indicated an increased risk for stroke in patients with atrial fibrillation according to ROC analysis data (12). In our study, seven of eight atrial fibrillation patients passed away after getting an acute ischemic stroke attack. However, our study showed no association between atrial fibrillation and survival in ischemic stroke (p=0.063). In our study, we found the mortality rate to be high. This may be due to the fact that the number of patients is high with bilateral affected brain region in the deceased group. It may also be due to the high number of patients with atrial fibrillation in the dying group.

Previous studies that investigated the impact of MPV levels on prognosis of stroke patients showed different results. In a study conducted by Farah and Samra (13) in 2018, no association was found between MPV values of stroke patients and development risk of a new stroke attack. In the study with 136 participants by Oz et al. (14), it was found that MPV has no value in predicting the development of a cerebrovascular event in coronary artery disease. In addition, a previous study which compared MPV values of 70 first time atherothrombotic acute ischemic stroke patients, 50 transient ischemic attack patients, and 70 healthy individuals, no statistically significant difference was found between the groups (15). Another study by Nataios et al. (16) measured MPV values within the first 24 hours after the onset of stroke and found that MPV levels were not associated with stroke severity and limitation of neurological functions. Further, a retrospective study by Lok et al. (17) in 2017 which 798 first time acute ischemic stroke patients participated, showed that MPV values were not associated with short-term stroke prognosis and neurological functions. Also, a study compared MPV values of 281 first-episode acute ischemic stroke and 164 first-episode hemorrhagic stroke patients and found that MPV values were high in both groups but it is not associated with the prognosis (5). In contrast, in a 2017 study conducted on 100 acute cerebral infarction patients and 80 healthy controls by Wan and Ma (18), it was found that MPV values were high in the patient group. The same study suggested that MPV may have the potential to be a sensitive index for the prediction of acute cerebral infarct prognosis. Similarly, a study conducted on 776 patients with acute or transient ischemic attacks by Greisenegger et al. (6) which evaluated patients with Rankin scale after one week from the stroke attack, observed that higher MPV values were associated with worse clinical outcomes. In addition, a correlation between high MPV values and severity of stroke was observed in a study which 100 first time stroke patients participated. The same study suggested that this finding could be used to differentiate between mild and severe ischemic stroke (19). Furthermore, Arikanoglu et al. (20) found that MPV levels were high in 63 acute ischemic stroke patients. Also, a previous study observed that patients who passed away within 10 days after the acute ischemic stroke attack had higher MPV values than survivors, and suggested that it could be used as an indicator for mortality. In a prospective study conducted by Arévalo-Lorido et al. (21), MPV values of 379 stroke patients were examined. As a result of the study, it was found that those with high MPV (>12) had low survival or high rate of re-hospitalization, and functional disabilities were developed mostly in this group. Another study also conducted by Arévalo-Lorido et al. (22) in 215 atherothrombotic stroke patients, observed

an association between high MPV values and severity of carotid stenosis. Moreover, a study which included 692 patients with ischemic or hemorrhagic stroke and 208 healthy controls, high MPV level was found to be an independent risk factor for the development of ischemic stroke, and was associated with poor prognosis, but not with the risk of hemorrhagic stroke (23). In a previous prospective study which 3134 patients participated, 402 ischemic events in 383 patients were observed and found that the risk of stroke attack increased 11% in patients with high MPV values (24). In parallel with some mentioned studies, we observed worse clinical outcomes in acute ischemic stroke patients with higher MPV levels in our study. Our result suggests that high MPV levels may be considered as a risk factor in patients with acute cerebral ischemic stroke, and may be associated with high morbidity and mortality. It also indicates that high MPV levels may be used as an indicator to differentiate severe ischemic stroke from mild ischemic stroke. According to our study's results MPV which is an easily obtained blood parameter may be an indicator of poor prognosis and high mortality. We also observed that platelet count was higher in survived patients than deceased patients. When we evaluate our results on MPV and platelet count together, we suggest that there may be a connection between platelet dysfunction and poor stroke prognosis.

Also, some previous studies suggest that MPV values can be used for predicting the treatment outcomes in ischemic stroke patients. In a 2018 study conducted by İnanç et al. (25), MPV values of 129 stroke patients were found to be associated with neurological scale score improvement after intravenous thrombolytic therapy. In addition, a previous study by Ha et al. (26) in which 200 atrial fibrillation patients participated, suggested that MPV is a predictive factor for stroke development, independent of age and gender. They also suggested that anticoagulation treatment may be necessary for patients with high MPV values, even if they have low or moderate thromboembolic risk for a stroke attack. A 2017 study evaluated elevated MPV levels of 196 non-cardioembolic ischemic stroke patients before clopidogrel treatment as a risk factor for ischemic stroke treatment resistance (27). Similarly, we found higher MPV values in deceased patients both before and after the treatment. Considering this finding, we suggest that high MPV values may be an important factor for treatment resistance and can be used as an independent predictor of poor prognosis in ischemic stroke patients.

Previous studies showed that the effects of a stroke attack depend on the part and size of the brain area affected. Pikija et al. (28) found that high MPV level was independently associated with greater infarct volume, and its value at 7th day and third month after stroke was associated with increased risk of death in 81 acute ischemic stroke patients. Similarly, we observed that stroke patients with bilateral hemisphere involvement had an increased risk of death.

Conclusion

This study showed that MPV and platelet count may be associated with survival rate in acute ischemic stroke patients, and may be used as prognostic indicators. With conforming future large-scale prospective studies in stroke patients, our findings may lead to better clinical follow-up and a more extensive understanding of stroke pathogenesis.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

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CASE REPORT

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A Rare Case: Malignant Granular Cell Tumor in Axillary Region

Nadir Bir Olgu: Aksiller Bölgede Malign Granüler Hücreli Tümör

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Abstract

Granular cell tumors (GCT) are rare soft tissue tumors. Although it is frequently seen in the upper extremity, it can be seen anywhere in the human body. The majority of tumor cases are benign and approximately 2% are malignant. It is seen in the breast at a rate of 5-8%. They present with a slow growing, painless, mobile mass. The definitive diagnosis is made histopathologically and the treatment is wide excision. A 75-year-old woman presented with an ulcerated exudative mass in the right axilla. Mastectomy and axillary dissection were performed by general surgery 8 months ago for BIRADS 3 mass that was determined on mammography in the right breast. Breast specimen was identified as a phyllodes tumor. GCT was detected in five of thirty lmph nodes in the axilla. Incisional biopsy was performed on the axillary mass. Histopathological measurements showed S-100 and CD68 positivity, eosinophilic staining in tumor cells and pleomorphic nuclei with marked nucleolus. The tumor was removed with wide excision and the defect area was closed with a splint thickness skin graft. The pathological measurements revealed that the GCT in the axilla was not a breast metastasis, it was actually malignant GCT which was originated from skin. Ki-67 proliferation index was found as 10%. Surgical margins were seen as tumor free. There were no complications in the postoperative follow-up. GCTs in the axilla are generally seen as a result of breast metastasis and the vast majority are benign. Malignant skin-derived GCT is a rare case.

Keywords: Granular cell tumor, axillary, rare tumors

Öz

Granüler hücreli tümör (GHT) nadir görülen yumuşak doku tümörüdür. Sıklıkla üst ekstremitede görülse de vücudun herhangi bir yerinde görülebilir. Tümör olgularının büyük çoğunluğu benigndir yaklaşık %2'lik kısmı maligndir. Tümör %5-8 oranında memede görülmektedir. Yavaş büyüyen, ağrısız, mobil kitle ile ortaya çıkar. Kesin tanı histopatolojik olarak konulmaktadır. Tedavisi geniş eksizyondur. Yetmiş beş yaşında kadın hasta sağ aksillada ülsere eksüdalı kitle ile başvurdu. Sekiz ay önce sağ memedeki mamografi sonucu BIRADS 3 olan kitle için genel cerrahi tarafından mastektomi ve aksiller diseksiyon yapıldı. Meme patolojisi filloides tümör olarak belirlendi. Aksilladaki otuz lenf nodundan beş tanesinde GHT'ye rastlandı. Aksilladaki kitleye insizyonel biyopsi yapıldı. Histopatolojik ölçümlerde S-100 ve CD-68 pozitifliği, tümör hücrelerinde eozinofilik boyanma ile belirgin nükleolusua sahip pleomorfik nükleuslar görülmüştür. Tümör geniş eksizyonla çıkartıldı defekt alanı kısmi kalınlıkta deri greft ile kapatıldı. Patolojik ölçümlerde aksilladaki GHT'nin meme metastazı olarak değil, deri kaynaklı malign GHT'si olduğu belirlendi. Ki-67 proliferasyon indeksi %10 olarak saptandı. Cerrahi sınırlar salim olarak görüldü. Hastanın postoperatif takiplerinde herhangi bir komplikasyona rastlanmadı. Aksilladaki GHT'ler genel olarak meme metastazı sonucu görülmektedir ve büyük çoğunluğu benigndir. Malign deri kaynaklı GHT nadir görülen bir olgudur.

Anahtar kelimeler: Granüler hücreli tümör, aksilla, nadir tümörler

Introduction

Granular cell tumor (GCT) is a rare soft tissue tumor that is usually seen in the head, neck, skin, abdomen, upper extremity, breast and female genital organs (1). It was first described in 1854 by Weber and Virchow (2) in a patient's tongue. Also it was defined by Abrikossoff (3) in 1926 in the breast and named as granular cell myoblastoma. It is generally seen in African-American women in the perimenopausal period (4). Although estrogen and progesterone may be thought to play role for pathogenesis, most cases are hormone receptor negative.

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Initially it was thought that GCT was derived from skeletal muscle cells. Because of the S-100 protein positivity of tumor cells, it was found that it originated from neurogenic mesenchymal cells, especially Schwann cells (5,6,7,8,9). The definitive diagnosis is made by histopathological confirmation. The most effective treatment is wide excision.

5-8% of GCTs are seen in the breast (1,6). It is very important to distinguish the tumor from breast cancer because the similarity between the two entities is remarkable, especially at the diagnostic stage. In this case, we present a patient who underwent mastectomy and axillary lymph node dissection due to breast cancer and a biopsy of the mass in the axillary region of the same side revealed a malign GCT derived from skin not breast.

Case Report

Seventy-five years old female presented to our clinic with complain of mass in her axillar region (Figure 1). Physical examination revealed that there was a mastectomy scar with her right side and approximately 7x8 cm mass which is painless, exudative and ulcerated. Before eight month ago patient refered to general surgery department for painless mass in her right breast and right axillar region. Mammography revealed that there was lesion which was a stage of BIRADS 3 (Breast Imaging Reporting and Data System), which shows generally benign lesion. Mastectomy and axillary dissection were performed and for breast specimen benign phyllodes tumor was diagnosed by postoperative histopathologic examination. Five of thirty lymph nodes from which removed axilla were diagnosed as GCT. Incisional biopsy was performed lesion and pathology reports confirmed GCT. After written informed consent that is appropriate to Declaration of Helsinki was obtained from the patient. Under general anesthesia the patient was underwent excisional biopsy with 1 cm surgical margin and area where tumor was removed was covered with splint thickness skin graft (Figure 2). Histological evalutaion of surgical specimens revealed macroscopically grayish yellowish colored solid lesion that setteled under skin and caused ulcer. Also with Hematoxylin and Eosin stain on magnification x100 and x200 the fact that tumor cells had pleomorphic nuclei with prominent nucleolus and solid pattern infiltration of tumor cells with eosinophilic granules cytoplasm were seen. Showing diffuse strong immunostaining with S-100 protein was observed

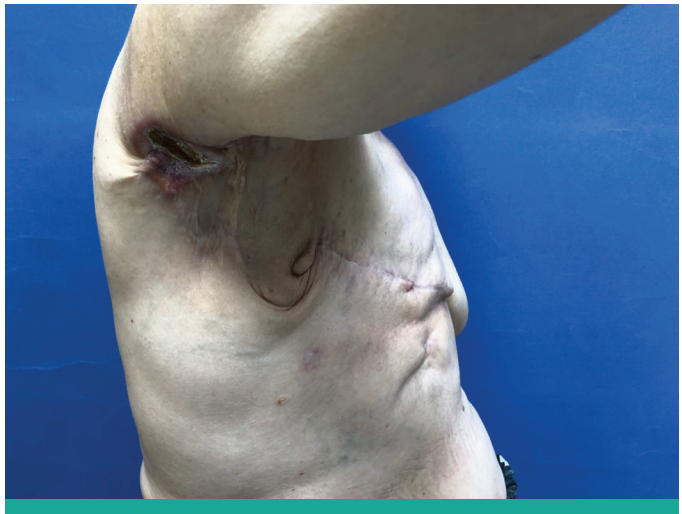

Figure 1. Preoperative view

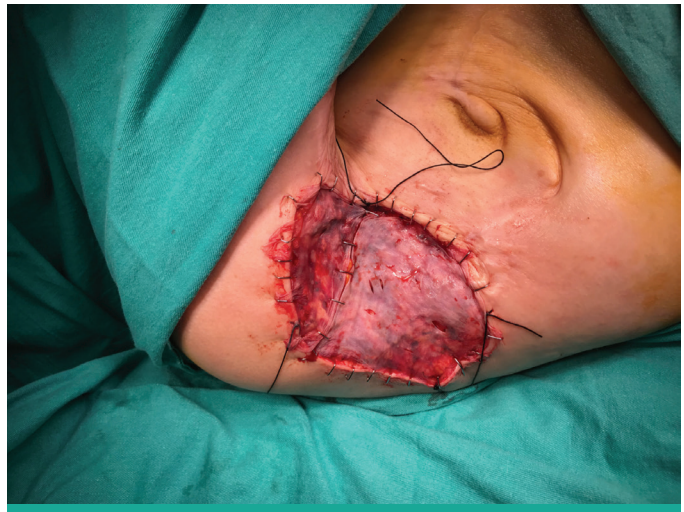

Figure 2. After tumor resection covered with splint thickness skin graft

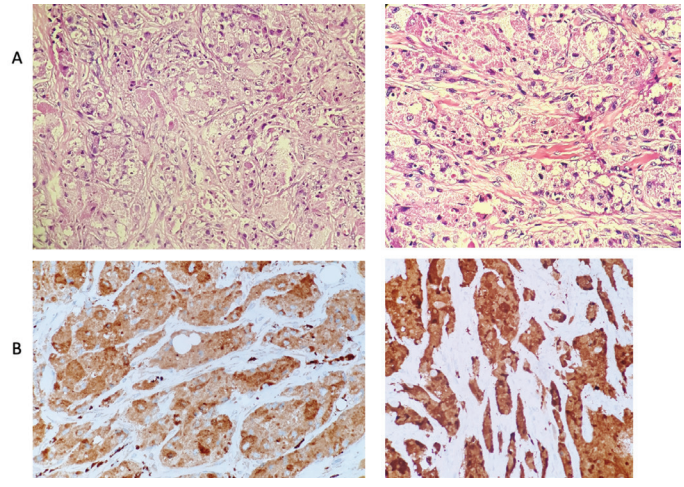

Figure 3. Tumor cells have plemorphic nuclei with prominent nucleous and solid patern infiltration of tumor cells with eosinophilic granules cytoplasm with Hemotoxylin and Eosin stain on magnification x100 and x200, respectively (A). Diffuse strong immunostaining with S-100P protein and CD-68, respectively (B)

and tumor cells showed 10% Ki-67 proliferation index (Figure 3). Tumor was diagnosed as malign GCT derived from skin by patology department because of mentioned above and they reported all surgical margins were safe and tumor-free. After follow up period no complications were seen at the wound site and the graft was intact (Figure 4).

Discussion

Cases of GCTs, first described in 1854, have increased over the years. It composes 0.5% of all soft tissue tumors (10). Although it is generally seen in adult women, it has been reported in children. The majority of tumor cases are benign, but about 2% are malignant and also 5-10% are multiples (1). Although the most common site is the head and neck region also skin, heart, lung, abdominal wall, pelvis, bladder, vulva and esophagus are parts of the body where the tumor is seen. (11,12,13,14,15,16,17,18) Clinical presentation varies depending on localization, but generally presents with slow-growing painless mobile masses.

The origin of GCTs were thought to be myocytes, histiocytes, fibroblasts in the first years, but histochemical tests showed that the tumor originated from neural cells especially Schwann cells (1). Alpha tubulin, cytokeratin, inhibin and calterin negativity proves that the tumor is not orginated from epithelial cells. Tumor cells shows S-100 the protein positivity which is secreted from neural cells and melanocytes. Tumor is stained with CD68 and Neuron Specific enolase. CD68 is a marker of lysosomal activity in Schwann cells. Enolase is also secreted from neural cells (Carcinoembryonicantigen) and vimentin positivity have been reported in some cases.

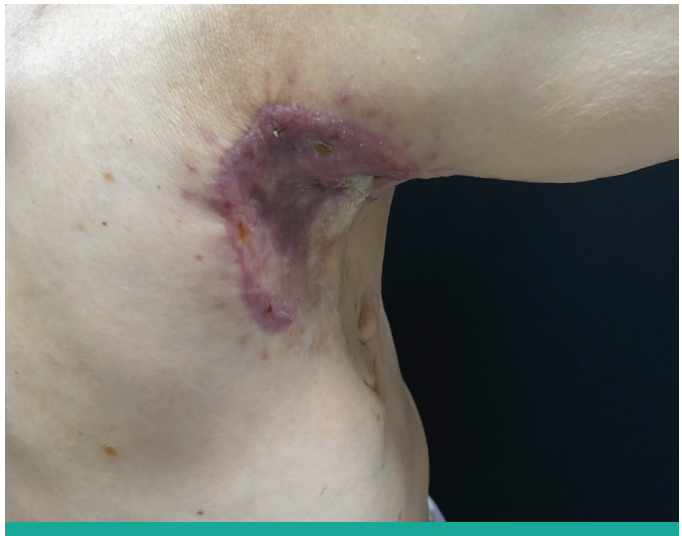

Figure 4. Postoperative view

Wang et al. (19) presented six criteria to determine the malignancy of the tumor. Necrosis, spindle cell shape, vesicular nucleus having large nucleolus, high mitosis rate, height of cytoplasma/nucleus ratio and pleomorphism. With two of these criteria they define such a mass ''atypical'' and with three or more criteria as ''malignant''.

Histopathological confirmation is the gold standard in the diagnosis of GCT.

The tumor may cause a painless mass in the breast. The most common localization is upper middle and medial part (6). The tumor mimics breast cancer because it retracts nipple and skin. 5-8% of GCTs are seen in the breast, most of these tumors are benign but 1-2% have malignant features (9). GCT mimics breast cancer because of showing irregulation, spiculation stellation, isodensity and heterogeneity on USG or mammography. Also, excisional biopsy is the gold standard for effective diagnosis and treatment. Recurrence rate with wide excision is 2-8% (20).

Conclusion

GCTs in the axilla are usually associated with the focus in the breast due to the similarity. In our case, the mass in the axilla was found to be malign GCT which is derived from skin, which malignancy is a rare condition for GCT.

Ethics

Informed Consent: Informed conset was signatured by patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.E.T., Concept: M.S., Design: P.K., Data Collection or Processing: C.G., Analysis or Interpretation: S.K., Literature Search: C.U., Writing: B.E.T.

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

Financial Disclosure: Conflict of interest was declared by the authors.

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CASE REPORT

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Acute Urticaria Related to Cow's Milk Allergy in Newborn Period

Yenidoğan Döneminde Akut Ürtiker İle Prezente Olan İnek Sütü Proteini Alerjisi

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Abstract

Urticaria is a common disease in children. But there are few case reports in neonatal period. Urticaria has many causes, unfortunately it cannot be figured out in some of the cases. Drug and food allergies, infections are common reasons that have been commonly shown. IgE-mediated food allergy should be considered in patients with acute urticaria and/or angioedema after food intake. Here we present a case of acute urticaria due to cow's milk protein allergy in the newborn period. A 21-day-old male patient was admitted to our emergency department with the complaint of widespread rash on the body which started one day earlier. Medical history has revealed that he did not have a different drug intake before the onset of complaints, had no previous rashes, upper respiratory tract infection or other infective-inflammatory disease since birth. His parents did not admit to another hospital. We obtained blood tests for food allergy. Total IgE: 38 IU/L and cow's milk protein-specific IgE (f2): 2.26 kU/L were found to be suspicious for food allergy. According to these results, the formula which the baby was treated before has been stopped and extensively hydrolyzed formula has been started. After 12 hours, urticaria had started to fade. While going on our treatment, on 5th day the urticaria lesions totally disappeared. Although urticaria is a common disease, it is rarely reported in patients under six months. We want to emphasize that food allergies may be considered in cases presenting with urticaria in neonatal period.

Keywords: Cow's milk allergy, urticaria, newborn

Öz

Ürtiker, küçük çocuklarda çok sık görülen medikal bir problemdir. Yenidoğan döneminde ise az sayıda olgu bildirimi vardır. Ürtikerin birçok olguda nedeni bulunamasa da oldukça fazla nedeni vardır. Daha çok gıda alerjisi, ilaç etkisi veya enfeksiyonlara bağlı meydana geldiği gösterilmiştir. Besin alımı sonrası akut ürtiker ve/veya anjioödem görülen hastalarda IgE aracılı besin alerjisinin olabileceği mutlaka akla getirilmelidir. Bu yazıda ise yenidoğan döneminde inek sütü proteini alerjisine bağlı gelişen akut ürtiker olgusu sunulmuştur. Yirmi bir günlük erkek hasta acil servisimize 1 gün önce başlayan vücuttaki yaygın döküntü şikayeti ile başvurdu. Hastanın öyküsünde şikayetleri başlamadan önce farklı bir ilaç alımı olmadığı, daha önce döküntülerinin olmadığı, doğumundan bu yana üst solunum yolu enfeksiyonu veya başka bir enfektif-enflamatuvar hastalık geçirmediği ve başka bir tıbbi kuruma başvurmadıkları öğrenildi. Hastanın besin alerjisi şüphesi açısından alınan tetkiklerinde Total IgE: 38 IU/L, süt spesifik IgE (f2): 2,26 kU/L olarak saptandı. Bu sonuçlara göre olgunun almış olduğu formüla mama kesilerek ileri derece hidrolize formüla başlanıldı. İzlemde olgunun 12 saat sonra vücuttaki döküntülü lezyonlar solmaya başladı ve tedavisinin 5. gününde tüm lezyonları düzeldi. Ürtiker, sık görülen bir hastalık olsa da 6 aydan küçük olgularda nadir olarak bildirilmektedir. Yenidoğan döneminde ürtiker tablosu ile başvuran olgularda besin alerjisi olabileceğinin akılda tutulması gerektiğini vurgulamak için olgumuz sunulmuştur.

Anahtar kelimeler: İnek sütü protein alerjisi, ürtiker, yenidoğan

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Introduction

Urticaria is a very common medical problem in young children. Although the exact prevalence is unknown, it is estimated to be 20% (1). Characteristic finding in urticaria is well-circumscribed, surface-raised erythematous plaques. They are transient lesions with marked margins or tendency to converge and fade by pressing. Each swelling doesn't exist more than 24 hours and the lesions are often itchy. Mast cells in the superficial dermis play a key role in the pathogenesis of urticarial (1,2). Clinical manifestations lasting less than 6 weeks are called "acute urticaria" and the ones which exist 6 weeks or more are called chronic urticarial (3,4). Although the cause of urticaria is not found in many cases, there are many reasons. It should be kept in mind that patients with acute urticaria and/or angioedema after food intake may have IgE-mediated food allergy (1,2). IgE-mediated food allergy is observed in approximately 10% of pediatric patients presenting with acute urticaria, whereas food is rarely (2%) causative in chronic urticaria patients (1). Eggs, milk, soy, peanuts and wheat are the most commonly accused foods in young children, while fish, shellfish and nuts are blamed in older children (3).

Although urticaria is a common disease, it is rare to occur at a age of less than 6 months. There are few reports in the neonatal period (5). It is mostly linked to food allergy, drug action or infections. Since urticaria is rare at age less than 6 months and only a few treatments have been tried for its efficacy and safety, little information is available about treatment in the literature (6,7,8,9). In this report, we present a case of acute urticaria due to cow's milk protein allergy in the newborn period.

Case Report

A 21-day-old male patient was admitted to our emergency department with the complaint of widespread rash on the body that started one day earlier. The patient's history revealed that he did not have a different drug intake before the onset of complaints, had no previous rashes, did not experience upper respiratory tract infection or other infective-inflammatory disease since birth, and had not consulted another medical institution. It was learned from the patient's history and family history that she was the first child of unrelated parents, that he was born vaginally at the 40th gestational week following a problem-free pregnancy and that the mother started breastfeeding from the first hour. It was learned that intermittent formula was initiated because of insufficient breast milk in the first week of the patient's nutrition and that he fed on only formula due to the discontinuation of breast milk during follow-up. In the skin examination; there were widespread plaques that held the extremities and trunk, tend to merge in places, puffy from the skin, migratory, fading with pressure, and occasionally left a purplish discoloration (Figure 1). No mucosal involvement was observed. Laboratory examination of the patient revealed white cells of 16.350 mm^3, hgb: 17.3 gr/dL, plt: 288.000 mm^3, eosinophil count: 500 mm^3 and a normal total biochemistry except a rise in Crp which was 3.21 mg/L (N: 0-5). Bleeding profile was normal. Serological examinations for congenital infections were negative. Complete urinalysis was normal. No fecal occult blood was detected. Total IgE: 38 IU/L, milk specific IgE (f2) levels were detected in the patient's food allergy suspicion; 2.26 kU/L. According to these results, the formula taken was stopped and the hydrolyzed form was started. During the follow-up, the rash lesions began to fade within 12 hours and all lesions disappeared on the 5th day of treatment. The patient was advised to continue with a highly hydrolyzed form and was discharged with an appointment for oral loading test after a 2-week elimination diet. But oral food loading test could not be performed because the family did not consent. The milk specific IgE (f2) level at the age of 4 months was found to be 5.8 kU/L, andthe diet elimination was continued.

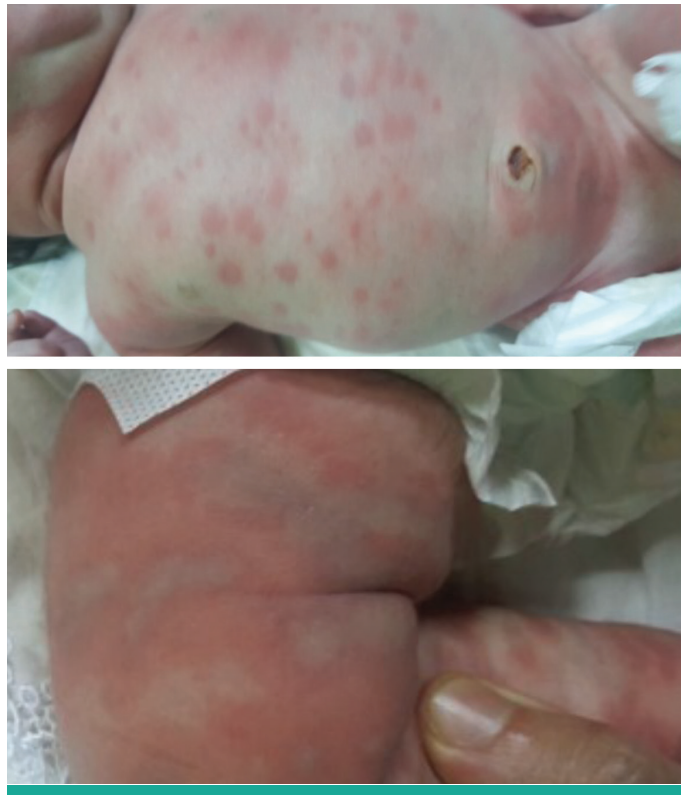

Figure 1. Skin examination

Discussion

IgE-mediated food allergy should be considered in patients with acute urticaria and/or angioedema after food intake. Our case was an acute urticaria due to cow's milk protein allergy in the newborn period.

Classical findings of urticaria consists of papules and plaques of pink, red, edematous, different sizes of geographic or annular character. It can hold any place on the skin. If it is generalized, the lesions may merge. But the lesions are temporary, they can be displaced within hours. It is typically less than 24 hours in the same location. In the literature, all types of urticaria described in patients younger than 6 months showed an acute course (6,7). There were no reports of chronic urticaria at this age. In our case, the lesions in the body were evaluated as acute urticaria due to the non-sequelae healing within 5 days after starting with the highly hydrolyzed form.

The most common causes of urticaria in children are infections, food allergy, medications, insect bites. However, the majority of patients younger than 6 months present with food allergy and infections as the cause (6,7,8,9). Legrain et al. (7) accused cow's milk responsible for 75% as the causative agent of acute urticaria in patients younger than 6 months. Hon and So (10) reported annular target-like rashes in the literature in a 24-day-old male patient. During the follow-up examinations, no infectious etiology (blood, cerebrospinal cultures: negative) was detected in laboratory examinations, but as evidence of atopy; reported high levels of eosinophilia (eosinophil percentage: 13%) and IgE (216 kIU/L). The authors suggested that atopic newborns may be prone to acute urticaria and eczematous rashes and should be monitored in this respect. Huston et al. (11) found that the content of the parenteral nutritional, namely; amino acid solution, lipid solution, multivitamins and magnesium sulfate may also be associated with hypersensitivity reactions in the study performed in the neonatal intensive care unit receiving parenteral nutritional therapy.

Demirdöven et al. (12) reported a case of anaphylaxis after feeding with cow's milk-based formula in a newborn on postnatal 16th day. The patient was treated with intravenous adrenaline, antihistaminic and dexamethasone, and nebulized salbutamol (albuterol). The patient was fed only breast milk during the follow-up and the mother started a diet that did not contain cow's milk protein. Again, in the literature, Lifschitz et al. (13) reported that anaphylaxis was observed following the use of cow milk protein-based formula in an 8-day-old newborn. Tarım et al. (14) reported that anaphylaxis developed with partial-hydrolyzed formula in a 7-week-old baby with a familial history of atopy who was admitted to the hospital with cardiac arrest and died 21 hours later. In our case, cow's milk protein allergy was considered only because he had been taking formula due to the discontinuation of breast milk. Later cow's milk protein allergy was confirmed by the diagnostic tests as well.

It is important to take a detailed history in the diagnosis of cow's milk allergy. The age of patient, onset of symptoms, the frequency of occurrence, the time between food intake and the reaction, triggering factors ant the amount and type of cow's milk that triggers symptoms should be questioned (15,16). Detailed history and laboratory tests are essential for the diagnosis. Milk specific IgE, skin prick tests, skin patch tests are helpful; however oral food loading test is the gold standard in diagnosis (17,18). Cow milk specific IgE measurement is a high sensitivity and low specificity test with quantitative method (CAP or Immulite system) in serum which is frequently used in diagnosis. This test is not affected by the drugs used by the patient; there is no risk of reaction during the test (19). Milk specific IgE levels higher than 0.35 kU/L indicate sensitization; however, it is not enough for the diagnosis. Positive results must be correlated with the clinic. For milk-specific IgE, ≥5 kU/L in children younger than 2 years and ≥15 kU/L in children older than 2 years have been reported to be diagnostic with 95% positive predictive value (18). In our case, the elimination diet was continued as the milk-specific IgE level at the age of 4 months was above the positive predictive value of 5.8 kU/L.

In the classical treatment of cow's milk allergy, it is necessary to start a cow milk elimination diet. Elimination diet is a very difficult process, affecting the quality of life of the patient and the family and preventing accidental intake is difficult. Elimination diet should be given to each patient with a list of nutrients that should not be consumed, information about alternative foods, and with a whole education for compliance of patients and their parents, prevention of accidental ingestions, and immediate treatment of acute reactions. The follow-up of patient's growth and development should be planned in the treatment as well. If there is a symptom while feeding with breast milk, it is necessary to remove milk and dairy products from the mother's diet and start with 1000 mg/day calcium supplementation appropriately. Highly hydrolyzed or amino acid-based formulas are used in children under two years of age who have insufficient breastfeeding or who cannot eat at all. In the absence of severe symptoms,

the first choice is highly hydrolyzed formulas. Amino acid-based formulas are used as the first choice if there is no response to treatment with highly hydrolyzed formulas, or in high-risk situations (such as anaphylaxis), or if growth and developmental retardation accompany, or in the presence of eosinophilic esophagitis or other severe symptoms (20). Due to the absence of breast milk, our case was started with highly hydrolyzed formula. In our patient who had clinical improvement with treatment, outpatient follow-up is continued in terms of monitoring growth and tolerance development.

Conclusion

It is important to keep in mind that the rashes observed in the neonatal period may be worrisome and sometimes may be associated with sepsis, which is life-threatening. It should be kept in mind that atopic neonates may present with acute urticaria and eczematous rashes as well.

Ethics

Informed Consent: Informed consent was obtained from the patients.

Peer-review: Externally peer-review.

Authorship Contributions

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

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

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