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

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databases, author should be sure that abstract represents the content of the article accurately. Abstract should inform about the basis of the study and include the purpose, basic procedures (selection of cases and laboratory animals, observatory and analytical methods), key findings and conclusions. New and significant apects of the study or observations should be stated. 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).

Manuscript Types

Original Research

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

Abstract

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

Key Words

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

Introduction

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

Material and Methods

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

The selection and description of the participants

The election, source of population, inclusion and exclusion criteria of the people who participate to experimental or clinical study must be clearly defined in this section. The particular study sample must be explained by the authors (i.e., why the study is performed in a definite age, race or sex population, etc.)

Technical information

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.

Statistics

The statistical methods must be described with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. If possible, findings should be quantified and presented with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Relying solely on statistical hypothesis testing, such as P values, which fail to convey important information about effect size must be avoided. References for the design of the study and statistical methods should be to standard works when possible (with pages stated). Define statistical terms, abbreviations, and most symbols. The computer software used must be specified.

Results

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.

Conclusions

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.

Tables, Graphics and Illustrations

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.

Brief Research

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.

Case Report

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

Review

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

The manuscript should have an unstructured abstract representing an accurate summary of the article, key words, introduction, conclusion. Authors submitting review article should include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.

Letter to the Editor

Letter to the Editor is short and decisive manuscript. They should be preferably related to articles previously published in the Journal or views expressed in the Journal. The letter should not include preliminary observations that need a later study for validation.

Tables

Tables capture information concisely and display it efficiently; they also provide information at any desired level of detail and precision. Including data in tables rather than text frequently makes it possible to reduce the length of the text. Each table should be typed or printed with double spacing on a separate sheet of paper. The tables should be numbered consecutively in the order of their first citation in the text and a brief title for each table should be supplied. Any internal horizontal or vertical lines should not be used and a short or an abbreviated heading should be given to each column. Authors should place explanatory matter in footnotes, not in the heading. All nonstandard abbreviations should be explained in footnotes, and the following symbols should be used in sequence: *,†,‡,§,ǁ,¶,**,††,‡‡. The statistical measures of variations, such as standard deviation and standard error of the mean should be identified. Be sure that each table is cited in the text. If you use data from another published or unpublished source, obtain permission and acknowledge that source fully. Additional tables containing backup data too extensive to publish in print may be appropriate for publication in the electronic version of the journal, deposited with an archival service, or made available to readers directly by the authors. An appropriate statement should be added to the text. Such tables should be submitted for consideration with the paper so that they will be available to the peer reviewers.

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Bağcılar Tıp Bülteni

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Illustrations (Figures)

Figures should be either professionally drawn and photographed, or submitted as digital prints in photographic-quality. In addition to requiring a version of the figures suitable for printing, authors are asked for electronic files of figures in a format (for example, JPEG or GIF) that will produce high-quality images in the Web version of the journal; authors should review the images of such files on a computer screen before submitting them to be sure they meet their own quality standards. For X-ray films, scans, and other diagnostic images, as well as pictures of pathology specimens or photomicrographs, sharp, glossy, black-and-white or color photographic prints should be sent, usually 127x173 mm. Letters, numbers, and symbols on figures should therefore be clear and consistent throughout, and large enough to remain legible when the figure is reduced for publication. Figures should be made as self-explanatory as possible, since many will be used directly in slide presentations. Titles and detailed explanations belong in the legends-not on the illustrations themselves. Photomicrographs should have internal scale markers. Symbols, arrows, or letters used in photomicrographs should contrast with the background. Photographs of potentially identifiable people must be accompanied by written permission to use the photograph. Figures should be numbered consecutively according to the order in which they have been cited in the text. If a figure has been published previously, the original source should be acknowledged and written permission from the copyright holder should be submitted to reproduce the figure. Permission is required irrespective of authorship or publisher except for documents in the public domain. Accompanying drawings marked to indicate the region to be reproduced might be useful to the editor. We publish illustrations in color only if the author pays the additional cost.

Legends for Illustrations (Figures)

The legends for illustrations should be typed or printed out using one spacing, starting on a separate page, with Arabic numerals corresponding to the illustrations. When symbols, arrows, numbers, or letters are used to identify parts of the illustrations, each one clearly should be identified and explained in the legend. The internal scale should be explained and the method of staining in photomicrographs should be identified. Units of Measurement.

Measurements of length, height, weight, and volume should be reported in metric units (meter, kilogram, or liter) or their decimal multiples. Temperatures should be in degrees Celsius, blood pressures should be in millimeters of mercury. Authors must consult the Information for Authors of the particular journal and should report laboratory information in both local and International System of Units (SI). Drug concentrations may be reported in either SI or mass units, but the alternative should be provided in parentheses where appropriate.

Abbreviations and Symbols

Use only standard abbreviations; use of nonstandard abbreviations can be confusing to readers. Avoid abbreviations in the title of the manuscript. The spelled-out abbreviation followed by the abbreviation in parenthesis should be used on first mention unless the abbreviation is a standard unit of measurement.

Acknowledgement(s)

All forms of support, including individual technical support or material support must be acknowledged in the author's footnote before references.

Case Reports and Word Limitation

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

Preparation of Manuscripts

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

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

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

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

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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.

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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.

YAZARLARA BİLGİ

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.

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

Referans Stili ve Formatı

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

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

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

Kaynaklar için örnekler aşağıda belirtilmiştir:

1. Dergilerdeki makaleler için örnekler:

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

Makalenin Dergiye Gönderilmesi

Çevrimiçi gönderim (online submission) ile birlikte Bağcılar Tıp Bülteni web sitesinin (www.ijfed.org) ilgili kısımlarındaki talimatlara uyarak makale gönderilebilmekte, hakem süreçleri de bu yolla yapılabilmektedir.

Makalelere eşlik eden ve aşağıdaki bilgileri içeren bir kapak mektubu olmalıdır.

• 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.

• Eğer makalenin kendisinde ya da yazar formunda belirtilmemişse çıkar çatışmasına neden olabilecek mâli ya da diğer ilişkileri belirten bir ifade olmalıdır.

• Makalenin tüm yazarlar tarafından okunup kabul edildiğini, önceden belirtilen şekilde yazarlık ölçütlerinin karşılandığını, her yazarın makalenin dürüst bir çalışmayı yansıttığına inandığını belirten bir ifade olmalıdır. Mektup editöre yardımcı olabilecek tüm diğer bilgileri içermelidir. Eğer makale önceden başka bir dergiye gönderilmişse önceki editörün ve hakemlerin yorumları ve yazarların bunlara verdiği cevapların gönderilmesi faydalıdır. Editör, önceki yazışmaların gönderilmesini hakem sürecini dolayısıyla yazının yayınlanma sürecini hızlandırabileceğinden istemektedir.

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

SON KONTROL LİSTESİ

- Editöre sunum sayfası
- Makalenin kategorisi
- Başka bir dergiye gönderilmemiş olduğu bilgisi
- Sponsor veya ticari bir firma ile ilişkisi (varsa belirtiniz)

YAZARLARA BİLGİ

- İstatistik kontrolünün yapıldığı (araştırma makaleleri için)
- İngilizce yönünden kontrolünün yapıldığı
- Telif Hakkı Devir Formu
- Yazar Katkı Formu
- ICMJE Potansiyel Çıkar Çatışması Beyan Formu
- Daha önce basılmış materyal (yazı-resim-tablo) kullanılmış ise izin belgesi
- İnsan öğesi bulunan çalışmalarda "gereç ve yöntemler" bölümünde Helsinki Deklarasyonu prensiplerine uygunluk, kendi kurumlarından alınan etik kurul onayının ve hastalardan "bilgilendirilmiş olur (rıza)" alındığının belirtilmesi
- Hayvan öğesi kullanılmış ise "gereç ve yöntemler" bölümünde "Guide for the Care and Use of Laboratory Animals" prensiplerine uygunluğunun belirtilmesi

- Kapak sayfası
- Makalenin Türkçe ve İngilizce başlığı (tercihen birer satır)
- Yazarlar ve kurumları
- Tüm yazarların yazışma adresi, iş telefonu, faks numarası, GSM, e-posta adresleri
- Özler (400-500 kelime) (Türkçe ve İngilizce)
- Anahtar Kelimeler: 3-10 arası (Türkçe ve İngilizce)
- Tam metin makale
- Teşekkür
- Kaynaklar
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ORIGINAL RESEARCH

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The Assessment of the Neutrophil-lymphocyte Ratio and Platelet-lymphocyte Ratio in Dyslipidemic Obese Children

Dislipidemik Obez Çocuklarda Nötrofil Lenfosit Oranı ve Platelet Lenfosit Oranının Değerlendirilmesi

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Abstract

Objective: Childhood obesity is one of the most important children's health problems that is gradually increasing all over the world. Dyslipidemia which coexists with obesity is a risk factor for atherosclerotic diseases in adulthood. In this study, the usability of the neutrophil-lymphocyte ratio (NLR) and the platelet-lymphocyte ratio (PLR) in predicting dyslipidemia, a serious complication of obesity, in children were investigated.

Method: Two hundred and seven cases aged between 11-17 years who were diagnosed with obesity at the Pediatrics Clinic of our hospital and 50 cases with no disorders whose complete blood count was performed for routine purposes were retrospectively investigated. The genders, ages, and examination findings of the cases were recorded. In obese children, leukocyte, hemoglobin, platelet, mean platelet volume, neutrophil and lymphocyte levels were evaluated in the complete blood count performed at the first admission. The NLR and the PLR were calculated. Preprandial blood glucose and preprandial insulin, serum aminotransferase values, and the lipid profile were recorded.

Results: While dyslipidemia was determined in 99 (47.82%) of 207 cases who were diagnosed with obesity, it was not determined in 108 (52.18%) cases. The systolic blood pressure, diastolic blood pressure, and preprandial insulin level were higher in cases with dyslipidemia than the group without dyslipidemia. The PLR average of the dyslipidemic group was 112.75±39.11, the PLR average of the non-dyslipidemic group was 104.78±31.38, and the PLR average of the control group was 110.20±39.35, and there was no statistically significant difference between the PLR averages of the groups (p=0.353). The NLR average was 1.52±0.69 in

Öz

Amaç: Çocukluk çağı obezitesi tüm dünyada giderek artan en önemli çocuk sağlığı sorunlarından biridir. Obezite ile birlikte olan dislipidemi, erişkin dönemde aterosklerotik hastalıklar için bir risk faktörüdür. Bu çalışmada çocuklarda, obezitenin ciddi bir komplikasyonu olan dislipidemiyi öngörmede nötrofil-lenfosit oranı (NLO) ve platelet-lenfosit oranının (PLO) kullanılabilirliğini araştırdık.

Yöntem: Hastanemiz Çocuk Sağlığı ve Hastalıkları Kliniği'nde obezite tanısı alan 11-17 yaş arası 207 olgu ve herhangi bir rahatsızlığı olmayıp rutin amaçlı tam kan tahlili yapılan 50 olgu retrospektif olarak incelendi. Olguların cinsiyetleri, yaşları, muayene bulguları kaydedildi. Obez çocuklarda ilk başvuruda alınan tam kan sayımında lökosit, hemoglobin, trombosit, ortalama trombosit hacmi, nötrofil ve lenfosit düzeyleri değerlendirildi. NLO ve PLO hesaplandı. Açlık kan şekeri ve açlık insülin, serum aminotransferaz değerleri ve lipid profili kaydedildi.

Bulgular: Obezite tanısı alan 207 olgunun 99'unda (%47,82) dislipidemi saptanırken, 108 olguda (%52,18) dislipidemi saptanmadı. Dislipidemi saptanan olguların sistolik kan basıncı, diastolik kan basıncı ve açlık insülin düzeyi dislipidemi olmayan gruptan daha yüksekti. Dislipidemik grubun PLO ortalaması 112,75±39,11, dispidemik olmayan grubun PLO ortalaması 104,78±31,38, kontrol grubunun PLO ortalaması 110,20±39,35 olup grupların PLO ortalamaları arasında istatistiksel olarak anlamlı farklılık gözlenmemiştir (p=0,353). NLO ortalaması dislipidemik grupta 1,52±0,69, dislipidemik olmayan grupta 1,66±0,81, kontrol grubunda 1,72±1,26 idi. Her üç grubun NLO ortalaması arasında istatistiksel olarak anlamlı farklılık gözlenmemiştir (p=0,295).

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Abstract

the dyslipidemic group, 1.66±0.81 in the non-dyslipidemic group, and 1.72±1.26 in the control group. No statistically significant difference was observed between the NLR averages of all three groups (p=0.295).

Conclusion: In this study, no relationship was determined between the PLR and NLR and dyslipidemia in obese children.

Keywords: Children, dyslipidemia, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio

Öz

Sonuç: Çalışmamızda obez çocuklarda PLO ve NLO ile dislipidemi arasında ilişki saptanmadı.

Anahtar kelimeler: Çocuk, dislipidemi, nötrofil-lenfosit oranı, platelet-lenfosit oranı

Introduction

Obesity, which is an important cause of morbidity and mortality, is gradually rising in the young people (1,2). Many health problems such as cardiovascular diseases, hypertension, type 2 diabetes, and fatty liver are associated with obesity (3).

Elevation of triglyceride (TG), LDL and total cholesterol values and a decrease in HDL cholesterol values in obese children cause an increase in the risk of cardiovascular diseases in childhood (4). Therefore, the early diagnosis and treatment of risk factors in obesity gains importance.

Recently, obesity is also known to be associated with immunological abnormalities (5). Inflammatory cells infiltrate adipose tissue in obese individuals, and these inflammatory cells and fat cells cause a low level of chronic systemic inflammation by producing cytokines (2,6,7). The neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR), which are considered to be indicators of subclinical inflammation, are cheap and easily calculable haemogram parameters, and in recent years, their relationship with obesity and obesity-associated diseases has been investigated (8-13).

Complications of obesity in children are now better known. Therefore, the treatment and prevention of obesity have remained a problem that should be solved urgently. In this study, we investigated the usability of NLR and PLR, which are easy methods, in the prediction of the presence of dyslipidemia in obese children.

Material and Methods

Two hundred and seven cases, who were diagnosed with obesity upon applying to the outpatient clinic of our hospital pediatrics clinic between January 2017 and May 2017 and who were between 11-17 years of age, and 50 cases, who did not have any disorder and who underwent a complete blood test for routine purposes, were retrospectively examined. Children with the body mass index (BMI) determined to 95 percentiles and higher according to age and gender were considered as obese. By using height and weight measurements, the BMIs [weight (kg)/height^2 (m^2)] of the cases were calculated. Patients with chronic disease, syndromic obesity, or hypothyroidism were not included in the study. Children with systemic infection or immunological disorders were excluded from the study.

The genders, ages and examination results of the cases were recorded. In the complete blood count taken at first admission in obese children, leukocyte, hemoglobin, platelet, mean platelet volume, neutrophil, and lymphocyte levels were evaluated. NLR and PLR were calculated. Fasting blood glucose and fasting insulin, serum aminotransferase values and lipid profile were recorded. Children with the LDL level >130 mg/dL or TG level >130 mg/dL, total cholesterol level >200 mg/dL or HDL level <35 mg/dL were considered to be dyslipidemic (14).

Ethics committee approval of the study was obtained from the Local Ethics Committee of our hospital (No: 2018.03.1.06.028), and an informed consent form was signed in accordance with the Declaration of Helsinki.

Statistical Analysis

The data were analyzed on the computer using SPSS 25.0 (Statistical Packages of Social Sciences) program. The appropriateness of the data to the normal distribution was evaluated by the Kolmogorov-Smirnov test. Descriptive statistics were demonstrated as mean ± standard deviation and median for continuous variables and as frequency and percentage for categorical variables. The two independent samples t-test was used to compare the normally distributed variables of two independent groups. The chi-square test was performed to analyze the difference between categorical variables. The Kruskal-Wallis test was conducted to compare the not normally distributed variables of more than two groups. The Mann-Whitney U test was used to perform the pairwise comparison of the variables that were statistically significant. It was interpreted by performing Bonferroni

correction. In the case of p<0.05, the difference was considered significant.

Results

While dyslipidemia was detected in 99 (47.82%) of the 207 cases diagnosed with obesity, dyslipidemia was not detected in 108 cases (52.18%).

The mean age of obese patients with dyslipidemia was 13.39±1.28 years and the mean age of obese subjects without dyslipidemia was 13.49±1.20 years. The mean BMI of the group with dyslipidemia was 31.48±1.81 kg/m^2, and the mean BMI of the group without dyslipidemia was 31.44±1.79 kg/m^2, and no significant difference was determined between the two groups (p=0.872).

The mean systolic blood pressure (SBP), mean diastolic blood pressure (DBP) and mean fasting insulin of the dyslipidemic group were found to be statistically significantly higher compared to those of the group without dyslipidemia (Table 1).

Table 1. Clinical and laboratory findings of obese children with and without dyslipidemia

	Dyslipidemia (-) n=108	Dyslipidemia (+) n=99	p value
Age	13.49±1.20	13.39±1.28	0.576
BMI	31.44±1.79	31.48±1.81	0.872
Fasting insulin	21.11±9.56	27.03±19.71	0.008*
SBP	120.67±11.54	128.18±14.16	0.0001*
DBP	74.21±8.96	78.28±9.18	0.001*
AST	20.62±8.21	22.51±17.71	0.319
ALT	20.30±13.23	22.16±11.36	0.617

BMI: Body mass index, SBP: Systolic body pressure, DBP: Diastolic body pressure AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

*Statistical significance was defined as a p value <0.05

The mean age of the dyslipidemic group was 13.39±1.28 years and the mean age of the group without dyslipidemia was 13.49±1.20 years, and the mean age of the control group was 13.26±1.54 years, and there was no statistically significant difference between the mean ages of all three groups (p=0.365).

While the mean leukocyte and platelet counts were determined to be statistically significantly higher in obese children with and without dyslipidemia compared to the control group (p=0.037, p=0.0001), the mean lymphocyte count was found to be statistically significantly lower (p=0.007).

The mean PLR of the dyslipidemic group was 112.75±39.11, the mean PLR of the group without dyslipidemia was 104.78±31.38, and the mean PLR of the control group was 110.20±39.35, and no statistically significant difference was observed between the mean PLRs of the groups (p=0.353). The mean NLR was 1.52±0.69 in the dyslipidemic group, 1.66±0.81 in the group without dyslipidemia, and 1.72±1.26 in the control group. There was no statistically significant difference between the mean NLRs of all three groups (p=0.295) (Table 2).

Discussion

Obesity is the excessive accumulation of fat in the body over acceptable measurements (15). Childhood obesity has an increasing prevalence throughout the world (16). The fact that morbidity and mortality in adulthood increase in individuals who have been obese in childhood and that 50% of those who have been obese in adolescence are obese in adulthood make obesity a significant health problem (17).

Table 2. Hemogram parameters of obese children with and without dyslipidemia and control group

	Dyslipidemia (-) I (n=108)	Dyslipidemia (+) II (n=99)	Control III (n=50)	p value	I-II p value	I-III p value	II-III p value
Age	13.49±1.20	13.39±1.28	13.26±1.54	0.365	-	-	-
Leukocyte	8.60±1.94	8.64±1.98	7.94±12.14	0.037*	1.000	0.067	0.052
Neutrophil	4.72±1.56	4.51±1.51	4.31±1.73	0.100	-	-	-
Lymphocyte	3.03±0.79	3.10±0.67	6.76±28.76	0.007*	0.863	0.059	0.005*
Hemoglobin	13.41±1.19	13.64±1.07	13.03±1.80	0.189	-	-	-
MPV	9.18±1.64	9.06±1.66	8.42±2.15	0.053	-	-	-
Platelet	300.19±64.84	334.68±81.43	282.89±62.42	0.0001*	0.010*	0.536	0.001*
PLR	104.78±31.38	112.75±39.11	110.20±39.35	0.353	-	-	-
NLR	1.66±0.81	1.52±0.69	1.72±1.26	0.295	-	-	-

MPV: Mean platelet volume, PLR: Platelet-lymphocyte ratio, NLR: Neutrophil-lymphocyte ratio

*Statistical significance was defined as a p value <0.05

With the increasing prevalence of obesity, the incidence of many health problems such as cardiovascular diseases, hypertension, type 2 diabetes, and dyslipidemia is gradually increasing (3). Dyslipidemia that accompanies obesity is a significant risk factor for atherosclerotic diseases in adulthood (18). Dyslipidemia observed in obese children is explained by the lipolysis of visceral fat cells and by the increase in fatty acids produced as a result of this. In the study by Özer et al. (19), dyslipidemia was determined at a rate of 39%. Atabek et al. (20) found the frequency of dyslipidemia to be 47.3%. In our study, the rate of dyslipidemia was determined to be 47.82% in accordance with the literature.

In a community-based epidemiological study, people who were lost due to accidents or suicides were evaluated, and it was demonstrated that the fat lines were in 50% of the children and 85% of the adults and the formation of fibrous plaque increased with age (in 8% of the deceased children and in 69% of adults), and the presence of these lesions was found to be correlated with the elevation of total cholesterol, LDL, TG level, blood pressure, and body mass index (21). There is a close relationship between dyslipidemia and insulin resistance since insulin plays a controlling role in the elimination of blood TGs and the release of free fatty acids from adipose tissue, by activating the lipoprotein lipase (22). The incidence of hypertension in obese children is significantly higher than in normal weight children (23). In our study, we found out that SBP, DBP, and fasting insulin levels were higher in obese individuals with dyslipidemia compared to obese individuals without dyslipidemia.

Obesity itself is a chronic inflammatory process (24). Inflammatory cells infiltrate the adipose tissue in obese individuals, and these inflammatory cells and fat cells cause a low level of chronic systemic inflammation by producing cytokines (2,6,7). NLR, considered to be an indicator of subclinical inflammation, is an indicator which is calculated by using neutrophil and lymphocyte values in the hemogram and of which popularity is increasing with each passing day (25). Increased inflammation and endothelial dysfunction play an important role in the pathophysiology of atherosclerotic cardiovascular diseases (26). Aydın et al. (27) found out that NLR was higher in obese adolescents than the healthy control group. In a study conducted on adult obese individuals, the NLR was not found to be a good indicator of inflammation (11). In our study, we did not determine a relationship between dyslipidemia and the NLR in obese children.

Apart from the antithrombotic effects of platelets, it is believed that they lead to leukocyte migration and binding to endothelial cells, by secreting proinflammatory cytokines, and thus play an important role in inflammation (28). The PLR is a parameter calculated by using platelet and lymphocyte values in the hemogram, and it is determined to be high in cardiovascular diseases and in cases that increase the risk of cardiovascular diseases (29). Aydın et al. (27) found out that the PLR in obese adolescents was not different from the healthy control group. In our study, we did not determine a relationship between the PLR and dyslipidemia in obese children.

Conclusion

In our study, in obese children there was no relationship between the NLR and PLR and dyslipidemia respectively. This may be related to the fact that our age group includes children and in this period, metabolic and cardiovascular complications and inflammation are less. The weak aspect of our study is that it is a retrospective study. Therefore, prospective studies involving more cases are required.

Ethics

Ethics Committee Approval: Ethics committee approval of the study was obtained from the Local Ethics Committee of our hospital (No: 2018.03.1.06.028)

Informed Consent: Informed consent form was signed in accordance with the Declaration of Helsinki.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.D.D., S.K., Concept: Ö.B.G., M.E., Design: Ö.B.G. M.E., Data Collection or Processing: T.D.D., S.K., Analysis or Interpretation: Ö.Y., F.M., Literature Search: Ö.B.G., T.D.D., Writing: Ö.B.G., T.D.D.

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ORIGINAL RESEARCH

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The Role of Granulocyte-macrophage Colony Stimulating Factor in Recurrent Pregnancy Losses

Granül-makrofaj Koloni Uyarıcı Faktörünün Tekrarlayan Gebelik Kayıpları Üzerindeki Rolü

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Abstract

Objective: A specific factor cannot be detected in approximately half of recurrent pregnancy losses (RPL). The aim of the present study was to investigate the role of a cytokine, granulocyte-macrophage colony stimulating factor (GM-CSF), in the etiology of recurrent pregnancy losses.

Method: A total of 50 patients who had been admitted to the gynecology and obstetrics clinics of İstanbul University Medical School between January 1995 and September 2001 were included into the study and allocated to five groups including control and study groups. The study groups included 30 patients and the control groups included 20 patients. There were 3 study groups including non-pregnant women who had abortion (2 groups) and a spontaneous abortion group, which were selected among the recurrent pregnancy loss (RPL) subjects with unknown etiology. The spontaneous abortion, non-pregnant RPL group and pregnant RPL group were accepted as study group). These groups were compared with the control groups, which included pregnant and non-pregnant healthy women.

Results: Moderate and severe GM-CSF activity was detected in the decidua of all cases in fertile and elective termination groups. However no significant difference was detected in the surface epithelium, gland epithelium and stromal GCSF activities. Endometrial GM-CSF activity was determined to decrease in spontaneous abortion and RPL cases.

Conclusion: Reduced GM-CSF activity in the decidua may have a role in the etiology of RPL. Besides, the level and distribution of GM-CSF in different compartments of the decidua may be a determinant factor in the prognosis of pregnancy.

Keywords: Recurrent pregnancy loss, GM-CSF, endometrium

Öz

Amaç: Bu çalışma ile öncelikle implantasyon için önemli bir role sahip olduğu düşünülen GM-CSF'ün tekrarlayan gebelik kaybı (TGK) etiyolojisindeki yerini araştırmayı amaç edindik. İmplantasyon başlangıcı ve devamlılığı birçok karmaşık olgunun bir senkronizasyon içinde seyrini gerektirir. Tekrarlayan gebelik kayıplarının ortalama yarısı açıklanamaz durumda olup lokal immun faktörler ile ilişkili olabileceği ile ilgili çalışmalar yoğunluk kazanmaktadır. Düşüğün fizyopatolojisinde GM-CSF'nin bir sitokin olarak rolü henüz araştırılmaktadır.

Yöntem: İstanbul Tıp Fakültesi Kadın Hastalıkları ve Doğum Poliklinikleri'ne başvuran 50 olgudan kontrol ve çalışma grupları oluşturarak toplam beş grup araştırılmıştır. Çalışma grupları 30, kontrol grupları ise 20 hasta içermektedir. Çalışma grupları rutin TGK araştırması sonucu nedeni bulunamayan olgular arasından seçilen, gebe olmayan ve düşük yapanlar olmak üzere oluşturulan iki grup ile spontan düşük yapan bir başka grup beraber olmak üzere toplam olarak üç grup halinde çalışılmıştır. Bu gruplar, gebe olan ve olmayan sağlıklı kadınlardan oluşturulan kontrol grupları ile mukayese edilmişlerdir.

Bulgular: Bu çalışma göstermiştir ki spontan ya da TGK olgularında gebelikten bağımsız olarak endometriumda GM-CSF azalmış düzeyde bulunmaktadır. Söz konusu durum gebeliğin henüz gerçekleşmediği preimplantasyon endometriumunda söz konusu patolojinin bir devamlılık göstererek düşük için predispozisyon oluşturduğu tezini destekler görünmektedir. Çalışma gruplarında GM-CSF'ye ilişkin boyanma kontrol gruplarına kıyasla anlamlı derecede azalmış bulunurken, özellikle yüzey epiteli ve glandüler epitele ait farklılıklar dikkat çeker nitelikte idi. Kontrol grupları arasında farklı bir boyanma paterni izlemedi.

Sonuç: GM-CSF'nin tekrarlayan gebelik kayıplarındaki rolü immun mediatörler ve sitokinler hakkındaki bilgilerin yoğunlaşması ile daha da açıklık kazanacaktır. Bu tez çalışmasının immunodistrofik etkeninin araştırılması konusunda bir adım olarak kabul edilerek daha büyük hasta grupları ile ve prospektif yeni, detaylı çalışmalara gereksinim olduğu düşüncesindeyiz.

Anahtar kelimeler: Tekrarlayan gebelik kaybı, GM-CSF, uterus mukozası

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Introduction

Recurrent pregnancy loss (RPL) was defined as the loss of three consecutive pregnancies independently from being intrauterine pregnancies in 2006 (1,2). Later in 2013, loss of two or more failed clinical pregnancies, which were documented with ultrasonography and histopathological examination, was accepted as RPL considering that every sequential abortion would increase the likelihood of the failure of the next pregnancy depending on prospective studies (3). Early pregnancy loss is the most common complication of pregnancy and seen in about 10-15% of the clinical pregnancies under 20 weeks (4). Despite the fact that the etiology is unclear in about half of the RPLs although anatomical, hormonal and genetic factors have been accounted for (5).

The presence of cytokines is required for communication and synchronization besides oocyte, sperm, embryo, and an appropriate endometrium for a successful pregnancy. Cytokines and growth factors that are produced by endometrial tissue and trophoblastic cells play a role in regulation and differentiation of trophoblastic cell growth and myometrial invasion of trophoblasts (6). Colony stimulating factors (CSF) are glycoproteins, which affect the cellular differentiation and proliferation through binding to specific receptors in hematopoietic stem cells. Members of the CSF family have different gene locations, structures and receptors.

The aim of the present study was to investigate the role of Granulocyte-macrophage colony stimulating factor (GM-CSF), which is a member of the CSF family known to have a role in continuity of pregnancy together with ovulation and implantation in the etiology of recurrent early pregnancy losses and implantation failure.

Material and Methods

A total of 50 patients aged between 18-40 years, who were menstruating regularly, who knew the last date of menstruation, who were pregnant with shorter than 20 weeks of gestation, who had experienced two or more abortions and who had presented to the İstanbul University Medical School Clinic of Gynecology and Obstetrics between January 1995 and September 2001, were included in the study, retrospectively.

A detailed anamnesis was obtained from all patients and analyses were performed for complete blood count, urine analysis, blood group, fasting plasma glucose (4-hour oral glucose tolerance test with 100 gr glucose for risky patients), hysterosalpingograph (HSG), biopsy with endometrial pipelle, thyroid stimulant hormone (TSH), prolactin, aPTT, anti-cardiolipin antibody (aCL), IgM and IgG levels, karyotype detection for the couples and genetic counseling was given. The patients were recommended contraception with the barrier method during the tests.

Fifty patients were allocated to five groups as the fertile group (control 1 - group I), the elective termination group (control 2 - group II), the spontaneous abortion group (group III), the non-pregnant RPL group (RPL 1- group IV) and the pregnant RPL group (RPL 2 - group V) with 10 patients in each.

The patients who had at least one live and healthy child, those who did not have an additional endometrial pathology and those who had cervical polyps were assigned to the “fertile group”; the patients who met these criteria and who knew the date of the last menstruation, those who had electively terminated their singleton pregnancy, those who had at least one live and healthy child were assigned to the “elective termination group”. While endometrial biopsy was performed with pipelle following cervical polyp extirpation during the late secretory phase (between days 24-27 of the last menstruation) in patients in the fertile group, curettage material was obtained from the patients in the elective termination group. The patients who had been diagnosed with spontaneous abortion (impaired pregnancy, missed abortion, non-embryonic pregnancy) within the recent 2 years, those who had a history of at least one pregnancy above 20 weeks or those who had at least one live birth previously were included in the “spontaneous pregnancy group” and the curettage material of these patients were analyzed. The first RPL group (RPL 1) was composed of patients who previously had RPL with an unknown etiology (anatomical, genetic, endocrinological and autoimmune). Endometrial sampling was carried out with pipelle 2-3 days before the estimated day of menstruation. The second RPL group (RPL 2) was composed of patients who were pregnant and had RPL with an unknown etiology (impaired pregnancy, non-embryonic pregnancy, missed abortion) and abortion material was obtained.

The tissue samples were fixed within 4% (w/v) formalin for 12-18 hours; they were dehydrated and embedded into paraffin blocks. Tissue samples were cut into pieces 5 µm in thickness and placed onto clean lams, deparaffinized with xylene and alcohol, and washed with phosphate buffer solution (PBS). The tissue sections were then mixed with

3% (w/v) hydrogen peroxide for 45 min in order to block endogenous peroxidase activity and treated with blocking agent, Vectastain Elite ABC kit in order to block nonspecific avidin-biotin binding. The tissue samples were incubated with 10 µg/mL anti-GM-CSI, which was diluted with 0.1% (w/v) bovine serum albumin at pH 7.4 for 2 hours.

The control samples were composed of sections that did not contain primary antibody, which were incubated in GM-CSF antibody pre-absorbed with GM-CSF purified mice IgG1 and GM-CSF. Following the washing with PBS, tissue samples were incubated with secondary antibody against mice IgG was conjugated with peroxidase for one hour, centrifuged with PBS for 5 min and incubated with diaminobenzidine (DAB). The sections were dehydrated and slides were prepared by using permanent. The results were evaluated visually through comparing each positive sample with its control.

Statistical Analysis

The endometrial surface, the endometrial gland epithelium, and the endometrial stromal cells were evaluated separately. The fields in which immunoreactivity was most widespread and most intense were detected on small magnification (X40, X100). The location and severity of immunoreactivity were evaluated on high magnification (X250, X400). All sections were scored between 0 and 4 according to the severity of the reaction. The non-parametric statistical analyses were performed using the Fischer's chi-square test and a p level of <0.05 was accepted as statistically significant. The results were evaluated by comparing three different compartments of decidual tissue.

Results

The fertile and the elective termination groups were accepted as the control groups. The mean age was 29 in the control groups. The spontaneous abortion, the non-pregnant RPL group and the pregnant RPL groups were accepted as the study group. The mean age was 32 years in the study group. The mean age was similar in the control and the study groups. While six patients in non-pregnant RPL group had 3 consecutive abortions, two patients had 4, and the remaining two patients had five abortions.

Moderate-severe GM-CSF immunoreactivity was determined in the decidua of all cases in the fertile and the elective termination groups. However, the surface epithelium, the gland epithelium and the stromal GM-CSF activity did not differ significantly in those healthy subjects regardless of the presence of pregnancy. When compared with the spontaneous abortion and the RPL groups, the GM-CSF activity of the surface epithelium and gland epithelium was found to be significantly higher in the fertile and the elective termination groups (p<0.001).

Stromal cell GM-CSF immunoreactivity was found to be statistically similar in all groups, although stromal cell GM-CSF expression was determined to be high in the fertile groups. Superficial, glandular epithelium and stromal cell GM-CSF activity showed a significant difference in the spontaneous abortion, the non-pregnant RPL and the pregnant RPL groups. According to the results of our study, the GM-CSF expression was affected as the staining intensity was lost in the presence of a history of spontaneous abortion or RPL (Table 1); however, the presence or absence of pregnancy did not affect the degree of staining loss (Table 1).

Table 1. Statistical comparison of recurrent pregnancy lose groups

Group	Surface epithelium (p)	Gland epithelium (p)	Stroma (p)
Fertile group-elective termination group	0.8	0.8	0.9
Fertile group-spontaneous abortion group	*0.0001	*0.0005	0.18
Fertile group-non-pregnant RPL group	*0.04	*0.04	*0.04
Fertile group-pregnant RPL group	*0.05	*0.01	0.4
Elective termination group-spontaneous abortion group	*0.001	*0.001	0.8
Elective termination group-non-pregnant RPL group	*0.05	*0.04	0.09
Elective termination group pregnant RPL group	*0.004	*0.005	0.8
Spontaneous abortion group-non-pregnant RPL group	0.2	0.1	0.3
Spontaneous abortion group-pregnant RPL group	0.5	0.5	1
Non-pregnant RPL group-pregnant RPL group	0.8	0.8	0.4

p<0.05 (significant)

RPL: Recurrent pregnancy lose

All patients of fertile and elective termination groups have moderate-severe GM-CSF immunoreactivity. However, in healty patients there aren't any differences among surface epithelial, gland epithelial and stromal immunoreactivity

While the staining in the spontaneous abortion, pregnant and the non-pregnant RPL groups was significantly different from the staining in the fertile and the elective termination groups, the staining features were similar in the spontaneous abortion and RPL cases.

This finding suggests that abortion and GM-CSF pathology have a synchrony without showing a quantity difference regardless of the etiology.

Discussion

The CSF family is composed of three members including CSF 1 (macrophage CSF/M-CSF), CSF 2 (GM-CSF), CSF 3 (Granulocyte CSF/G-CSF). The main role of the CSF family is leukocyte proliferation and differentiation. They are of glycoprotein structure. They are encoded on different chromosomes despite belonging to the same family. While G-CSF is encoded from the single gene on chromosome 17 (7), GM-CSF is encoded from chromosome 5 (8).

Cytokines have been known to have effects on the reproductive system and known to be important for maternal-fetal communication since the 1970s (9). The CSF family has immune trophic, anti-apoptotic and immune modulatory effects in early pregnancy (10). CSFs have begun to be used for therapeutic purposes in assisted reproductive technology for women who have implantation failure and folliculogenesis problems due to their effect in pregnancy formation and in the early period.

In 1991, CSFs (particularly GM-CSF) were shown by Croy et al. to be present in the placenta, the decidua and the endometrium besides ovary and follicles. (11)

CSFs play a role in a successful implantation through creating a T-helper 2 dominant environment. Implantation occurs in the early period through a local tolerance development against the fetus. Although all CSFs show an immune modulatory effect, GM-CSFs show a local effect through regulating cytotoxicity of natural killer cells and reducing the interleukin production. GM-CF plays the main role in implantation (12). GM-CSF was also shown by Clark et al. (13) to play a control role in uterine cell cytotoxicity. In conclusion, while neutralizing, GM-CSF increases the likelihood of spontaneous abortion, and the chance for a successful pregnancy increases with GM-CSF supplementation.

In addition to its local immunological effects, the CSF family is necessary for a successful pregnancy due to having an angiogenic effect. The CSF family is required not only for the decidua, but also for placental development. GM-CSF is a promoter for placental growth and enables trophoblast migration (14,15).

GM-CSF may have an important role for endometrium's preparing to implantation. A healthy blastocyte, apposition, adhesion and penetration should be successful for achieving implantation. For this purpose, GM-CSF activity should be sufficient, particularly in decidual cells (16,17). The role of GM-CSF as a local regulator is important, not only at the implantation stage, but also for the healthy continuation of pregnancy (18). GM-CSF, which is produced at the fetomaternal surface, contributes to placental functions and embryo development through stimulating gonadotropin production (15). The inflammatory reactions that develop when pregnancy is formed lead to alterations in cytokine concentration including GM-CSF through enabling granulocyte migration to the field.

In the present study, we determined the presence of GM-CSF glycoprotein in the surface epithelium, glandular and stromal cells during the whole cycle in the fertile and the elective termination groups. The results in both groups have indicated the presence of similar amounts of GM-CSF, regardless of the presence of pregnancy (Table 1). In other words, no change occurs in GM-CSF expression in the pregnancy endometrium if there is no clinical pathology. However, the staining features of the cells have changed in the presence of a clinical pathology. The presence of GM-CSF was different in pregnant RPL2 cases and spontaneous abortion cases when compared to the elective termination group (Table 1). The cellular staining characteristic in these groups is similar to that of non-pregnant healthy RPL1 cases at all cellular levels (Table 1). No significant change was detected in stromal staining while superficial epithelium and glandular staining showed significant differences (Table 1).

GM-CSF is a local factor, which is effective on the distribution and rate of hematopoietic cells in the endometrium. Macrophages were seen to be the most effective cell group in the uterus in animal and human studies. Macrophages are cells that interact with steroid hormone levels (19). Presence of macrophage, granulocyte, and the peroxidase of some cytokines are known to be effective in eosinophilic cell concentration (20).

In the present study, GM-CSF expression was negatively affected at cellular level in patients diagnosed with RPL, and endometrial staining did not change significantly

independent from the presence of pregnancy. In fact, endometrial GM-CSF pathology persists in a case diagnosed with recurrent pregnancy loss with unknown etiology.

The present study has indicated that an insignificantly low level of GM-CSF in stromal cells is not significantly affected by factors that lead to RPL. Moreover, protein expression in the stromal cells of the study group similar to healthy cells may indicate that GM-CSF may not necessarily be required for implantation in the very early period of pregnancy. Various mediators such as TNFα, DDFG, TGFB and IL-1 may stimulate the GM-CSF production when the embryo passes the surface epithelium and invades the stroma (21,22,23,24,25).

Much lower GM-CSF activity was shown in superficial and glandular epithelial cells in group II, group III and group V when compared to the control group (Table 1). As known, apposition and adhesion procedures are arranged by the decidual superficial epithelium and glandular elements. Defective production of GM-CSF in the decidual epithelial compartments leads to recurrent pregnancy losses through the alterations described above.

Study Limitations

The limitations of the present study are its retrospective design and the limited number of patients. Despite the presence of studies investigating GM-CSF, M-CSF (CSF-1) and TNF, they have not been studied in pre- and post-pregnancy endometrium. Presence of different concentrations of GM-CSF was investigated in this study and significant reductions in semiquantitative GM-CSF levels were determined.

Conclusion

Decidual GM-CSF activity may play a role in etiology of recurrent pregnancy losses. The level and distribution of GM-CSF in different compartments of the decidua may be a determinant in the prognosis of pregnancy. The results of the present study reveal that GM-CSF production is negatively affected in spontaneous or recurrent abortions. In other words, abnormal GM-CSF activity begins in the superficial and glandular cells of the decidua regardless of the clinical type of abortion. In addition, the abortion procedure does not affect the stromal GM-CSF production; the stromal GM-CSF production does not have a necessary role in the survey of early pregnancy.

The role of GM-CSF as a cytokine is still being investigated in the pathophysiology of abortion. The results of the present study yield information about the location and expression of GM-CSF in endometrial cells and also draw attention to its role as a cytokine in recurrent pregnancy losses with unknown etiology and indicate that further studies should be performed on this issue.

According to the results of the study, the endometrial GM-CSF level is reduced independently from pregnancy in spontaneous or recurrent pregnancy losses contrary to the intensive GM-CSF presence in endometrial layers in healthy women. In presence of a pathological pregnancy, and even in the presence of an etiology that could accompany a pathological process, GM-CSF expression on the endometrial surface and glandular epithelium decrease; however, stromal expression does not change. More comprehensive studies that would follow this preliminary study would answer the questions whether the reduction in GM-CSF expression is the etiology itself or a reflection, and could render future supplemental treatments to contribute to the clinical process.

The role of GM-CSF in recurrent pregnancy losses would be clearer through accumulating data about immune mediators and cytokines. We consider that the present study would be accepted as a step for investigating the immune dystrophic factor and further prospective studies conducted with larger patient groups are required.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Ö.K.A., C.A., Design: Ö.K.A., C.A., Data Collection or Processing: Ö.K.A., Analysis or Interpretation: E.V.K., H.G., Literature Search: Ö.K.A., E.V.K, Writing: Ö.K.A., E.V.K., H.G., C.A.

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

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ORIGINAL RESEARCH

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Improvement of Spatial Learning and Memory Impairments by Fetal Neural Tissue Transplantation in Experimental Rat Model of Alzheimer's Disease

Sıçanlarda Deneysel Alzheimer Hastalığı Modelinde Hacimsel Öğrenme ve Bellek Bozukluklarının Fetal Nöral Doku Transplantasyonu ile Düzelmesi

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Abstract

Objective: It is known that the acetylcholinergic afferents of the neocortex from subcortical areas participate in learning and memory. Autopsy studies in cases of Alzheimer's disease (AD) have shown that most of the neurons of nucleus basalis magnocellularis (NBM) are atrophic or decreased in number. In this study, we searched for whether or not it was possible to improve the impaired learning and memory functions with foetal neural tissue transplantation in an experimental model of AD.

Method: A total of thirty seven young adult male Wistar albino rats were served as experimental subjects. NBM on the right side was destroyed by the injection of kainic acid stereotactically so as to make a model of AD. The grafts were obtained from 14-16 day foetuses of the same genus. After the tissue with cholinergic neurons dissected from ventral forebrain and tissue with non-cholinergic neurons dissected from telencephalic vesicle, cell suspensions were prepared and injected stereotactically to the ipsilateral frontal cortex. Spatial learning and memory functions were tested by Morris' water maze tasks.

Results: Spatial learning and memory functions in rats were impaired by unilateral lesions of nucleus basalis magnocellularis. The impairment observed during the early period partially improved by the time. It was observed that this amelioration was accelerated with both cholinergic and non-cholinergic foetal neural tissue implantation.

Öz

Amaç: Subkortikal alanlardan neokortekse uzanan asetilkolinerjik nöronların öğrenme ve bellek süreçlerinde rol aldığı bilinmektedir. Alzheimer hastalığında (AH) yapılan otopsi incelemeleri bazal magnoselüler çekirdekteki nöronlarda atrofi veya azalma olduğunu göstermiştir. Bu çalışmada deneysel AH modelinde bozuk öğrenme ve bellek fonksiyonlarının, fötal nöral doku transplantasyonu ile düzelmesinin mümkün olup olmadığı araştırıldı.

Yöntem: Deneysel çalışmada 37 adet Wistar albino cinsi genç erişkin erkek sıçan kullanıldı. AH modeli sağ bazal magnoselüler çekirdeğe stereotaktik yöntemle verilen, nörotoksik bir ajan olan kainik asit ile oluşturuldu. Greftler aynı cins sıçanların 14-16 günlük fetuslarından alındı. Kolinerjik nöronları içeren doku ventral ön beyinden, non-kolinerjik nöronların olduğu doku ise telensefalik vezikülden elde edilerek, hücre süspansiyonu haline getirildi ve stereotaktik yöntemle ipsilateral frontal kortekse implante edildi. Hacimsel öğrenme ve bellek fonksiyonları Morris'in "water maze" testi ile değerlendirildi.

Bulgular: Tek taraflı bazal magnoselüler nükleus lezyonları ile sıçanlarda hacimsel öğrenme ve bellek fonksiyonları bozuldu. Erken dönemde bozulan bu fonksiyonlar geç dönemde kısmen düzeldi. Hem kolinerjik hem de non-kolinerjik fötal doku implantasyonu ile bu düzelmenin hızlandığı saptandı.

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Abstract

Conclusion: In our study, improvement of spatial learning and memory impairment with both cholinergic and non-cholinergic foetal neural tissue implantation can be explained by re-establishment of impaired connections via proliferation of limited number of surviving cholinergic neurons creating new synapses, as a result of upregulation of endogenous neural stem cells and activation of trophic mechanisms by implantation, rather than creation of functional synapses between the graft and the recipient tissue.

Keywords: Alzheimer's disease, neural transplantation, nucleus basalis magnocellularis, spatial learning and memory

Öz

Sonuç: Çalışmamızda hem kolinerjik hem de non-kolinerjik fötal nöral doku implantasyonu ile hacimsel öğrenme ve bellek fonksiyonlarının düzelmesi, greftin alıcı doku ile fonksiyonel sinapslar oluşturmasından ziyade, implantasyonun endojen nöral kök hücrelerini regüle etmesi ve trofik mekanizmaları harekete geçirmesi sonucu, sağ kalan az sayıdaki kolinerjik nöronların çoğalması ve yeni sinapslar oluşturarak bozulmuş bağlantıları yeniden kurması ile açıklanabilir.

Anahtar kelimeler: Alzheimer hastalığı, nöral transplantasyon, nükleus basalis magnoselüler, hacimsel öğrenme ve bellek

Introduction

Many investigations have emphasized that some of non-myelinated and scarcely myelinated neurons in mammalian central nervous system (CNS) have regeneration capacity since the late 19th century (1-10). Inspired by these studies, fetal tissue graft models have been studied for the restoration of damaged circuits in the treatment of degenerative disorders. (4,6,7,10-24).

Neuroanatomy and neurophysiology of learning and memory functions have not been clearly defined yet. It is believed that they are regulated by a complex system including anatomic associations and chemical pathways (25,26). It has been shown that nucleus basalis magnocellularis (NBM), which was first microscopically defined by Meynert in 1872, and located in both anatomic and chemical pathways, plays an important role in learning and memory functions by acting as a bridge between cortex and limbic system (25-27). Autopsy studies performed on neurodegenerative diseases progressing with Alzheimer disease (AD) and dementia indicated that there was atrophy or decrease in neurons in NBM (28-32). Decreases were determined in cortical cholinesterase (ChAT), acetylcholine esterase (AchE) activities with acetylcholine (Ach) levels in these patients, and it was shown that these were directly correlated with the damage in NBM (28-33). As the result of histological, pharmacological, and biochemical studies, it is believed that clinical picture of dementia in AD is due to decreased acetylcholinergic inputs in cortex which is commonly associated to the degeneration in cholinergic neurons in nucleus of Meynert (25,30,31). In experimental animals, neurotoxic or electrolytic lesions in NBM causes 70-80% decrease in neocortical ChAT, and AchE activities along with similar learning and memory disorders in subjects with AD model (19,20). Both histological and biochemical studies have documented that Ach-rich ventral forebrain (VF) grafts can set up functional synaptic connections with host neurons in the neocortex. Besides, it was determined that clinical picture in sensorimotor and learning tests were recovered (19,20). The aim of the present study was to establish an experimental AD model by disrupting learning and memory functions by a unilateral NBM lesion in rats, and to investigate effects of fetal neural grafts on spatial learning and memory functions in this experimental model of AD.

Material and Methods

Experimental study was performed at İstanbul University, Center for Experimental Medical Research and Application (DETAM). Animal rights were followed according to Helsinki Declaration, and handling and use of laboratory animals were managed according to institution and national guidelines. The study was approved by the Local Ethics Committee (DETAM project number: 1990/31).

A total of 37 young adult male Wistar albino rats, which were grown up at DETAM and weighing about 200-300 g at time of surgery served as experimental subjects. Grafts were obtained from 14-16-day old fetuses of the same genus (Figure 1). Coordinates in stereotactic interventions were calculated by using Pellegrino's rat stereotaxis map.

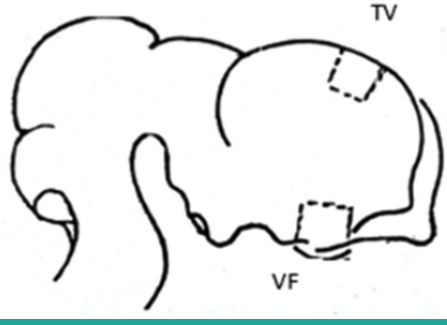

Figure 1. Location of grafts obtained in 14-16 days old fetus

VF: Ventral forebrain, TV: Telencephalic vesicle

A two-staged experiment was performed in the investigation (Table 1). Eighteen rats were used in the first experiment. Four of them had no surgical intervention and were included in the normal rat group. Neurotoxic lesions with kainic acid were induced stereotactically in the right NBM in 11 rats. In three rats, Hamilton needle was introduced into NBM, but no lesion was performed, so they were defined as the sham-operated (self help and actualization movement) group. Ten days after NBM lesion, spatial learning and memory functions were assessed by Morris' water maze tasks. At the end of this test, six out of 11 rats with NBM lesions received stereotaxic injections of cell suspensions containing tissue dissected from VF area of fetuses into the ipsilateral frontal cortex. At day 100 after NBM lesion, water maze tasks were repeated in all groups.

In the second experiment performed after the first one, 19 rats were used. Of them, four constituted normal group, whereas three formed the sham-operated group. In 12 rats, neurotoxic lesions of NBM with kainic acid were made stereotactically. Ten days after the NBM lesion, spatial learning and memory functions were assessed by Morris' water maze tasks. At the end of this test, cholinergic cell suspensions prepared from tissue obtained from VF area of fetuses were implanted stereotactically into the ipsilateral frontal cortex in five out of 12 rats with NBM lesions. In four out of 12 lesioned rats, cell suspensions prepared from the tissue dissected from the telencephalic vesicle (TV) of the same fetuses, which did not contain cholinergic neurons, were implanted stereotactically into the ipsilateral frontal cortex. At day 100 after NBM lesion, water maze tasks were repeated in all groups.

At the baseline, every rat was given a number by marking their tails. Procedures during surgical interventions were recorded for each rat. Until the end of the study, all rats were kept together in big rat cages located at the floor of experimental animals in DETAM. Subjects performing Morris' water maze tasks were blinded for groups of rats while performing the test.

Graft preparation: For each experiment, a total of four fetuses 14 to 16 day-old (crown-rump leng 12-16 mm) were dissected out by caeserian section from a deeply anesthetized pregnant rat under aseptic conditions. After a fetus was removed from the uterus, the brain tissue was submerged in 0.6% glucose-saline solution on a glass slide, and the area of interest was dissected, 2x2x2mm in size, under a operating microscope using a pair of iridectomy scissors and watchmaker's forceps. To prepare a cell suspension, the dissected regions were cut into smaller pieces and transferred to a test tube containing a trypsin-glucose-saline solution (0.1% trypsin, Sigma crude type II and 6% d-glucose in sterile saline) for 20 minutes incubation at 37 °C. Following the enzyme incubation, the trypsin solution was then rinsed off by 4-5 times with the glucose-saline solution. A cell suspension was made by mechanical dissociation, which was performed by gentle pipetting 15 times using a Pasteur pipette. A total of 3 µL cell suspension was injected through Hamilton needle no 24 with a speed of 1 µ/L/minute.

Morris' water maze test: A cylindrical tank, 100 cm in diameter and a depth of 40 cm, was filled to a depth up to 30 cm, and the water was made turbid by using milk powder. The pool was divided four equal imaginary quadrants. In the middle of a fixed quadrant, a glass platform with 10x10 cm was placed 1 cm under the water level, so that rats could not see the platform. The pool was placed in a fixed place in the experiment room with fixed objects such as wall, mirror, or hanger around. Rats, facing to borders of the pool, were placed in the water from four corners twice a day for 4 days with 24-hour intervals and their time to find the platform within 120 seconds was calculated by using a chronometer. In order to observe the surroundings, rats were kept on the platform for 30 seconds after each trial. A total of 32 trials were performed within 4 days. The platform was removed on the 5th day, and rats were placed in the pool from four different corners. Time spent in the place where platform was previously located was measured within 60 seconds.

Statistical Analysis

Results were assessed by using ANOVA statistically analysis program for Macintosh, repeated one-way variation analysis was used for each graphic, and the level of significance was determined at $p<0.05$.

Table 1. Study groups in two-staged experiments

	A Normal	B Sham-operated	C NBM lesions	D VF grafts	E TV grafts	Total
Experiment 1	4	3	5	6	-	18
Experiment 2	4	3	3	5	4	19

NBM: Nucleus basalis magnocellularis, VF: Ventral forebrain, TV: Telencephalic vesicle

Results

Experiment 1

Figure 2 shows the graphic of arithmetic means of the results of 8 trials in 4 consecutive days starting 10 days after lesion surgery. There was no significant difference between groups A (normal) and B (Sham-operated), whereas group C (NBM lesion) statistically differed from the others ($p<0.001$). Similar results were determined in assessment of day 5 results ($p<0.05$) (Figure 3).

The results of the first four days of the tasks performed 100 days after NBM lesions are shown in Figure 4. The statistically analyzes between all groups (A-normal, B-sham-operated, C- NBM lesion, D- VF implantation) revealed no difference between groups A and B, A and D, B and D; but significant difference was determined between groups A and C; B and C; C and D ($p<0.0001$). At the 5th day, the results between the same groups were again significant (Figure 5) ($p<0.001$).

The results of water maze tasks performed on lesioned rats 10 (group C1 n=11) and 100 days after lesion surgery (group C2 n=5) and on implanted rats 100 days after lesion surgery (group D n=6) were compared (Figure 6). The time-to-find the platform was shorter at day 100 than at day 10 among lesioned rats, but it was observed that learning was slower than the rats receiving implantation. Statistically significant differences were determined in this assessment between groups C1 and C2; C1 and D; C2 and D ($p<0.0001$).

Experiment 2

In Figure 7, the mean of groups within the first four days of water maze tasks performed on day 10-14 after NBM lesion is shown. Among rats in normal (A), sham-operated (B), and with NBM lesions (C), no significant difference between

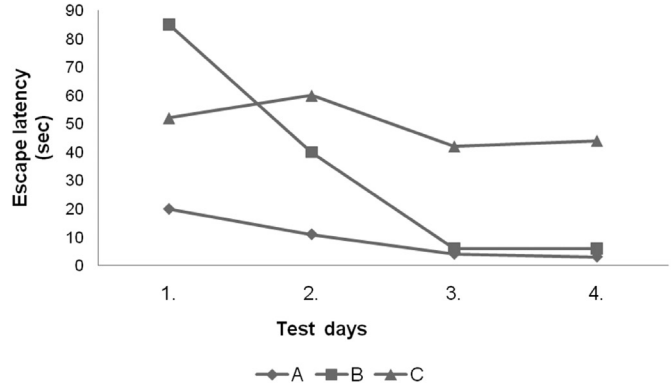

Figure 2. The results of the first 4 days of water maze tasks 10 days after lesion surgery. A: Normal, B: Sham-operated, C: NBM lesion

NBM: Nucleus basalis magnocellularis

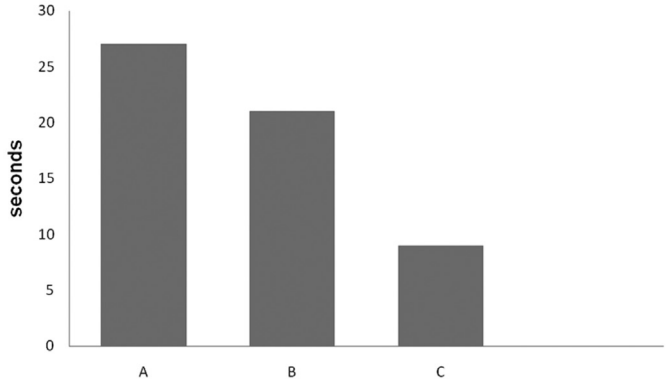

Figure 3. The results of the 5th day of water maze tasks 10 days after lesion surgery. A: Normal, B: Sham-operated, C: NBM lesion

NBM: Nucleus basalis magnocellularis

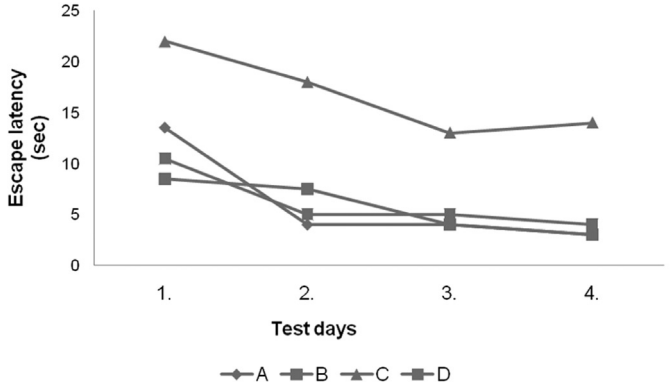

Figure 4. The results of the first 4 days of water maze tasks 100 days after lesion surgery. A: Normal, B: Sham-operated, C: NBM lesion, D: VF implantation

NBM: Nucleus basalis magnocellularis, VF: Ventral forebrain

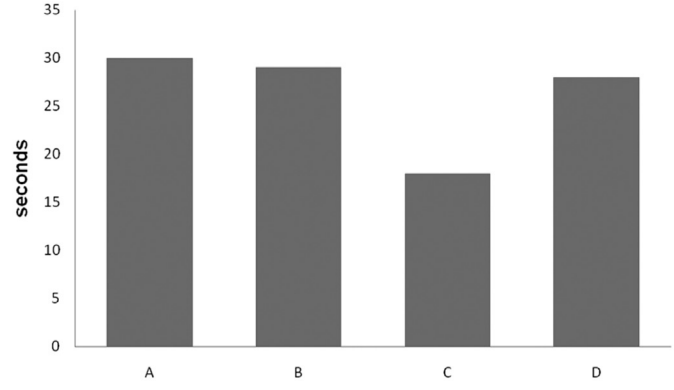

Figure 5. The results of the 5th day of water maze tasks 10 days after lesion surgery. A: Normal, B: Sham-operated, C: NBM lesion, D: VF implantation

NBM: Nucleus basalis magnocellularis, VF: Ventral forebrain

group A and B was found, but significance was determined in results between groups A and C; B and C ($p<0.01$). The results were similar in the assessment of 5th day ($p<0.001$) (Figure 8).

The means of water maze tasks in the first four days, which was performed between days 100 and 104 after formation of the NBM lesions, are shown in Figure 9. Among rats in normal group (A), sham-operated group (B), group with NBM lesion (C), group transplanted with VF grafts (D) and group transplanted with TV grafts (E), there were statistically significant differences between group C and other groups ($p<0.001$). The same results were determined in assessment of the 5th day's test results ($p<0.01$) (Figure 10).

Results of the test done on 10 days after NBM lesion were evaluated within the group (C1, n=12). Results of water maze test, which was repeated 100 days after the lesion were evaluated within the group (C2, n=3). Results of rats transplanted with VFGs (D, n=5), and transplanted with TVG (E, n=4) were also evaluated within their groups (Figure 11). Rats with lesion found the platform on day 100 (C2) in a shorter period of time than on the 10th day (C1). However, the learning among them was slower than the rats in groups D and E. For this assessment, there were statistically significant differences between C1 and C2 ($p<0.05$); C1 and D, E ($p<0.001$); C2 and D, E ($p<0.001$).

Discussion

It is believed that impairments of learning and memory functions in AD and other neurodegenerative diseases progressed with dementia are mainly due to decreased Ach, serotonin, and noradrenalin levels in the cortex in association with damage in the basal nuclei (25,28-30,32). AH-like learning and memory dysfunctions may be established in experimental animals by forming NBM

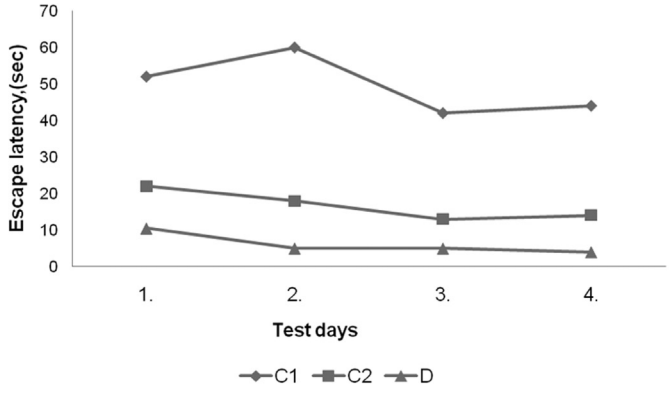

Figure 6. C1: NBM lesion (10th day), C2: NBM lesion (100th day), D: VF implantation (100th day)

NBM: Nucleus basalis magnocellularis, VF: Ventral forebrain

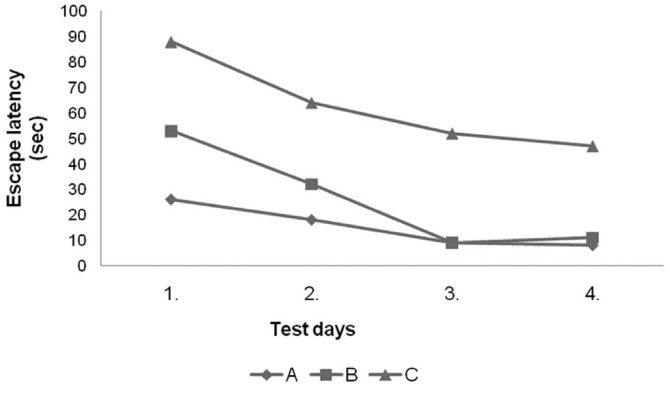

Figure 7. The results of the first 4 days of water maze tasks 10 days after lesion surgery. A: Normal, B: Sham-operated, C: NBM lesion

NBM: Nucleus basalis magnocellularis

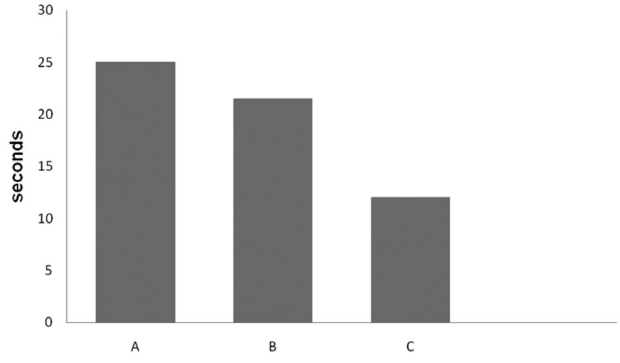

Figure 8. The results of the 5th day of water maze tasks 10 days after lesion surgery. A: Normal, B: Sham-operated, C: NBM lesion

NBM: Nucleus basalis magnocellularis

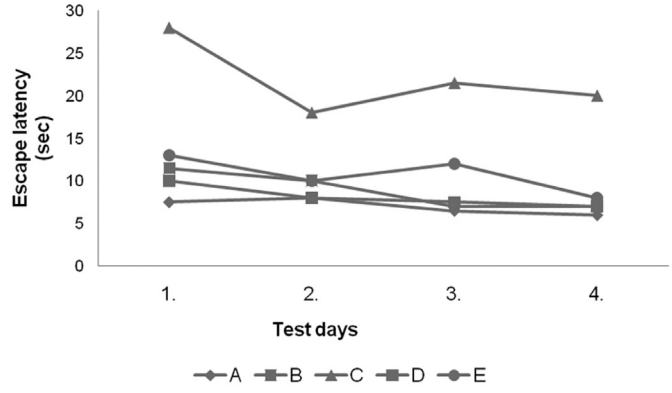

Figure 9. The results of the first 4 days of water maze tasks 100 days after lesion surgery. A: Normal, B: Sham-operated, C: NBM lesion, D: VF implantation, E: TV implantation

NBM: Nucleus basalis magnocellularis, VF: Ventral forebrain, TV: Telencephalic vesicle

or medial septal area lesions (34,35). In the present study, NBM lesion is selected, because it is the most debatable method.

Lesion should be extensive as neurons in NBM are scattered, and this may damage the adjacent structure. Surrounding fasciculi are also damaged along with neurons in electrolytic lesions formed by radiofrequency. Therefore, neurotoxic lesion is selected in the present study. To form neurotoxic lesions, different excitotoxic amino acids are used (27). Kainic acid, used in the present study, is the analogue of glutamic acid, which is an excitatory amino acid. In intraparenchymal injection, it binds nonspecifically to receptors on dendrites of neurons carrying excitatory amino acids, and it ruptures cell body and dendrites without damaging axons by overstimulation. As it is nonspecific, it ruptures other neurons along with

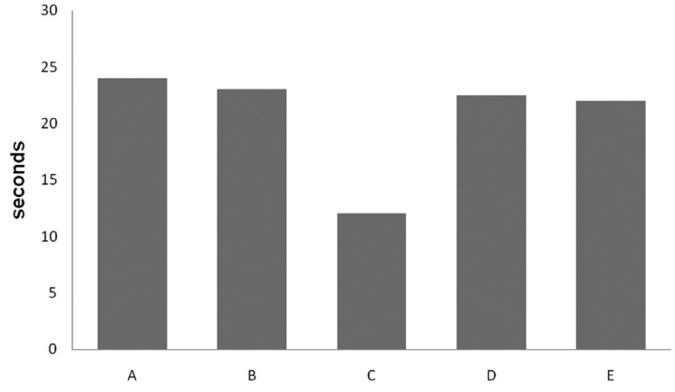

Figure 10. The results of the 5th day of water maze tasks 10 days after lesion surgery. A: Normal, B: Sham-operated, C: NBM lesion, D: VF implantation, E: TV implantation

NBM: Nucleus basalis magnocellularis, VF: Ventral forebrain, TV: Telencephalic vesicle

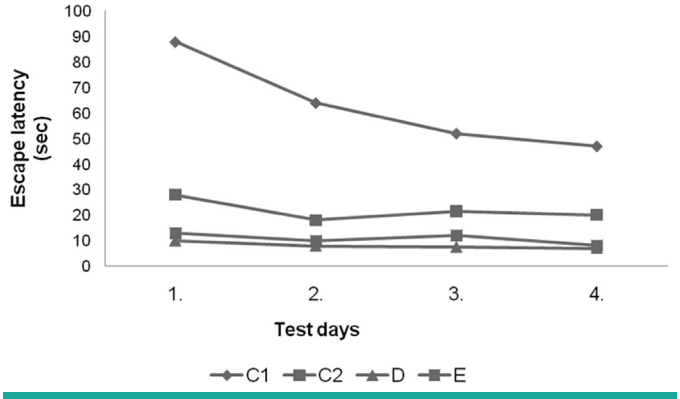

Figure 11. C1: NBM lesion (10th day), C2: NBM lesion (100th day), D: VF implantation (100th day), TV implantation (100th day)

NBM: Nucleus basalis magnocellularis, VF: Ventral forebrain, TV: Telencephalic vesicle

cholinergic neurons. In lesions formed by using kainic acid, medial globus pallidus, hippocampus, and ventrolateral thalamus are also partially damaged other than NBM. Since these areas are determined as partially damaged in AD, it is preferred to establish the model (33). In previous preliminary studies, bilateral NBM formation caused problems in water drinking, feeding, and related survival issues, unilateral lesion was formed in the present study. Since the right hemisphere is dominant in spatial learning (36), the lesion is formed on the right side.

Water maze test, which was originally created by Morris et al. (34), is excellent to assess spatial learning and memory performance in experimental animal models. In this test, the ability of rats to learn and remember the location of the hidden platform in a fixed quadrant by using the fixed surrounding objects is investigated. During the first 4 days normal rat learns to find the hidden platform quickly and directly by using the fixed cues around the tank. The rat spends more time in the same quadrant on the 5th day when the platform is removed. This reflects its ability to learn and remember the location of the platform.

Solid grafts and cell suspensions are used in transplantation studies. In studies by Björklund et al. (14,18), it was demonstrated that cell suspensions provided better results when compared to solid grafts. In studies by Plunnkett (37,38), it was observed that cells did not rupture if the suspension was given at 1 micro/min rate by using no 22-26 Hamilton needle. Administration of cell suspension by using stereotactic method eliminates neural tissue damage and high infection risks, which may be encountered during craniotomy, and it provides easy implantation.

It was observed that basocortical cholinergic system regenerated in unilateral lesions after 3-6 months (20). Therefore, Water maze test was performed 10 days later lesion formation, and it was repeated within the first 3 months after implantation.

In the first experiment, learning and memory functions, which were damaged after NBM lesion formation, were recovered after cholinergic neuron implantation. It was thought that primarily the graft survived, and might provide basocortical cholinergic system reconstruction by making functional synapses with recipient neural tissue. In the second experiment, which was conducted to investigate whether or not functional improvement resulted from cholinergic neuron reinnervation by the graft; similar recovery was observed in rats with noncholinergic neuron implantation as well as rats with cholinergic neuron

implantation. In both experiments, rats with lesion recovered partially in the late phase.

Underlying causes of functional recovery after neural tissue transplantation has not been clearly defined yet. Researches indicate four probable mechanisms.

The first mechanism is that graft tissue survives, and functions as a store releasing deficient neurotransmitters. Partial recovery observed in sensorimotor and behavioral disorders after adrenal medulla grafts in Parkinson disease (PD) model, and peripheral cholinergic ganglion grafts in AD model reinforces these mechanisms (39-54).

The second possibility is that neurons remain alive, and make functional synapses with recipient neural tissue, thus re-establishing the severed circuit. In studies with experimental animals, dopaminergic and cholinergic synapses were determined after transplantation in PD and AD models, respectively (5,10-13,15,16,19,20,23,41,46,52,55-59). It was observed that learning and memory functions were better in older rats after intrahippocampal fetal cholinergic grafts, and axons extending from the graft tissue to hippocampus were determined in histochemical studies (8,60).

It was postulated that locomotor activity recovery after adrenal medulla and fetal mesencephalon grafts used in PD model was associated to dopamine, norepinephrine, and epinephrine secreted from the graft in the early phase. The recovery was associated to dopaminergic connections, which were built up between the graft and striatum, in the late phase (21,41,42,47,48,50,54,61). Although partial recovery was detected in clinical picture in some Parkinson patients after adrenal medulla transplantation, few living cells or necrosis was observed in autopsy examination of these patients (53,62). In some studies, conducted on experimental animals, limited number of synapses was observed between the graft and recipient neural tissue in subjects with functional recovery (63). In the autopsy study of a patient, who received adrenal medulla transplantation in the striatum, and had poor recovery, it was determined that graft tissue remained alive and formed synapses (64).

It is thought provoking that bilateral response is gained with unilateral transplantation in Parkinson disease, and experimental PD models (65). If recovery is associated to functional synapses between the graft and striatum, then the response should have been unilateral. If the graft acts as a store secreting dopamine, then it should not be liable for bilateral recovery, because dopamine diffusion is limited to a few millimeters in the tissue (66).

In the present study, it has been shown that the recovery of learning and memory functions with both cholinergic and noncholinergic grafts cannot be explained by providing deficient neurotransmitters or cholinergic synapse formation from the graft to recipient neural tissue that are proposed in both mechanisms for functional recovery.

The third probability is stimulation of neurotrophic mechanisms. In recent 40 years, various neurotrophic factors, which prevent death of damaged neurons, and facilitate reinnervation of damaged circuits in CNS, have been defined (67-74). Nerve growth factor (NGF) is the most studied of all. It was reported that NGF pump implantation together with adrenal medulla implantation into putamen improved clinical recovery partially (75). It was observed in *in vivo* and *in vitro* studies that NGF prevented cell death in central cholinergic neurons and peripheral sympathetic ganglions, and also accelerated axonal growth (70,74). It was observed in tissue culture that NGF increased proliferation and differentiation of fetal basal forebrain neurons (76). In autopsy study on Alzheimer patients, Mufson et al. (77) observed in NGF-immunoperoxidase examinations that neurons carrying NGF receptor, especially in NBM, were quite decreased in basal forebrain neurons. Nieto-Sampedro et al. (78) showed that the graft tissue was alive 3-6 days after the lesion, and an NGF-like liquid, stimulating multiplication, accumulated in the cavity opening to the cortex. Korfalı et al. (79) reported that neurotrophic factors provided by gelfoam implantation in the cavitation ensured survival of adrenal medulla grafts implantation. In solid graft transplantations, grafts that were implanted after cavitation had better outcomes, and this was explained by activation of lesion-related trophic mechanisms (80,81). In the study performed with hemiparkinsonism model in monkeys, Bankiewicz et al. (23) reported that locomotor activity was recovered by both cavitations opened in caudate nucleus and dopaminergic and nondopaminergic tissue transplantations. In the study, dopaminergic axons extending from recipient neural tissue to the graft and cavity were detected (46,51,80). These findings indicated that functional recovery was obtained as the result of recipient neural tissue, itself, started to build up the damaged connections by using trophic mechanisms stimulated by cavitation and implantation. Bohn and Kanuicki (65) determined macrophages intensely around adrenal medulla grafts, and some of other investigators also reported similar findings. They proposed that recipient neural tissue developed an immunologic response against the graft, and macrophages secreted substances such as interleukins, which activated neurotrophic mechanisms

(46,65,80,82). It is believed that bilateral recovery after unilateral implantation may occur through this mechanism (54). Transplantation results are better in young experimental animals and young Parkinson patients, and it is explained by less trophic activity in elderly people (9,54).

The fourth probability is activation of neurogenesis by stimulation of endogenous stem cells. Stem cell is defined as cells, which can regenerate and have the potential to differentiate into different cell types. Stem cells do not have any predefined functions, and they provide *in vivo* functional reconstruction of a specific tissue by differentiating into different cell types according to signals they receive. They are classified as embryonic and adult according to their origin. Since the first embryonic stem cell growth in culture medium in 1998, experimental studies and investigations related to stem cell treatment have been conducted on many neurological degenerative disorders mainly spinal cord injuries, cerebral infarct, Parkinson disease, AD (83-91). Mainly two stem cell types are used: pluripotent stem cell/induced pluripotent stem cell originated from embryonic stem cell, and adult stem cells (neuronal stem cells, hematopoietic stem cells, mesenchymal stem cells). Neural stem cells are primarily located in hippocampal dental gyrus and subventricular zone in CNS (83-85,89). These cells are activated during conditions such as cerebral infarct, and facilitate recovery. However, their effects are limited, because of their inadequate number and gliosis. Therefore, administration from outside is considered as the suitable option. It was designated that neural stem cells decreased with age; hippocampal neurogenesis rate was slowed down with age; and there was progressive and diffuse cell death in these areas in AD (89). It was indicated that endogenous neural stem cells were regulated by various chemical agents and growth factors (89,90). In recent years, studies about prevention of death of neurons and glial cells, produced by the stem cells by the stimulation and regulation of primarily endogenous neural stem cells, have been performed (89,90). It is a known fact that in case of damage, endogenous neural stem cells prevent apoptosis in damaged cells by producing and secreting various trophic factors (90). In AD, experimental study findings indicated that neural stem cell transplantations, and neural progenitors might stimulate endogenous neural precursors and sinaptogenezis; and damaged cells might be rescued by secreted local neurotrophic and neuroprotective factors; and also, amyloid beta and tau protein accumulations might be diminished by therapeutic gene transfers (89,90). It is believed that symptoms and signs associated to cognitive disorders in AD may be improved by using these treatments.

The partial recovery in the late phase among rats with lesion may be explained as multiplication of limited number of alive cholinergic neurons as a result of lesion-related trophic mechanisms, and endogenous stem cell stimulation; thus, partial reconstruction of basocortical cholinergic system by re-establishing new axonal connections. Amelioration of spatial learning and memory impairments by both cholinergic and noncholinergic fetal neural tissue implantations may reflect that lesion stimulated trophic mechanisms and endogenous neural stem cells, namely hippocampal neurogenesis, become active after transplantation leading to acceleration of reconstruction.

When mechanisms playing a role in functional recovery are explained more clearly by anatomical and histochemical examinations, studies associated to neurogenesis activation will be a candidate treatment for many CNS disease involvements.

Conclusion

In rats, experimental AD model may be set up by performing unilateral NBM lesion, and damaging cortical cholinergic innervation, which leads to deterioration of learning and memory functions. İmpaired learning and memory functions in the early phase can recover in the late phase, which indicates that trophic mechanisms and hippocampal neurogenesis are stimulated due to the lesion itself. It is determined that improvement is accelerated both with cholinergic and noncholinergic fetal neural tissue implantations. Rather than functional synapses between the graft and recipient tissue, this condition can be explained by multiplication of limited number of living cholinergic neurons, and re-establishment of damaged connections by forming new synapses, as a result of endogenous neural stem cell regulation and activation of trophic mechanisms after implantation.

Ethics

Ethics Committee Approval: The study was approved by the local ethics committee (DETAM project number: 1990/31)

Informed Consent: This study does not include patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.M.C., O.B., Concept: S.M.C., O.B., Design: S.M.C., O.B., Data Collection or Processing: S.M.C., O.B., Analysis or Interpretation: S.M.C., O.B., Literature Search: S.M.C., O.B., Writing: S.M.C., O.B.

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

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ORIGINAL RESEARCH

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Determination of Prognostic Factors in Cerebral Contusions

Serebral Kontüzyonlarda Prognostik Faktörlerin Belirlenmesi

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Abstract

Objective: Cerebral contusion (CC) is vital because it is one of the most common traumatic brain injury (TBI) types and can lead to lifelong physical, cognitive, and psychological disorders. As with all other types of craniocerebral trauma, the correlation of prognosis with specific criteria in CC can provide more effective treatment methods with objective approaches.

Method: The results of 105 patients who were hospitalized in the emergency clinic with the diagnosis of CC and whose lesion did not require surgical intervention were evaluated. The demographic variables, Glasgow coma scale (GCS) score, radiographic findings, coexisting traumas and, type, number, and the midline shift of the contusions detected in computerized tomography (CT) were evaluated as a guide in determining the prognosis in one month.

Results: Twenty-five patients were female, and 80 were male, and the mean age was 37 years. The traffic accident was the most common cause of head injury. It was seen that while advancing age had a significant effect on mortality, sex factor had no impact on prognosis. Motor posture in GCS score, pupil light reactions, the number of contusions, and presence of accompanying subdural hemorrhage (SDH) on cranial CT were found to be substantial prognostic indicators. The presence of a cranial fracture and the degree of midline shift did not affect prognosis.

Conclusion: Advanced age, low GCS score, abnormal motor response, abnormal pupil light reaction, presence of other system traumas, multiple contusions, and accompanying SDH affected the prognosis of the cases adversely.

Keywords: Cerebral contusion, head injury, computerized tomography, Glasgow coma scale, intraparenchymal hemorrhage, prognosis, trauma, traumatic brain injury

Öz

Amaç: Kontüzyo serebri, en sık karşılaşılan travmatik beyin yaralanması olması ve ömür boyu süren fiziksel, bilişsel ve psikolojik bozukluklara yol açabilmesi nedeniyle önem taşımaktadır. Diğer tüm kraniyoserebral travma tiplerinde olduğu gibi kontüzyon serebride de prognozun belli kriterlere bağlanması objektif yaklaşımlarla vakit geçirmeden daha efektif tedavi yöntemlerinin belirlenmesini sağlayabilir.

Yöntem: Acil poliklinikte kontüzyon serebri saptanılarak yatırılan, lezyonu cerrahi müdahale gerektirmeyen 105 olgu araştırıldı. Demografik değişkenler, Glasgow koma skalası (GKS) skoru, radyografik bulgular, eşlik eden travmalar, kraniyal bilgisayarlı tomografide (BT) saptanılan kontüzyonların tipi, sayısı, ile oluşturduğu orta hat şiftine göre sonuçları bir aylık dönemde prognoz tayininde yol gösterici olarak değerlendirildi.

Bulgular: Çalışmadaki olguların 25'i kadın, 80'i erkek olup ortalama yaş 37 idi. Trafik kazalarının kontüzyon serebri oluşumunda ilk sırayı aldığı dikkati çekti. İlerleyen yaşın mortalite üzerinde belirgin etkisi olduğu, cins faktörünün ise prognoza etkisinin olmadığı görüldü. GKS skorunda yer alan motor postür, pupil ışık reaksiyonu, kraniyal BT'deki kontüzyonun sayısı ve eşlik eden subdural hematom (SDH) prognostik açıdan yol gösterici idi. Kranial fraktürün ve orta hat şiftinin prognoza etkisinin olmadığı görüldü.

Sonuç: İleri yaş, düşük GKS skoru, anormal motor cevap, anormal pupil ışık reaksiyonu, birlikte diğer sistem travmalarının bulunması, kontüzyonun multipl olması ve beraberinde SDH bulunması olguların prognozunu kötü yönde etkilemekteydi.

Anahtar kelimeler: Serebral kontüzyon, kafa travması, bilgisayarlı tomografi, Glasgow koma skalası, intraparankimal kanama, prognoz, travma, travmatik beyin yaralanması

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Introduction

In economically developing countries, most of the traumatic brain injury (TBI) is caused by motor vehicles and continues to be the fearful dream of today's technology age because it cause not only of disability and loss of life but also of financial losses (1-12).

In patients with trauma, a hemorrhagic contusion is the most common lesion detected on computerized tomography (CT), and in many series, account for approximately 13-35 % of traumas (2,6,12-15).

When the literature is examined, it is seen that many criteria were evaluated for the prognosis of TBI cases. The heterogeneity of TBI is the major obstacle to determining effective treatment and linking prognosis to specific criteria will provide objective approaches and effective treatment methods.

We aimed to evaluate the cases with CC and to determine the possible prognostic factors such as age, sex, brainstem findings (pupil reactions and motor postures), Glasgow coma scale (GCS) score, accompanying traumas, cranial CT findings, and presence of fracture images in the radiographic examination. When the Turkish and English literature were examined, no other study was seen to determine the prognosis of CC using all these criteria together.

Material and Methods

Including and Excluding Criteria

In this study, the head trauma cases with CC admitted to our emergency clinic within two years and treated with medical treatment were evaluated retrospectively. The exclusion criteria were as follows: Diffuse periorbital edema, ecchymosis, and lacerations to prevent eye-opening, facial fracture to avoid speech, spinal pathologies to prevent movements of limbs and immobilization due to fractures and alcohol intoxication were excluded from the study because of difficulties in GCS interpretation. Since it would be difficult to assess the consciousness because of the pharmacological sedation or muscle relaxants used for intubation, the patients who were prehospital intubated were not included in the study. Also, the patients with unilateral pupillary response disorder were not included in the survey as this may be due to direct trauma to the eye. In the radiological evaluation, all other fractures were included in the study except patients with open or closed depressed skull fractures. The patients required surgical intervention, and the patients with diffuse axonal injury (DAI) were not included in the study. Total of 105 cases was included in the study.

Demographic Data

The patients were introduced into 2-decade groups that as 0-20, 21-40, 41-60, 61-80, and ≥81 (Table 1). The effects of the patients' age and gender on one-month prognosis were evaluated.

Associated Traumas

Other system traumas of the patients were recorded, and their effects on the prognosis were evaluated.

Neurological Evaluation

The initial state of consciousness was evaluated according to the GCS score. The patients were divided into four groups according to their GCS score: GCS 3-5, GCS 6-8, GCS 9-11, and GCS 12-15. Direct and indirect light responses of both eyes were taken into consideration in the pupillary examination. In the motor system examination, response to a painful stimulus was evaluated separately from GCS. Patients with uni- and bilateral decorticated, uni- and bilateral decerebrated, or bilateral flask posture were compared with those without abnormal posture to determine the prognosis.

Radiological Findings

The prognosis was determined according to the type, number, and midline shift of the first cranial CT scans taken on the day of hospitalization. In the determination of contusion type, the classification defined by Lobato et al. (16) was used (Appendix 1).

Appendix 1. Lobato classification

Type 1. Pure extracerebral hematoma

Type 2. Extracerebral hematoma + Acute hemispheric swelling

Type 3. Single brain contusion +/- Extracerebral hematoma

Type 4. Multiple unilateral brain contusion +/- Subdural hematoma

Type 5. Multiple bilateral brain contusion

Type 6. General brain swelling +/- Small extracerebral hematoma

Type 7. Diffuse axonal injury

Type 8. Normal CT scans

The amount of shift caused by contusion was determined by measuring the distance between the inner tabulae and septum pellucidum in sections where septum pellucidum was seen.

For output status, the terms of recovery, disability, or dead were used, and these parameters were evaluated as a guide in determining the prognosis in the one month.

Statistical Analysis

The data were analyzed by SPSS (Statistical Package for Social Sciences) 15 package program, and the results were tested by chi-square test. Number and % were used as descriptive statistics in the evaluation of the data. A p value of less than 0.05 was considered significant, and a p value less than 0.005 was considered highly significant.

Results

Of the 105 cases in our study group, 24% were female, and 76% were male. Their ages ranged from 1.5 to 86, and the mean age was 37 (Table 1).

Relationship Between Demographic Data and Prognosis

Age is a statistically significant factor affecting the prognosis. Increasing age caused worse prognosis and higher mortality rate (Figure 1). This relationship was highly significant. The only exception was in the 61-80 age group, but this did not change significance (χ^2=22.010; p<0.005). When the relationship between sex and prognosis was examined, it was observed that 28% of 25 female patients and 15% of 80 male patients died. The relationship between gender and prognosis was not statistically significant (χ^2=3.373; p>0.05) (Figure 2).

Causes of Trauma

The causes of the trauma of the patients were summarized in Table 2. According to this, the most frequent cause was pedestrian traffic accidents (32.4%) followed by motor vehicle traffic accidents (21.9%) and fall from height (20%).

Table 1. Age and gender distribution of the patients

Year	Total		Female		Male	
	n	%	n	%	n	%
0-20	30	28.6	8	32	22	27.5
21-40	30	28.6	4	16	26	32.5
41-60	28	26.7	4	16	24	30
61-80	14	13.3	8	32	6	7.5
81-	3	2.8	1	4	2	2.5
Total	105	100	25	100	80	100

n: Number of the patients

The Effects of Associated Traumas

It was found that long bone fractures were most commonly associated with CC (58%) followed by chest trauma (21%), abdominal trauma (13%) and pelvic trauma (8%), respectively (Table 2). While the mortality rate was 11% in the case of TBI alone, the mortality rate increased to 42% in the presence of other system traumas (Figure 3). The effect of associated injuries on mortality was found to be statistically significant (χ^2=12.313; p<0.005).

The Effects of Neurological Status on Prognosis

Relationship between GCS and prognosis was found to be statistically significant (χ^2=47.462; p<0.005). It was seen that the healing rate was 0% in score between 3-5 and 62.2 % in those with a score of 12-15. While the mortality rates are 100 % in patients with scores 3-5, the rate is 3% in score 12-15 patients (Table 3).

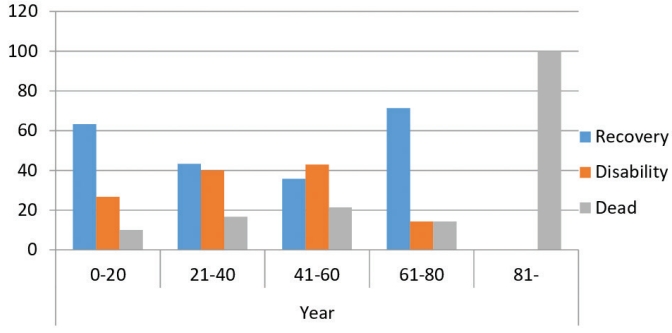

Figure 1. The relationship between age and prognosis

Table 2. Types of trauma and additional injuries

Types of trauma	n	%
Pedestrian traffic accidents	34	32.4
Motor vehicle traffic accidents	23	21.9
Fall from height	21	20
Fall from stairs	10	9.5
Assault	9	8.6
Head hitting against hard objects	1	0.9
Falls on the same level	7	6.7
Additional Injuries	**n**	**%**
Long bone fractures	14	58.3
Chest trauma	5	20.9
Abdominal trauma	3	12.5
Pelvic trauma	2	8.3

n: Number of the patients

The relationships between abnormal motor response and prognosis, and between the bilateral response of pupils to light were also statistically significant (χ^2=18.822; p<0.005, and χ^2=18 822; p<0.005, respectively). The mortality rate was 100% in patients with abnormal posture response to painful stimuli (Table 3). While the recovery was 0% in patients with bilateral abnormal (decreased or lost) pupil reaction, the mortality rate was found to be only 15% in patients with a normal response (Figure 4).

The Effects of Radiological Findings

Presence of cranial fracture did not affect the one-month prognosis (χ^2=1.171; p>0.05) (Table 4). While the mortality rate was 50% in cases with midline shift in cranial CT, it decreased to 16.8% in cases without shift (Table 4). However, the relationship between the degree of midline shift and the prognosis was not statistically significant (χ^2=2.914; p>0.05).

The relationship between contusion type and prognosis was statistically significant (χ^2=9.808; p<0.05) (Table 4).

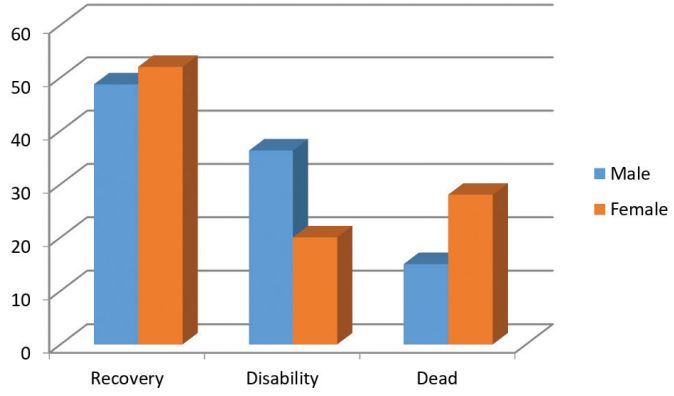

Figure 2. The relationship between gender and prognosis

The highest mortality rate was found in type 4 of Lobato classification (multiple unilateral CC +/- Subdural hematoma) (38.5%), which was 4 times higher than the mortality rate in type 3 (Single CC +/- Extra cerebral hematoma) (10%). The relationship between the number of contusions and prognosis was also statistically significant (χ^2=6.111; p<0.05). If the number of contusions detected on cranial CT was more than one, the mortality rate (28.6%) was two times higher than that of single ones (11.1%) (Table 4).

Length of Hospitalization

The length of hospitalization of the patients ranged from 1 to 23 days, and the mean duration of hospitalization was nine days. The hospitalization period of our deceased patients was between 1-18 (mean 7.5 days), and 53% of the cases who died was lost between 1-10 days (Table 5).

Discussion

The presence of CC is a factor affecting the outcome of the patients with a head injury. In the literature, mortality in CC was reported as 34% (17), and this rate was found to be 18% in our series. There are some studies evaluating the factors affecting the mortality in these cases. Age is one of these factors. The mean age of the patients with CC was reported to be 27 to 38 in the studies of Lobato et al. and Miller et al. (16,17). In the series of Miller et al. (17) was consisting of non-operated 225 cases, 72% of the cases were between 0 and 40 years of age.

Similarly, Narayan et al. (18) reported that the rate of cases in the 0-40 age group was 72%. The mean age of our patients was 37, and the majority (57%) were composed of male patients aged 0-40 years. At the end of the study, it was seen that age had a significant effect on mortality. While mortality was 10% in the 0-20 age group, it reached 100% in

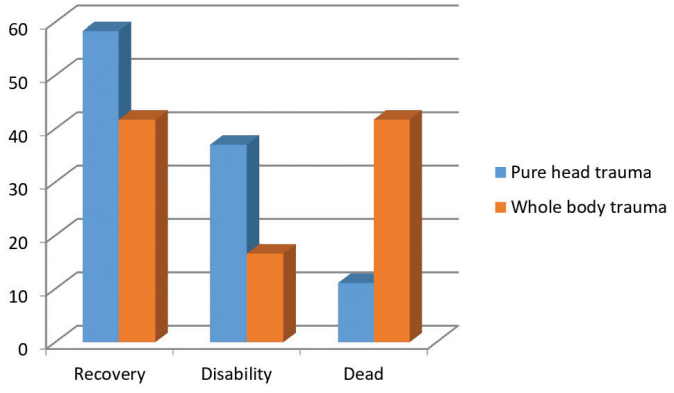

Figure 3. The relationship between trauma types and prognosis

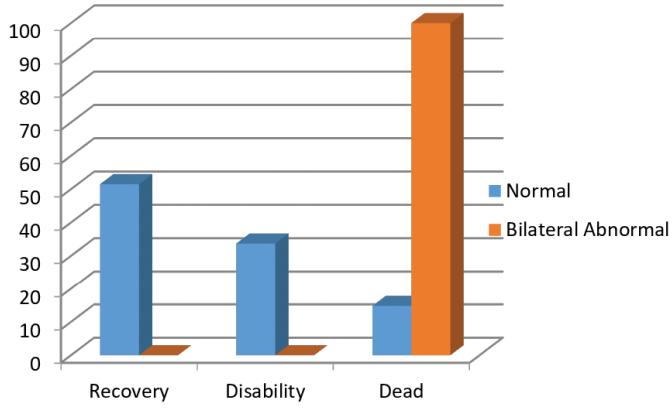

Figure 4. The relationship between pupillary responses and prognosis

Table 3. Initial GCS, motor responses and prognosis relationships

		Total		Recovery		Disability		Dead	
		n	%	n	%	n	%	n	%
GCS	3 - 5	4	3.8	0	0	0	31.8	4	100
	6 - 8	15	14.3	2	13.3	4	26.7	9	60
	9 - 11	20	19	9	45	7	35	4	20
	12 - 15	66	62.9	41	62.2	23	34.8	2	3
Motor response	Postured	101	96.2	52	51.5	34	33.7	15	14.8
	W/O postured	4	3.8	0	0	0	0	4	100

GCS: Glasgow coma scale, n: Number of the patients, W/O: Without

Table 4. Prognosis according to the radiographic findings

		Total		Recovery		Disability		Dead	
		n	%	n	%	n	%	n	%
Skull fracture	Present	65	61.9	32	49.3	23	35.3	10	15.4
	Absent	40	38.1	20	50	11	27.5	9	22.5
CC types in CT-scans	Type 3	62	59	36	58	20	32.3	6	9.7
	Type 4	13	12.4	3	23	5	38.5	5	38.5
	Type 5	30	28.6	13	43.3	9	30	8	26.7
CC number in CT-scans	Single	63	60	36	57.1	20	31.8	7	11.1
	Multiple	42	40	16	38.1	14	33.3	12	28.6
Midline shift in CT-scan	Present	4	3.8	1	25	1	25	2	50
	Absent	101	96.2	51	50.5	33	32.7	17	16.8

CT: Computered tomography, CC: Cerebral contusion, n: Number of the patients

Table 5. Hospitalization period of the dead cases

	n	%
0-1 day	4	21.1
1- 10 day	10	52.6
11 day and ↑	5	26.3
Total	19	100

n: Number of the patients

the group over 81 years. In the literature, it is also seen that mortality increases with increasing age (8,17-22).

The gender was also evaluated for its effect on mortality in our study. 24% of our cases were female, and 76% were male. We found no relationship between gender and the prognosis. In the literature also, although the incidence of TBI in men is higher than in women, there is no significant relationship between gender and prognosis (3,17,20).

It was reported that the leading cause of TBI is traffic accidents in underdeveloped countries. Since improved road safety, falls is in the first place in developed countries (4,12,15). When our patients were ranked according to the type of trauma they were exposed to, traffic accidents were at the forefront (54%).

In 23% of our cases, CC was accompanied by other system traumas, and the mortality rate was 11% in pure TBI, but when poly-trauma added mortality was seen raised to 42%. In the literature, the presence of significant extracranial injury has been reported to be one of the important prognostic indicators in TBIs (8,19,23). In our study, the most common systemic traumas were long bone fractures (58%), followed by chest trauma (21%), abdominal trauma (13%), pelvic trauma (8%), respectively. In Miller et al. 's series, 48% of patients had multi-system trauma, and as in our series, extremity injuries were reported to be the most common (17).

Although there are many methods in neurological evaluation, GCS has been reported to be the easiest method of rapid assessment of the patient and predicting the correct outcome early (24,25).

Rimel and Jane (26) divided head trauma into three groups according to GCS, and GCS value 3-8 was accepted as severe, 9-12 as moderate, and 13-15 as mild head trauma. In our study, we found a statistically significant relationship between GCS scores and prognosis (27). As the GCS score increased, the recovery rate increased, and the mortality rate gradually decreased. Similarly, it has been reported in the literature that mortality rates are inversely proportional

to GCS scores. Moreover, in cases with GCS score 9 or higher, mortality or morbidity may occur in the presence of advanced age or other additional complications (2,8,17,18,22,24,28-30). However, it was noteworthy that there were differences between the rates in the literature. The reasons for the differences where they had included the cases requiring operation in their studies, and also, they had formed GCS groups at different levels.

In our study, it was found that motor posture on the coma scale was an additional parameter in prognosis determination, and high rates of mortality were observed in patients with abnormal motor posture. Similarly, it has been reported in the literature that the neurological status is one of the well-established prognostic factors (8,17,18,20,22).

The effect of both pupils' reactions to light on prognosis was also investigated statistically. According to our results, the mortality rate was 100% in patients with a bilateral abnormal pupillary response and 15% in patients with a normal pupillary response. When different series were examined, it was seen that there was a significant relationship between pupillary light response and prognosis (8,17,18).

In our study, the skull fracture rate was 61.9%. However, the effect of the presence of fracture on prognosis was not significant. There was not any data on this issue in the literature.

It was reported in 1977 by Koo and La Roque (6) that neuropathological changes in hemorrhagic contusion can be visualized by CT. Currently, cranial CT is the ideal method for the diagnosis of CC in the first 24 hours after trauma (12,16,31-35). It was reported that the increase in the volume of traumatic cerebral hemorrhage occurs in the first few hours after the trauma in 38 to 59% of the cases. Also, the findings in the first non-contrast cranial CT taken after the injury were related to the quality of life score at 12 months after the accident (14,36-38). In our study, cranial CT was found to be helpful in the determination of short-term prognosis in CC. In particular, the relationship between the type of contusion and the outcome was remarkable. We found that mortality was the lowest in type 3 of Lobato CC classification (10%), and was the highest in type 4 (39%). The higher mortality in Lobato type 4 can be explained by the fact that acute hemispheric swelling in the case of SDH is much more than EDH. It was reported in the literature that the prognosis is negatively affected when acute SDH is added to the traumatic intracerebral hemorrhage (13,21,22,36). It was shown that increases in intracranial pressure in multiple bilateral CCs could be tolerated longer than in multiple unilateral contusions, which may explain the low mortality rate in type 5 compared with type 4 (7) as to be in our study also. These rates found in our study are in line with Lobato et al.'s study (16). Mortality rates in Lobato' s series are twice that of our series. However, when the series was examined, it was observed that most of the cases had advanced shift and accompanying diffuse hemorrhage requiring surgical intervention, which explains the rate differences. We excluded the cases requiring surgical intervention in our series. Another factor guiding the prognosis in cranial CT was the number of contusions. In our series, 60% of cases had single, and 40% had multiple contusions. The mortality rate was 11% in single contusions, and 29% in multiple contusions. There are also studies in the literature showing that multiple contusions are not associated with poor prognosis (30). The results show why the mortality rate in Lobato's type 5 is lower in the literature to be in our study (39).

Contusions located in the deep gray matter, corpus callosum and internal capsule are among the criteria considered to be a poor prognostic marker in cranial CT today. Gennarelli et al. (40) and Adams et al. (39) were described these types of contusions as DAI. In our study, DAI cases were excluded from the study. Because DAI is not clearly and adequately diagnosed by CT, and the diagnosis is usually made by pathological anatomical studies or in patients who are unconscious after two weeks or by magnetic resonance examination (33).

It was emphasized in many studies that the presence of a midline shift was one of the poor prognostic factors on CT image (5,8,16,25,34). However, Raj et al. (41) reported that midline shift was not very important in determining prognosis. In our series, in only four cases, midline shift was detected, and two of these cases died. Since the number of cases was not sufficient, a statistically significant relationship was not determined.

The limitation of our study was that it was a retrospective study, the number of cases was low, and it was performed in a broad range age group. Since the clarification of the prognostic factors in CCs will determine the treatment protocols, prospective studies evaluating the late prognosis with a large number of cases are needed.

Conclusion

Advanced age, low GCS score, abnormal motor response, abnormal pupil light response, presence of other system traumas, multiple contusions and accompanying SDH had

a negative effect on the in one-month prognosis in the head injury cases with CC.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.S., M.S.D. Concept: N.S., M.S.D. Design: N.S., M.S.D. Data Collection or Processing: N.S., M.S.D. Analysis or Interpretation: N.S., M.S.D. Literature Search: N.S., M.S.D. Writing: N.S., M.S.D.

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

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