Year: June 2017 Volume: 4 Issue: 2

ISSN: 2147-9445

The Journal of Pediatric Research

Official Journal of Ege University Children's Hospital

galenos yayınevi

The Journal of Pediatric Research

JPR

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The Journal of Pediatric Research, Ege Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı'nın bir yayın organıdır.

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Yeşilce Mah. Aytekin Sk. No: 21 34418 4. Levent, İstanbul, Türkiye
Telefon/Phone: +90 (212) 280 00 09
Basım Tarihi/Printing Date: Haziran 2017/June 2017
ISSN: 2147-9445
Üç ayda bir yayımlanan süreli yayındır.
International scientific journal published quarterly.

The
Journal of Pediatric Research

Official Journal of Ege University Children's Hospital

Dergi Hakkında

The Journal of Pediatric Research, Ege Üniversitesi Tıp Fakültesi Çocuk Sağlığı ve Hastalıkları Anabilim Dalı'nın bir yayın organıdır. Dergi üç ayda bir, Mart, Haziran, Eylül, Aralık aylarında Türkçe ve İngilizce dillerinde yayınlanır.

The Journal of Pediatric Research hakemli, online erişilebilir bir dergidir ve pediatri alanında araştırma makaleleri, davetli derlemeler, klinik çalışmalar ve olgu sunumları yayınlar.

Derginin amacı araştırmacılara ve sağlık alanında çalışanlara çocuk sağlığı ve hastalıklarının tanısı, izlemi, tedavisi, yeni araştırma alanlarının yaratılması ve klinik yaklaşım gibi konularda rehberlik yapmak ve yeni araştırma alanlarının yaratılmasına aracılık etmektir. Derginin web sayfasına http://www.jpedres.org/ yoluyla ulaşabilirsiniz.

Yayın politikası, "ICMJE Recommendations" (2016, http://www.icmje.org/) kuralları temel alınarak belirlenmiştir.

Araştırma bulgularının denetlenmesi istatistik editörü tarafından yapılır.

Dergi içeriği pediatri ile ilgili öncelikle genel pediatri konuları olmakla birlikte, pediatri yan dallarını (Acil Tıp, Allerji ve İmmünoloji, Endokrinoloji, Gastroenteroloji, Beslenme ve Hepatoloji, Genetik, Kardiyoloji, Hematoloji-Onkoloji, Enfeksiyon Hastalıkları, Metabolizma, Nefroloji, Nöroloji, Romatoloji, Solunum Yolları, Sosyal Pediatri, Yenidoğan, Yoğun Bakım, Etik ve Sağlık Servisleri), Çocuk Psikiyatrisi, Çocuk Cerrahisi, Çocukluk Yaş Grubunun Ağız ve Diş Sağlığı ve Çocuk Sağlığı ve Hastalıkları Hemşireliği ile ilgili genel konuları kapsamaktadır.

The Journal of Pediatric Research'e gönderilen çalışmalarınızın ortalama değerlendirme süresi 6 haftadır.

Makalenin kabulünü takiben bütün yazarların makalenin son halini görmesi ve içeriğini onaylaması beklenmektedir. Başka bir yayın organında basılmış ya da değerlendirme aşamasında olan makaleler kesinlikle değerlendirme sürecine giremezler. Araştırma makalelerinde etik onay belgesi (etik onay numarası ile birlikte), olgu sunumlarında bilgilendirilmiş onam formu istenir.

The Journal of Pediatric Research, **Web of Science-Emerging Sources Citation Index (ESCI), Directory of Open Access Journals (DOAJ), EBSCO, CINAHL Complete Database, ProQuest, Tübitak/Ulakbim TR Dizini, TurkMedline ve Türkiye Atıf Dizini'nde** indekslenmektedir.

Açık Erişim Politikası

Dergide açık erişim politikası uygulanmaktadır. Açık erişim politikası Budapest Open Access Initiative (BOAI) http://www.budapestopenaccessinitiative.org/ kuralları esas alınarak uygulanmaktadır.

Açık Erişim, "[hakem değerlendirmesinden geçmiş bilimsel literatürün], İnternet aracılığıyla; finansal, yasal ve teknik engeller olmaksızın, serbestçe erişilebilir, okunabilir, indirilebilir, kopyalanabilir, dağıtılabilir, basılabilir, taranabilir, tam metinlere bağlantı verilebilir, dizinlenebilir, yazılıma veri olarak aktarılabilir ve her türlü yasal amaç için kullanılabilir olması"dır. Çoğaltma ve dağıtım üzerindeki tek kısıtlama yetkisi ve bu alandaki tek telif hakkı rolü; kendi çalışmalarının bütünlüğü üzerinde kontrol sahibi olabilmeleri, gerektiği gibi tanınmalarının ve alıntılanmalarının sağlanması için, yazarlara verilmelidir.

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Yazarlara Bilgi

Yazarlara bilgi dergi sayfasında ve www.jpedres.org web sayfasında yayınlanmaktadır.

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The Journal of Pediatric Research, yayınlanan tüm yazılarda görüş ve raporlar yazar(lar)ın görüşüdür ve Editör, Editörler Kurulu ya da yayıncının görüşü değildir; Editör, Editörler Kurulu ve yayıncı bu yazılar için herhangi bir sorumluluk kabul etmemektedir.

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The Journal of Pediatric Research abonelik işlemleri için Galenos Yayınevi ile iletişime geçmeleri gerekmektedir. Ait olduğu dönemler içinde dergi eline ulaşmamış aboneler, Galenos Yayınevi'ne müracaat etmelidirler. Derginin tüm sayılarına ücretsiz olarak www.jpedres.org adresinden tam metin olarak ulaşılabilinir.

Kapak Fotoğrafı

Yazarlar dergimizde yayınlanmak üzere çocuk temalı ve düşündürücü özelliği olan fotoğraflar gönderebilirler. Uygun görülen fotoğraflar ilgili sayıda yayınlanacaktır. Fotoğraflarınızı ozgur.cogulu@ege.edu.tr adresine göndermenizi rica ederiz.

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About Journal

The Journal of Pediatric Research is the official publication of Ege University and Ege Children's Foundation. It is a peer-reviewed journal published quarterly in March, June, September and December in Turkish and English languages.

The Journal of Pediatric Research is a peer-reviewed, open access journal, which publishes original research articles, invited review articles, clinical reports and case reports in all areas of pediatric research.

The journal publishes original research and review articles, which summarize recent developments about a particular subject based on standards of excellence and expert review and case reports. Target audience includes specialists in general pediatrics and pediatric subspecialties (Emergency Medicine, Allegy and Immunology, Endocrinology, Gastroenterology, Hepatology and Nutrition, Genetics, Cardiology, Hematology-Oncology, Infectious Diseases, Metabolism, Nephrology, Neurology, Rheumatology, Pulmonology, Social Pediatrics, Newborn, Critical Care Medicine, Ethics and Health Service Research), as well as relevant specialties such as Pediatric Surgery, Child and Adolescent Psychiatry, Pedodontics, Pediatric Nursing and Family Physicians. The web page of The Journal of Pediatric Research is http://www.jpedres.org/.

The journal's editorial policies are based on "ICMJE Recommendations" (2016, http://www.icmje.org/) rules.

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The Journal of Pediatric Research is indexed in **Web of Science-Emerging Sources Citation Index (ESCI), Directory of Open Access Journals (DOAJ), EBSCO, CINAHL Complete Database, ProQuest, Tübitak/ Ulakbim TR Index, TurkMedline and Turkiye Citation Index.**

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Yazarlara Bilgi

The Journal of Pediatric Research, Ege Üniversitesi Tıp Fakültesi Çocuk Sağlığı ve Hastalıkları Anabilim Dalı ve Ege Sağlık Vakfı'nın yayın organı olup, çocuk sağlığı ve hastalıkları ile doğrudan ya da dolaylı olarak ilgili konularda özgün klinik ve laboratuvar araştırmaları, olgu sunumları, derleme yazıları yayınlar. Derginin yayın dili Türkçe ve İngilizce'dir.

Türkçe yazılarda Türk Dil Kurumu'nun Türkçe Sözlüğü ve Yazım Kılavuzu temel alınmalıdır. Kullanılan terimlerin Türkçe kullanılmasına özen gösterilmelidir.

The Journal of Pediatric Research Dergisi makale başvuru ücreti veya makale işlem ücreti uygulamamaktadır.

The Journal of Pediatric Research'nin kısaltması JPR'dir, ancak kaynaklarda kullanılırken J Pediatr Res şeklinde belirtilmelidir. Uluslararası indekslerde ve veritabanında, derginin adı The Journal of Pediatric Research, İngilizce kısaltması J Pediatr Res olarak kaydedilmiştir.

Dergiye kabul edilen eserlerin özgün ve daha önceden başka ortamlarda yayınlanmamış olması esas alınır. Yayın için dergiye yollanan her yazı hakem değerlendirmesine gönderilir. Yazarlar 6 hafta içinde süreçle ilgili haberdar edilir. Değerlendirme sonucunda basılması kabul edilen yazılar dergide basılır ve dergi web sayfası olan http://www.jpedres.org adresinde yayınlanır.

Yazıların bilimsel ve etik sorumlulukları yazarlara, telif hakkı ise JPR'ye aittir. Yazıların içeriğinden ve kaynakların doğruluğundan yazarlar sorumludur. Yazarlar, yayın haklarının devredildiğini belirten onay belgesini (Yayın Hakları Devir Formu) yazıları ile birlikte göndermelidirler. Bu belgenin tüm yazarlar tarafından imzalanarak dergiye gönderilmesi ile birlikte yazarlar, gönderdikleri çalışmanın başka bir dergide yayınlanmadığı ve/veya yayınlanmak üzere incelemede olmadığı konusunda garanti vermiş, bilimsel katkı ve sorumluluklarını beyan etmiş sayılırlar.

Dergiye yayımlanmak üzere gönderilen tüm yazılar 'iThenticate' programı ile taranarak intihal kontrolünden geçmektedir. İntihal taraması sonucuna göre yazılar red ya da iade edilebilir.

The Journal of Pediatric Research'te yayınlanmak amacıyla gönderilen ve etik kurul onayı alınması zorunluluğu olan deneysel, klinik ve ilaç araştırmaları için uluslararası anlaşmalara ve 2013'te gözden geçirilmiş Helsinki Bildirisi'ne uygun etik kurul onay raporu gereklidir (http://www.wma.net/en/30publications/10policies/b3/). Etik kurul onayı ve "bilgilendirilmiş gönüllü onam formu" alındığı araştırmanın "Gereç ve Yöntem" bölümünde belirtilmelidir. Deneysel hayvan çalışmalarında ise yazarlar, "Guide for the care and use of laboratory animals" (http://oacu.od.nih.gov/regs/guide/guide.pdf) doğrultusunda hayvan haklarını koruduklarını belirtmeli ve kurumlarından etik kurul onay raporu almalıdır.

Yayın, direkt ya da indirekt ticari bağlantı içeriyorsa veya çalışmaya materyal desteği veren bir kuruluş varsa, yazarlar kullanılan ticari ürün, ilaç, firma vs. ile ticari hiçbir ilişkisinin olmadığını ya da var ise nasıl bir ilişkisinin olduğunu (konsültan, diğer anlaşmalar), editöre sunum sayfasında belirtmek zorundadır.

Araştırmalara yapılan her türlü yardım ve diğer desteklerin alındığı kişi ve kuruluşlar beyan edilmeli ve çıkar çatışmasıyla ilgili durumları açıklamak amacıyla Çıkar Çatışmaları Bildirim Formu doldurulmalıdır.

Tüm yazılar, editör ve editör yardımcıları ile danışman hakemler tarafından incelenir.

The Journal of Pediatric Research bağımsız, önyargısız ve çift-kör hakemlik ilkeleri çerçevesinde yayın yapan süreli bir yayın organıdır. Hakemler, yazının konusuyla ilgili uluslararası literatürde yayınları ve atıfları olan bağımsız uzmanlar arasından seçilmektedir. Makale baş editöre ulaşınca değerlendirmeye alınır ve bölüm editörüne gönderilir. Bölüm editörü ilk değerlendirmeyi takiben makaleyi hakemlere gönderir. Hakemler 21 gün içinde kararlarını bildirmelidirler. Bölüm editörü hakem kararlarına kendi değerlendirme ve önerisini ekleyerek baş editöre gönderir ve son kararı hakemlerin görüşleri doğrultusunda bölüm editörü verir. Hakemlerin kararları birbirleriyle çelişkili ise dergi editörü gerektiğinde yeni hakem atayabilir.

Dergide yayınlanacak yazıları değerlendiren hakemler dergide belirtilen danışmanlar ve gerekirse yurt içi/dışı konu ile ilgili uzmanlar arasından seçilir. Yazarlar, yayına kabul edilen yazılarda, metinde temel değişiklik yapmamak kaydı ile editör, editör yardımcıları, biyoistatistik uzmanı ve İngilizce dil uzmanının düzeltme yapmalarını kabul etmiş sayılır.

İncelemeye sunulan araştırmada olası bir bilimsel hata, etik ihlal şüphesi veya iddiasıyla karşılaşılırsa, bu dergi verilen yazıyı destek kuruluşların veya diğer yetkililerin soruşturmasına sunma hakkını saklı tutar. Bu dergi sorunun düzgün biçimde takip edilmesi sorumluluğunu kabul eder ancak gerçek soruşturmayı veya hatalar hakkında karar verme yetkisini üstlenmez.

Yayın Politikası ve Makale Yazım Kuralları aşağıda belirtilen maddeler "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations)" (2016, http://www.icmje.org/) temel alınarak hazırlanmıştır.

Araştırma makalelerinin hazırlığı, sistematik derleme, meta-analizleri ve sunumu ise uluslararası kılavuzlara uygun olmalıdır:

Araştırma makalelerinin hazırlığında sistematik derlemeler ve meta analizler için aşağıdaki tasarım klavuzları:Randomize çalışmalar için; CONSORT (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/).

Sistematik derleme ve meta-analizlerin raporlamaları için; PRISMA (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/).

Tanısal değerli çalışmalar için; STARD (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/).

Gözlemsel çalışmalar için; STROBE (http://www.strobe-statement.org/).

Meta-analizleri ve gözlemsel çalışmaların sistematik derlemeleri için; MOOSE (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).

GENEL KURALLAR

Yazılar sadece çevrim-içi olarak kabul edilmektedir. Yazarların makale gönderebilmesi için Journal Agent web sayfasına (http://www.journalagent.com/jpr/) kayıt olup, şifre almaları gerekmektedir. Bu sistem

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çevrim-içi yazı gönderilmesine ve değerlendirilmesine olanak tanımaktadır. Bu sistem ile toplanan makaleler Web of Science-Emerging Sources Citation Index (ESCI), Directory of Open Access Journals (DOAJ), EBSCO, CINAHL Complete Database, ProQuest, Tübitak/Ulakbim TR Dizini, TurkMedline ve Türkiye Atıf Dizini kurallarına uygun olarak sisteme alınmakta ve arşivlenmektedir.

Sayfa düzeni: Özgün Araştırmalar, klinik araştırma, klinik gözlem, yeni teknikler, deneysel ve laboratuvar çalışmalarını kapsar. Özgün araştırmalar, başlık, özet, yazının ana konusu ile ilgili anahtar kelimeler, giriş, gereç ve yöntem, bulgular, tartışma, teşekkür, kaynaklar, tablolar, resimler bölümlerini içermelidir. Özet bölümü, "Öz" başlığı ile yazılmalıdır. Metin "Times New Roman" yazı stili, 12 punto, 1,5 satır aralığı ile yazılmalıdır. Metnin tümü 2500 kelimeyi geçmemelidir. Olgu Sunumları, nadir görülen ya da tanı ve tedavide farklılık gösteren, mevcut bilgilerimize katkıda bulunan, eğitici olguyu/olguları içermeli, giriş, olgu sunumu, tartışma bölümlerini kapsamalıdır. Metnin tümü 1500 kelimeyi geçmemelidir. Derlemeler güncel bir konuyu, bağımsız, literatür bilgisini de içerecek şekilde derinlemesine inceleyen yazılardır. Metnin tümü 18 adet A4 sayfasını geçmemelidir. Editöre Mektuplar yayınlanmış makaleler hakkında ya da güncel pediatrideki gelişmeleri içeren 1000 kelimeyi geçmeyen ve kaynak belirten yazılar olmalıdır. Özet bölümü içermez. Kaynak sayısı 5 ile sınırlıdır.

Kısaltmalar: Kelimenin ilk geçtiği yerde parantez içinde ve tüm metin boyunca kullanılır. Uluslararası kullanılan kısaltmalar için "Bilimsel Yazım Kuralları" kaynağına başvurulabilir.

Editöre sunum sayfası: Gönderilen makalenin kategorisi, daha önce başka bir dergiye gönderilmemiş olduğu, var ise çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ve bu kuruluşların yazarlarla ilişkileri, makale İngilizce ise; İngilizce yönünden kontrolünün ve araştırma makalesi ise biyoistatistiksel kontrolünün yapıldığı belirtilmelidir.

KAYNAKLAR

Kaynakların gerçekliğinden yazarlar sorumludur.

Metin içinde: Kullanılan kaynaklar, ilgili cümlenin içinde veya sonunda parantez içinde belirtilmelidir. Eğer, kullanılan kaynağın yazar/yazarları cümle başında belirtiliyorsa, kaynak isimden hemen sonra gelecek şekilde parantez içi olarak yazılmalıdır. Tüm yazılarda Türk yazarlarca yapılmış yerli veya yabancı yayınların kullanılmasına özellikle dikkat edilmeli ve Türkçe dil kurallarına uyulmasına özen gösterilmelidir.

Kongrelerde sunulan bildiriler, basılmamış yayınlar, tezler, internet kaynaklı adresler, kişisel görüşme ya da deneyimler kaynak olarak belirtilmemelidir. Adı geçen kaynaklardan bahsedilmek isteniyorsa, yazıda geçtiği cümlenin sonunda kaynak numarası belirtilmeden, açık yazı ile parantez içine alınarak kaynağın niteliği belirtilmelidir.

Kaynaklar bölümünde: Kaynaklar metin içerisinde geçiş sırasına göre Arap rakamları ile numaralandırılmalıdır. Kaynaklarda tüm yazarlar belirtilmelidir. Ancak yazar sayısı 6'dan fazla olan çalışmalarda ilk 3 yazarın adı yazılmalı, daha sonra Türkçe makalede (ve ark.), İngilizce makalede (et al.) eki yapılmalıdır. Dergilerin isimleri Index Medicus'ta kullanılan stillere göre kısaltılmalıdır.

Kaynak yazılımı için örnekler:

Dergi: Yazar(lar)ın soy isim(ler)i ve yazar isim(ler)inin ilk harfi, makale başlığı, dergi adı (dergide belirtilen orijinal kısaltması), yıl, cilt ve sayfa numaraları.

Örnek: Koening JQ. Air pollution and asthma. J Allergy Clin Immunol 1999;104:717-22.

Kitap: Yazar(lar)ın soy isim(ler)i ve yazar isim(ler)inin ilk harfi, bölüm başlığı, editörün(lerin) ismi, kitap ismi, kaçıncı baskı olduğu, basıldığı şehir, basım yeri, yayınevi, basım yılı ve sayfa numaraları.

Örnek: Fletcher CDM, Unni KK, Mertens F. Genetics of Tumours of Soft Tissue and Bone. Lyon, France, IARC Press, 2002. p. 225-419.

Kitap bölümü: Yazar(lar)ın soy isim(ler)i ve yazar isim(ler)inin ilk harfi, bölüm ve kısım, editörün(lerin) ismi, kitap adı, basım yeri, yayınevi adı, basım yılı, sayfa numaraları.

Örnek: Whitsett JA, Pryhuber GS, Rice WR. Acute respiratory disorders. In: Avery GB, Mac- Donald MG (eds). Neonatology: Pathophysiology and Management of the Newborn, 5th ed. Philadelphia, Lippincott Williams&Wilkins, 1999;505-15.

RESİM, TABLO, GRAFİK VE ŞEKİLLER

Tüm görsel materyaller metnin sonunda ayrı birer sayfa olarak hazırlanmalıdır. Şekil, resim, tablo ve grafiklerin açıklamaları makale sonuna eklenmelidir. Orijinal filmler, EKG kayıtları gibi belgeler kesinlikle yollanmamalıdır. Renkli resimlerin masrafları yazarlar tarafından bizzat karşılanacaktır.

Resimler: Resimlere metindeki geçiş sırasına göre numara verilmeli ve kısa birer başlık yazılmalıdır. Başka bir yayından alıntı yapılıyorsa yazılı baskı izni birlikte yollanmalıdır. Fotoğrafların ayrıntıları seçilmeli, JPEG formatında ve en az 300 dpi (çözünürlük) olarak kaydedilmelidir.

Tablolar, Grafikler, Şekiller: Tüm tablolara, grafiklere ve şekillere metinde geçiş sırasına göre numara verilmeli ve kısa birer başlık yazılmalıdır. Tablolar yazıda geçiş sıralamasına göre Romen rakamlarıyla (I, II) sıralandırılmalı ve başlık taşımalıdır. Şekiller geçiş sıralamasına göre Arap harfleri (1,2) ile sıralanmalıdır. Kullanılan kısaltmalar alt kısımda mutlaka açıklanmalıdır. Özellikle tablolar metni açıklayıcı ve kolay anlaşılır hale getirme amacı ile hazırlanmalı ve metnin tekrarı olmamalıdır. Olgu sunumlarında en çok 2 şekil veya resim kullanılmalıdır.

BİYOİSTATİSTİK

Araştırma bulgularının denetlenebilirliğini sağlamak için, araştırma düzeni, örneklem, yöntem, bilimsel yaklaşımlar ve uygulamalar tanımlanarak kaynakları sunulmalıdır.

Anlamlılık sınırı olarak seçilen "p" değeri ile birlikte uygun hata ve belirsizlik payları (güven aralıkları, vs) belirtilmelidir. Kullanılan istatistiksel terimler, kısaltmalar ve semboller tanımlanmalı, kullanılan yazılım (software) belirtilmelidir. İstatistik terminolojisi (random, signifikant, korelasyon, vs.) istatistik dışı anlamlarda kullanılmamalıdır.

Verilerin ve analizin tüm sonuçları tablo, şekil veya grafik olarak "Bulgular" bölümünde, kullanılan biyoistatistiksel yöntemler ve uygulama ayrıntıları yazının "Gereç ve Yöntem" bölümünde veya ayrı bir başlık altında sunulmalıdır.

YAZI ÇEŞİTLERİ

Özgün Araştırmalar

Klinik araştırma, klinik gözlem, yeni teknikler, deneysel ve laboratuvar çalışmalarını kapsar. Özgün araştırmalar; başlık, özet, yazının ana konusu

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Yazarlara Bilgi

ile ilgili anahtar kelimeler, giriş, gereç ve yöntem, bulgular, tartışma, çalışmanın kısıtlılıkları, sonuç, teşekkür, kaynaklar, tablolar, grafikler, resimler bölümlerini içermelidir. Başlık, özet ve anahtar kelimeler Türkçe ve İngilizce olarak yazılmalıdır. Makale yukarıda belirtilen yazım kuralları ile yazılı 16 A4 sayfasını aşmamalıdır.

Başlık sayfası: Makalenin başlığı, kısa başlık, yazar isimleri ve yazar bilgilerini kapsayan sayfadır. Sırasıyla şu tanımlar yapılmalıdır;

1. Makalenin başlığı (Türkçe ve İngilizce) mümkün olduğunca kısa ve açıklayıcı olmalı, boşluklar dahil 135 karakteri geçmemeli, kısaltma içermemelidir.

2. Kısa başlık (Türkçe ve İngilizce), en fazla 60 karakterden oluşmalıdır.

3. Yazar isimleri (yazarların isimleri tam olarak kısaltılmadan yazılmalıdır, yazarın akademik görevi yazılmamalıdır) ve bağlı bulunduğu kurumlar.

4. İletişim kurulacak yazarın ismi, adresi, telefon ve faks numarası ile e-posta bilgileri.

5. Bilimsel toplantılarda sunulan ve özeti kongre kitabında yer almış eserlerin toplantı yeri ve tarihi.

Öz: Yazının ana hatlarını içeren, en fazla 200 kelimeden oluşan öz Türkçe ve İngilizce olarak hazırlanmalıdır. Öz bölümünde kaynak gösterilmemeli, kısaltmalardan mümkün olduğunca kaçınılmalıdır. Yapılacak kısaltmalar metindekilerden bağımsız olarak ele alınmalıdır.

Araştırma makalelerinde öz 5 alt başlık olarak hazırlanmalıdır:

Amaç: Çalışmanın amacı açıkça belirtilmelidir.

Gereç ve Yöntemler: Çalışma tanımlanmalı, standart kriterleri, randomize olup olmadığı, retrospektif veya prospektif olduğu ve varsa istatistiksel yöntem belirtilmelidir.

Bulgular: Çalışmanın detaylı sonucu verilmeli, istatistik anlamlılık derecesi belirtilmelidir.

Sonuç: Çalışmanın sonuçlarını yansıtmalı, klinik uygulanabilirliği tanımlamalı, olumlu ve olumsuz yönleri gösterilmelidir.

Anahtar Kelimeler: En az 3, en çok 5 anahtar kelime özetin sonunda yer almalıdır. İngilizce anahtar kelimeler "Medical Subject Headings'e (MESH) uygun olarak verilmelidir (www.nlm.nih.gov/mesh/MBrowser.html). Türkçe anahtar kelimeler ise MESH terimlerinin aynen çevirisi olmalıdır. Anahtar kelimeler uygun nitelikte ve standart terminolojide yazılmalıdır. Türkçe anahtar kelimeler "Türkiye Bilim Terimleri" arasından seçilmelidir. Yazarlar bilgilendirme için http://www.bilimterimleri.com adresini kullanabilir.

Araştırma makalelerinde ana metin aşağıdaki başlıkları içermelidir;

Giriş: Konu hakkında kısa ve öz bilgi verilmeli, çalışmanın amacı belirtilmeli, bunlar literatür bilgisi ile desteklenmelidir.

Gereç ve Yöntem: Çalışma planı verilmeli, randomize olup olmadığı, retrospektif veya prospektif olduğu, denek sayısı, özellikleri, çalışmaya dahil edilme ve dışlanma kriterleri, kullanılan istatistiksel yöntem belirtilmelidir.

Bulgular: Elde edilen sonuçlar belirtilmeli, tablo ve resimler numara sırasıyla verilmeli, sonuçlar uygulanan istatistiki analiz yöntemine göre değerlendirilmelidir. Görsel materyallerin yazım kuralları hakkında gerekli bilgi "Genel Kurallar" başlığı altında bulunan "Resim, Tablo, Grafik ve Şekiller" bölümünde bulunmaktadır.

Tartışma: Elde edilen değerler olumlu ve olumsuz yönleriyle tartışılmalı, literatür ile karşılaştırılmalı, çalışmadan elde edilen sonuç vurgulanmalıdır.

Sonuç: Çalışmadan elde edilen sonuç vurgulanmalıdır.

Teşekkür: Her türlü çıkar çatışması, finansal destek, bağış ve diğer editöryal (istatistik analiz, İngilizce/Türkçe değerlendirme) ve/veya teknik yardım var ise metnin sonunda sunulmalıdır.

Kaynaklar: Kaynakların gerçekliğinden yazarlar sorumludur. Kaynakların yazım kuralları hakkında gerekli bilgi "Genel Kurallar" başlığı altında bulunan "Kaynaklar" bölümünde bulunmaktadır.

Olgu Sunumları

Nadir görülen, tanı ve tedavide farklılık gösteren, mevcut bilgilerimize yenilerini ekleyip, katkı sağlayan olguları içermelidir. Türkçe ve İngilizce başlık, 50 kelimeyi aşmayan, yapılandırılmamış özet ve anahtar kelimeler ilk sayfada yer almalıdır. Sunum metni, giriş, olgu sunumu, tartışma ve kaynaklardan oluşmalıdır. Metnin tümü yukarıda bahsedilen yazım kuralları çerçevesinde 1500 kelimeyi geçmemelidir. Olgu sunumları için en fazla 10 kaynak kullanılmalıdır.

Derlemeler

Bir bilgi ya da konunun klinikte kullanılması için vardığı son düzeyi anlatan, tartışan, değerlendiren ve gelecekte yapılacak olan çalışmalara yön veren bir formatta hazırlanmalıdır. **Dergi yalnızca davetli derleme kabul eder ve yayınlar.** Derleme başvurusu yapılmadan önce konunun editör ile görüşülmesi önerilir.

Güncel bir konuyu, bağımsız, hiçbir farklı görüşü öne çıkarmadan derinlemesine inceleyen yazılardır. Yazının ilk bölümünde Türkçe ve İngilizce başlık, özet, anahtar kelimeler bulunmalıdır. Özet bölümü yapılandırılmamalıdır. Konuda geçen her alıntının kaynağı mutlak gösterilmelidir. Tümü 18 A4 sayfayı geçmemelidir.

Editöre Mektuplar

Yayınlanmış makaleler hakkında ya da güncel pediatrideki, bilimsel ve sosyal yönden irdeleyen veya özellikle The Journal of Pediatric Research Dergisi'nde yayınlanan yazılarla ilgili soru veya katkı içerikli 1000 kelimeyi geçmeyen ve kaynak belirten yazılar olmalıdır. Başlık ve özet bölümleri içermez. Kaynak sayısı 5 ile sınırlıdır.

REKLAMLAR

Reklamlar için Editör ile görüşülmelidir. Derginin dış ve iç kapakları ile iç sayfalarında renkli reklam yayınlanması mümkündür.

YAYIN HAKKI

The Journal of Pediatric Research, Ege Çocuk Vakfı (EÇV) tarafından desteklenen, Ege Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı'nın yayın organıdır.

YAZIŞMA

Prof. Dr. Özgür Çoğulu

The Journal of Pediatric Research

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Intructions to Authors

The Journal of Pediatric Research is an official peer-reviewed publication of the Ege University, Faculty of Medicine, Department of Pediatrics and Ege Children's Foundation. This publication organ is responsible for the issue of unique clinical and laboratory research papers, case reports, reviews directly or indirectly related to children's health and diseases. The publication languages of the journal are Turkish and English.

Manuscripts written in Turkish should be in accordance with the Turkish Dictionary and Writing Guide ("Türkçe Sözlüğü ve Yazım Kılavuzu") of the Turkish Language Association.

The Journal of Pediatric Research does not charge any article submission or processing charges.

The abbreviation of The Journal of Pediatric Research is JPR, however, it should be denoted as J Pediatr Res when referenced. In the international index and database, the name of the journal has been registered as The Journal of Pediatric Research and abbreviated as J Pediatr Res.

A manuscript will be considered only with the understanding that it is an original contribution that has not been published elsewhere. All manuscripts submitted to the journal for publication are peer-reviewed. Authors shall be informed within a period of 6 weeks about the process. Upon review, those manuscripts, which are accepted, shall be published in the journal and issued on the http://www.jpedres.org official internet address.

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Experimental, clinical and drug studies requiring approval by an ethics committee must be submitted to The Journal of Pediatric Research with an ethics committee approval report confirming that the study was conducted in accordance with international agreements and the Declaration of Helsinki (revised 2013) (http://www.wma.net/en/30publications/10policies/b3/). The approval of the ethics committee and the fact that informed consent was given by the patients should be indicated in the Materials and Methods section. In experimental animal studies, the authors should indicate that the procedures followed were in accordance with animal rights as per the Guide for the Care and Use of Laboratory Animals (http://oacu.od.nih.gov/regs/guide/guide.pdf) and they should obtain animal ethics committee approval.

Authors must provide disclosure/acknowledgment of financial or material support, if any was received, for the current study.

If the article includes any direct or indirect commercial links or if any institution provided material support to the study, authors must state in the cover letter that they have no relationship with the commercial product, drug, pharmaceutical company, etc. concerned; or specify the type of relationship (consultant, other agreements), if any.

Authors must provide a statement on the absence of conflicts of interest among the authors and provide authorship contributions.

The Journal of Pediatric Research is an independent international journal based on double-blind peer-review principles. The manuscript is assigned to the Editor-in-Chief, who reviews the manuscript and makes an initial decision based on manuscript quality and editorial priorities. Manuscripts that pass initial evaluation are sent for external peer review, and the Editor-in-Chief assigns an Associate Editor. The Associate Editor sends the manuscript to reviewers (internal and/or external reviewers). The reviewers must review the manuscript within 21 days. The Associate Editor recommends a decision based on the reviewers' recommendations and returns the manuscript to the Editor-in-Chief. The Editor-in-Chief makes a final decision based on editorial priorities, manuscript quality, and reviewer recommendations. If there are any conflicting recommendations from reviewers, the Editor-in-Chief can assign a new reviewer.

The scientific board guiding the selection of the papers to be published in the Journal consists of elected experts of the Journal and if necessary, selected from national and international authorities. The Editor-in-Chief, Associate Editors, biostatistics expert and English language consultant may make minor corrections to accepted manuscripts that do not change the main text of the paper.

In case of any suspicion or claim regarding scientific shortcomings or ethical infringement, the Journal reserves the right to submit the manuscript to the supporting institutions or other authorities for investigation. The Journal accepts the responsibility of initiating action but does not undertake any responsibility for an actual investigation or any power of decision.

The Editorial Policies and General Guidelines for manuscript preparation specified below are based on "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations)" by the International Committee of Medical Journal Editors (2016, archived at http://www.icmje.org/).

Preparation of research articles, systematic reviews and meta-analyses must comply with study design guidelines:

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 statement of 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/);

STROBE statement, a 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).

GENERAL GUIDELINES

Manuscripts can only be submitted electronically through the Journal Agent website (http://journalagent.com/tjo/) after creating an account. This system allows online submission and review.

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The manuscripts are archived according to Web of Science-Emerging Sources Citation Index (ESCI), Directory of Open Access Journals (DOAJ), EBSCO, CINAHL Complete Database, ProQuest, Tübitak/Ulakbim TR Index, TurkMedline and Turkiye Citation Index.

Format: Unique research papers cover clinical research, observational studies, novel techniques, and experimental and laboratory studies. Unique research papers shall consist of a heading, abstract, keywords related to the main topic of the paper, introduction, materials and methods, results, discussion, acknowledgements, bibliography, tables and figures. Manuscripts should be prepared using 12 pt "Times New Roman" and 1.5 line spacing. The text shall not exceed 2500 words. Case reports must contain rare cases or those that are unique in diagnosis and treatment, those which contribute to current knowledge and provide educational information, along with the introduction, case reporting and discussion sections. The whole text must not exceed 1500 words. Reviews are texts in which a current subject is examined independently, with reference to scientific literature. The whole text must not exceed 18 A4 paper sheets. Letters to the Editor must be manuscripts, which do not exceed 1000 words, with reference to scientific literature, and those written in response to issued literature or those, which include development in the field of pediatrics. These manuscripts do not contain an abstract. The number of references is limited to 5.

Abbreviations: Abbreviations should be defined at first mention and used consistently thereafter. Internationally accepted abbreviations should be used; refer to scientific writing guides as necessary.

Cover letter: The cover letter should include statements about manuscript type, single-journal submission affirmation, conflict of interest statement, sources of outside funding, equipment (if applicable), approval of language for articles in English and approval of statistical analysis for original research articles.

REFERENCES

Authors are solely responsible for the accuracy of all references.

In-text citations: References shall be listed as the below formats on a separate page according to their sequence within the text and referred to within the text in parentheses.

Presentations presented in congresses, unpublished manuscripts, theses, Internet addresses, and personal interviews or experiences should not be indicated as references. If such references are used, they should be indicated in parentheses at the end of the relevant sentence in the text, without reference number and written in full, in order to clarify their nature. In all manuscripts, care must be given to the inclusion of references related to domestic and international studies performed by Turkish authors and compliance to Turkish written language rules.

References section: All author names shall be stated within all references. References shall be listed as the below formats on a separate page according to their sequence within the text and referred to within the text in parentheses. However, in studies where author numbers exceed 6, names of the first 3 authors shall be stated; "ve ark." and "et al." additions shall be made to the list of authors in Turkish and English references, respectively. The titles of journals should be abbreviated according to the style used in the Index Medicus.

Reference Format

Journal: Last name(s) of the author(s) and initials, article title, publication title and its original abbreviation, publication date, volume, the inclusive page numbers.

Example: Koening JQ. Airpollutionandasthma. J Allergy Clin Immunol 1999; 104:717-22.

Book: Last name(s) of the author(s) and initials, chapter title, book editors, book title, edition, place of publication, date of publication and inclusive page numbers of the extract cited.

Example: Fletcher CDM, Unni KK, Mertens F. Genetics of Tumours of Soft Tissue and Bone. Lyon, France, IARC Press, 2002. p. 225-419.

Book Chapter: Last name(s) of the author(s) and initials, chapter title, book editors, book title, edition, place of publication, date of publication and inclusive page numbers of the cited piece.

Example: Whitsett JA, Pryhuber GS, Rice WR. Acuteres piratory disorders. In: Avery GB, Mac- Donald MG (eds). Neonatology: Pathophysiology and Management of the Newborn, 5th ed. Philadelphia, Lippincott Williams & Wilkins, 1999;505-15.

TABLES, GRAPHICS, FIGURES, AND IMAGES

All visual materials together with their legends should be located on separate pages that follow the main text. Original documents such as films, ECG records must not be delivered. All cost related to colored printouts shall be covered by the authors' own expenses.

Images: Images (pictures) should be numbered and include a brief title. Permission to reproduce pictures that were published elsewhere must be included. All pictures should be of the highest quality possible, in JPEG format, and at a minimum resolution of 300 dpi.

Tables, Graphics, Figures: All tables, graphics or figures should be enumerated according to their sequence within the text and a brief descriptive caption should be written. Tables shall be numbered by Roman numerals (I, II) according to their sequence, and shall include a heading. Figures shall be numbered by Arabic numerals (1,2) according to their sequence. Any abbreviations used should be defined in the accompanying legend. Tables in particular should be explanatory and facilitate readers' understanding of the manuscript, and should not repeat data presented in the main text. A maximum of 2 figures or photographs shall be added to case reports.

BIOSTATISTICS

To ensure controllability of the research findings, the study design, study sample, and the methodological approaches and applications should be explained and their sources should be presented.

The "p" value defined as the limit of significance along with appropriate indicators of measurement error and uncertainty (confidence interval, etc.) should be specified. Statistical terms, abbreviations and symbols used in the article should be described and the software used should be defined. Statistical terminology (random, significant, correlation, etc.) should not be used in non-statistical contexts.

All results of data and analysis should be presented in the Results section as tables, figures and graphics; biostatistical methods used and application details should be presented in the Materials and Methods section or under a separate title.

MANUSCRIPT TYPES

Original Articles

Unique research papers cover clinical research, observational studies, novel techniques, and experimental and laboratory studies. Unique research papers shall consist of a heading, abstract, keywords related to the main topic of the paper, introduction, materials and methods, results, discussion, acknowledgements, bibliography, tables and figures. The text shall not exceed 2500 words. Case reports must contain rare cases or those that are unique in diagnosis and treatment, those which contribute to current knowledge and

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provide educational information, along with the introduction, case reporting and discussion sections. The whole text must not exceed 1500 words. Reviews are texts in which a current subject is examined independently, with reference to scientific literature. The whole text must not exceed 18 A4 paper sheets. Letters to the Editor must be manuscripts, which do not exceed 1000 words, with reference to scientific literature, and those written in response to issued literature or those, which include development in the field of pediatrics. These manuscripts do not contain an abstract. The number of references is limited to 5.

Title Page: This page should include the title of the manuscript, short title, name(s) of the authors and author information. The following descriptions should be stated in the given order:

1. Title of the manuscript (Turkish and English), as concise and explanatory as possible, including no abbreviations, up to 135 characters

2. Short title (Turkish and English), up to 60 characters

3. Name(s) and surname(s) of the author(s) (without abbreviations and academic titles) and affiliations

4. Name, address, e-mail, phone and fax number of the corresponding author

5. The place and date of scientific meeting in which the manuscript was presented and its abstract published in the abstract book, if applicable

Abstract: A summary of the manuscript should be written in both Turkish and English. References should not be cited in the abstract. Use of abbreviations should be avoided as much as possible; if any abbreviations are used, they must be taken into consideration independently of the abbreviations used in the text.

For original articles, the structured abstract should include the following sub-headings:

Aim: The aim of the study should be clearly stated.

Materials and Methods: The study and standard criteria used should be defined; it should also be indicated whether the study is randomized or not, whether it is retrospective or prospective, and the statistical methods applied should be indicated, if applicable.

Results: The detailed results of the study should be given and the statistical significance level should be indicated.

Conclusion: Should summarize the results of the study, the clinical applicability of the results should be defined, and the favorable and unfavorable aspects should be declared.

Keywords: A list of minimum 3, but no more than 5 key words must follow the abstract. Key words in English should be consistent with "Medical Subject Headings (MESH)" (www.nlm.nih.gov/mesh/MBrowser.html). Turkish key words should be direct translations of the terms in MESH.

Original research articles should have the following sections:

Introduction: Should consist of a brief explanation of the topic and indicate the objective of the study, supported by information from the literature.

Materials and Methods: The study plan should be clearly described, indicating whether the study is randomized or not, whether it is retrospective or prospective, the number of trials, the characteristics, and the statistical methods used.

Results: The results of the study should be stated, with tables/figures given in numerical order; the results should be evaluated according to the statistical analysis methods applied. See General Guidelines for details about the preparation of visual material.

Discussion: The study results should be discussed in terms of their favorable and unfavorable aspects and they should be compared with the literature. The conclusion of the study should be highlighted.

Study Limitations: Limitations of the study should be discussed. In addition, an evaluation of the implications of the obtained findings/results for future research should be outlined.

Conclusion: The conclusion of the study should be highlighted.

Acknowledgements: Any technical or financial support or editorial contributions (statistical analysis, English/Turkish evaluation) towards the study should appear at the end of the article.

References: Authors are responsible for the accuracy of the references. See General Guidelines for details about the usage and formatting required.

Case Reports

Case reports should present cases which are rarely seen, feature novelty in diagnosis and treatment, and contribute to our current knowledge. The first page should include the title in Turkish and English, an unstructured summary not exceeding 50 words, and key words. The main text should consist of introduction, case report, discussion and references. The entire text should not exceed 1500 words (A4, formatted as specified above). A maximum of 10 references shall be used in case reports.

Review Articles

Review articles can address any aspect of clinical or laboratory pediatry. Review articles must provide critical analyses of contemporary evidence and provide directions of or future research. **The journal only accepts and publishes invited reviews.** Before sending a review, discussion with the editor is recommended.

Reviews articles analyze topics in depth, independently and objectively. The first chapter should include the title in Turkish and English, an unstructured summary and key words. Source of all citations should be indicated. The entire text should not exceed 18 pages (A4, formatted as specified above

Letters to the Editor

Letters to the Editor should be short commentaries related to current developments in ophthalmology and their scientific and social aspects, or may be submitted to ask questions or offer further contributions in response to work that has been published in the Journal. Letters do not include a title or an abstract; they should not exceed 1.000 words and can have up to 5 references.

COMMERCIALIZATION

Commercialization issues shall be discussed with the editor. It is possible to include an advertisement on the outer and inner pages of the journal.

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Editorial / Editörden

Dear Readers,

Welcome to the second issue of "The Journal of Pediatric Research" of 2017. In this issue, all the articles have been written in English. As of 2018, our journal will be published in English. The Journal of Pediatric Research is listed in Web of Science-Emerging Sources Citation Index (ESCI), Directory of Open Access Journals (DOAJ), EBSCO, CINAHL Complete Database, ProQuest, Tübitak/Ulakbim TR Index, TurkMedline and Turkiye Citation Index.

The cover photo of this issue is the painting named "The Sea of Life". This awesome pastel painting is by Dr. Sibel Polater, one of our pediatric residents in Ege University Hospital. Most of us have witnessed that doctors are interested in art. Actually, medicine is itself an art; it must employ the finest tools available; not just the finest in technology and science, but also the finest in knowledge, skills, and the personality of the physician. In fact, the medicine, like the art, is a passion. There is a close relationship between art and medicine, and they share a common role. They have a common substrata, the physical, visible world of matter. More significant however, are the similar qualities of mind, body, and spirit demanded of the practitioners of each; painter and physician. The chief among them is the eye: the ability not only to observe, but to observe keenly - to ferret out the tiny details from the jumble of facts, lines, colors - the tiny detail that unlocks a painting, or a patient's predicament. Observation demands attention, and this is the key to both art and medicine. Attention is nothing more than a state of receptiveness to its object; the artist to nature, the viewer to the work of art, the physician to the patient.

In the June issue, there is a review about PFAPA syndrome, summarizing the current diagnosis and treatment. There are interesting case reports about TAR syndrome, the association between choledochal cyst and pancreatitis, rhabdomyosarcoma. Unfortunately, consanguineous marriages are still common in our country; so, metabolic diseases are not very rare. Also in the June issue, you can read two important articles about urea cycle disorders and mucopolysaccaridosis as well as interesting research articles about febrile seizures and the anxiety of the parents of premature babies.

As the Editor of the June issue, I would like to thank the members of our editorial board, reviewers, authors, and Galenos Publishing House for their tremendous help in preparing this featured issue of 2017.

We look forward to your future scientific articles, and wish you good and productive reading.

Sincerely yours,

Prof. Dr. Zülal Ülger Tutar

Section Editor

J Pediatr Res 2017;4(2):42-5
DOI: 10.4274/jpr.32757

Review / Derleme

Current Diagnosis and Treatment Models of Periodic Fever, Aphthous Stomatitis, Pharyngitis and Cervical Lymphadenitis Syndrome

Periyodik Ateş, Aftöz Stomatit, Farenjit ve Servikal Lenfadenit Sendromuna Güncel Tanı ve Tedavi Yaklaşımları

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ABSTRACT

Periodic fever, aphthous stomatitis, pharyngitis, and cervical lymphadenitis (PFAPA) syndrome is the most frequent cause of periodic fever in childhood. The pathogenesis of PFAPA is still unknown. Differantial diagnosis must be made with cyclic neutropenia and other autoinflammatory diseases. Because PFAPA is self limiting and benign, there is no certain treatment model. Treatment options must be specific to the patient, with a strong family and doctor relationship.

Keywords: Periodic fever, aphthous stomatitis, pharyngitis, and cervical lymphadenitis syndrome, diagnosis, therapy

ÖZ

Periyodik ateş, aftöz stomatit, farenjit ve servikal lenfadenit (PFAPA) sendromu çocukluk çağında görülen, en sık tekrarlayan ateş nedenidir. PFAPA patogenezi halen tam olarak bilinmemektedir. Siklik nötropeni ve diğer monogenik otoenflamatuvar hastalıklarla ayırıcı tanısının yapılması gerekmektedir. Kendini sınırlayan ve benign bir hastalık olduğu için henüz netlik kazanmış bir tedavi şekli yoktur. Tedavi seçeneklerinin ise güçlü bir ebeveyn-doktor ilişkisi yardımıyla hastaya özel olarak seçilmesi gerekmektedir.

Anahtar Kelimeler: Periyodik ateş, aftöz stomatit, farenjit ve servikal lenfadenit sendromu, tanı, tedavi

Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Cervical Lymphadenitis Syndrome

Periodic fever, aphthous stomatitis, pharyngitis, and cervical lymphadenitis (PFAPA) syndrome is the most frequent cause of recurrent fevers in childhood. It was first described by Marshall et al. (1) in 1987. PFAPA is diagnosed with recurrent episodes of fever continuing for 3-6 days and following 3 to 8-week intervals; with at least one of the following findings: Aphthous stomatitis, cervical lymphadenitis, and pharyngitis. The disease often starts before the age of 5 and mostly ends in adolescence. The general condition, growth and development of patients are normal between the episodes (1,2).

Epidemiology

Most of the patients are between the ages of 2 and 5 with mild male predominance and no racial or ethnic

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Received/Geliş tarihi: *01.09.2015* **Accepted/Kabul tarihi:** *26.10.2015*

predominance (3). Rarely, familial cases have been reported (4,5). In the majority of patients the attacks last until the age of 10, but it has also been reported in adults (6).

Pathogenesis

Autoinflammatory syndromes are a group of diseases characterized by inflammatory attacks that occur independently of autoreactive T lymphocytes or external triggering agents. The common termination of genes associated with these syndromes is interleukin (IL)-1β activation. Although the pathogenesis of PFAPA syndrome is not fully understood, it is evaluated in autoinflammatory syndromes. Studies have shown that IL-1β, IL-18, tumor necrosis factor-α, interferon (IFN)-γ from proinflammatory cytokines increase in the early phase of fever and IL-6 increases rapidly in the late phase (7-12). In contrast, levels of T-cell-associated cytokines IL-7, IL-17 and anti-inflammatory cytokines IL-10 and IL-4 decrease during exacerbation (8). Dysregulation of IL-1 production from monocytes has been shown in patients (9). In addition, increased expression of inflammation-associated genes (AIM2, CASP1) and IL-1 were detected during the episode (11). In the fever episodes, dysregulation in natural immunity together with an increase in Th1 response, and reduction in Th2 response lead to changes in cytokine levels (8-10,12). Increased levels of monocytes, and decreased levels of eosinophiles and lymphocytes are observed during exacerbations (9,10).

Genetic background is one of the most controversial features of this syndrome. Although it is generally accepted as a sporadic disease, familial clustering suggests the presence of a possible hereditary component (13). The link to genes associated with other autoinflammatory diseases has been investigated. Specifically observed was the MEFV mutation which plays a modifying role in PFAPA disease activation and it has been determined that with MEFV mutations the duration of attacks are irregular and shorter, the frequency of aphthous stomatitis and the need for glucocorticoid treatment is rare (14).

In a large cohort study, 68 individuals and 14 families were enrolled to elucidate the genetic orientation of PFAPA syndrome. It was suggested that PFAPA is not a monogenic disease, but polygenic and/or is influenced by non-genetic factors (15).

Clinical Findings

In a multicentre cohort analysis by Hofer et al. (16), 301 patients with PFAPA were evaluated and clinical manifestations were reported. The study results reported so far are presented in Table I (2,8,17-21). Fever starts suddenly with shudders. Body temperature ranges from 38.9 to 41.1 °C for 3-6 days. The period between fever episodes is around 28.2 days (26-30.4 days). The average number of attacks is 11.5 per year (2,14). Aphthous ulcer is frequently seen on the lips and in buccal mucosa, accompanied by fever attacks in 40-70% of cases, and heals without scarring (2,16,17). Pharyngitis is detected in 90% of the patients. Exudative pharyngitis occurs in 41% of the cases (17). Cervical adenopathy is associated with 78% of attacks, and 86% is bilateral (17). Adenopathy is sensitive to touch. The clinical findings may also be accompanied by headache, muscle aches, diarrhea, arthralgia, cough and flu-like symptoms, and rash.

Laboratory Findings

There is no diagnostic laboratory test. Attacks may be diagnosed as tonsillitis or viral infection. Group A *Streptococcus* can be detected in 9.8% of cases in the throat culture (2). PFAPA attacks do not respond to penicillin therapy. C-reactive protein (CRP) is high at the beginning of the attack, sedimentation may

Table I. Clinical features of patients with periodic fever, aphthous stomatitis, pharyngitis, and cervical

	Thomas et al. (2)	Padeh et al. (17)	Tasher et al. (18)	Gattorno et al. (19)	Feder and Salazar (20)	Wurster et al. (21)	Stojanov et al. (8)
Number of patients	66	28	54	130	105	59	21
Pharyngitis (%)	65	100	96	83.8	85	75	86
Cervical adenitis (%)	77	100	61	83.8	62	88.3	100
Aphthous stomatitis (%)	67	68	39	58.5	38	71.7	62
Headache (%)	65	18	46	40.8	44	70	-
Abdominal pain (%)	45	18	65	53.1	41	33.3	57
Diarrhea (%)	30	-	13	29.2	-	-	10
Arthralgia (%)	-	11	-	43.8	-	26.7	29
Trembling (%)	80	-	61	-	-	83.3	-
Skin eruption (%)	15	-	4	22.3	-	-	10

be normal but it may increase after a few days (20). Procalcitonin does not increase like other acute phase reactants (22). Serum immunoglobulin (Ig) levels are normal, IgD is normal or slightly elevated (20,23). All inflammatory parameters return to normal between the attacks (22).

Differential Diagnosis

Cyclic neutropenia, whose attacks occur at specific intervals, is the most important differential diagnosis (2). Cyclic neutropenic episodes occur every 18-24 days and the absolute neutrophil count falls below 500/mm^3 during the attack. Promyelocytic arrest is detected in the bone marrow, and attacks do not respond to steroid therapy (24). Many monogenic autoinflammatory diseases may emerge with regular attacks and mimic or coincide with PFAPA syndrome. Especially in hyperimmunoglobulinemia D syndrome, familial Mediterranean fever and tumor necrosis factor receptor-associated periodic syndrome patients, PFAPA-like findings can be seen. Further research should be done if there are coughs, colds, severe abdominal pain, severe diarrhea, rash, arthritis and neuromuscular symptoms, increased acute phase response between episodes, and family history of periodic fever. In 2008, Gattorno et al. (19) formed a gaslini scoring system to help further investigation, which is recommended if the total score is higher than 1.32 in this scoring system, where abdominal pain, aphthous stomatitis, chest pain, presence of diarrhea, as well as the age at the onset of symptoms and family history are questioned.

Treatment

Since PFAPA syndrome is a self-limiting and benign disease, there is no clear treatment yet. The family and the physician should decide on the treatment together considering potential side effects, and social factors such as not being able to go to work and/or school in this febrile period (25). Clinical experience has shown that paracetamol and nonsteroid anti-inflammatory drugs used in the treatment of PFAPA syndrome can not control symptoms other than fever.

Glucocorticoids: The administration of 1-2 mg/kg prednisolone at the onset of fever will control fever and pharyngitis, but not aphthous stomatitis and adenitis. This rapid response has a diagnostic feature that also helps to distinguish PFAPA syndrome from other periodic fever syndromes (6,20). However, glucocorticoids have been shown to shorten the time between attacks in 25% of patients (26). Symptoms may recur within 48-72 hours after the first dose (27). In this case, prednisolone 1 mg/kg on days 1 and 2; 0.5 mg/kg on day 2 and 3 can be repeated. There are studies recommending a single dose of betamethasone (0.3 mg/kg) at the onset of fever as an alternative to this treatment (23). In some recent uncontrolled studies, low-dose (0.6 mg/kg/g) prednisolone therapy has also been shown to improve the symptoms (24). The most frequently reported side effects of glucocorticoid therapy are–restlessness and sleep disturbance. These may be reduced if the prednisolone dose is given 4-6 hours before bedtime.

Tonsillectomy: Because PFAPA syndrome has a spontaneous remission, tonsillectomy, which has possible risks, is a controversial treatment. It is reported that in 1/3 of the patients symptoms repeat 0.5-10 years after tonsillectomy (25). In another study evaluating the efficacy of the treatment, steroid therapy (90%), tonsillectomy (75%), tonsillectomy and adenoidectomy (86%) were found successful (2). According to the results obtained from the meta-analysis performed by Burton et al. (28), tonsillectomy (± adenoidectomy) was an effective treatment in children with PFAPA, and post-operative symptoms occurred four times more slowly. There was also a significant decrease in the number of PFAPA attacks and the use of corticosteroids after tonsillectomy. However, due to the disadvantages inherent in the surgical procedure, the choice of patients to be offered this treatment should be done carefully.

Among the less frequently applied therapies are colchicine, anti IL-1 and vitamin D treatments. In a study group in which colchicine treatment was given at 0.5-1 mg/day together with prednisolone, there was a decrease in the frequency of attacks (18). However, routine use of colchicine in the treatment of PFAPA is not recommended because of its short term effect, and the lack of studies on a sufficient number of patients (25). IL-1β has been seen to elevate during PFAPA attacks. Acting on this, anakinra (recombinant IL-1β receptor antagonist) was used on a small group of patients, and there was a reduction in IFN-γ induced protein 10 and CXCL10 (chemokine, CXC motif, ligand 10) levels. Also clinical improvement was observed (9).

Vitamin D: In addition to regulating calcium and phosphorus metabolism, it also has an immunomodulator effect. Vitamin D levels in PFAPA patients were found to be deficient and insufficient especially in winter. Vitamin D level is related with the number of attacks and CRP levels (29).

Conclusion

Timely and accurate recognition of the most common PFAPA syndrome among periodic fever syndromes can be achieved with good patient follow-up. Treatment options should be selected specifically for the patient with the help of a strong parent-doctor relationship.

Ethics

Peer-review: Internally peer-reviewed.

Authorship Contributions

Medical Practices: A.P.K., E.K.Ü., B.S., Concept: B.S., Design: A.P.K., E.K.Ü., B.S., Literature Search: A.P.K., E.K.Ü., B.S., Writing: A.P.K., E.K.Ü., B.S.

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

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

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J Pediatr Res 2017;4(2):46-52
DOI: 10.4274/jpr.02408

Original Article / Orijinal Araştırma

Evaluation of the Knowledge and Attitude Changes of Mothers in Neonatal Care

Annelerin Yenidoğan Bakımında Bilgi ve Tutum Değişimlerinin Değerlendirilmesi

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ABSTRACT

Aim: The aim was to determine the initial knowledge of mothers about neonatal care and evaluate their knowledge, care and attitude changes following individual education.

Materials and Methods: Questionnaire forms designed on the subject of infant care and nutrition were given to mothers right after delivery. Before being discharged they were informed by the doctor and breastfeeding nurse about nutrition, infant care, and the most common mistakes. These forms were reapplied on the 15th and 30th days in neonatal polyclinic controls and the changes were evaluated. The correct information was repeated to the mothers who were detected to have misinformation and wrong attitudes in the evaluations in each form application period.

Results: A total of 100 mothers and their infants were included in the study. No difference was determined in the nutrition rates of infants with food other than breast milk on the first day, 15th and 30th days. However, the breastfeeding rates obtained were higher on the 30th day than on the 15th, with an interval of two hours, and in general breastfeeding rates were low on the 15th and 30th days. The rates of bathing the infants with and without a bathtub net were determined to be high on the 15th and 30th days. The change in the infants' sleeping positions, the place of sleep, and the presence of rails/guards around the crib on the 15th and 30th days were not found to be significant compared to the 1st day. There was a significant increase in the umbilical care rates on the 15th and 30th days. The increase in washing the clothes of the infants with soap powder, and the decrease in swaddling after the education were found to be significant. Furthermore, it was determined that the mothers received infant care information more frequently from the healthcare organisation

ÖZ

Amaç: Annelerin yenidoğan bakımı hakkında ilk bilgilerinin saptanması ve bireysel eğitim sonrası bilgi, bakım ve tutum değişimlerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Doğum yapan annelere doğumdan hemen sonra yenidoğan bebeklerin bakımı ve beslenmesi konusunda düzenlenen anket formları verildi. Anneler taburcu olmadan önce doktor ve emzirme hemşiresi tarafından beslenme, bebek bakımı ve en sık yapılan yanlışlar konusunda bilgilendirildi. Yenidoğan polikliniği kontrollerinde bu formlar 15-30. günlerde tekrar uygulanarak aradaki değişim değerlendirildi. Değerlendirmelerde yanlış bilgi ve tutum saptanan annelere doğru bilgiler her form uygulama döneminde yinelendi.

Bulgular: Çalışmaya toplam 100 anne ve bebeği dahil edildi. Bebeklerin ilk gün, 15. gün ve 30. gün anne sütü harici gıda ile beslenme oranlarında fark saptanmadı. Ancak bebeklerin 30. günde, 15. güne göre iki saat ara ile emzirme oranları daha yüksek; genel olarak anne sütü ile beslenme oranları ise 15. gün ve 30. günde düşük olarak elde edildi. Bebeklerin 15. günde ve 30. günde banyo yapma oranı ve file üzerinde banyo yapma oranları yüksek tespit edildi. Bebeklerin ilk güne göre 15. gün ve 30. günlerde uyku pozisyonları, uyudukları yer ve beşikte parmaklık/koruyucularının olma oranlarındaki değişim anlamlı bulunmadı. Göbek bakımı yapma oranlarında artış 15. gün ve 30. gün için anlamlı bulundu. Eğitim sonrası bebek kıyafetlerinin sabun tozu ile yıkanmasındaki yükseliş ve bebeklere kundak yapılmasındaki düşüş anlamlı olarak bulundu. Ayrıca annelerin ilk güne göre 15. gün ve 30. günlerde bebek bakım bilgilerini daha yüksek sıklıkta sağlık kuruluşundan aldıkları tespit

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Received/Geliş tarihi: *06.12.2016* **Accepted/Kabul tarihi:** *10.01.2017*

on the 15th and 30th days compared to the 1st day. The highest correlation between the maternal education level and the post-education knowledge and attitude change was determined in uneducated and primary school graduate mothers (r^2=0.35).
Conclusion: The frequency and duration of the breastfeeding, infant umbilical care, swaddling, bathing, sensitivity to pinning jewellery on the infants, and whether or not mothers receive information about infant care from a healthcare organisation have changed positively after the education.
Keywords: Neonatal care, breast milk, maternal education

edildi. Annelerin eğitim düzeyleri ile eğitim sonrası bilgi ve davranış değişikliği arasında en yüksek ilişki, eğitimsiz ve ilkokul mezunu olan annelerde saptandı (r^2=0,35).
Sonuç: Annelerin yenidoğan bebeklerini emzirme sıklığı ve süresi, bebeklerin göbek bakımı, kundak yapma, bebeklerini yıkama, bebeklere takı takma hassasiyeti, bebek bakımı hakkında bilgileri sağlık kuruluşundan alma durumları eğitim sonrası olumlu yönde değişmektedir.
Anahtar Kelimeler: Yenidoğan bakımı, anne sütü, anne eğitimi

Introduction

When parents decide to have a baby, the first evaluation of the parents' health should be performed by specialists in the pre-pregnancy period, and this observation and informing should be continued after the pregnancy. Health promotion is defined as activities that help an individual to improve resources that maintain and increase the well-being of the individual (1).

Various education and counselling programs are offered at different times to ensure that pregnancy, delivery, and postnatal period are spent healthfully in terms of the mother and the baby. In these programs, the late prenatal classes begin in the third trimester of pregnancy, and the expectant parents are trained on the subjects of delivery, infant care and infant nutrition (2).

In this study, we aimed to determine the levels of knowledge on newborn nutrition and care of the mothers whose infants were born through normal spontaneous vaginal delivery or cesarean section at Bağcılar Training and Research Hospital, and to evaluate the change in these knowledge levels with education.

Materials and Methods

The study was conducted as a cross-sectional study with mothers, and their infants born at Bağcılar Training and Research Hospital, Obstetric Unit between January 2016 and September 2016. Questionnaire forms designed on the subject of infant nutrition, infant care, and traditional practices were given to mothers right after delivery. The questionnaire forms included questions about the educational levels of the mothers, time of the first breastfeeding, nutrition type and frequency, form of nutrition other than breastfeeding, the first bathing time and place, umbilical care, infant sleeping patterns, attitudes towards traditional practices (jewellery, pacifier, putting infant to sleep with a blanket covering its face, swaddling); and information acquisition resources were addressed to the mothers and situation determination was done. The mothers' information was evaluated by a doctor and breastfeeding nurse after the questionnaire and the mothers were informed about nutrition, infant care, and traditional practices. The questionnaire forms were repeated on the 15th and 30th days in the neonatal policlinic controls and the changes were evaluated. Mothers who were determined to have wrong information and attitudes in the evaluations were supplied with the correct forms after the application.

The ethical approval of the study was obtained from the hospital ethics committee (approval number: 2016-12). Written consent was obtained from the mothers before the study.

Statistical Analysis

Number Cruncher Statistical System (NCSS) 2007 (Kaysville, Utah, USA) program was used for statistical analyses. Descriptive statistical variables were used for quantitative variables in the study data. The Friedman test was used for the evaluations and comparisons between the variables and the Wilcoxon signed-rank test and the Spearman correlation test were used in paired evaluations. The level of $p<0.05$ was accepted to be significant.

Results

A total of 100 mothers and their infants were included in the study. 47% of the infants included in the study were born via cesarean section, and 53% through normal vaginal delivery. 52% of the cases were boys and 48% were girls. The educational levels of the mothers, the time of the first breastfeeding, the delivery method, and the gender of the infants are presented in Table I. No difference was determined in the nutrition rates of the infants with food other than breast milk on the first day, 15th and 30th days. However, the breastfeeding rates of the infants were higher on the 30th day than on the 15th day, with an interval of two

hours, and in general, breastfeeding rates obtained on the 15th and 30th days were low.

The rates of bathing the infants with and without a bathtub net were determined to be high on the 15th and 30th days. The change in the sleeping positions of the infants, the place of sleep, and the presence of rails/guards around the crib on the 15th day and the 30th day was not found to be significant compared to the first day. The increase in the rates of sleeping in the dark after receiving the education was significant as well as the increase in the umbilical care rates on the 15th and 30th days in comparison to the first day. The results regarding the form of nutrition other than breastfeeding, the first bath, sleeping position, place and environment of sleep and umbilical care of the infants are presented in Table II.

No significant change was determined on the 15th and 30th days compared to the first day in the diaper changing tools for infants, pacifier use and its reasons, and in the evaluation of covering the face while sleeping and the reasons for covering the face. After the education, the increase in washing the clothes of the infant with soap powder, and the decrease in swaddling were found to be significant. No change was determined in the rates of pinning jewellery to the infants' clothes after the education. Furthermore, a significant increase was determined in the rates of mothers receiving infant care information from the healthcare organisation on the 15th and 30th days compared to the first day (Table III).

The highest correlation between maternal educational levels and post-education knowledge, and attitude and

Table I. Distribution of descriptive characteristics

		n	%
Method of delivery	Vaginal	53	53.0
	Cesarean section	47	47.0
Gender	Female	48	48
	Male	52	52
Maternal educational level	Illiterate	17	17.0
	Primary school	27	27.0
	Secondary school	36	36.0
	High school	13	13.0
	University	7	7.0
Time of the first breastfeeding of the infant	Did not breastfeed	5	5.0
	30 minutes	30	30.0
	1 hour	40	40.0
	2 hours and more	25	25.0

Table II. Evaluations for breastfeeding, bathing and umbilical care

	1st day	15th day	30th day	p			
	n (%)	n (%)	n (%)		1st day- 15th day	1st day-30th day	15th day-30thday
Form of nutrition other than breastfeeding	15 (15.0)	10 (10.0)	9 (9.0)	**0.060**	0.132	0.058	0.317
	1 (1.0)	99 (99.0)	100 (100)	**0.001**	0.001	0.001	0.317
First bathing time							
As soon as discharged from the hospital	89 (89.0)	90 (90.0)	90 (90.0)	**0.368**	0.317	0.317	1.000
After the umbilical cord has fallen off	11 (11.0)	10 (10.0)	10 (10.0)				
First bathing place							
Bathtub	24 (24.0)	15 (15.0)	10 (10.0)	**0.001**	0.001	0.001	0.020
Plastic basin	51 (51.0)	15 (15.0)	15 (15.0)				
On a bathtub net	25 (25.0)	70 (70.0)	75 (75.0)				
Sleeping position							
While breastfeeding	96 (96.0)	96 (96.0)	95 (95.0)	**0.867**	1.000	0.705	0.317
Lying position	4 (4.0)	4 (4.0)	5 (5.0)				
Place of sleep							
Crib	98 (98.0)	99 (99.0)	99 (99.0)	**0.368**	0.317	0.317	1.000
No bed	2 (2.0)	1 (1.0)	1 (1.0)				
Rail, guard	94 (94.0)	95 (95.0)	94 (94.0)	**0.779**	0.564	1.000	0.317
Sleeping environment							
In the dark	49 (49.0)	58 (58.0)	56 (56.0)	**0.084**	0.018	0.040	0.739
Illuminated	31 (31.0)	26 (26.0)	29 (29.0)				
Umbilical care	27 (27.0)	83 (83.0)	52 (52.0)	**0.001**	0.001	0.001	0.001

Table III. Evaluation of primary care and traditional practices							
	1st day	**15th day**	**30th day**	**p**			
	n (%)	**n (%)**	**n (%)**		**1st day-15th day**	**1st day-30th day**	**15th day-30th day**
Diaper changing tool							
Wet wipes	**90 (90.0)**	**89 (89.0)**	**88 (88.0)**	**0.607**	0.783	0.589	0.317
Wet cotton	6 (6.0)	7 (7.0)	8 (8.0)				
Washing	4 (4.0)	4 (4.0)	4 (4.0)				
Cleaning of clothes							
Soap powder	**58 (58.0)**	**71 (71.0)**	**73 (73.0)**	**0.001**	0.001	0.001	0.157
Detergent	42 (42.0)	29 (29.0)	27 (27.0)				
Pacifier use	**53 (53.0)**	**55 (55.0)**	**55 (55.0)**	**0.135**	0.157	0.157	1.000
Reason for pacifier use							
Sleep	**6 (11.3)**	**7 (12.7)**	**7 (12.7)**	**0.368**	0.180	0.257	1.000
Crying	37 (69.8)	40 (72.7)	40 (72.7)				
Does not know	10 (18.9)	8 (14.5)	8 (14.5)				
Swaddling	**39 (39.0)**	**16 (16.0)**	**11 (11.0)**	**0.001**	0.001	0.001	0.025
Reason for swaddling							
Culture	**13 (33.3)**	**9 (56.3)**	**5 (45.5)**	-	1.000	1.000	1.000
To make baby stay still	26 (66.7)	7 (43.8)	6 (54.5)				
Pinning jewellery	3 (3.0)	3 (3.0)	4 (4.0)	**0.717**	1.000	0.564	0.564
The use of face cover	**71 (71.0)**	68 (68.0)	**65 (65.0)**	**0.034**	0.180	0.034	0.083
Reason for covering the face							
Family education	**5 (7.0)**	**3 (4.4)**	**3 (4.6)**	**0.135**	0.180	0.180	1.000
Prevention of jaundice	22 (31.0)	20 (29.4)	20 (30.8)				
Prevention of dust	18 (25.4)	19 (27.9)	18 (27.7)				
Prevention of light	26 (36.6)	26 (38.2)	24 (36.9)				
Receiving care information							
Family	**92 (92.0)**	**49 (49.0)**	**38 (38.0)**	**0.001**	0.001	0.001	0.001
Internet	1 (1.0)	0 (0)	0 (0)				
Healthcare organization	7 (7.0)	51 (51.0)	62 (62.0)				

behaviour change was seen in uneducated and primary school graduate mothers (r^2=0.35).

Discussion

A mother's maternal role, acceptance of her baby and acquisition of the necessary knowledge and care skills as of the pre-pregnancy period, during pregnancy and after delivery, and performing the care of the infant with proper practices are very important for neonatal and maternal health. While emphasising the importance of education and information, the evaluation of this especially during the postpartum period, and the improvement of the knowledge and attitude by providing the necessary feedback should be one of the primary duties of neonatal health centres (3-5).

The level of education can create a number of differences, especially in reaching the information and in the process of using it. According to the Turkey Demographic and Health Survey 2013 (TDHS-2013), the mothers' education rates were reported as follows: 11.8% of mothers were uneducated, 32.3% were primary school graduates, 25% secondary school graduates, and 30.9% were high school and higher education graduates (6). In our study, the ratio of uneducated mothers was 17%, primary school graduates 27%, secondary school graduates 36%, and high school and higher education graduates was 20%. These ratios seem to be consistent with the averages in our country. Our study revealed that mostly primary school graduates and uneducated mothers benefited from the education provided to them. These results suggest that mothers have little experience in infant care, mothers with low educational levels are more sensitive to the education provided, and they can develop their attitudes and behaviors in a positive way rapidly. As the educational level increases, individual

information acquisition increases, and new information and practices cannot be accepted readily.

All mothers need information about infant care, but especially those who are going through their first pregnancies have been determined to have more difficulties in infant care and need information on various topics regarding the care of babies (7). This lack of information can be valid both for the mother's self-care and her infant (8). It is reported that in the postpartum period, mothers often receive information from their friends and relatives, and infant nutrition takes the first place among maternal concerns (8,9).

Breastfeeding is a significant contributor in terms of the cost for mother and infant, health promoter and disease preventer (9). The UNICEF and World Health Organization emphasise the vital importance of breast milk by stating that breastfeeding the infant within the first hour after birth prevents 22% of neonatal deaths, and within the first day prevents 16% (6). In our study, it was determined that mothers were willing to breastfeed their infants in the first days but there was generally a decrease in the rates of feeding only with breast milk in the following days despite the provided education and that mothers fed their infants with food other than breast milk. The first feeding time and intake of colostrum by the infant are very important and therefore it is recommended that the infant is given breast milk within the first 30 minutes, especially in the case of vaginal delivery. According to the TDHS-2013 data, 50% of the infants are breastfed within the first hour after birth. In our study, the ratio of starting breastfeeding is 30% in the first 30 minutes and 40% in the first hour. These data are generally above the country average. This difference can be explained by the fact that our hospital is a baby-friendly hospital and the personnel receive training on encouraging mothers to breastfeed.

It has been observed that mothers apply wrong practices, and neonates are deprived of breast milk in cases when no education is provided on subjects such as the benefits of breast milk, and breastfeeding technique before delivery, and mothers are not encouraged to breastfeed after delivery (10). In the TDHS-2013 data, 27% of infants were not breastfed in the first 24 hours after birth (6). In our study, this rate was determined as 5%.

Infants can be bathed two or three times a week. The water temperature can be checked by inserting the elbow into the water. The infant should be held from his chest and washed face down. Also, the infant can be washed on a bathtub net vertically in the bath (11). In our study, the accuracy of washing habits in the evaluations on the 15th and 30th days following the first interview with family members show that the education has been successful.

The infant should be laid down in a crib or a cot on a flat surface. The room temperature should be kept between 21 and 24 ^{0}C. There should be no pillow and the bed sheet should be stretched (11). In our study, it was found that the mothers put their infants to sleep while breastfeeding, and in a crib with rails, and in the dark. These results suggested that infants slept in a proper environment and that the mothers' consciousness of putting infants to sleep in the dark increased after the training.

Infection can be prevented by keeping the umbilical cord clean and dry, without applying anything, and this can help the umbilicus to fall off early (11,12). Furthermore, diapers should be fastened below the umbilical cord so that it will not be in contact with urine and faeces. It was determined that in the conditions of our country, umbilical care with only sterile gauze is sufficient in healthy neonates (13). In our study, after the first interview with the mothers, dry care was recommended for umbilical care, and there was a positive change after the training.

Due to the sensitivity of the neonatal skin, irritation or rash may occur as a result of contact with faeces and urine for a long time. To prevent this, it is important to wipe off, or wash and dry the infant every time he wets his diaper. A baby girl's bottom must be wiped from front to back in order to prevent infections because of the shortness of the urethra in baby girls (14). In the study, it was determined that nearly all of the mothers obtained the correct information about neonatal bottom care after the education. This issue is very important for protection against future urinary tract infections and diaper dermatitis.

It is also important that baby clothes have cotton content, and some issues should be taken into consideration when washing clothes. It is known that soap powder is less allergenic than detergents, and this is important in terms of atopic dermatitis (15). In our study, it was determined that the mothers washed the baby clothes mainly with soap powder and that these tendencies increased even more on the 15th and 30th days.

Negative results have been reported on the use of a pacifier in the studies conducted. According to these, infants are reported to have decreased sucking durations due to breast confusion created after using the pacifier (16). The rate of pacifier use was 55% in our study, and despite the education provided, this rate did not change and the mothers continued to use pacifiers to prevent their babies from crying.

Swaddling still continues as a tradition in some regions of our country. However, it has been reported that swaddling an infant may be associated with congenital hip dysplasia (11). In a study conducted, 64% of the women said that they

swaddled their infants 30 minutes after delivery (17). In our study, while 39% of the mothers said that they swaddled their infants on the first day, this ratio regressed to 16% on the 15th day and to 11% on the 30th day, with the education provided.

The rate of mothers pinning evil eye pendants with a safety pin to their infants' clothes to protect them from the evil eye is 25% in our country (18). The rate of this cultural practice was found to be around 4% in our study.

It is known that mothers adopt various methods to put their infants to sleep. One of the traditional practices is covering the face of the infant with a cheesecloth (19). Our study showed that mothers cover the face of their infants for various reasons such as putting them to sleep, protecting from dust. However, in the studies conducted, it has been reported that the infant's sleeping with his face covered is associated with sudden infant death syndrome (20,21). In our study, it was determined that this behaviour did not change despite the maternal education provided.

In a study covering eight provinces in our country, it was found out that 54.8% of the women acquired information about self-care and infant care from the elder members of the family, and only 16% of the women received help from healthcare personnel. This shows that women in our country cannot sufficiently benefit from health services in infant health in the postpartum period (22). In our study, while mothers acquired infant care information from the elders in the family by 92% on the first day, on the 30th day, with the education provided, this rate turned into receiving information from healthcare institutions by 62%.

Study Limitations

There were some limitations of the study. There was limited number of mothers, the results should be confirmed with a higher number of mothers and neonates.

Conclusion

This study has shown that the frequency and duration of the breastfeeding of the neonates, infant umbilical care, swaddling, bathing of the infants, sensitivity to pinning jewellery on the infants' clothes, and the mothers' receiving information about infant care from a healthcare organisation have changed positively after the education.

Ethics

Ethics Committee Approval: The study was approved by the Bağcılar Training Research Hospital Local Ethics Committee (Approval number: 2016-12).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ş.H., Y.P., Concept: Ş.H., Y.P., Design: Ş.H., E.C., Data Collection or Processing: Ş.H., E.C., M.E., Analysis or Interpretation: Ş.H., M.E., Ö.Y., Literature Search: Ş.H., Y.P., Ö.B.G., Ö.Y., Writing: Ş.H., E.C.

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

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

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J Pediatr Res 2017;4(2):53-8
DOI: 10.4274/jpr.43433

Original Article / Orijinal Araştırma

Information is Power: An Interventional Study on Parents of Children with Febrile Seizures

Bilgi Güçtür: Febril Konvülsiyon Geçiren Çocukların Aileleri Üzerine Müdahaleli Bir Çalışma

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ABSTRACT

Aim: Febrile seizures (FS) cause great fear and panic in the families. The majority of parents think that they may lose their child during a seizure, and feel anxious about the possibility of seizures recurring in the future. We believe that educating the families with high levels of anxiety due to FS may help to reduce the level of anxiety. In this study, we aimed to determine the needs of parents regarding FS, and the effect of education on FS on the approach and anxiety of the parents.

Materials and Methods: In our study, we interviewed the parents of 113 children who suffered from FS. We conducted a survey aiming at detailed detection of knowledge, attitudes, thoughts and concerns of the families about FS, and their approaches to fever and FS. We also performed Hospital Anxiety and Depression Scale and State-Trait Anxiety Inventory to determine the levels of anxiety and depression of the parents.

Results: In this study, we found that parents were misinformed and had misbeliefs suggesting that FS damage the brain and cause epilepsy, that they are life-threatening and electroencephalography, magnetic resonance imaging and computed tomography scans of the brain are required. We also determined a significant lack of information about interventions during a seizure and thus, a high level of anxiety.

Conclusion: We concluded that parents provided with sufficient information and given psychosocial support have their anxiety levels significantly reduced, making them better in first aid practices and reducing their requests for unnecessary preventive interventions.

Keywords: Febrile seizures, parental anxiety, education program

ÖZ

Amaç: Febril konvülsiyonlar (FK) ailelerde büyük korku ve paniğe yol açar. Çoğu aile nöbet anında çocuğunu kaybedeceğini düşünür ve gelecekte nöbetlerin tekrarlaması endişesini yaşarlar. Ailelerin eğitimi ile FK'nin yarattığı endişe düzeyini azaltabileceğimize inanmaktayız. Bu çalışmada, ailelerin FK ile ilişkili ihtiyaçlarını tespit edip, FK hakkındaki eğitimin FK'ye yaklaşım ve ailelerin anksiyetesi üzerine etkisini belirlemeyi amaçladık.

Gereç ve Yöntemler: Çalışmamızda çocuğu FK geçiren 113 aile ile görüşüldü. Anket uygulaması ile ailelerin FK hakkındaki bilgi, düşünce, tutum ve endişelerini detaylı olarak saptamaya çalıştık. Ayrıca ailelerin depresyon ve anksiyetesini belirlemek için Hastane Anksiyete ve Depresyon Skalası ile Anksiyete Kişisel Bildiri Envanteri'ni uyguladık.

Bulgular: Bu çalışmada, ailelerin FK'nin beyine hasar verip epilepsiye yol açtığı, yaşamı tehdit eden bir hastalık olduğu, elektroensefalografi, manyetik rezonans görüntüleme ve bilgisayarlı tomografi ile değerlendirme gerektiğine dair yanlış bilgi ve inanışa sahip olduklarını gördük. Bunun yanında nöbet anında nasıl müdahale edeceklerini bilmedikleri ve bunun da yüksek anksiyeteye yol açtığını gördük.

Sonuç: Yeterli bilgi ve psikososyal destek verilen ailelerin anksiyete seviyelerinde belirgin azalma olduğunu tespit ettik. Böylece ilk yardım pratiğinde düzelme ve gereksiz önleyici müdahalede azalma beklemekteyiz.

Anahtar Kelimeler: Febril konvülsiyon, aile anksiyetesi, eğitici program

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Received/Geliş tarihi: *02.12.2016* **Accepted/Kabul tarihi:** *25.01.2017*

Introduction

Febrile seizures (FS) are of a benign character but remain important and relevant because of the risk of recurrence, and progression to epileptic seizures albeit very rarely (1-3). FS are the most common seizure type in childhood, and parental anxiety and misconceptions contribute to a relevant reduction in the quality of life of children and families after a FS.

The probability of an internal or external hazard, or the perception or interpretation of a situation as hazardous by the person arouses the feeling of anxiety. Anxiety is a normal feeling that everyone experiences from time to time but sometimes it can aggravate and turn into a pathological condition. Anxiety can be experienced in different severities from a slight feeling of unease and tension up to a degree of panic. Parental concern causes overprotection, and leads to the limitation of the activities of the child, resulting in a decrease in the quality of life of both the parents and the children. FS, especially if experienced for the first time, cause fear and panic in the family. The majority of the parents think that their child may die during a seizure (4,5). Especially the parents of children with recurrent FS are more troublesome, being quite apprehensive of the risk of recurrence, and they may even experience sleep disorders or other functional disorders for weeks (6,7).

Previous studies have tried to obtain qualitative information by questioning the attitudes and emotional state of the parents during and after previous seizures (5,8,9). It is suggested that educating the families with high levels of anxiety may be helpful in reducing the levels of anxiety.

In this study, we tested the effect of a modular education program on parental anxiety regarding febrile convulsions.

Materials and Methods

The study sample: A total of 172 children who attended the pediatric emergency department, pediatric outpatient clinic, and pediatric neurology clinic were included in the study with 113 children in the patient group and 59 children in the control group.

Selection of the patient group: Diagnosis of FS was made according to the occurrence of FS with a body temperature of >37.8 °C in children between 3 months and 5 years old without any defined reason such as central nervous system infection, acute electrolyte disturbances, intoxication, or a history of an afebrile or newborn seizure (3,10).

Selection of the control group: The control group consisted of children who had similar characteristics with the patient group in terms of age, sex and socio-cultural level. None of the children in this group had epilepsy, FS or a chronic disease. All the children in this group were normal neurologically, and displayed normal developmental stages.

Socio-demographic and clinical data sheet: A 42-question survey was conducted among the parents of the children who were included in the study with the aim of detecting the knowledge, thoughts, concerns, of the parents about fever and FS, and their attitudes and approaches towards them. A family history of FS, and educational status (less and more than 8 years) of the family were recorded.

Psychometric scales: The following psychiatric scales were used to determine the levels of anxiety and depression:

1. Hospital Anxiety and Depression Scale (HADS) which was originally developed by Zigmond and Snaith (11) and studied by Aydemir et al. (12) for the validity and reliability of the Turkish version.

2. State-Trait Anxiety Inventory (STAI) which was originally developed by Spielberger et al. (13) and translated into Turkish by Öner and LeCompte (14).

After the intervention of febrile convulsions, the families answered the questionnaires for the first time at admission to hospital. Also, the anxiety levels of the parents were determined by anxiety tests prior to education. The families received a 30-minute education program from the same pediatrician before their children were discharged. Each family was interviewed individually, not in a group.

The education program included 3 modules (10 minutes were allotted to each module):

Module I: (Step 1) The type of seizure (generalized tonic-clonic focal, or atonic) was watched using hometype video clips; (step 2) the seizure was classified as complex (focal, lasting more than 15 minutes, and recurrences in 24 hours or within the same febrile illness); or simple (the time elapsed between the fever and the seizure (1st hour, >1 and ≤24 hours, or <24 hours); and (step 3) the effects of FS on children were explained using printed cartons.

Module II: The proper management of the child during the episodes of fever and seizure were explained to the parents and caregivers with a power-point presentation.

Module III: The experiences of parents on previous FS issues including typical reactions of the families to FS, the etiology of the fever and FS, advice on first aid during fever and FS, treatment requirements, risk factors for recurrence, and the transformation of FS into epilepsy, prophylaxis and its potential side effects were discussed during the education program. It was explained to the families that FS are not as scary as they seem and have a benign character.

Anxiety levels of the parents were determined by anxiety tests prior to education. The survey and anxiety tests were re-conducted 4 weeks after the education to see their effects on the thoughts and approaches of the parents towards fever and FS, and on the anxiety levels of the parents.

The study was approved by the Celal Bayar University Local Ethics Committee (approval number: 50, 23.02.2011).

Statistical Analysis

Statistical Package for Social Sciences for Windows 10.0 software was used for the statistical analysis of the findings obtained in this study. After basic and descriptive statistical (frequency, mean, etc.) analysis, independent samples t test was used for continuous variables, and chi-square (χ^2) test was used for categorical variables in the comparison between parents of children with FS and the control group.

McNemar's test was used for categorical variables to compare the parents of children with FS before and after education.

Results

Of the patients diagnosed with FS, 52 (46%) cases were female and 61 (54%) cases were male. Male/female ratio was 1.17/1. Of the control group subjects, 27 (45.8%) children were female and 32 (54.2%) were male. Male/female ratio was 1.18/1. There was no significant difference between sexes. Family history of FS was significantly higher in the patient group compared to the controls (p=0.01). The education levels of the mothers and fathers of the control group were higher than those of the parents of the patients (p=0.005-0.004, respectively).

As for the duration of the seizures, they lasted less than 1 minute in 25.9% of the children, 1-5 minutes in 44.6%, 5-10 minutes in 21.4%, more than 10 minutes in 8.1%, and more than 30 minutes in 0.9% of the children. Recurrence was observed in 39 of the cases (34.5%). Only one seizure was experienced by 65.5% of the children, while 19.5% of them experienced two seizures, 9.7% experienced three, and 5.3% of the children experienced more than three seizures.

In the patient group, when parents were asked about their feelings on witnessing or being informed of their children's seizure, 61.9% stated fear, 20.4% said panic, 8.8% expressed sadness, 7.1% stated cool-headedness, and 1.8% claimed guilt.

The parents' level of anxiety significantly decreased after the education program (p=0.01) (Table I). Calculated values for the anxiety levels of the parents in the patient group were 43.3±7.5 for STAI trait, and 46.7±6.1 for STAI continuity, 7.2±4.4 for HADS anxiety, and 6.6±3.9 for HADS depression before education. After the education program, the values were detected as 38.7±7.1 for STAI trait, and 44.3±6.6 for STAI continuity, 5.5±3.8 for HADS anxiety, and 5.6±3.3 for HADS depression.

Before the education program, parents' perception of FS as a kind of epilepsy and electroencephalography (EEG) as a requirement was significantly more common in the patient group compared to the control group (p=0.001 and 0.004, respectively), but this difference disappeared after the program. Also after the education, the number of parents who believed FS to be an age-dependent disorder turned out significantly higher in the FS group, while the number of parents who thought that brain computed tomography (CT) or magnetic resonance imaging (MRI) were required for children with FS appeared to be significantly higher in the control group (p=0.01 and 0.04, respectively).

When the concerns of the families about FS were questioned, there was no significant difference between the FS group and the control group before the education program. After the education, the number of parents who believed that FS damage the brain, lead to epilepsy in the future, and are a life-threatening condition was found to be significantly lower in the patient group compared to the control group (p=0.01, 0.02, and 0.01, respectively) (Table II).

The opinion that anti-epileptic drugs (this terminus refers to a long-term medication) should be prescribed for FS was significantly more common among the parents of the patients compared to those of the control group before the education program (p=0.002), but this difference disappeared after education.

The intervention of putting the child on a flat surface, turning his/her head to one side, and giving rectal diazepam or midazolam (if the FS lasted for at least five minutes) were known by significantly more people in the FS group compared to the control group before education (p=0.03 and 0.01, respectively). After the program, the additional intervention of cleaning the nasal and oral secretions became known by significantly more people in the patient group (p=0.01).

When the interventions not recommended during FS were questioned in the FS group before and after the education program, a significant decrease was observed in

Table I. Scores of anxiety-depression scale in febrile seizures group

Scales	Before education	After education	p
STAI state	43.3±7.5	38.7±7.1	**0.01**
STAI trait	46.7±6.1	44.3±6.6	**0.01**
HADS anxiety	7.2±4.4	5.5±3.8	**0.01**
HADS depression	6.6±3.9	5.6±3.3	**0.01**

STAI: State-Trait Anxiety Inventory, HADS: Hospital Anxiety and Depression Scale

Table II. Concerns of the families about febrile seizures

Concerns of families	Before education					After education of FS group				
	Group 1		Group 2		p	Group 1		Group 2		p
	n	%	n	%		n	%	n	%	
FS damage the brain	99	88.4	54	91.5	0.36	61	54.0	54	91.5	**0.01**
FS cause epilepsy in the future	55	48.7	22	37.3	0.10	24	21.2	22	37.3	**0.02**
FS recur	104	92.0	54	93.1	0.53	105	92.9	54	93.1	0.62
FS are a life-threatening condition	99	87.6	55	93.2	0.19	82	72.6	55	93.2	**0.01**

Group 1: Febrile seizures group, Group 2: Control group, FS: Febrile seizures

interventions such as shaking the child to wake him/her up, placing something in the mouth in order to open the jaws, giving a shower, and splashing water or cologne to the face (p=0.002, 0.01, 0.01, 0.01, respectively) (Table III).

Discussion

The appearance of a child during a FS is such a terrible sight for the family that they may think their child is dying (8). There are a number of studies on the reactions of parents during and after FS (5,15,16). These reactions include physical, psychological and behavioral symptoms. FS are a potential cause for the deterioration of the quality of family life. Parents feel extreme anxiety and fear during fever, and they also think that their child is weak and vulnerable. It is important for the doctors to know about the misperceptions, anxiety, and fears of the parents. Discussion with the family has been suggested as the best medicine for FS (17). Thus, the fears and expectations of the families for medical therapy may be reduced.

In this study, the effect of a modular education program on parental anxiety and depression in febrile convulsions were investigated. The level of anxiety and depression of the parents were significantly decreased after a 4-week period with a modular education program. STAI and HADS were used to determine the levels of anxiety and depression of the parents. The calculated values for the anxiety levels of the parents in the patient group were 43.3±7.5 for STAI trait, and 46.7±6.1 for STAI continuity, which decreased to 38.7±7.1 for STAI trait, and 44.3±6.6 for STAI continuity. Hospital anxiety and depression values of the parents decreased from 7.2±4.4 for HADS anxiety, and 6.6±3.9 for HADS depression to 5.5±3.8, and 5.6±3.3 respectively.

Shuper et al. (18) determined that the parents' insufficient knowledge occupies an important place in parental anxiety, and Melnyk et al. (19) determined that parents need information on understanding the reactions of their children and coping with stress. In a study of Rutter and Metcalfe (9), 82% of the children had their family members nearby during the seizure, and 50% of these children had only their mothers near them. Also in this study, it was stated that families defined their first reactions as fear and panic (9).

Flury et al. (20) concluded that anxiety during the first seizure is associated with lower levels of education, and specific and repetitive education may provide a significant advantage for these families. Balslev (5) demonstrated the positive effect of having knowledge about FS on the behaviors of family members, reducing unnecessary anxiety levels. Similarly, Shuper et al. (18) also found a significant relationship between lower levels of knowledge and higher anxiety levels. Many parents stated that receiving education before FS was beneficial, especially via the posters in the waiting room and from health care workers rather than books (21).

There are some misbeliefs about FS, like causing suffocation, damaging or biting the tongue, damaging the brain, and resulting in epilepsy or death. These ideas play a key role through lack of information in the feeling of vulnerability the parents experience (17), and unnecessary fear may cause incorrect interventions (22). When asked the question whether therapy with anti-epileptic drugs should be initiated in each case of FS, 62.8% of the parents in the FS group, and 39% in the control group answered: "yes". 45.1% of the parents in the patient group who attended the education program continued to think that an anti-epileptic drug should be given, despite a significant decrease on this point. Parmar et al. (23) suggested similar results in their study. Huang et al. (24) noted that the requirement of initiating an anti-epileptic drug in every child with FS is very common.

We determined that families lack practice in first aid, have little information about the risk of recurrence of FS, and the measures to be taken for the disease. When we asked them about their first interventions during FS, the majority of the parents in the FS group said that they would put something in the child's mouth and try to open the jaws, or take the child to the shower. A study by Kayserili et al. (25), revealed that 70% of the parents directly consulted a doctor without making any intervention. Similar studies found the rates

Table III. The interventions during febrile seizures

The interventions	Before education		After education		p
	n	%	n	%	
Putting the child on a flat surface, turning his/her head to one side	29	25.7	99	87.6	**0.01**
Removing the oral and nasal secretions	11	9.7	61	54.0	**0.01**
Giving rectal diazepam or midazolam	14	12.4	39	34.5	**0.01**
Being calm	19	16.8	32	28.3	**0.001**
Shaking to wake	17	15	4	3.5	**0.002**
Placing something in mouth in order to open the chin	37	32.7	4	3.5	**0.01**
Taking to the shower	37	32.7	10	8.8	**0.01**
Splashing water or cologne to the face	11	9.7	2	1.8	**0.01**

of 36-90% for the same parameter (5,23,26). In a study of Flury et al. (20), 42% of the parents said that they would try to reduce the fever, and 29% stated that they would safely lay the child on a flat surface. In contrast, 16% of the parents said they would give mouth-to-mouth resuscitation, 5% would do cardiac massage, and 12% would hit the child on the back. After the education, some of the incorrect interventions continued, 10% of the parents said that they would do cardiac massage, 18% would give mouth-to-mouth resuscitation, and 15% would try to wake up the child by shaking him/her. Nonetheless, there was a significant increase in correct applications, and 64% of the parents said that they would put the child on a flat surface, 90% stated they would take precautions against aspiration and 95% said they would give the child diazepam rectally (20).

When asked whether EEG should be performed for every child with FS, 91.2% of the parents in the FS group, and 74.1% in the control group stated that it was a necessity. In the patient group 74% and in the control group 64.4% of the parents believed brain CT or MRI to be a requirement. There was no significant difference between the groups. After the education, 77% of the parents thought that EEG was necessary, while 49.1% said brain MRI should be done. Parents' opinions on the necessity of EEG and MRI significantly changed by education, but still appeared to be supported in high rates. In a study of Huang et al. (24), it was observed that 80% of the parents thought of EEG and/or brain CT as a requirement, but the rate of the same parameter decreased to 30% after they received education. Parents deem EEG as a requirement because it causes no side effects, it is the best method to see whether there is epileptic activity, and it provides relief for families and even for the physicians.

Seizures can be regarded shameful by the families in developing countries (27). In our study, 4 (3.5%) families stated that they were ashamed of having a child with FS. After the education, however, only one parent insisted on his opinion. In a study of Kayserili et al. (25), 60 (49.2%) parents were seen to be ashamed of having a child with FS. Compared to our study, this figure is very high. We believe that this is because the ratio of the participants living in villages and towns were higher in their study, and people in small social circles may influence each other more.

When we asked whether FS recur, 92% of the parents in the FS group, and 91.5% of the parents in the control group said "yes". In a study of Huang et al. (24), when the question was asked as "Do all FS recur?," 63.9% of the parents answered "definitely", but this rate decreased to 41.6% after the education.

Study Limitations

A randomised controlled trial comparing groups of parents educated and not educated on FS would be more optimal in assessing the impact of the study. This can be considered as a limitation of this study.

Conclusion

The presented study provides additional support to the fact that the majority of the parents have a fear of fever and misbeliefs about FS, and they significantly lack information about interventions. A three-step modular education program developed to relieve parental anxiety was found to be highly effective in families who had children with febrile convulsions. We would like to emphasize the importance of providing parents with correct and sufficient information at the emergency department despite the fact that it is a very busy environment, and inviting them to the clinical controls in order to be given detailed information.

Ethics

Ethics Committee Approval: The study was approved by the Celal Bayar University Local Ethics Committee (Approval number: 50, 23.02.2011).

Informed Consent: Consent form was filled out by all participants.

Peer-review: External and internal peer-reviewed.

Authorship Contributions

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

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

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

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J Pediatr Res 2017;4(2):59-62
DOI: 10.4274/jpr.15870

Original Article / Orijinal Araştırma

Evaluation of Demographic and Clinical Characteristics of Patients with Mucopolysaccharidosis

Mukopolisakkaridoz Hastalarının Demografik ve Klinik Özelliklerinin Değerlendirilmesi

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ABSTRACT

Aim: Mucopolysaccharidoses (MPSs) are a group of lysosomal storage disorders caused by the deficiency of spesific lysosomal enzymes required to break down glycosaminoglycans. MPSs should be suspected in a child with coarse facial features, organomegaly, and bone disease (dysostosis multiplex), with central nervous system abnormalities. Early diagnosis and treatment can improve outcomes in MPS. The aim of this study was to evaluate the demographic characteristics and clinical findings of our MPS patients.

Materials and Methods: This is a retrospective study which included 27 MPS patients who were diagnosed and treated in our center.

Results: The mean age of the group was 112.3±52.5 months (36-196 months); the mean onset age of symptoms was 40.8±30.6 months (4-112 months), and the mean time from symptom onset to diagnosis was 16.3±21.4 months (0-80 months). MPS subgroups were Type III in 13 (48%) patients, Type II in seven (26%), Type VI in four (15%), Type I in two (7%) patients and Type IV in one patient. Nine (33.3%) patients received enzyme replacement therapy (ERT). The mean duration of ERT was 31.3±21.5 months (9-67 months).

Conclusion: MPS Type III was found to be the most common subgroup in our center. We can speculate that the mean time from symptom onset to diagnosis was found too long for MPS in which early diagnosis improves the prognosis. Increasing awareness of the disease in physicians encountering these patients in different clinics will be an important factor in the early diagnosis of the disease.

Keywords: Mucopolysaccharidosis, pediatrics, consanguinity, enzyme replacement therapy

ÖZ

Amaç: Mukopolisakkaridozlar (MPS) glikozaminoglikanların yıkımında görev alan spesifik lizozomal enzimlerin eksikliği sonucu görülen bir grup lizozomal depo hastalıklarıdır. Kaba yüz, organomegali, kemik hastalığı (disostoz multipleks) ve merkezi sinir sistemi bulguları görülen hastalarda MPS hastalığı akla gelmelidir. MPS hastalığında erken tanı ve tedavi prognozda önemlidir. Bu çalışmanın amacı MPS tanısıyla takip edilen hastalarımızın klinik ve demografik verilerinin araştırılmasıdır.

Gereç ve Yöntemler: Bu çalışmada 27 MPS'li hastanın demografik ve klinik özellikleri retrospektif olarak kaydedildi.

Bulgular: Hastaların yaş ortalaması 112,3±52,5 ay (36-196 ay), semptomların başlama yaşı ortalama 40,8±30,6 ay idi (4-112 ay). Semptom başlangıcından tanıya kadar geçen süre ortalama 16,3±21,4 ay idi. Hastaların 13'ü (%48) MPS Tip III, yedisi (%26) MPS Tip II, dördü (%15) MPS Tip VI, ikisi (%7) MPS Tip I ve biri (%4) MPS Tip IV tanısı almışlardı. Dokuz (%33,3) hastaya enzim replasman tedavisi (ERT) başlandı. Ortalama ERT süresi 31,3±21,5 ay idi.

Sonuç: Çalışmamızda en sık görülen MPS alt grubu MPS Tip III olarak bulundu. Çalışmamızda hastaların semptomlarının başlangıcından tanı konulmasına kadar geçen süre uzun bulunmuştur. Bu hastalarla farklı kliniklerde karşılaşan hekimlerin hastalık hakkındaki farkındalığının artırılması hastalara daha erken tanı konulmasında önemli bir faktör olacaktır.

Anahtar Kelimeler: Mukopolisakkaridoz, çocuk, akrabalık, enzim replasman tedavisi

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Received/Geliş tarihi: *19.02.2017* **Accepted/Kabul tarihi:** *07.03.2017*

Introduction

Mucopolysaccharidoses (MPSs) are lysosomal storage disorders that are characterized by the dysfunction of the lysosomal enzymes involved in the catabolism of glycosaminoglycans (GAGs) due to a genetic mutation and GAG accumulation in the tissues (1). This accumulation differs depending on the deficiency of the specific enzyme (1). Seven types of MPS have been defined. MPS III and MPS IV have two or more subtypes biochemically. MPS I is divided into three subtypes according to the severity of the disease: Hurler syndrome (severe form), Hurler-Scheie syndrome, and Scheie syndrome (mild form) (2). MPS II is also divided into two subtypes as neurological and non-neurological (3). In MPS patients, clinical manifestations including cardiovascular diseases (common and early finding), obstructive type respiratory diseases, auditory impairment, visual problems (corneal clouding, glaucoma, retinal degeneration), and musculoskeletal diseases (short stature, joint stiffness or hyperlaxity, peripheral nerve entrapment neuropathy), where multiple organs are involved, can be observed (1,4). In patients who are suspected of having MPS based on clinical findings, firstly urinary GAG measurement is performed followed by specific lysosomal enzyme activity in leukocytes for definitive diagnosis (5).

Today, enzyme replacement therapy (ERT) and hematopoietic stem cell transplantation are used as therapeutic choices in MPS (6-9). However, as is the case with all other degenerative diseases, early diagnosis and onset of treatment prior to the occurrence of permanent injuries is of great significance with respect to treatment response (10). In this study, we present the demographic and clinical features of 27 MPS patients who were diagnosed, treated, and followed up at our hospital.

Materials and Methods

Twenty-seven MPS patients who were diagnosed at Dokuz Eylül University, Department of Pediatric Metabolism and Nutrition were included in our study. Demographics, blood relation between parents, clinical and imaging findings, time of diagnosis and monitoring, ERT treatment, age and cause of death were retrospectively investigated. The diagnosis of MPS was established based on clinical and imaging findings, urinary GAG assay, specific enzyme level measurement and genetic mutation assay.

Statistical Analysis

Data analysis was performed using the software, "SPSS for Windows 22". Descriptive statistics were expressed as mean ± standard deviation or median (minimum-maximum) for discontinuous numeric variables, and categorical variables were expressed as case number and (%).

Results

The mean age of the patients was 112.3±52.5 months (36-196 months), the mean age of symptom onset was 40.8±30.6 months (4-112 months), the age of diagnosis was 57.7±39.0 months (6-112 months), and the mean duration from symptom onset to diagnosis was 16.3±21.4 months (0-80 months). There were 10 females (37%) and 17 males (63%). Thirteen patients (48%) were diagnosed with MPS Type III, seven (26%) with Type II, four (15%) with Type VI, two (7%) with Type I, and one patient (4%) with MPS Type IV.

There was consanguinity between parents in 13 (48%) patients. Ten patients (37%) had history of sibling death, MPS findings were detected in the relatives or siblings of eight (29%) patients. Twenty-five patients (96.3%) had typical face, and 18 had (66.7%) hepatosplenomegaly (Figure 1). Echocardiographic investigation revealed 16 patients (59.3%) with cardiac involvement (mitral failure, mitral stenosis, tricuspid failure, aortic failure, aortic stenosis, interventricular septal hypertrophy, left ventricular hypertrophy) (Figure 1). There were eight patients (29.6%) with corneal opacity. Nineteen patients (74.1%) were detected to have dysostosis multiplex on bone imaging (Figure 1). Nine patients (33%) were operated on due to inguinal/umbilical hernia, adenoid vegetation, and hip dysplasia.

ERT was started on nine patients (33.3%), and all patients except one received regular treatment. The mean duration of ERT was 31.3±21.5 months (9-67 months). One patient was detected to have an allergic reaction during ERT. All patients were given a physical therapy programme for the treatment of their joint contractures. Two patients died during follow-up; the cause of death was respiratory failure and infection (sepsis).

Discussion

In this study, we retrospectively investigated the demographic and clinical features of MPS patients who were followed up at our hospital. The majority of the patients in our study consisted of MPS Type III (48%) and MPS Type II (26%) cases. Reviewing the European studies, we saw that MPS Type III and MPS Type I (11) in Germany, MPS Type III and MPS Type I (12) in Switzerland and MPS Type III and MPS Type II (13) were the most commonly detected types.

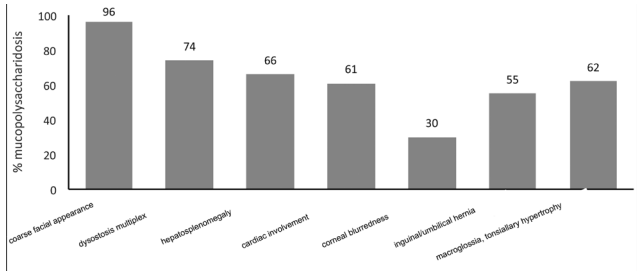

Figure 1. Clinical features of cases with mucopolysaccharidosis

Reviewing different geographic regions showed us that MPS III and MPS I were detected frequently in Tunisia (14) while MPS VI was relatively more common in Egypt, different from the other countries (15). Australian studies revealed MPS III and MPS I (16) as the most common types; and MPS II was the most common type in the Philippines (17). As for the studies in our country, the most common types of MPS detected by several authors (18) are as follows: Koca et al. (18) detected MPS Type III and MPS Type I in 42 MPS patients; Kılıç et al. (19) detected Type III and Type IV in 177 patients, and Kara et al. detected Type VI and Type IV in 61 patients (Kara A. Evaluation of diagnosis, clinical and laboratory parameters and follow-up findings of inborn errors of metabolism patients who get diagnosed or followed up in Çukurova University Medical Faculty, Pediatric Metabolism Unit. Çukurova University, unpublished doctoral dissertation, Adana. 2012). In our study, 48% of our patients had consanguinity between parents. Other studies from Turkey report this rate as between 82 and 91% (18,20).

Our patients applied to us most frequently with complaints of growth retardation and bone deformities. Physical examination findings showed that the most commonly detected clinical findings were coarse facial appearance, skeletal findings, and hepatosplenomegaly. In the literature, published demographic studies involving different types of MPS reveal the most common clinical findings as follows: coarse face, corneal opacity, macroglossia in MPS I (21); short stature, joint stiffness, and coarse facial appearance in MPS II (17); growth retardation, coarse face, hepatosplenomegaly in MPS III (22); short stature, limited joint movement, pectus carinatum in MPS IV (23); coarse face, joint and skeletal abnormalities in MPS VI (24). In our study, since the number of patients with subtypes of MPS was limited, no differentiation based on subtype could be made.

In this disease group, for which early diagnosis and early treatment onset are important in determining the prognosis, mean duration from symptom onset to diagnosis was 16.3 months in our study. Similar to ours, several studies from different countries showed that the diagnosis was established on average 2-3 years after the onset of symptoms (20,25-29). In a case of MPS, since patients exhibit different organ/system manifestations, they present to physicians from different branches including pediatricians, geneticists, cardiologists, ophthalmologists, orthopedists, and neurosurgery, and are diagnosed with different disorders such as primary valvular heart disease, Perthes disease, congenital talipes equinovarus, spondyloepiphyseal dysplasia, cataract, rheumatoid arthritis, craniosynostosis, pseudoachondroplasia, and inguinal hernia (23,27,29,30). In a study, patients were detected to be evaluated by 5 physicians on average before the diagnosis was made (29). Many studies involving different MPS types have demonstrated that early onset of ERT has many benefits including reduction of cardiac hypertrophy, slowing down somatic findings, and increasing quality of life (31-34). Therefore, it is very important to increase awareness of the disease among physicians from different branches so that the patients can be diagnosed as early as possible and treatment initiated in the early stage.

Study Limitations

This study has some limitations. Firstly, the sample size of the group was small. We could not make the subgroup comparisons of different MPS types regarding main complaints, clinical findings and prognosis. Secondly, we did not perform mutation analysis of all the patients in this study. Last limitation was the relative short follow-up duration of the patients.

Conclusion

In our study, we detected that MPS patients were diagnosed 16 months after the onset of symptoms on average, and the ratio of consanguinity between parents was 48%. Early diagnosis and treatment are important for the prognosis in MPS. Training practitioners, pediatricians, cardiologists, rheumatologists, radiologists, and specialists of other branches involved in the treatment of MPS, and increasing awareness of the slow-progressing symptoms would contribute to the early diagnosis and treatment of MPS.

Ethics

Ethics Committee Approval: Retrospective study.
Informed Consent: Retrospective study.
Peer-review: External and internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: P.T.K., E.K., Concept: N.A., P.T.K., Design: N.A., Data Collection or Processing: E.K., M.A., P.T.K., Analysis or Interpretation: E.K., M.A., Literature Search: P.T.K., Writing: N.A., P.T.K.

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

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

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J Pediatr Res 2017;4(2):63-7
DOI: 10.4274/jpr.09326

Original Article / Orijinal Araştırma

Gorlin Syndrome in Eleven Patients

On Bir Hastada Gorlin Sendromu

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ABSTRACT

Aim: Gorlin syndrome is an autosomal dominant disorder characterized by cutaneous basal cell carcinomas, odontogenic keratocysts and skeletal anomalies. Predisposition to certain types of cancers is among the main features of the disease. Chromosome instability was suspected as a mechanism for cancer predisposition. However, previous studies failed to prove the presence of chromosome instability.

Materials and Methods: We present 11 patients with Gorlin syndrome.

Results: Six of the patients were checked for increased sister chromatid exchange and were found normal. Two other patients had concurrent chromosome anomalies.

Conclusion: Evidence for chromosome instability was not found in our patients. Occurrence of chromosome instability in a subgroup of patients and mechanisms underlying cancer predisposition requires further studies for full elucidation. Hairy patches and pigmentary skin lesions are among the recently defined common features of the syndrome.

Keywords: Gorlin syndrome, hairy patch, chromosome instability, sister chromatid exchange, hypopigmented lesion

ÖZ

Amaç: Gorlin sendromu kutanöz bazal hücreli karsinomlar, odontojenik keratokistler ve iskelet anomalileriyle karakterize otozomal dominant bir sendromdur. Bazı kanser tiplerine yatkınlık hastalığın başlıca özelliklerindendir. Kromozom kırıklarına yatkınlık kanser yatkınlığı için öne sürülen mekanizmadır, ancak daha önceki çalışmalarda kromozom kırıklarına yatkınlık varlığı kanıtlanamamıştır.

Gereç ve Yöntemler: Bu yazıda Gorlin sendromu tanısıyla izlenen 11 hastanın klinik bulguları sunulmuştur.

Bulgular: Bu hastalardan altısında artmış kardeş kromatid değişimi izlenmemiştir. İki hastada eş zamanlı kromozom anomalileri bulunmuştur.

Sonuç: Gorlin sendromlu hastalarda kromozom kırıklarına dair yeterli kanıt bu çalışmada gösterilememiştir ve bunun için daha çok olgu incelenmelidir. Saçlı yamalar ve pigmenter deri lezyonları hastalığın yeni tanınan sık bulguları arasındadır.

Anahtar Kelimeler: Gorlin sendromu, saçlı yama, kromozom kırıklarına yatkınlık, kardeş kromatid değişimi, hipopigmente lezyon

Introduction

Gorlin syndrome or nevoid basal cell carcinoma syndrome is an autosomal dominant disorder in which multiple basal cell carcinomas, odontogenic keratocysts, skeletal malformations, and soft tissue calcifications are seen (1). Initial description in 1960 included a triad of multiple basal cell nevi, keratocysts in the jaw and skeletal anomalies (2). However, a variety of other manifestations involving ocular, cranial and genital systems are now known to be parts of the clinical presentation.

The syndrome is a cancer-prone condition which may predispose to, besides basal cell carcinomas of the skin, malignant or benign tumors like medulloblastoma, uterine and ovarian fibromas/fibrosarcomas, meningioma and cardiac fibromas (3). Chromosomal instability was suspected as one of the pathogenetic mechanisms of the cancer predisposition in Gorlin syndrome but this was not proven. Chromosome anomalies were rarely reported in patients with nevoid basal cell carcinoma syndrome, which included deletions of chromosome 9q in a few patients (4-7), where the causative

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Received/Geliş tarihi: *03.02.2017* **Accepted/Kabul tarihi:** *20.03.2017*

gene *PTCH* was later localized. This gene is a multifunctional developmental gene, it functions both in body patterning via Hedgehog signalling pathway, and also as a tumor suppressor gene (3). Sporadic mutations in *PTCH* gene were also associated with sporadic basal cell carcinomas in 1997 (8).

Herein we report on a series of 11 patients with Gorlin syndrome, in the order of admittance to our department. Six were checked for increased sister chromatid exchange with ultraviolet (UV) exposure and they were all normal. Two others had concurrent chromosome anomalies.

Materials and Methods

A series of 11 consecutive patients with Gorlin syndrome was retrospectively analysed. A review of clinical features was performed and standard karyotyping procedures were applied. Sister chromatid exchange analysis results were also included where available. The study was approved by Hacettepe University Non-Interventional Clinical Research Ethics Board.

Results

Clinical and cytogenetic features of the patients are summarised in Table I.

Patient 1

This female patient had presented at 6.5 years of age with severe headaches. She had a history of late eruption and hypoplasia of teeth. Developmental stages were on time. Physical examination revealed prominent maxilla and mandibula, gingival hypertrophy and absence of teeth. Panoramic X-ray showed a mandibular cystic lesion. Until she was 8 years old, curettage of jaw cysts had been performed three times. Cranial magnetic resonance imaging revealed triventricular widening and aqueductal narrowing. Menstruation had begun at 11 years of age and ceased after two years when hypogonadotropic hypogonadism was diagnosed. Chromosome analysis revealed 46,XX/46,X,t(X;11)(q24;q13). On physical examination at the age of 21, she weighed 75 kg and measured 151 cm. She had macrocephaly (head circumference was 52 cm at 8 years of age), coarse facies with prominent supraorbital ridges and thick eyebrows, ptosis, a flat maxillary region, prognathism and squared mandibula, multiple hyperpigmented lesions on the back (Figure 1a) and below axilla.

Patients 2 and 3

These two patients were a mother and her daughter. The 31-year-old mother had maxillary and mandibular odontogenic cysts for which she had been operated on three times. Two periorbital lesions were excised and histopathological examination revealed a pigmented basal cell carcinoma and the second was trichoepithelioma. All the cervical vertebrae were deformed and there was cervical scoliosis at the craniocervical junction. Her father had died of skin cancer.

Table I. Clinical and cytogenetic features of the presented patients with Gorlin syndrome

Features	Patients	1	2	3	4	5	6	7	8	9	10	11
Age (years)		6.5	31	5	19	15	18	47	42	13	17	51
Sex (F/M)		F	F	F	M	M	M	M	M	F	M	M
Odontogenic keratocysts		+	+	-	+	+	+	+	+	+	+	-
Basal cell carcinomas		-	+	-	-	-	-	+	-	-	-	-
Calcification of falx cerebri		-	-	-	+	-	+	+	-	-	+	-
Characteristic facial features		+	-	+	-	-	+	+	+	+	+	-
Head circumference >97th centile		+	-	+	-	-	+	+	+	-	+	-
Weight or height >97th centile		-	-	+	-	-	-	-	-	+	-	-
CNS abnormalities		+	-	+	-	-	+	-	-	-	-	-
Palmar or plantar pits		-	-	-	+	-	-	+	+	+	+	+
Hairy patch		-	-	-	+	-	-	+	+	-	-	+
Atrophic or pigmentary skin lesions		+	-	+	+	+	+	+	+	-	-	-
Other tumors		-	T	-	-	-	-	-	-	-	-	-
Teeth hypoplasia or late eruption		+	-	-	-	-	-	-	-	-	-	-
Developmental delay		+	-	-	-	+	-	-	-	-	-	-
Hypogonadotropic hypogonadism		+	-	-	-	-	-	-	-	-	-	-
Extracranial skeletal abnormalities		-	+	-	-	-	-	-	+	+	-	-
Chromosomal abnormalities		+	?	-	-	+	-	-	-	-	-	-
Increased SCEs		?	?	?	?	?	-	-	-	-	-	-

F: Female, M: Male, CNS: Central nervous system, T: Trichoepithelioma, SCE: Sister chromatid exchange

The 5-year-old daughter had macrocephaly (head circumference was 56 cm), coarse facies with frontal bossing, and a café-au-lait spot over the left wrist. Cranial tomography revealed partial agenesis of splenium of the corpus callosum, cerebral atrophy and bilateral frontotemporoparietal subdural effusion. Her karyotype was 46,XX.

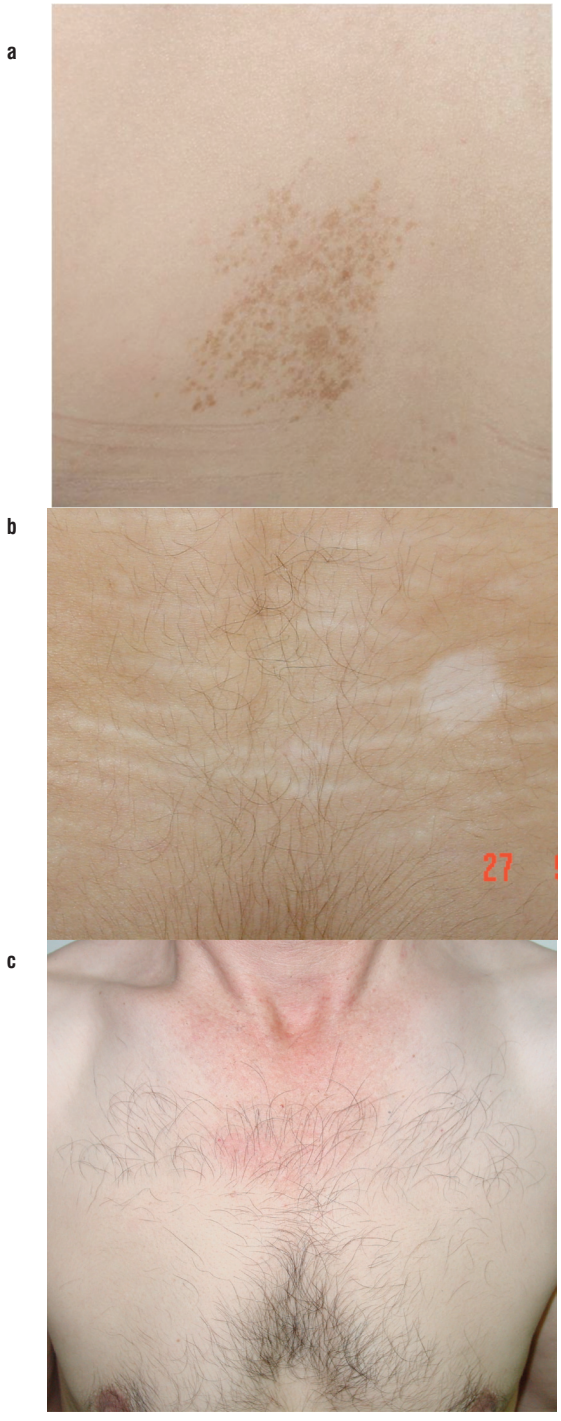

Figure 1. a) Hyperpigmented lesion over the shoulder of patient 1, b) Hairy patch and depigmented lesion over the lower back of patient 4, c) Hairy patch over the anterior thoracic wall of patient 7

Patients 4 and 5

These two were brothers, both having gingival hyperplasia and odontogenic cysts. The elder brother, who was 19 years old, had milimetric calcifications on the anterior part of falx cerebri, as demonstrated by cranial tomography. His head circumference was 55 cm (25^{th}-50^{th} percentile), his weight was 63 kg (10^{th}-25^{th} percentile) and his height was 180 cm (75^{th}-90^{th} percentile). He had palmar pits and atrophic depigmented skin lesions over the back, the forearms and the lower limbs. He also had a hairy patch over his lower back (Figure 1b).

The 15-year-old younger brother had similarly located depigmented lesions as well; however, he did not have palmar pits. In cranial tomography, he was seen to have diffuse calvarial thickening. His head circumference was 53 cm (25^{th}-50^{th} percentile), body weight was 57 kg (25^{th}-50^{th} percentile), and height was 173 cm (75^{th}-90^{th} percentile). He was mildly retarded and unable to read. The karyotype was 47,XXY.

Patient 6

The sixth patient was an 18-year-old male who had undergone surgery several times for mandibular and maxillary odontogenic keratocysts. When he was two years old, hydrocephalus had been diagnosed. On physical examination, he had macrocephaly (head circumference was 59.5 cm), coarse facies with prominent supraorbital ridges and very thick eyebrows, synophrys, a prominent nose with a high nasal bridge, down-slanting and wide palpebral fissures, generalized skin hyperpigmentation with a single 3x3-cm area of hyperpigmentation on the back, and mild prognathism. He weighed 60 kg (10^{th}-25^{th} percentiles) and was 179.5 cm tall (75^{th}-90^{th} percentiles). Echocardiographic examination showed floppiness of the mitral valve, mild tricuspid regurgitation and mild pulmonary hypertension. Ophthalmologic examination and renal ultrasonography gave normal results. Chromosome analysis was not done.

Patient 7

The seventh patient was a 47-year-old man operated on several times for odontogenic keratocysts in mandibular and maxillary alveolar processes. He had undergone surgery five times for the excision of facial skin lesions which were histologically diagnosed as basal cell carcinomas. On physical examination, his head circumference was 58.7 cm (over 97^{th} percentile), he had a coarse face with prominent supraorbital ridges and thick eyebrows, maxillary hypoplasia and prognathism, hyperpigmented and hypopigmented lesions over the scalp and the back, palmar pits and patches of hair over the anterior thoracic wall (Figure 1c). An anteroposterior cranial radiogram showed calcification of falx. Spontaneous sister chromatid exchange was increased, when analysed as previously described (9).

Patients 8 and 9

These two patients were a father and daughter. The 42-year-old father had been operated on three times for odontogenic keratocysts. His head circumference was 61 cm (over 97th percentile), his weight 82.5 kg (90th-97th percentiles), and his height was 168 cm (10th-25th percentiles). He had a coarse facial appearance with thick eyebrows and prominent supraorbital ridges, a patch of hair over the chest, pectus carinatum, palmar pits and generalized hyperpigmentation. His karyotype was 46,XY and there was no increase in sister chromatid exchanges.

His 13-year-old daughter was born 4500 gr at term, and she developed normally until 5 months of age when she contracted meningitis. Then she had bilateral deafness and severe developmental delay. She presented with left mandibular swelling at the age of 13 when a diagnosis of odontogenic keratocyst was made. Her head circumference was 54 cm (50th percentile), weight 55 kg (75th percentile), and height was 158 cm (50th-75th percentiles). She had coarse facies with prominent supraorbital ridges and thick eyebrows, and a high palate. She also had an asymmetry of the thorax and palmar pits. There was a post-axial polydactyly on the right hand. She had no pigmentary abnormalities. Her karyotype was 46,XX with no increase in sister chromatid exchanges.

Patients 10 and 11

The last two patients were a father and son. The 17-year-old son had received surgery 4 times for odontogenic keratocysts of the jaw. On physical examination, his head circumference was 58 cm (over 97th percentile), he was 168 cm tall (10th-25th percentiles), and weighed 75 kg (75th-90th percentile). He had a coarse face with thick eyebrows, and there were several palmar pits bilaterally. Posteroanterior cranial radiogram demonstrated calcification of falx cerebri.

His 51-year-old father had hairy patches over the anterior thorax and a few palmar pits. However, he did not have any history regarding the presence of odontogenic keratocysts and basal cell carcinomas. His head circumference was 59 cm (50th percentile). Calcification of falx cerebri was absent. He was considered to have Gorlin syndrome as his son was affected.

Discussion

Gorlin syndrome is an autosomal dominant disorder characterized by multiple basal cell carcinomas, jaw keratocysts and skeletal malformations (2). Soft tissue calcifications and dyskeratotic palmar/plantar pits are frequent features (3). The patients may be affected by various types of cancers including medulloblastoma, ovarian fibroma and fibrosarcoma, meningioma, rhabdomyoma, and cardiac fibroma (3).

The presence of the hairy patches is a recenty recognized feature of the syndrome (10). This feature was present in patient 7 and patient 8, who had the full-blown presentation of the disease. Patient 7 and patient 2, who were 47 and 31 years old respectively, had basal cell carcinomas. The remaining patients who were younger, did not have basal carcinoma which generally arise in older ages. All the patients, except patient 3 who was very young, were referred by dentists after the detection of odontogenic keratocysts, no patient was referred due to basal cell carcinoma. We believe that earlier onset for the odontogenic cysts is an important factor for diagnosis. However, considering the variability in the clinical presentation of Gorlin syndrome, physicians taking care of basal cell carcinomas, including surgeons, dermatologists and dermatopathologists, should be highly prudent in looking for other features of the syndrome. We suggest that generalized hyperpigmentation and/or localized hypo/hyperpigmented areas, which were present in all the patients in our series, may be common features of the syndrome.

The mutated gene in Gorlin syndrome is called *PTCH* and lies at 9q22.3 (11). Several patients with deletions involving this region have been reported (4-7). Co-occurrence of the condition with Klinefelter syndrome and (X;11) translocation in our patients was considered coincidental.

Gorlin syndrome has been suspected as a chromosome instability syndrome. An early study in 1985 (12) showed that there were higher spontaneous and mitomycin-C induced sister chromatid exchange rates in nine Gorlin syndrome patients than in controls. A second study in 1987 showed that the frequency of spontaneous sister chromatid exchange was high in three patients with Gorlin syndrome. Later studies showed no evidence of chromosomal instability compared to controls, when both spontaneous and induced chromosomal breaks were considered (13-16). However, one study involving seven patients in 1995 confirmed the disease as being a chromosome instability syndrome, though spontaneous chromatid breaks occurred more frequently in a subset of patients, indicating a variable expression of this feature (17). In the present series, six of the patients were checked for increased sister chromatid exchange via UV exposure. None showed an increase in the number of sister chromatid exchanges. We were unable to perform sister chromatid exchange analysis in the other patients. Fibroblasts were not tested, since lymphocytes would be appropriately representative of somatic UV susceptibility for DNA breakages. Increased sister chromatid exchanges might be associated with acquired chromosomal abnormalities, both in tissues affected by carcinogenesis and in those without cancer (1). In our cohort, two patients had chromosomal rearrangements; one was a balanced translocation in mosaic and the other was a constitutional aberration, 47,XXY. These two were considered unrelated to a possible UV susceptibility for increased DNA breakages.

Patients with Gorlin syndrome should receive counselling on certain important issues. One is that the disease is inherited in an autosomal dominant fashion, and the future generations may be affected with a 50% probability. The

disease is mostly inherited from a parent but may be sporadic in one-fifth. Therefore, parents, siblings and offsprings should be evaluated accordingly. Another point is that all those with consistent findings should be followed-up for carcinogenesis. One major preventive approach is avoiding sunlight exposure. Another should include prudent follow-up after cranial or spinal radiotherapy for medulloblastoma, since sunlight and radiotherapy may be provocative for the development of basal cell carcinomas of the exposed skin (3).

Study Limitations

Sister chromatid exchange analysis was not done in all of the patients. Testing fibroblasts would also be further informative, since lymphocytes would be appropriately representative of somatic UV susceptibility for DNA breakages.

Conclusion

Gorlin syndrome is a clinically heterogeneous condition. We conclude that the detection of odontogenic keratocysts and basal cell carcinomas should raise the suspicion of Gorlin syndrome, and the patients should be examined for other clinical findings. Presence of hairy skin patches and pigmentary skin lesions represent the recently recognized physical signs of the disease. Although evidence for chromosome instability was not found in our patients, occurrence of chromosome instability in a subgroup of patients, and mechanisms underlying cancer predisposition require further studies for full elucidation.

Ethics

Ethics Committee Approval: The study was approved by Hacettepe University Non-Interventional Clinical Research Ethics Board.

Informed Consent: Consent form was filled out by all participants.

Peer-review: External and internal peer-reviewed.

Authorship Contributions

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

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

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

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J Pediatr Res 2017;4(2):68-74
DOI: 10.4274/jpr.65882

Original Article / Orijinal Araştırma

The Anxiety Levels of the Parents of Premature Infants and Related Factors

Prematüre Bebeği Olan Anne ve Babaların Kaygı Düzeyleri ve İlişkili Faktörler

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ABSTRACT

Aim: The aim was to determine the anxiety levels of parents with premature infants and related factors.

Materials and Methods: This comparative descriptive study was conducted in the neonatal intensive care unit of four hospitals located in Konya, Turkey between March and April 2012 with the parents (n=194; 97 mothers, 97 fathers) of premature infants who were 32-37 weeks gestational. Data were collected using Parents and Infant Information Form prepared by the researchers, and State-Trait Anxiety Inventory Scale.

Results: The mean state anxiety scores of the mothers and fathers were similar (p>0.05). The mothers had higher mean trait anxiety scores compared to the fathers and this difference was found to be statistically significant (p<0.05).

Conclusion: It was observed that parents with premature infants experienced mild anxiety.

Keywords: Anxiety, parents, premature, related factors, State-Trait Anxiety Inventory

ÖZ

Amaç: Çalışma prematüre bebeği olan anne ve babaların kaygı düzeyleri ve ilişkili faktörleri belirlemek amacıyla yapıldı.

Gereç ve Yöntemler: Karşılaştırmalı tanımlayıcı çalışma, Konya ili kent merkezinde yer alan, yenidoğan yoğun bakım ünitesi bulunan dört hastanede, Mart-Nisan 2012 tarihleri arasında yapıldı. Örneklem grubunu 97 prematüre bebeğin anne ve babası oluşturdu (n=194). Verilerin toplanmasında araştırmacılar tarafından oluşturulan Ebeveyn ve Bebek Bilgi Formu ve Durumluk-Sürekli Kaygı Ölçeği kullanıldı.

Bulgular: Annelerin ve babaların durumluk kaygı puan ortalamaları benzer olduğu saptandı (p>0,05). Annelerin sürekli kaygı puan ortalamalarının babalara göre yüksek olduğu ve bu farkın istatistiksel olarak anlamlı olduğu bulundu (p<0,05).

Sonuç: Prematüre bebeği olan anne ve babaların hafif düzeyde kaygı yaşadıkları görüldü.

Anahtar Kelimeler: Anksiyete, anne-baba, prematüre, ilişkili faktörler, Durumluk-Sürekli Kaygı Ölçeği

Introduction

Premature delivery is a major critical problem that causes high perinatal morbidity and mortality rates (1-3). The World Health Organization reports that one of every 10 births is premature (2). In Turkey, the rate of premature delivery is reported to be 12% (4).

Parents who are not psychologically ready for a preterm delivery, go through high levels of anxiety (5-7). The fact that a premature infant has more common health problems also affects the anxiety levels of the parents. Factors such as family and infant characteristics, the severity of the infant's health condition, parent-infant relationship are related to the outcome of premature infants (8). The mother and father

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This study was presented orally in the 5th Congress of the European Academy of Pediatric Societies on 17-21 October 2014, in Barcelona, Spain.
Received/Geliş tarihi: *24.01.2017* **Accepted/Kabul tarihi:** *20.04.2017*

must adapt to their new roles in providing a safe environment for and taking care of their infant. In this process, they should learn how to communicate with their infant as well as how to manage the baby's problems. Also social support should be provided for both the mothers and fathers to prevent stress and anxiety during this period (9,10).

The parents of infants in neonatal intensive care units (NICUs) may feel high anxiety due to the severity of their infant's illness, the ambiance of the unit, and the psychosocial feeling of seperation (9). Previous studies show that the mothers of premature infants in the NICU may have a mild level (11,12), medium level (13,14) and high level (15,16) of anxiety.

Most of the studies focus on maternal stress in general; there is even less information about a father's long-term adaptation (9,17,18). However, the family should be evaluated as a whole including both parents. More studies are needed as the number of premature deliveries is high and this group of babies require special care. Studies conducted in this field shall make positive contributions to creating awareness among parents and nurses of newborns, and create an important literature specific to this field.

The aim of our study was to determine the anxiety levels of the parents of premature infants. We also aimed to determine the factors that could impact anxiety on these parents.

Materials and Methods

Setting

This comparative descriptive study was conducted in the NICU of four hospitals located in Konya between March and April 2012.

Sample

The table presented in "determine sample size of descriptive studies with dependent variables" (19) was used to determine the sample size of the study, and we used the rate reported by Özyazıcıoğlu and Tüfekci (20) (52.88±10.18). The aim was to determine the score to be taken from the state trait anxiety scale within 95% confidence level and ±2 point confidence interval. Accordingly, the total width was taken as 4 points (2 points above and 2 points below). In the calculation standardized range width= the total width/ standard deviation (SD) (4/10.18=0.37 approximately 0.40) was found (19). The calculated sample size in each group was 97 (97 mothers, 97 fathers). Considering 10% drop out rate the study sample size was set to 107. Three fathers among these did not agree to join the study for confidentiality reasons, and seven parents did not complete the questionnaire.

Inclusion criterion was to be the mother and father of a premature infant of 32-37 weeks of gestational age, hospitalized at the NICU, and planned to be discharged from the NICU in 2-3 days. All the parents were required to sign the informed consent.

Exclusion criteria were the infants diagnosed with a genetic disorder and/or major congenital malformations, and parents who had a previously hospitalized premature infant younger than 32 weeks of gestational age.

Data Collection

Data were collected from the parents by the researcher via face-to-face interview in a separate room outside the NICU.

Measures

"Parents and Infant Information Form" and "State-Trait Anxiety Inventory (STAI)" were used.

Parents and Infant Information Form was developed by the researcher (21-23). The form included five questions regarding the socio-demographic characteristics of the parents (age, education level, working status, health insurance, perceived income), 11 questions concerning the mother and the infant (gender, delivery method, gestational week of the mother, postmenstrual age of the infant, diagnosis, interventions implemented to the infants in the postpartum period, feeding methods, number of children, having premature infants previously, birth weights, the hospitalization period of the infants), and the opinions of the parents regarding the care of the premature infant (currently experienced anxiety regarding the infant's care), and 6 questions on the perception of the mothers concerning their adequacy fields in the field of infant care (feeling sufficient for the baby's care, moniliasis care, evaluating respiration, discharge training regarding infant care).

STAI Scale, Spielberger STAI (STAI-I), developed by Spielberger et al. (24) in 1983 and adapted to Turkish by Öner and Le Compte (25) in 1985 was used to assess the anxiety level. This assesses both state anxiety, i.e. current mood; and trait anxiety, i.e. general predisposition towards anxiety. It is a 4-point scale consisting of 40 items. Both scales include 20 items, such as I am worried (state anxiety) and I feel nervous and restless (trait anxiety). Both showed good internal consistency-Cronbach's α=0.86 and 0.89. Internal consistency was adequate in this sample (Cronbach's α=0.92 and 0.89).

Ethical Considerations

Before the study was started, Ethical Committee consent was received from Selçuk University Faculty of Medicine in January 2012 (approval number: 2012/01) and the related permissions were obtained from each hospital where the study took place, and from the all parents within the study population.

Statistical Analysis

Data were analysed using the SPSS version 20 (SPSS; IBM, New York, USA). Normal distribution of dependent variables was evaluated by conducting a normality analysis through Kolmogorov-Smirnov test and it was found that they showed normal distribution. Number, percentage and mean ± SD were used to determine descriptive data. Independent

samples t test, Mann-Whitney U (U) tests, and Kruskal-Wallis (KW) and Bonferroni-corrected Mann-Whitney U (for KW test) were used to determine the differences between groups. P<0.05 value was accepted significant in all the analyses.

Results

Features of the Parents and Infants

Mean age of the mothers participating in the study was 26.77±5.31 and mean age of the fathers was 30.13±5.35. Of the mothers 38.2% were primary school graduates, 86.6% were unemployed, 66% evaluated their monthly income as mediocre, while 37% of the fathers were primary school graduates, 91.8% had a wage-earning employment, and 72.2% evaluated their monthly income as mediocre (Table I). In addition, 87.6% of the parents had a health insurance, 44.2% had one child, and 14.4% previously had a premature infant.

Of the premature infants 52.6% were born in gestational weeks 35-37, 55.7% were planned to be discharged in gestational weeks 35-37, 50.5% were male, 67% were born via cesarean section, and 44.3% were in hospital only because of being premature. While 81.5% of the infants stayed in an incubator, 76.3% were fed only with breast milk (Table II). The gestational weeks of the premature infants were 34.51±1.68, and their postmenstrual ages were 36.12±2.01 weeks. Their birth weights were 2210.03±568.17 grams, and postmenstrual weights were 2264.36±568.72 grams. Mean hospitalization period of the premature infants was found to be 8.49±6.66 days (minimum: 2.00, maximum: 35.00).

Table I. Socio-demographic characteristics of parents (n=194)

	Mothers (n=97)		Fathers (n=97)	
Characteristics	**n**	**%**	**n**	**%**
Age*				
18-24 years	38	39.2	14	14.5
25-31 years	39	40.2	46	47.4
32 and more years	20	20.6	37	38.1
Educational levels				
Primary school	37	38.2	36	37.0
Secondary school	33	34.0	18	18.6
High school	14	14.4	25	25.8
University	13	13.4	18	18.6
Working status				
Working	13	13.4	89	91.8
Not working	84	86.6	8	8.2
Perceived income status				
Good	29	29.9	19	19.6
Mediocre	64	66.0	70	72.2
Low	4	4.1	8	8.2

*Mothers' mean age=26.77±5.31, fathers' mean age=30.13±5.35

State-Trait Anxiety Levels of the Parents

While mean state anxiety score of the mothers was 40.15±11.25 (minimum: 20, maximum: 72), that of the fathers was 37.32±10.87 (minimum: 20, maximum: 67), and this difference was not found to be statistically significant (t=1.785, p=0.076). However, mean trait anxiety score of the mothers was 44.30±8.98 (minimum: 26, maximum: 65), while that of the fathers was 39.45±8.58 (minimum: 20, maximum: 67), and this difference was found to be statistically significant at an advanced level (t=3.842, p=0.000) (Table III).

Factors Related to the Anxiety Levels of the Parents

When the anxiety levels were examined according to the socio-demographic features of the parents, no statistically significant difference was found between the mothers' ages, educational levels, employment status, perceived income, number of children, previously having had premature infants,

Table II. Characteristics of premature infants (n=97)

Characteristics	**n**	**%**
Gender		
Female	48	49.5
Male	49	50.5
Delivery method		
Vaginal	32	33.0
Cesarean	65	67.0
Gestational age		
32-34 weeks	46	47.4
35-37 weeks	51	52.6
Postmenstrual age		
32-34 weeks	21	21.6
35-37 weeks	54	55.7
38 weeks and over	22	22.7
Diagnosis		
Premature	43	44.3
Premature + additional problems*	54	55.7
Interventions implemented to infants in postpartum period		
Incubator	79	81.5
Cot	4	4.1
Mechanical ventilation	14	14.4
Feeding methods of infants		
Breast milk	74	76.3
Breast milk and formula	23	23.7

*Additional problems (hyperbilirubinemia, respiratory distress syndrome, meconium aspiration syndrome, malnutrition, intrauterine growth retardation)

and state-trait anxiety mean scores (p>0.05). No significant difference was found between the fathers' ages, number of children, previously having premature infants, and state-trait anxiety mean scores (p>0.05). The difference between the education levels and trait anxiety mean scores of the fathers was statistically significant in the study (trait anxiety KW=11.042 p=0.012). In the advanced analysis conducted through Bonferroni-corrected Mann-Whitney U test, it was determined that primary school graduate fathers had higher trait anxiety mean scores (43.33±8.48) compared to high school graduate fathers (36.32±7.94) and this difference was significant (p=0.003). Trait anxiety mean scores of unemployed fathers (46.75±11.25) were significantly higher (trait anxiety U=161.0 p=0.010). Trait anxiety mean scores of the fathers were also significant according to their perceived income status (trait anxiety KW=8.300 p=0.016). In the advanced analysis conducted through Bonferroni-corrected Mann-Whitney U test, it was determined that the fathers who perceived their income levels to be low had significantly higher trait anxiety mean scores than those who perceived their income to be good or mediocre (Table IV).

When anxiety levels of the parents were evaluated according to the features of the premature infants, no significant difference was found between gender, delivery method, gestational age (GA), postmenstrual age (PMA) (trait anxiety mean score), diagnosis, feeding methods, and state and trait mean scores of the parents (p>0.05). However, when the PMA of the infants and state anxiety levels of the mothers were examined, a significant difference was found between the groups (KW=7.701 p=0.021). In the advanced analysis performed in order to determine between which groups there was a difference, it was noted that the mothers whose PMA was 38 weeks or more, had significantly higher state anxiety scores than those whose PMA was 35-37 weeks.

When anxiety levels of the parents were assessed according to their current anxiety experience regarding the care of their premature infants, parents who stated they currently experienced anxiety had higher state and trait anxiety mean scores, and this difference was found to

Table III. Comparison of mean anxiety score of the mothers and fathers (n=194)

Status of anxiety	Mothers (n=97)	Fathers (n=97)	t	p
	$\bar{x}$ ± SD	$\bar{x}$ ± SD		
State anxiety	40.15±11.25	37.32±10.87	1.785	0.076
Trait anxiety	44.30±8.98	39.45±8.58	3.842	**0.000**

SD: Standard deviation

Table IV. Comparison of mean anxiety score by socio-demographic characteristics of the mothers and fathers

Characteristics	Mothers (n=97)			Fathers (n=97)		
	n	State anxiety $\bar{x}$ ± SD	Trait anxiety $\bar{x}$ ± SD	n	State anxiety $\bar{x}$ ± SD	Trait anxiety $\bar{x}$ ± SD
Educational levels						
Primary school	37	41.24±11.53	45.22±10.48	36	40.14±9.73	43.33±8.48[a]
Secondary school	33	38.94±11.74	45.33±9.01	18	37.50±13.46	37.56±5.85
High school	14	41.36±10.75	40.57±6.47	25	33.68±11.37	36.32±7.94[b]
University	13	38.85±10.46	43.08±5.48	18	36.56±8.51	37.94±9.59
KW (SD: 3)		1.392	3.463		6.542	11.042
p		0.707	0.326		0.088	**0.012 (a>b)**
Working status						
Working	13	38.69±9.83	43.46±7.04	89	36.76±10.85	38.80±8.06
Not working	84	40.38±11.49	44.43±9.27	8	43.50±9.78	46.75±11.25
U		510.5	488.0		218.0	161.0
p		0.707	0.539		0.070	**0.010**
Perceived income status						
Good	29	36.97±9.76	43.41±7.43	19	37.00±9.79	36.68±7.49[a]
Mediocre	64	41.02±11.29	43.92±9.33	70	37.29±11.29	39.13±7.83[b]
Low*	4	-	-	8	38.38±10.88	48.88±11.74[c]
U		735.50	870.50	**KW (SD: 2)**	0.119	8.300
p		0.110	0.633		0.942	**0.016 (a<c, b<c)**

*Data excluded from the analysis because the number of sample was small
KW: Kruskal-Wallis test, SD: Standard deviation, U: Mann-Whitney U test

be statistically significant (mothers state anxiety t=3.728 p=0.000, trait anxiety t=2.239 p=0.027; fathers state anxiety t=3.697 p=0.000, trait anxiety t=2.436 p=0.017). When anxiety levels of the mothers were evaluated according to their perceptions of regarding their adequacy in the field of care, mothers who did not feel sufficient had higher state and trait anxiety mean scores (state anxiety 46.11±8.88, trait anxiety 49.74±7.24), and this difference was found to be significant in the advanced analysis (state anxiety U=428.50 p=0.004, trait anxiety U=405.00 p=0.002 respectively). In terms of counting and evaluating the infant's respiration, mothers who did not feel adequate had higher state anxiety mean scores, and this difference was found to be statistically significant (state anxiety t=-2.233 p=0.028), whereas the difference between trait anxiety mean scores was not significant (p>0.05) (Table V). The difference between the state and trait anxiety mean scores of the mothers in providing moniliasis care for the infant was not statistically significant (p>0.05). Nor was the difference statistically different (p>0.05) when the mothers' state and trait anxiety mean scores were evaluated according to the hospital discharge training to be received regarding the infant's care.

Discussion

The study determined that the mothers of premature infants had higher anxiety than their fathers. While the anxiety of the father was more influenced by reasons such as being primary school graduates, unemployment and low income; the anxiety of the mothers was mostly related to infant care.

It was also determined that the mothers included in the study had higher state anxiety mean scores than the fathers (p>0.05). The trait anxiety levels of the mothers were also higher than those of the fathers and they experienced mild anxiety (p=0.000) (Table III). State anxiety levels of the parents are thought to be changing depending on the momentary behaviors and reactions of their infants. The fact that infants were kept in a safe environment where medical intervention could be provided for 24 hours in case of a problem could have affected the state anxiety levels of parents positively, and the fact that the mothers had higher state anxiety levels than the fathers may be associated with the mothers' being more sensitive to the negative changes in the infants compared to the fathers. The study also determined that the mothers had higher trait anxiety

Table V. Comparison of mean anxiety score by the feeling of sufficiency of the mothers regarding infant care, and opinions of the mothers and fathers regarding infant care

	n	%	State anxiety	Trait anxiety
			$\bar{x}$ ± SD	$\bar{x}$ ± SD
Current anxiety experience status of the mothers regarding the care of their infants				
Yes	47	48.5	44.28±9.64	46.36±8.30
No	50	51.5	36.28±11.35	42.36±9.24
t			3.728	2.239
p			**0.000**	**0.027**
Current anxiety experience status of the fathers regarding the care of their infants				
Yes	40	41.2	41.90±10.38	41.93±9.38
No	57	58.8	34.11±10.11	37.72±7.58
t			3.697	2.436
p			**0.000**	**0.017**
Feeling of sufficiency of the mothers regarding infant care				
Yes	78	80.4	38.71±11.33	42.97±8.90
No	19	19.6	46.11±8.88	49.74±7.24
U			428.50	405.00
p			**0.004**	**0.002**
Feeling of sufficiency of the mothers in terms of counting and evaluating infant's respiration				
Yes	32	33.0	36.59±10.16	42.97±7.80
No	65	67.0	41.91±11.41	44.95±9.49
t			-2.233	-1.024
p			**0.028**	0.308

SD: Standard deviation

mean scores than the fathers, and mothers experienced a mild anxiety, which may be arising from the uncertainty related to the future, inability to continue infant care at home sufficiently, distress about how to cope with problems after being discharged from hospital, and the fear of losing her infant. Additionally, the mothers' more intense anxiety levels may be explained with the fact that they play the primary role in providing care for their infant and other children, and they are affected more by an unreliable environment. Ghorbani et al. (13) and Gambina et al. (26) showed that anxiety levels in parents of preterm infants were higher than those of term infants. In another study, it was reported that the mothers whose infants stayed in NICU attached to their infants earlier in the postpartum period compared to the fathers, they were more sensitive to negative changes in the infant, and they experienced more fear, depression, feeling of worthlessness and uneasiness (27).

It was seen that only trait anxiety levels of the fathers differed with three variables. In the study, primary school graduate fathers had significantly higher trait anxiety levels (p=0.012) (Table IV). This may be due to the fact that the fathers with lower education levels could not comprehend sufficiently the explanations made regarding the infant's state of health, and they were unsuccessful in developing solutions for problems they encountered. In a study conducted by Miles et al. (28), the mothers with lower education levels were reported to be more worried about the medical conditions of their infants compared to the mothers who had higher education levels.

In this study, fathers who did not work had higher trait anxiety levels compared to those who were working and had mild levels of anxiety (p=0.010) (Table IV). Unemployment of the fathers affected the economical status and welfare of the family directly in a negative way. Fathers with low income levels also had high levels of trait anxiety (p=0.016) (Table IV), which may be related to the anxiety that they may not be able to afford care and medical services for the infant. Additionally, economic status plays an important role in reaching information and meeting requirements.

Mothers whose PMA was 38 or more weeks were found to have higher state anxiety levels than those whose PMA was 35-37 weeks (p=0.008) because premature infants in 35-37 weeks PMA have been in hospital for a longer period and their mothers may have adapted to the situation. They might have had slight anxiety because their infants would be discharged, and they were worried that they were not fully recovered and they did not feel ready for discharge.

It was observed that both the mothers and fathers had different anxiety scores. Parents who stated that they currently experienced anxiety were found to have high state and trait anxiety scores (mothers state anxiety p=0.000 trait anxiety p=0.027; fathers state anxiety p=0.000 trait anxiety p=0.017) (Table V). Parents may have experienced mild anxiety by thinking that home care would not be sufficient for the infant after being discharged from the hospital, or the infant is too young or they could not be discharged due to some reasons. In a study conducted by Kurnaz and Gençalp (12), no statistically significant difference was found in terms of state anxiety scores between the mothers who stated and those who did not state anxiety before their infants were discharged from the hospital. However, when their state anxiety scores were considered, the mothers stated that they experienced mild anxiety about themselves and their infants (12).

Our results showed that the mothers who did not feel self-sufficient concerning the infant's care had higher anxiety levels compared to those who felt adequate (Table V). A higher anxiety level is expected as a result of the inadequate information had by mothers regarding the infant's care, the fact that almost half of them were primipara, and they did not have a premature infant before. This result reveals the need that mothers should be informed regarding premature infant care.

Mothers who were not sufficient in counting and evaluating respiration had higher state anxiety scores (p=0.028) (Table V), which may be associated with the inadequate information received by the mothers from the medical personnel, and inadequate practices conducted in the clinic with the NICU nurses before being discharged from the hospital.

Study Limitations

This study has some limitations. First of all, self-report measures like STAI may only indicate the level of anxiety without yielding information about the clinical diagnosis. A further limitation of the study was that the parents of premature infants younger than 32 weeks GA were not included in the study. Finally, we included both first time parents and parents that already had children. So they could have experienced anxiety at different levels.

Conclusion

Parents of premature infants had mild anxiety, also the mothers had higher trait anxiety levels than the fathers. Being primary school graduates, unemployment, low income affected the anxiety levels of the fathers. Anxiety levels of the mothers whose premature infants were in 38 weeks or more PMA, who did not feel adequate about their infant's care, were found to be higher. State anxiety levels of the mothers who felt inadequate in counting and evaluating the respiration of their infants, were found high. Also current anxiety levels of both the mothers and fathers were high.

Family-centered care practices should be developed to support both the mother/father-infant attachment and parents' empowerment in the care of their infant. Nurses have a vital role in family-centered care and they should apply supportive nursing interventions such as encouraging parents to visit and touch their infants; and explaining the intended use of medical devices.

Ethics

Ethics Committee Approval: The study was approved by the Selçuk University Faculty of Medicine Ethics Committee (Approval number: 2012/01, 31.01.2012).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: R.Ç., F.T.A., Design: R.Ç., F.T.A., Data Collection or Processing: R.Ç., Analysis or Interpretation: R.Ç., F.T.A., Literature Search: R.Ç., Writing: R.Ç., F.T.A.

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

Financial Disclosure: This research was financially supported both via oral presentation and the thesis by the Selçuk University Scientific Research Projects Coordinatorship in Konya, Turkey.

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J Pediatr Res 2017;4(2):75-7
DOI: 10.4274/jpr.57070

Late Preterm Infant Diagnosed with Thrombocytopenia Absent Radius Syndrome

Geç Preterm Bir Yenidoğanda Tanı Alan Trombositopeni Radius Yokluğu Sendromu

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ABSTRACT

Thrombocytopenia absent radius (TAR) syndrome is a rare genetic anomaly presenting with bilateral radial aplasia and thrombocytopenia. Pathophysiology is not fully understood. Patients may need to receive thrombocyte transfusions for better neurological outcome and frequent follow-up may prevent serious complications such as intracranial hemorrhage. Here we report a one-day-old late preterm neonate diagnosed with TAR syndrome by clinical and laboratory data, and confirmed by genetic studies.

Keywords: Thrombocytopenia absent radius, thrombocytopenia, radius, neonate, preterm

ÖZ

Trombositopeni radius yokluğu (TAR) sendromu, nadir görülen bilateral radius yokluğu ve trombositopeni ile karakterize bir sendromdur. Patofizyolojisi tam olarak anlaşılamamıştır. Hastalar nörolojik gelişimlerinin etkilenmemesi ve intrakraniyal kanama gibi izlemde gelişebilecek komplikasyonlardan korunmak için trombosit transfüzyonuna gereksinim duyabilirler. Burada bir günlük geç preterm bir yenidoğanda klinik ve laboratuvar olarak tanı konulan ve genetik çalışmalar ile konfirme edilen TAR sendromu olgusu sunulmuştur.

Anahtar Kelimeler: Trombositopeni radius yokluğu, trombositopeni, radius, yenidoğan, prematüre

Introduction

Thrombocytopenia absent radius (TAR) syndrome is a rare genetic condition, characterized by bilateral absence of the radii while both thumbs are present, and thrombocytopenia. Skeletal, hematologic, and cardiac system involvement may also occur. Incidence of TAR syndrome is 0.42 per 100000 births. Intracranial hemorrhages due to thrombocytopenia or serious cardiac defects are often the cause of death (1). Mental retardation may develop secondary to intracranial hemorrhage (2). Epilepsy, learning difficulties, intracranial vascular malformations, sensorineural hearing loss, hypoplasia of corpus callosum and cerebellar dysgenesis have been reported as associated neurological abnormalities. Although primordial megakaryocytes are suspected to take part in pathogenesis due to their role in formation of blood vessels, the mechanism leading to this congenital phenomenon is not fully understood (3).

Herein we report a late preterm one-day-old neonate diagnosed with TAR syndrome by clinical and laboratory data, and confirmed by genetic studies.

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Received/Geliş tarihi: *15.02.2016* **Accepted/Kabul tarihi:** *14.04.2016*

Case Report

A 36 5/7-week gestation male infant, with a birth weight of 2600 grams, was born by normal vaginal delivery to a 28-year-old Syrian mother and admitted to neonatal intensive care unit for upper limb hypoplasia. Detailed prenatal history was absent due to communication issues.

Physical examination revealed radially deviated upper limbs with no thumb deformity but hypoplastic fingers. There were no deformities in the lower limbs other than laterally deviated bilateral halluces (Figure 1). Abdominal examination revealed no organomegaly. On cardiac auscultation, a soft (2/6) systolic murmur was heard over the left sternal side.

Complete blood count showed white cell count of 29800/mm^3 and platelet count of 36000/mm^3. Other laboratory results were within normal ranges. Radiography of forearms revealed bilateral absence of radii (Figure 2). Echocardiography was performed, which showed ventricular septal defect (VSD), patent ductus arteriosus (PDA), atrial septal defect (ASD) and pulmonary hypertension. Transcranial and abdominal ultrasonography were normal. The patient was administered platelet transfusion when complete blood count revealed that the platelet count was below 25000/mm^3. Platelet levels increased to 129000/mm^3 following transfusion. Monitoring the case continues in the postnatal 3rd month.

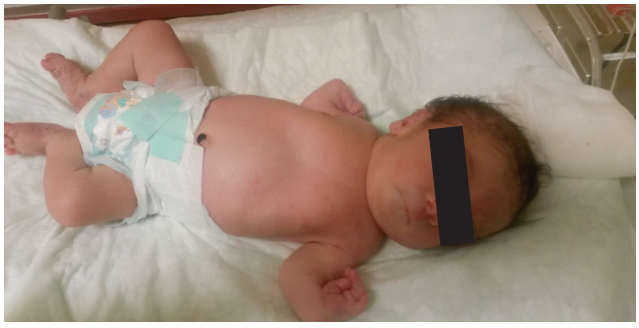

Figure 1. General appearance of the patient

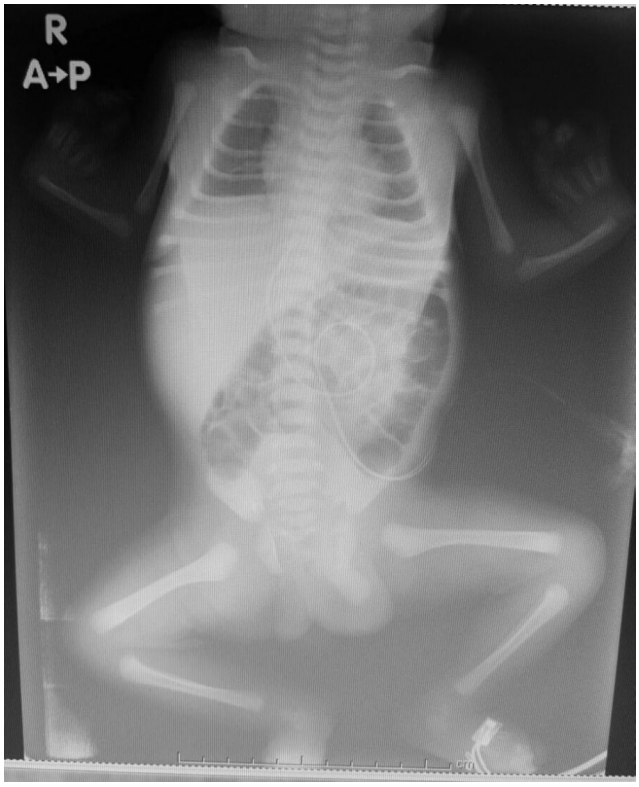

Figure 2. On the X ray-graphy, absence of bilateral radius was shown

Discussion

Thrombocytopenia associated with TAR syndrome is believed to be related to a process of defective megakaryopoiesis resulting from a faulty progenitor cell. Patients usually become symptomatic within the first 4 months of life, and deaths from intracranial hemorrhages often occur in this period (2,4). In a previously published case series of 77 patients, overall mortality rate was 27% and of these, 21 deaths (66.6%) occurred within the first four months, 28.5% in between 4-14 months, and 4.7% after one month (5). Episodes of thrombocytopenia often are triggered by infections, surgical interventions and in some cases, after ingestion of cow's milk. Episode intervals become less frequent, and the severity of the attacks decreases by the time patient reaches the age of two. In our case, the patient received platelet transfusion when severe thrombocytopenia was detected in order to prevent complications.

Leukemoid reaction triggered by stress and infections may occur mostly within the first year of life (6). Leukocyte levels can increase up to 35000/mm^3. Thrombocytopenia may worsen and hepatomegaly can be detected on physical examination (3). We didn't determine leukemoid reaction in the laboratory analysis of our case.

Pathophysiology of anemia, developing in the patients with TAR syndrome within the first year of life, is not clear. It may be due to hemolysis, thrombocytopenia related blood loss, or short lifespan of the erythrocytes (3). We neither observed symptoms related to anemia, nor determined abnormal laboratory analysis in the reported case. The most important skeletal abnormality detected in TAR syndrome is bilateral radius hypoplasia. Autopsy findings have shown that patients have normally attached muscles to carpal bones, and they always have both thumbs and fingers. Upper extremity anomalies associated with TAR syndrome include hypoplastic ulna, hypoplastic humerus and syndactyly. In the reported case, bilateral radii were absent and the hands were deviated toward ulna, but there was no finger abnormality. Abnormalities associated with the lower extremity in TAR syndrome are mild (5,7). In the reported patient, we did not observe pathological findings related to lower limbs, except laterally deviated halluces. The ratio of cardiac problems is 30% among patients with TAR syndrome, and the most common heart defects are tetralogy of Fallot (17.6%), ASD (17.6%), and VSD (17.6%). Echocardiographic evaluation

of our case revealed VSD, PDA, ASD, and pulmonary hypertension.

Hedberg and Lipton (5) showed that TAR syndrome has 18% mortality and the most common causes of death include hemorrhages (88.8%) (intracranial, visceral, and pulmonary), sepsis (5.5%), and congestive heart failure (5.5%).

TAR syndrome can be diagnosed antenatally after 16 weeks of gestation by fetoscopy, X-rays and ultrasonography (8). In our case, the mother had no follow-up during pregnancy. When diagnosed, patients with TAR syndrome should be monitored closely and collaboration should be made with an orthopedics department. Life expectancy is reported normal with successful follow-up. The treatment of thrombocytopenia is also important to prevent complications, and thrombocyte transfusion is necessary when values reach critical level.

Ethics

Informed Consent: Written informed consent was declared by the authors.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ö.B., T.D.T., Ş.H., Design: E.C., Ö.B., T.D.T., Data Collection or Processing: Ö.B., S.B., Literature Search: S.B., Ş.H., Writing: T.D.T., E.C.

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

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

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J Pediatr Res 2017;4(2):78-81
DOI: 10.4274/jpr.08860

The Association of Choledochal Cyst and Pancreatitis: A Case Report and Review of the Literature

Koledok Kisti ve Pankreatit Birlikteliği: Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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ABSTRACT
Choledochal cysts are relatively rare congenital anomalies which are characterized by dilatation of the extra-and/or intra-hepatic bile ducts. Pancreatic involvement before choledochal cyst operation might be a risk factor for postoperative pancreatitis. In this case report, we present a patient who had pancreatic enzyme elevation before choledochal cyst operation and who developed acute pancreatitis after surgery.
Keywords: Choledochal cyst, pancreatitis, child

ÖZ
Koledok kistleri oldukça nadir görülen, karaciğer içi ve/veya dışı safra yollarının dilatasyonu ile karakterize konjenital anomalilerdir. Koledok kist operasyonu öncesi pankreas tutulumunun varlığı operasyon sonrası pankreatik komplikasyonlar için risk faktörü olabilir. Burada koledok kist operasyonu öncesi pankreas enzim yüksekliği bulunan ve operasyon sonrasında akut pankreatit gelişen bir olgu sunulmuştur.
Anahtar Kelimeler: Koledok kisti, pankreatit, çocuk

Introduction

Choledochal cysts are uncommon congenital anomalies of the bile ducts. The incidence of choledochal cyst is reported to be 1/100000-150000 in western societies, whereas it is 1/1000 in Asian societies (1). Although choledochal cysts are usually observed in childhood, they are seen in adults in 25 percent of the cases. Many complications can occur before and after surgery in patients with choledochal cyst. It was argued that pre-operational pancreas involvement could be a risk factor for a possible post-operational pancreatitis (2). This case report aims to discuss the association of choledochal cyst and pancreatitis in the light of the literature, and emphasize the necessity of being careful about acute pancreatitis after choledochal cyst operations.

Case Report

An 18-month-old male patient was guided to our department upon detection of high aspartate aminotransferase (AST): 220 U/L, alanine aminotransferase (ALT): 295 U/L in the examinations held upon his vomiting in an eruptive manner 5 to 6 times in the last 2 days following a fever that started 5 days previously. No medication was

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Received/Geliş tarihi: *24.02.2016* **Accepted/Kabul tarihi:** *06.06.2016*

used by the patient who did not have a known disease, but the father had a history of cholelithiasis. At physical examination, body weight was 11 kg (25 p), height was 84 cm (50-75 p), the patient did not have a significant sensitivity in the abdomen, and system examinations were normal. White blood cell count was: 6500/uL, hemoglobin: 11,8 g/dL, platelets: 412000/uL, AST: 442 U/L, ALT: 607 U/L, total bilirubin: 0.5 mg/dL, direct bilirubin: 0.2 mg/dL, total protein: 7.4 gr/dL, albumin: 4.7 g/dL, gamma-glutamyl transferase: 486 U/L, amylase: 190 U/L, and lipase was: 227 U/L. Abdominal ultrasonography (USG) showed no dilatation in the intrahepatic bile ducts. The main hepatic bile duct was dilated from proximal to the head of the pancreas, and it measured 2.5 cm at the widest point. The cystic duct was dilated and was 5 mm. The gall bladder size, the wall, and the lumen were normal. While the total bilirubin rose to 2.4 mg/dL and the direct bilirubin to 1.8 mg/dL; AST decreased to 67 U/L, ALT to 185 U/L, amylase to 64 U/L and lipase to 63 U/L, following the initiation of intravenous hydration therapy. In the abdominal computed tomography (CT), choledoch was observed to be tortuous and dilated, and the largest area was measured as 28 mm. Pre-operative cholangiography revealed the choledochal cyst as Type I A (Figure 1). Choledochal cyst excision, cholecystectomy, Roux-en-Y hepaticojejunostomy, and appendectomy procedures were performed on the patient. On the first post-operative day, the general condition of the patient was good, with amylase: 68 U/L and lipase: 56 U/L. With the follow-up, feeding began. On post-operative day 9, amylase was found to be 1538 U/L and lipase was 1460 U/L. The patient developed fever and started vomiting. Total parenteral nutritional support, intravenous hydration and antibiotic therapy were initiated and oral nutrition was stopped. Amylase and lipase values gradually decreased and were observed at normal range on postoperative day 23.

Discussion

Choledochal cysts are congenital anomalies of the bile duct and are defined as the abnormal, disproportionate cystic dilatation of the bile duct. More than 60% of the cases are diagnosed in the first year of life. The symptoms are often nonspecific and ambiguous as observed in our patient at diagnosis, and clinical findings vary with age in choledochal cysts cases. The three classical findings are abdominal pain, palpable mass in the upper right quadrant and jaundice. Adults may more frequently present complications. Jaundice and acholic stool in the infant, and intermittent biliary obstruction, or recurrent episodes of pancreatitis in the child are probable findings (3).

Choledochal cysts are classified according to the modified Todani classification (Figure 2) (4). Type I is the most common with a rate of 75-85%. In the diagnosis of choledochal cyst, USG is the best method for evaluating intrahepatic and extrahepatic bile ducts, and gallstones. USG is also important in demonstrating complications such as cystolithiasis, cholangitis, and malignancy. In a study, abdominal pain and jaundice were found to be the most common complaints of patients with choledochal cyst (5). These findings are nonspecific and therefore make the diagnosis difficult, especially during infancy (5). Antenatal diagnosis with USG is also important in terms of the prevention of complications with early surgery (5,6). CT can be used in conditions where distal choledoch duct cannot be monitored due to intestinal gas. CT and USG are useful methods for typing according to the location, size and intra-extra hepatic involvement of the choledochal cysts. Magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP) are other options in bile duct pathologies. As a highly sensitive and non-invasive examination, MRCP has priority over ERCP in patients with suspected choledochal cysts (7).

There may be many hepatobiliary pathologies associated with choledochal cyst. Cystolithiasis is the most common condition associated with choledochal cyst in adults. Many of the intracystic stones have a soft, muddy and pigmented appearance that supports the biliary stasis, which is the primary etiologic factor. Hepatolithiasis is frequently seen in Type IV A choledochal cysts, and is being observed in increasing frequency in the long follow-up. Pancreatitis is a common complaint of referral for patients, especially adults with choledochal cysts. Cholangitis is also a common complication. Malignancy may occur in the choledochal cyst associated cyst, liver and pancreaticobiliary duct.

Treatment varies according to the type of choledochal cyst and associated hepatobiliary pathology. The treatment of Type I includes the excision of the cyst and Roux-en-Y hepaticojejunostomy. In Type II, the diverticulum is excised, and in Type III, cyst excision with or without sphincterotomy was being performed until very recently. The opening of the choledochal and pancreatic duct into the cyst was important in terms of protecting these ducts in the re-anastomosis. Today, endoscopic sphincterotomy, and opening of the upper part of the cyst is preferred. In Type IV B, as in Type I, dilated extrahepatic cysts are completely excised and Roux-en-Y hepaticojejunostomy is applied. Resection of cysts in Type IV A is contradictive. Increased risk of malignancy has been reported in intrahepatic cysts even after the total excision of extrahepatic cysts. The intraductal disease does not require treatment unless hepatolithiasis, intrahepatic ductal stenosis, and hepatic abscess are present, in which situation the affected segment or lobe of the liver can be resected. If Type V is present in a single hepatic lobe, hepatic lobectomy can be performed. Patients with widespread involvement should be followed closely for the development of liver failure, biliary cirrhosis and portal hypertension. These patients may require liver transplantation (7).

The diagnosis of acute pancreatitis is based on the sudden onset of typical abdominal pain with at least three fold increase in the upper limit of the normal range of amylase or lipase. However, serum amylase and lipase

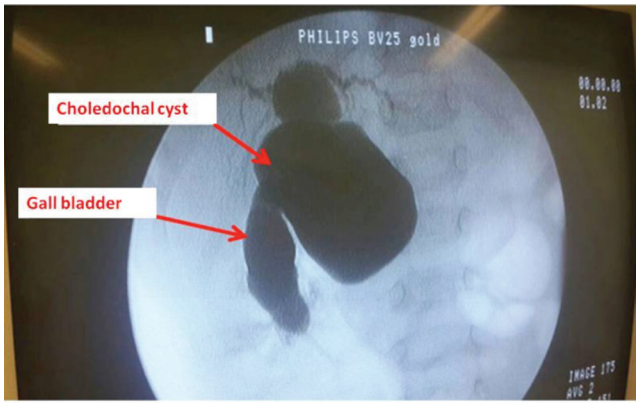
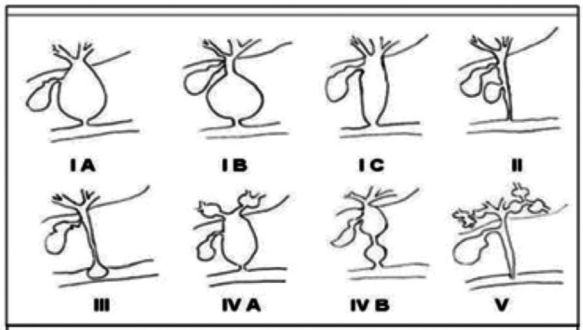


Figure 1. Choledochal cyst image on pre-operative cholongiography



Type I: Cystic dilatation of entire common bile duct I A: Cystic I B: Saccular I C: Fusiform
Type II: Diverticulum of extrahepatic biliary tree
Type III: Cystic dilatation of the intraduodenal portion of common bile duct (choledochocele)
Type IV: Multiple cysts of the intrahepatic and extrahepatic biliary tree IV A: Both intrahepatic and extrahepatic cysts IV B: Multiple extrahepatic cysts without intrahepatic
Type V: Isolated intrahepatic cystic disease (Caroli disease)

Figure 2. Modified Todani classification of choledochal cysts (9)

may be normal in 20% of the cases that are clinically and radiologically considered as acute pancreatitis. As observed in our patient diagnosed with choledochal cyst, amylase and lipase elevation in the serum may occur in cases of biliary system diseases, biliary and pancreatic duct obstructions as well as choledochal cyst. Chronic pancreatitis, which is defined as the chronic inflammation of the pancreas, is rarely observed in children. The most important difference between chronic pancreatitis and acute pancreatitis is that the former causes permanent and progressive morphological and functional damage. No evidence of chronic pancreatitis was found in our patient, who presented a high level of lipase and no radiologic evidence of pancreatitis before the operation. He was clinically and radiologically evaluated as acute pancreatitis after the cyst operation.

There are few studies in the literature on the pancreatic complications of choledochal cysts, especially in children. In their study, Fujishiro et al. (2) found that pre-operative pancreatitis was most commonly seen in Todani Type I C among children with choledochal cysts. Following choledochal cyst operation, pancreatitis findings were seen in 9.7% of patients with pre-operational pancreatitis findings, as was the case with our patient (2). In patients with pancreaticobiliary junction abnormality, reflux of bile to the pancreatic duct, and bile stasis in the distal bile duct may activate pancreatic enzymes and result in pancreatitis. Studies in the field revealed that the incidence of acute pancreatitis in children with choledochal cysts was 0-70.6%, whereas it was observed in a range as wide as 10-54.5% in adults (8,9). Protein plugs are also common in patients with choledochal cysts. It is argued that bile reflux to the pancreatic duct changes the distribution of pancreatic secretion, and given the mucin production in the bile duct, reflux of the pancreatic fluid to the bile duct, and the activation of pancreatic enzymes result in protein plugs in the choledochal cyst (10). Patients with protein plug formation were found to be highly susceptible to pre-operative pancreatitis (2). If protein plugs are soft and fragile, there can be spontaneous regression; the irrigation of the main duct during surgery is a simple and effective way for removing protein plugs. Thus, the risk of post-operative pancreatitis may be reduced (2).

In conclusion, it is important to diagnose the choledochal cyst in the antenatal period, and to treat patients appropriately before any complications develop. It should be kept in mind that patients with pancreatic findings, as in our case, are in the risk group for developing pancreatitis after the operation. Cyst excision and the resolution of bile and pancreatic fluid with hepaticojejunostomy, complete excision of the distal canal, and complete removal of the protein plugs are especially important in cases of choledochal cyst with pre-operative pancreatic complications.

Ethics

Informed Consent: Consent form was filled out by the participant.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Y.Ç.A., C.G., S.T., E.K., Concept: Y.Ç.A., E.K., Design: Y.Ç.A., G.D., Data Collection or Processing: Y.Ç.A., G.D., Analysis or Interpretation: Y.Ç.A., E.K., Literature Search: Y.Ç.A., Writing: Y.Ç.A.

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

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

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J Pediatr Res 2017;4(2):82-4
DOI: 10.4274/jpr.43043

Perianal-Perineal Localized Alveolar-Embryonal (Mixed) Type Rhabdomyosarcoma: Rare Localization, Case Report

Perianal-Perineal Yerleşimli Alveolar-Embriyonel (Mikst) Tip Rabdomiyosarkom: Seyrek Yerleşim, Olgu Sunumu

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ABSTRACT

A 17-year old girl who had been admitted to another hospital with perianal swelling and pain was diagnosed with perianal abscess. She had been given anti-biotheraphy and anti-inflamatory medication. Because her swelling and pain got worse, she was referred to our pediatric clinic. After her physical examination, she was prediagnosed with perianal abscess/tumor, and reffered to our department for magnetic resonance imaging examination, after which she was diagnosed with perianal tumor, and biopsy was performed. Alveolar-embryonal (mixed) type rhabdomyosarcoma (RMS) was diagnosed in the histopathology. Even though RMS is diagnosed frequently in childhood and adolescence, perianal and perineal location for this tumor is relatively rare. We wanted to highlight the rare localization and possible differential diagnosis for this type of tumor.

Keywords: Magnetic resonance imaging, perineal, perianal, rhabdomyosarcoma

ÖZ

Perianal şişlik ve ağrı şikayeti ile apse tanısı alarak izlenen 17 yaşında kız olgu şikayetlerinin geçmemesi ve şişliğin giderek büyümesi üzerine hastanemiz çocuk hastalıkları bölümüne başvurdu. Yapılan fizik muayene sonucunda perianal apse/kitle ön tanısıyla bölümümüzde uygulanan manyetik rezonans görüntülemede perianal/perineal kitle saptanarak yapılan biyopsi ile alveolar-embriyonel (mikst) tip rabdomiyosarkom (RMS) tanısı aldı. RMS, çocukluk ve adölesan döneminde en sık izlenen yumuşak doku sarkomu iken, perianal ve perineal yerleşim oldukça nadirdir. Burada nadir bölge tutulumunu vurgulamayı ve apse gibi farklı klinik ön tanının malignite göstergesi olabileceğini hatırlatmayı amaçladık.

Anahtar Kelimeler: Manyetik rezonans görüntüleme, perineal, perianal, rabdomiyosarkom

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Received/Geliş tarihi: *21.10.2015* **Accepted/Kabul tarihi:** *01.08.2016*
This study was presented as a poster at the 20th Annual Scientific Meeting of Turkish Society of Magnetic Resonance on 21-23 May 2015.

Introduction

Rhabdomyosarcoma (RMS) is a common mesenchymal originated soft tissue tumor in childhood (1-3). The age specific incidence rates of RMS show a bimodal distribution, with the first peak between the ages 2-6, and the second peak between 15-19. The most common location for RMS is the head and neck region with 40% incidence (1). Even though RMS is a common soft tissue sarcoma seen in the childhood and adolescence periods, the perianal and perineal location in genitourinary RMS subgroup is rare with less then a 2% incidence rate (4-6). RMS has four histological types being the embryological, alveolar, botryoid, and pleomorhic. Although in all locations the most common histological type is embryonal; for the perineal region it is the alveolar type (4).

For diagnosis, age, location, clinical-laboratory findings, local invasion, and metastasis are considered. At the time of diagnosis the metastasis rate is 10-20%. The primary imaging modality is magnetic resonance imaging (MRI).

Treatment of RMS needs a multidisciplinary approach involving radiotherapy, chemotherapy, and surgery. Here, we present a case of perianal/perineal RMS, considered as perianal abscess after the first evaluation. With this case, we aimed to emphasize the rare location for RMS, and the fact that different pre-diagnoses such as abscess may be indicative of malignancy.

Case Report

A 17-year-old girl was admitted to the pediatric clinic in another center with a complaint of swelling in the anal region for the last 6 weeks. After the first evaluation, the drainage was planned with the diagnosis of pearianal abscess and during the intervention. During the drainage intervention, there was no infected material and hyperemic mass lesion was observed. The patient was referred to our pediatric department for further evaluation. The first examination at the department of pediatric oncology in our center revealed anal mass accompanied with pain. Erythrocyte sedimentation rate was slightly elevated, and lactate dehydrogenase was detected in the blood. C-reactive protein level was normal. Her pelvic MRI, which was obtained from her first admission, showed an ill circumsribed mass in the perianal region. Because of the non-contrast pelvic MRI protocol from the first admission, and the time interval with the new symptom (pain), we performed the abdominal MRI protocol with contrast medium in our department using Philips Achieva 1.5 Tesla MR machine. The abdominal MRI revealed a subdermal soft tissue mass located in the right ischiopubic fossa, 9x8.5 cm in size, ill circumscribed, and disrupting the anterior borders between the rectal distal segment-anal canal-anus, isointense with muscle in T1 weighted images (T1WI), hyperintense in T2WI, which was heterogeneous and poorly contrasted (Figures 1, 2 and 3). Ultrasound (USG) guided fine needle Tru-cut biopsy was performed. Microscopic review showed a partially diffuse growth pattern and a partially alveolar tumor tissue filling all areas (Figure 4, 5). In some regions tumor cells are rabdomyoblastic and in some regions they are round cells. For this reason, our case was diagnosed as alveolar and embryonal type RMS. Immunohistochemically, tumor cells showed nuclear staining with Myo D1 and cytoplasmic staining with Desmin (Figure 6, 7). Because of the location and the extention of the tumor, our case was not eligible for surgery, so chemotheraphy with ARST 0431 protocol (ifosfamide, etoposide, vincristine, doxorubicin and cyclophosphamide) was started, and on the 20th week of the treatment one session of radiotheraphy was performed. In the follow up a marked regression was detected in the tumor. The treatment and follow up are still ongoing.

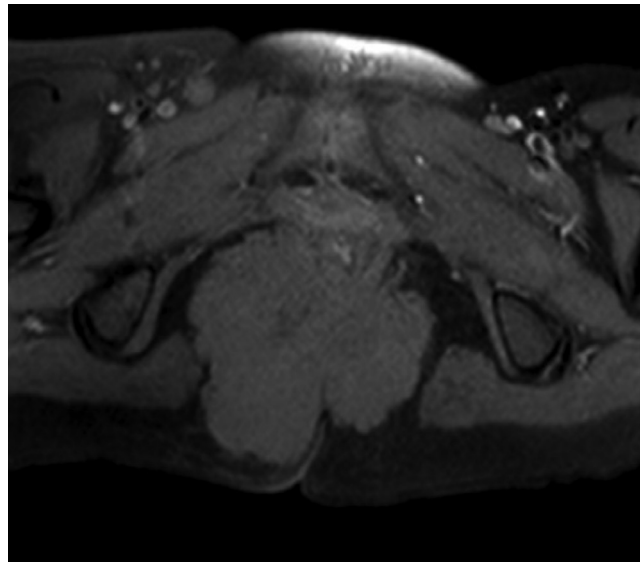

Figure 1. Axial T1 weighted magnetic resonance imaging image shows poorly defined mass in the perianal region

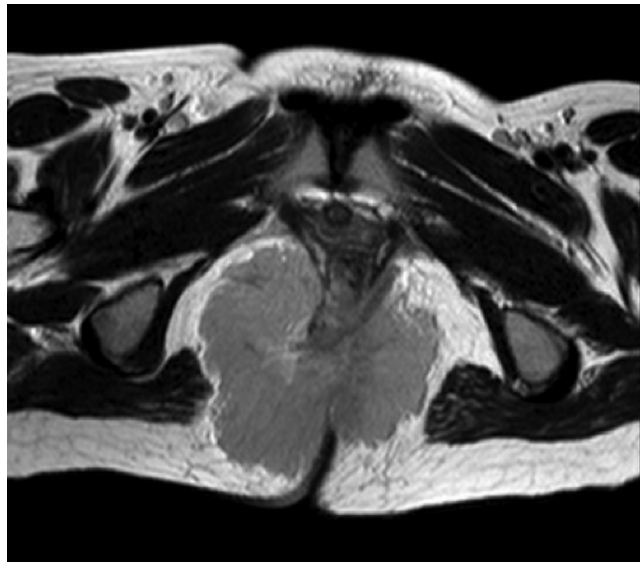

Figure 2. Mass is hyperintense on axial T2 weighted magnetic resonance imaging image

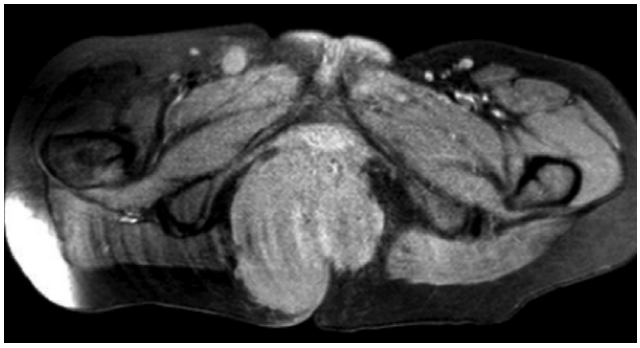

Figure 3. Axial post-contrast T1 weighted image shows homogeneous contrast enhancement of the mass

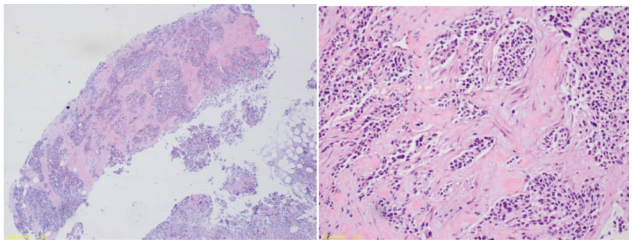

Figure 4, 5. Tumor tissue shows alveolar and diffuse growth pattern for rhabdomyosarcoma

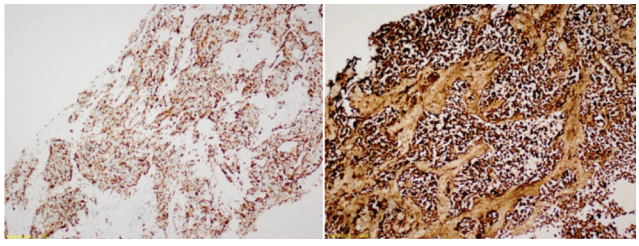

Figure 6, 7. Immunohistochemically tumor cells show nuclear staining with cytoplasmic Myo D1 with Desmin

Discussion

Although RMS is a common soft tissue sarcoma of childhood and adolescence, perianal and perineal location is very rare (5,6). RMS in this location is thought to originate from the muscle layers of the intestinal and genitourinary tract.

For diagnosis a complete blood count and urine test must be done, and tumor markers from blood should be taken. USG, computerised tomography and MRI should be performed according to physical examination signs. Definitive diagnosis is based on histopathology. According to the literature, perineal RMS is mostly the alveolar type (4). Alveolar RMS is a generally ill circumsribed, locally aggressive and oval or round shaped tumor (7). In our case, the histopathology of the tumor was reported as embryonal/alveolar type.

Perineal/perianal RMS has a high rate of misdiagnosis, especially in terms of infectious and inflamatory pathologies such as perianal abscess. Although there is no underlying disease in most cases, it has been shown that RMS is associated with neurofibromatosis, fetal alcohol syndrome, congenital central system anomalies (8). No relationship to any known disease has been detected in our case.

In MRI, like many other soft tissue tumors, RMS is mid-intense in T1WI, mid-hyperintense in T2WI. In other words, the imaging properties of RMS are non-specific. The tumor can be lobulated and multi-septated. The imaging findings of our case are consistent with the literature.

The differential diagnoses of RMS are quite broad because of its placement in many different anatomical areas. This broad differential diagnosis list includes; hemangioma, vascular malformations, adult type soft tissue sarcomas, primitive neuroectodermal tumor, infantile fibrosarcoma, desmoplastic small round cell tumors, rabdoid tumor, non-osseos Ewing's sarcoma.

Although the perianal/perineal region is rare for RMS with no particular imaging findings, it should be considered in the differential diagnosis for perianal/perineal tumors of childhood, and it should be kept in mind that it may interfere with perianal abscess.

Ethics

Informed Consent: Consent form was filled out by the participant.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Y.D., Concept: Y.D., Design: Y.D., Data Collection or Processing: Y.D., H.M., C.T., Analysis or Interpretation: Y.D., H.M., M.G., Literature Search: Y.D., Writing: Y.D., M.G.

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

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

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J Pediatr Res 2017;4(2):85-9
DOI: 10.4274/jpr.52724

Case Report / Olgu Sunumu

Urea Cycle Disorders in Neonates: Six Case Reports

Yenidoğanlarda Üre Döngüsü Bozukluğu: Altı Olgu Sunumu

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ABSTRACT
Urea cycle disorders are a group of diseases associated with hyperammonemia, which causes severe neurological sequelae, seizures and psychomotor retardation. In this study, six newborn cases diagnosed between 2010-2014 as citrullinemia Type I (four cases) and argininosuccinic aciduria (two cases) are presented in terms of clinical course and treatment responses.
Keywords: Newborn, urea cycle disorder, peritoneal dialysis

ÖZ
Üre döngüsü bozukluğu hiperamonyemi ile seyreden ve ciddi nörolojik sekeller, nöbetler, psikomotor retardasyona neden olabilen bir grup hastalıktır. Bu çalışmada 2010-2014 yıllarında yenidoğan döneminde tanı alan dördü sitrülinemi Tip I, ikisi argininosüksinik asidüri olmak üzere altı üre döngü bozukluğu olgusunun klinik seyri ve tedavi yanıtları sunulmuştur.
Anahtar Kelimeler: Yenidoğan, üre döngüsü bozukluğu, periton diyalizi

Introduction

The urea cycle is a metabolic pathway that allows the ammonia to turn into a product so as to remove it from the body. Enzyme deficiencies and transport defects on this pathway lead to hyperuricemia-induced urea cycle disorders (UCD). These enzymes are carbamoyl phosphate synthetase 1 (CPS1), ornithine transcarbamylase (OTC), argininosuccinate synthetase (ASS), argininosuccinate lyase (ASL), arginase and N-acetylglutamate synthetase. Mitochondrial ornithine transporter 1 and aspartate/glutamate transporter deficiency is also responsible for UCD (1). Except for the OTC defect due to the X-linked transition; UCD, an autosomal recessive familial disorder, is seen in 30.000 live births. In the newborn period, UCD presents by different clinical tables ranging from severe disease to very mild findings in childhood and adulthood (2,3). The neonate is the age at which the predisposition to hyperammonemia is more common, and approximately half of the cases give evidence in the neonatal period. Serious neurological sequelae, seizures, severe psychomotor retardation are seen in the survivors of hyperammonic decompensation (1-3). Despite early diagnosis and treatment, there is no good clinical course in the neonatal severe hyperammonemia, but the prognosis could be affected positively. Therefore, immediate diagnosis and treatment is important.

In this article, four cases of citrulinemia Type I, two cases of argininosuccinic aciduria that were diagnosed and started to receive treatment during the neonatal period as

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Received/Geliş tarihi: *03.07.2016* **Accepted/Kabul tarihi:** *12.10.2016*

well as the signs, diagnosis and treatment responses have been presented.

Case Report

Data were obtained by retrospectively examining the files of six patients who were diagnosed as UCD in the neonatal intensive care unit between 2010 and 2014. The gestational weeks of the cases ranged from 36 to 41 weeks, and birth weights ranged from 1990 to 4200 g. Three were girls, three boys. There was consanguinity between the parents of five patients. The demographic data of the cases are given in Table I. The application to hospital took place between the 3rd and 19th days of the postnatal period. They came with nonspecific and similar complaints like nourishment problems, vomiting, sleepiness. Intrusive breathing was remarkable among the complaints. A physical examination of all cases revealed dehydrated appearance, hypotonia and a decrease in newborn reflexes. Due to possibility of sepsis, ampiric antibiotherapy was started after taking blood culture. Blood gas and ammonia levels were studied with a preliminary diagnosis of metabolic disease in the cases in which infectious markers were negative. Respiratory alkalosis was present in the blood gases of all patients, and initial ammonia levels were determined to be between 689 and 1575 µg/dL (N: 68-136 µg/dL). When the results of the metabolic screenings that were sent with the pre-diagnosis of metabolic disease were evaluated, two patients with high argininosuccinic acid (ASA) levels in the plasma and urine were diagnosed with argininosuccinic aciduria, and four patients with no evidence of ASA and anhydrides in the blood and urine, but high serum citrulline levels both in the blood and urine were evaluated as citrullinemia Type I (Table II). Enzyme analysis and genetic tests could not be done.

High-calorie total parenteral nutrition was initiated by stopping protein intake for the cases of hyperammonemia. Oral sodium benzoate was applied at 250-500 mg/kg/day with intervals of six hours. Sodium phenyl acetate (250 mg/kg) and sodium benzoate (250 mg/kg) were administered intravenously for 90 to 120 minutes after the initial (loading) doses of 250 to 500 mg/kg/day. Carbamoyl glutamate (carglumic acid) was administered by enteral route at a dose of 25 mg/kg for six hours after the 100 mg/kg loading. The treatment of patients with no decrease in the control ammonia levels was regulated with oral and intravenous sodium benzoate at 750 mg/kg/day. In the follow-up, it was observed that the ammonia level increased rapidly except for one case, and that one case was observed at the same level. Due to the fact that the control ammonia level did not decrease six hours after the ammonia-removing medical treatment agents (Table III), peritoneal dialysis (PD) was initiated with a PD catheter because of the lack of response of the patients to medical treatment, and the fact that hemodiafiltration is not available in our unit.

Phenobarbital therapy was started because of convulsions in the follow-up of five cases. Electroencephalography (EEG) could not be performed in two cases due to the infusion of midazolam and loss of the patient in early period. EEG was pathologic in two cases, in one case generalized burst suppression pattern, and in the other mild epileptiform disorder originating from the centrotemporal regions of both hemispheres was detected. In one case without convulsion, a sharp wave appearance was observed in the EEG in the right parieto-occipital region due to convulsions following discharge, and phenobarbital treatment was started. Cranial ultrasonography of the cases revealed no pathology. Eyeground examinations were usually normal. Cranial magnetic resonance (MR) and MR spectroscopy (MRS) could be applied to one patient. A myelination defect in both cerebral hemispheres was detected in the MR, while a peak of macromolecules was found to the right of the N-acetylaspartate (NAA) picin in the MRS.

Except for one patient that was admitted on postnatal day 19, five patients required mechanical ventilation support during the first day of admission, showing respiratory disturbance. Decrease in ammonia levels due to PD were detected (Table III). The ammonia level of the three patients decreased to the normal range (<200 µg/dL) between the 1st and 4th days of the PD treatment, and the patients were given oral sodium benzoate. However, a patient with metabolic balance was lost due to sepsis on postnatal day 41. In the other three cases, ammonia levels decreased in the first hours of PD, but patients lost follow-up because PD could not be continued due to catheter dysfunction (Table III).

Table I. Demographic data of cases

Case no	Gestation week	Birth weight (grams)	Gender	Consanguineous marriage	Admission day	Admission symptom
1	38	4100	Female	(+)	3rd day	Nourishment problems
2	41	4200	Male	(+)	3rd day	Vomiting
3	36+2/7	1990	Female	(+)	19th day	Nourishment problems
4	38	3600	Female	(+)	3rd day	Intrusive breathing
5	38	3500	Male	(+)	4th day	Intrusive breathing
6	39	3750	Male	(-)	4th day	Intrusive breathing

Discussion

The UCD mostly has an early onset (<28 days) (except for OTC deficiency), and high mortality especially in the neonatal period (4). Delay may occur due to the imitation of neonatal sepsis during the newborn period. Early diagnosis and urgent treatment are important in terms of prognosis and the influence of the accumulation of toxic metabolites. Continuous veno-venous hemodialysis or PD should be initiated urgently in patients unresponsive to dietary and pharmacological treatment, and continuing ammonio levels above 500 µmol/L (5). Because of the hemodynamic

Table II. Diagnostic laboratory data of cases

Case	Blood gas	Ammonia (µg/dL)	Blood amino acids	Urine amino acids	Urinary orotic acid	Diagnosis
1	Respiratory alkalosis	1126	Glutamine, alanine, citrulline high, ASA very high, Arginine low	*ASA high	High	**ASL deficiency Argininosuccinic aciduria
2	Respiratory alkalosis	1575	Glutamine, alanine, citrulline high, ASA very high, Arginine very low	*ASA high	Could not performed	**ASL deficiency Argininosuccinic aciduria
3	Respiratory alkalosis	748	Glutamine, alanine moderately high, Citrulline very high, Arginine and ornithine low	Citrulline high	Could not performed	**ASS deficiency Citrullinemia Type I
4	Respiratory alkalosis	1133	Glutamine, alanine high, Citrulline very high, Arginine and ornithine moderately low	Citrulline high	High	***ASS deficiency Citrullinemia Type I
5	Respiratory alkalosis	689	Glutamine, alanine moderately high, Citrulline very high, Arginine and ornithine low	Citrulline high	High	***ASS deficiency Citrullinemia Type I
6	Respiratory alkalosis	975	Glutamine, alanine high, Citrulline very high, Arginine and ornithine low	Citrulline high	High	***ASS deficiency Citrullinemia Type I

*ASA: Argininosuccinic acid
**ASL: Argininosuccinate lyase
***ASS: Argininosuccinate synthetase

Table III. Treatment findings and prognosis

Case no/diagnosis	Pre-treatment ammonia (µg/dL)	After medical treatment-before peritoneal dialysis ammonia (µg/dL)	Time to start peritoneal dialysis (days)	24 hr ammonia after dialysis (µg/dL)	Total effective peritoneal dialysis duration (days)	Prognosis
1 Argininosuccinic aciduria	1126	1981	3	713	4	Postnatal exitus due to sepsis at 41 days
2 Argininosuccinic aciduria	1575	1810	3	384	3	Postnatal exitus on day 8
3 Citrullinemia Type I	748	744	19	73	1	Follow-up case
4 Citrullinemia Type I	1133	2359	3	1363	2	Postnatal exitus on day 6
5 Citrullinemia Type I	689	1004	4	702	2	Postnatal exitus on day 8
6 Citrullinemia Type I	975	1387	4	167	4	Follow-up case

and technical complication frequency during the neonatal period, continuous veno-venous hemodiafiltration is recommended instead of hemodialysis. Continuous veno-venous hemodialysis has been shown to be more effective and safer in the removal of toxic metabolites; the duration of dialysis is shorter, and the neurological outcomes are more favorable compared to those of PD (6). PD should be applied as an alternative method to cases where hemodiafiltration is not an option. Although hemodialysis has been considered more effective, some studies have shown that PD is still an effective treatment for hyperammonemic patients (4,5). In our study, PD seemed to be effective when the level of ammonia decreased. PD can be effectively used in the neonatal period with the different indications besides metabolic diseases (7). Due to invasive interventions during PD, many complications like catheter leakage, catheter dysfunction, peritonitis, intestinal perforation can be observed. In our three cases, due to catheter dysfunction, PD can not be continued.

For UCD cases, since the maternal urea cycle metabolizes waste nitrogen that comes from the fetus, there are no complaints or signs during pregnancy and the first few days after birth. Hyperammonemic encephalopathy, which develops following this period of several days of well being, causes neurological findings. As ammonia levels increase; lethargy, vomiting, nourishment problems, hyperventilation, and intrusive breathing occur (2,3,8). Cerebral edema due to hyperammonia causes hyperventilation and respiratory alkalosis (6,8). In our cases, respiratory alkalosis was accompanied by hyperammonia. The prognosis is directly related to the duration of hyperammonemic encephalopathy, the level of ammonia, the type of metabolic disease causing hyperammonia (9). For this reason, treatment should be started in the early period, and the patient transferred without delay to centres specializing in this field.

Blood gas, blood sugar, plasma acyl carnitine profile, blood lactate level, plasma and urine amino acids, urine organic acids, urine ketone and urinary orotic acid levels should initially be tested in cases of high ammonia level for the diagnosis of UCD. In addition, enzyme analysis and molecular genetic tests should be performed. Plasma citrulline level in UCD is helpful in locating the disorder. There is a significant increase in plasma citrulline levels in ASS deficiency (citrulline Type I). In the absence of ASL (argininosuccinic aciduria), plasma citrulline levels increase moderately (5,8). If the plasma citrulline level is at or below trace level, CPS1 and OTC deficiency should be considered. In four of our cases, plasma citrulline levels were found to be very high, with moderate increase in two cases.

Neurological imaging findings in UCD are also associated with the duration of hyperammonemia as well as the level of ammonia. During the acute phase, cranial computed tomography and MR shows cerebral edema, whereas prolonged hyperammonemia shows similar findings to those of hypoxic ischemic encephalopathy. Cortical atrophy, cystic changes in white matter and hypomyelination are detected due to prolonged hyperammonia in OTC deficiency. In UCD, glutamate and glutamine are increased in MRS, and myosinolite is decreased. In addition, a decrease in NAA, cholinergic and creatinine may be detected (8,10). In the MRS in our study a peak of macromolecules was found to the right of the NAA peak, while cranial MR, which could be applied to only one of our patients, showed myelinational defects in both cerebral regions.

During the neonatal period mortality was found to be 50% in severe cases (4). Similar mortality rates in our patients suggest that early initiation of PD may be an alternative treatment in centers where other treatment options are not available.

UCD should be kept in mind in our country, where consanguineous marriages are frequently encountered, in cases normal at birth but showing rapid progressive clinical deterioration, accompanied by convulsions and neurological findings, especially respiratory alkalosis in blood gas. In cases of severe hyperammonemia, early diagnosis and appropriate treatment should reduce mortality. However, since both mortality and severe neurological problems in living cases would increase morbidity, the ammonia should be removed rapidly.

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: External and internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: K.Ç., Ş.K.G., M.K., Concept: K.Ç., Ö.O., Design: D.T., S.A., Data Collection or Processing: K.Ç., D.T., Analysis or Interpretation: E.S., Ş.Ç., S.A., Literature Search: K.Ç., Ö.O., Writing: K.Ç., D.T.

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

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

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