CANPOLAT & OLGAÇ DÜNDAR

Çocukluk Çağında Otizm Spektrum Bozukluğu Multidisipliner Yaklaşım

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ÖNSÖZ

Otizm spektrum bozukluğu, sosyal iletişim ve sosyal etkileşimde bozulmayla birlikte sınırlı ve tekrarlayıcı davranışlar, ilgi alanları ve / veya aktivitelerle karakterize nörogelişimsel bir bozukluk olup sıklığının 1000'de 23 olduğu tahmin edilmektedir. Sıklığı son yıllarda tanı uygulamalarına, sunulan imkanlara ve daha çok tanınmasına bağlı olarak belirgin artış göstermiştir.

Otizmin adı konmadan önce otistik bulgular ve tedavisinin tanımlandığı bilinmektedir. Neo-Latin autismus sözcüğünü, İsviçreli psikiyatri uzmanı Eugen Bleuler şizofreninin belirtilerini tanımlarken 1910 yılında Yunanca autos (αὐτός, kendi anlamında) sözcüğünden türetmiş ve kişinin kendisine olan hastalıklı hayranlığı anlamında kullanmıştır. Otizm sözcüğü günümüzdeki anlamında ilk defa 1938 yılında Viyana Üniversite Hastanesi'nden Hans Asperger tarafından çocuk psikolojisi üzerine verdiği bir derste otistik psikopatlar terminolojisi ile kullanılmıştır. Johns Hopkins Hastanesi'nden Leo Kanner 1943 yılında ilk olarak erken infantil otizm terimini kullanmıştır. Aynı makalede tanımlanan, otistik yalnızlık ve tek düzelikte ısrar gibi özelliklerin tümü hala otistik spektrum bozukluklarının tipik özellikleri olarak görülmektedir. 1960'lı yılların sonunda otizm, yaşam boyu süren, zekâ geriliği, şizofreni ve diğer gelişimsel bozukluklardan farklı ayrı bir sendrom olarak kabul edilmiştir. Otizmin net bir etiyolojisi yoktur. Multifaktöryel etyolojiye sahiptir Çeşitli mutasyonların, genetik, çevresel ve epigenetik faktörlerin etkileşime girdiği ve bozukluğun gelişimi için risk faktörleri olarak katkıda bulunduğu düşünülmektedir. Otizm şüphesi olan her çocuk multidisipliner bir ekip tarafından değerlendirilmelidir. Amerikan Pediatri Akademisi, 18 ve 24 ay arasındaki tüm çocuklarda rutin tarama önermektedir.

Günlük hasta pratiğinde hekimlerimizin sıklıkla karşılaştığı başlıca nörogelişimsel bozukluklardan olan otizm konusunu ele alan bu kitapta, epidemiyoloji, genetik, patogenez, klinik bulgular, eşlik eden komorbid durumlar, tanısal yaklaşım ve testler, biyobelirteçler ve güncel gelişmeler, farmakolojik tedavi dışında davranışsal ve eğitimsel girişimler, gelecekteki tedaviler Çocuk Ruh Sağlığı ve Hastalıkları ve Çocuk Nörolojisi alanında yetkin bilim insanları tarafından ele alınmıştır.

Alanında temel eser niteliği taşıyan bu kitabın, pediatrik hasta tanı ve tedavisini gerçekleştiren çok değerli asistan ve uzman hekimlerimize, eğitim süreçleri boyunca ve günlük pratik uygulamalarında yararlı olmasını temenni ediyor. Bu vesile ile 14 Mart Tıp Bayramımızı kutluyoruz. Yine "Çocukluk Çağında Otizm Spektrum Bozukluğu Multidisipliner Yaklaşım" kitabının baskısında yer alarak katkı sağlayan çok değerli hekimlerimize, Akademisyen Kitabevi'nin çok değerli yönetici ve çalışanlarına teşekkürlerimizi sunarız.

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BÖLÜM 1

OTİZM TANIM VE TARİHÇESİ

Serkan KIRIK[1]

GİRİŞ VE TANIM

Otizm spektrum bozukluğu (OSB), son yıllarda önemi giderek artan, bulguları erken çocukluk çağında başlayan, iletişim ve sosyal etkileşim alanlarında belirgin yetersizlik, basmakalıp ve stereotipik yani yineleyici davranışlar, sınırlı ilgi alanları ve kısıtlı işlevsellik ile kendini ortaya koyan, ömür boyu devam edebilen nörogelişimsel bir bozukluktur. Klinik durumun şiddeti, hastalar arasında hafiften ağıra doğru değişkenlik gösterir. "Otizm" terimi, Yunanca "Autos" kelimesinden türemiş olup "Kendi" anlamına gelir. Bleuler tarafından bu terim ilk olarak 1911 yılında kullanmıştır. Hem şizofreni hastalarında hem de dementia praecoks hastalarında "Bireyin kendi iç dünyasına kapanıp, dış dünya ile olan ilişkilerini kaybetmesi ya da minimalize etmesi" durumunu bu terimle açıklamıştır.[1]

Otizm Spektrum Bozukluğu (OSB), yaygın ancak karmaşık ve heterojen bir nörogelişimsel bozukluktur. Bu nedenle, kişiye özel değerlendirmeler ve müdahale stratejileri, tıbbi, eğitimsel ve toplumsal destek hizmetlerinin koordinasyonu ve uzun vadeli bakım gerektirir. Son 15 yılda, bu alanda önemli değişiklikler yaşanmıştır. Bu değişiklikler arasında; OSB'nin yaygınlığındaki artış, en yaygın kabul gören tanı kriterleri ve sınıflandırma sistemlerindeki değişiklikler, OSB ile ilişkili özelliklerin ve eşlik eden hastalıkların öneminin daha iyi anlaşılması, kanıta dayalı tedavi yöntemlerinin genişlemesi, genetik nedenlerin belirlenmesinde hızlı ilerleme kaydedilmesi, OSB ile ilgili araştırmalara ayrılan fonların ve yapılan yayınların önemli ölçüde artması yer almaktadır. OSB'nin tanı ve yönetimine yönelik klinik kılavuzlar, Amerikan Çocuk ve Ergen Psikiyatrisi Akademisi

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sınıflandırma sisteminde otizm tanısı zamanla birlikte değişime uğrayarak, ICD 10' da YGB başlığı ile isimlendirilmiştir.[2,3,10,16]

Sonuç olarak otizm, yıllar içinde farklı isimler ve tanımlamalar altında incelenmiş; bu tanımlamalar zamanla evrimleşmiştir. Ancak günümüzdeki anlamıyla ilk kez 20. yüzyılda tanımlanmıştır. Otizmin tanı kriterlerindeki değişikliklere ek olarak bireysel eğitimin etkisinin kanıtlanmasıyla önemli mesafeler katedilmiştir. Genetik ve nörobiyolojik çalışmaların hızlanmasıyla otizmin kalıtsal yönü daha iyi anlaşılmıştır. Tüm bunlar OSB'nun erken teşhisinin, bireyselleştirilmiş eğitimin ve sosyal desteklerin otizmli bireylerin yaşam kalitesini artırmada kritik bir rol oynadığı ortaya koymaktadır. İlerleyen zamanda yapılacak araştırmalar; genetik faktörler, çevresel etkileşimler ve bireyselleştirilmiş tedavi yaklaşımlarını daha iyi anlamaya odaklanacaktır.

KAYNAKLAR

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BÖLÜM 2

ÇOCUKLUK ÇAĞINDA OTİZM SPEKTRUM BOZUKLUĞU: EPİDEMİYOLOJİ

Fatma SARGIN [1]
Hurşit FERAHKAYA [2]
Ahmet Sami GÜVEN [3]

GİRİŞ

Otizm Spektrum Bozukluğu (OSB), bireylerin sosyal etkileşimde bulunma, iletişim kurma ve davranışsal esneklik konusunda zorluk yaşadıkları, geniş bir klinik spektrumda yer alan nörogelişimsel bir bozukluktur. OSB semptomları genellikle erken çocukluk döneminde başlamaktadır ve etiyolojisinde genetik, çevresel ve nörobiyolojik faktörlerin etkileşimi önemli rol oynamaktadır. Çocukluk çağında OSB'nin prevalansı, tanı kriterlerinin ve tanı süreçlerine dair bilgi ve veriler zamanla değişim göstermiştir. Bu bölümde, çocukluk çağındaki OSB'nin epidemiyolojik özellikleri, prevalansı, risk faktörleri ve coğrafi farklılıklar ile birlikte eşlik eden tıbbi durumlar ele alınacaktır.

EPİDEMİYOLOJİK ÖZELLİKLERİ, PREVALANSI, RİSK FAKTÖRLERİ VE COĞRAFİ FARKLILIKLAR

Otizm Spektrum Bozukluğu prevalansına ilişkin tahminler, çalışma metodolojisine ve değerlendirilen popülasyona göre değişiklik göstermektedir. Avrupa, Asya ve Amerika Birleşik Devletleri'nde genel OSB prevalansı, 1000 kişide 2 ile

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şı, tanı süreçlerinin iyileşmesi ve çevresel faktörlerin etkisi ile ilişkilidir. OSB'de erken tanının öneminin vurgulanması gerektiği bu alanda yapılan çalışmalarda öne çıkmaktadır. Gelecekte, genetik ve çevresel etkileşimlerin daha derinlemesine incelenmesi, otizm spektrumundaki bireylerin ihtiyaçlarına yönelik daha etkili tedavi ve destek stratejilerinin geliştirilmesine olanak sağlayacaktır.

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BÖLÜM 3

OTİZM SPEKTRUM BOZUKLUĞU ETİYOLOJİSİ

Mürşide ŞAHİN [1]
Esra DEMİRCİ [2]

GİRİŞ

Otizm spektrum bozukluğu (OSB), DSM 5'te sosyal iletişim ve etkileşiminde kısıtlılık anormal ve sabit ilgi alanları ve tekrarlayan davranışlarla kendini gösteren bir nörogelişimsel bozukluk olarak tanımlanmaktadır.[1] Amerika Birleşik Devletleri'ndeki en son tahminlere göre, 36 çocuktan 1'i OSB'den etkilenmektedir.[2] Prevelansı gittikçe artmakla birlikte etyopatogenezi hala gizemini korumaktadır.

OSB'ye ilişkin ilk araştırmalar davranışsal gözlemlere ve psikanalize odaklanmıştır. Yirminci yüzyılın ikinci yarısında, genetik ve nörobilimdeki ilerlemelerle birlikte araştırmacıların OSB'nin biyolojik temelini keşfetmeye başlamasıyla birlikte çalışmalar genetik faktörlere, beyin yapısı ve işlevindeki anormalliklere odaklanmıştır. Yirmibirinci yüzyılda araştırmacılar yalnızca OSB ile ilişkili belirli genetik varyantları tanımlamakla kalmamış, aynı zamanda çevresel faktörler ile genetik duyarlılık arasındaki etkileşimi de keşfetmeye başlamışlardır.[3]

Yapılan çalışmalar OSB'nin etyolojisinde hem genetik hem de çevresel faktörlerin önemli bir rol oynadığını göstermekte[4] olup; etyolojisinde genetik temelin bulunduğu, çevresel etmenlerin epigenetik değişiklikler üzerinden riski arttırdığı, nöroimmunilojik mekanizmaların nöronal bağlanırlığı etkilediği nörogelişimsel bir bozukluk olarak tanımlanmaktadır.[5] Etyopatogenezine dair yapılan

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ğunu ve epigenetik mekanizmaların otizmin gelişimine nasıl katkıda bulunduğunu anlamak önemli bir araştırma alanıdır.

3. **Multi-Omik Veri Entegrasyonu:** Genomik, transkriptomik, proteomik ve metabolomik verilerin entegrasyonu, otizmin moleküler düzeyde daha kapsamlı bir şekilde anlaşılmasına ve tedavi hedeflerinin belirlenmesine yardımcı olabilir.
4. **Nörogelişimsel ve Beyin Görüntüleme Çalışmaları:** Beyin gelişimiyle ilgili yapısal ve fonksiyonel farklılıkları inceleyen nörogörüntüleme tekniklerinin kullanımı, erken dönemde biyomarkerler belirlememize ve müdahale için kritik zaman dilimlerini saptamamıza yardımcı olabilir.
5. **Bireysel Farklılıklar ve Kişiye Özel Tedavi Yaklaşımları:** OSB'nin heterojen doğası göz önünde bulundurularak, bireysel genetik, nörobiyolojik ve davranışsal özelliklere dayalı otizm alt gruplarının belirlenmesi ve kişiye özel tedavi yöntemlerinin geliştirilmesi önemlidir.

Bu alanlarda yapılacak araştırmalar, OSB'nin çok faktörlü doğasını daha derinlemesine anlamamıza, daha erken tanı konmasına ve daha etkili müdahalelere olanak sağlayarak, otizmli bireylerin yaşam kalitesini artıracaktır.

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BÖLÜM 4

OTİZM GENETİĞİ

Elif Funda ŞENER[1]

OTİZMİN GENETİK TEMELLERİ

Otizm spektrum bozukluğu (OSB), anormal sosyal etkileşim, tekrarlayıcı davranışlar ve gecikmiş dil ve bilişsel beceriler ile karakterize bir hastalıktır.[1,2] OSB, çocukluk döneminde ortaya çıkan ve yaşam boyu devam eden nörolojik bir işlev bozukluktur.[3,4] Dünya genelinde nüfusun yaklaşık %1'inde OSB teşhis edilir ve erkek:kız prevalans oranı 3-4:1'dir.[5,6] Dil gelişiminde gecikme olmayanlar veya kızlar genellikle daha geç teşhis alırlar.[7] Hatta bazı OSB vakalarının önemli bir kısmı, yetişkinliğe kadar bile göz ardı edilebilir.[8] OSB'nin altında yatan nedenleri belirlemek, hasta ve ailelerine destek sağlamak için çok önemlidir. Bu alanda atılacak her adım erken teşhis konulmasına ve tedaviye destek sağlayabilir. Birincil klinik semptomların ötesinde, otizm teşhisi konulan önemli sayıda bireye aynı zamanda zihinsel engellilik, epilepsi, anksiyete, obsesif-kompulsif bozukluk, uyku bozuklukları, depresyon ve gastrointestinal sorunlar, otoimmün bozukluklar ve obezite gibi fiziksel rahatsızlıklar da eşlik etmektedir.[9,10]

OSB'nin etiyopatogenezi karmaşıktır ve heterojen bir doğaya sahiptir. Klinik fenotipteki değişkenlikle birlikte bu heterojenlik, OSB için kesin bir temel oluşturulmasını engelleyen en önemli faktör arasında yer almaktadır[11]. OSB'nin etiyolojisinde çeşitli ve kümülatif yollarla etkileşime giren çevresel, metabolik, immün ve genetik mekanizmalar bulunmaktadır.[12,13] OSB'ye katkıda bulunduğu bilinen çevresel faktörler arasında ebeveyn yaşı, perinatal faktörler, seks steroidleri, anne sağlığı ve anne beslenmesi ve ayrıca fetüsün uyuşturuculara, toksinle-

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luyla tanımlanabilir. Bugün için bozulduğunda saf OSB ile benzersiz bir şekilde ilişkili olduğu bilinen tek bir moleküler yolak yoktur. Sadece OSB'ye neden olan ve diğer nörogelişimsel veya psikiyatrik bozukluklara atfedilemeyen gen varyantlarının sınıflandırılması araştırılmaktadır.[9] Sinaptik işlevlerle ilişkili genlere odaklanmak, OSB'nin altında yatan genetik ve nöral mekanizmaların daha iyi anlaşılmasına yol açabilir.

Özetle; otizmin genetik kökeni olsa da bu genetik risk genellikle tek bir gen mutasyonundan değil, potansiyel olarak yüzlerce ila binlerce gendeki birçok küçük varyasyonun kümülatif etkisinden kaynaklanır ve bu durum vakaların büyük bir çoğunluğunu açıklamak için yetersiz kalır.[15,35,203,204] Gen ifadesindeki bu ince değişiklikler, toplu olarak bir bireyin OSB'ye yakalanma olasılığı üzerinde önemli bir etkiye sahip olabilir. Gen ifade profilindeki değişiklikler, OSB patogenezini ve ilerlemesini belirlemede çok önemlidir ve OSB nedenlerini anlamada gen ifadesi çalışmalarının ayrıca bir önemi vardır. Gelecekte de OSB'nin genetiğini anlamaya yönelik yapılacak çalışmalarda bu noktaların ve özellikle epigenetiğin etkilerinin de dikkate alınması yararlı olacaktır. Davranışsal terapiler ve müdahaleler OSB'li bireylerin yaşam kalitesini artırabilse de, şu anda bu bozukluk için genel bir tedavi seçeneği yoktur.[38] Gelecekte daha etkili farmakolojik tedavilerin geliştirilmesi için yeni ilaç hedeflerinin bu alanda belirlenmesi gereklidir.

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BÖLÜM 5

OTİZM SPEKTRUM BOZUKLUĞU PATOGENEZİ

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GİRİŞ

Otizm spektrum bozukluğu (OSB); erken başlangıçlı anormal sosyal iletişim, kısıtlı tekrarlayıcı davranışlar ve ilgi alanlarıyla karakterize bir grup gelişimsel nörolojik bozukluktur. İlk olarak 1980 yılında ebeveyn davranışından ziyade beyindeki yapısal farklılıklar nedeniyle ortaya çıktığı dile getirilmiştir.[1] OSB, genetik ve çevresel faktörlerin karmaşık bir etkileşiminden kaynaklanan, davranışsal anormallikler olarak ortaya çıkan etiyolojisi son derece karmaşık heterojen bir durumdur. Etiyolojik, fenotipik ve prognositik heterojenite OSB için klinik tanıyı ve tedavinin bireyselleştirilmesini zorlaştırır ve çeşitlendirir.[2]

1.GENETİK FAKTÖRLER

Otizm, genetik ve çevresel faktörlerin etkileşimi ile ortaya çıkmaktadır. Yapılan çalışmalarda, otizmin gelişiminde hem nadir mutasyonların hem de sık görülen genetik varyasyonların önemli rol oynadığını gösterilmiştir. Bu çalışmalar, transkripsiyon, translasyon, sinaptik bağlantılar, epigenetik modifikasyonlar ve bağışıklık sistemine ilişkin sinyal yolları gibi ortak moleküler mekanizmaların otizmin patogenezinde önemli bir rol aldığını ortaya koymaktadır. Sinaptik proteinlerin işlevindeki bozukluklar, nöronlar arasındaki iletişimin bozulmasına ve otizme özgü klinik semptomların gelişimine zemin hazırlamaktadır. İkiz,

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göre daha güçlü olması ve oksidatif strese karşı daha az duyarlılık koruyucu etki olarak değerlendirilmiştir.[47]

7.BEYİN – BAĞIRSAK AKSI

OSB tanılı çocuklarda kabızlık, diyare, reflü ve besin intoleransı gibi gastrointestinal sorunlar sık karşımıza çıkmaktadır. Otizm ve mikrobiyata ilişkisini inceleyen çeşitli çalışmalar bulunmaktadır. Bu çalışmalar, otizmli çocuklarda gastrointestinal işlev bozukluklarının yaygın olduğunu göstermektedir. Bağırsak geçirgenliğinin artışı ve mikrobiyom değişiklikleri, enflamatuar süreçleri tetikleyerek serebral fonksiyonlarını etkilemektedir. Ayrıca, bazı genetik mutasyonların bağırsak motilite bozukluklarına yol açtığı bildirilmitir. Bağırsak-mikrobiyom-beyin ekseninin ASD'deki rolü giderek daha fazla önem kazanmaktadır.[48-48] Ketojenik diyetin ASD hayvan çalışmasında bağırsak mikrobiyal dengesini düzenleyerek sosyal iletişimi ve davranış biçimini iyileştirdiği gösterilmiştir.[50] Ketojenik diyet; mitokondriyal fonksiyonun desteklenmesini, oksidatif stresin azaltılmasını ve GABA seviyelerinin düzenlenmesini sağlamaktadır.[51]

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BÖLÜM 6

OTİZM KLİNİK BULGULARI

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Nilüfer ELDEŞ HACIFAZLIOĞLU [2]
Şaziye Senem BAŞGÜL [3]

GİRİŞ

Otizm spektrum bozukluğu (OSB); sözel ya da sözel olmayan iletişimde zorluk, sosyal etkileşimde bozukluk, tekrarlayıcı davranışlar ve kısıtlı ilgi alanı ile karakterize nörogelişimsel bir bozukluktur (DSM 5, *Diagnostic and Statistical Manual of Mental Disorders*).[1] Klinik belirtilerin hastalar arasında ve zaman içinde değişebildiği, yaşam boyu devam eden bir durumdur.[2] Çevresel faktörler (klinik heterojenite, yaş, zeka düzeyi, bireyselleştirilmiş eğitim hizmetleri, konuşma, dil ve davranışsal müdahaleler) fenotipi etkileyebilirler.[3] Ayrıca OSB'ye özgü belirtiler diğer nörolojik, genetik ve metabolik hastalıklarda da görülebilirler.

OSB terimi ilk kez 1911'de Bleuler tarafından gerçekle bağın kopması ve iletişim kurmada zorluk olarak tanımlanmıştır.[4] Leo Kanner, iletişim ve sosyal becerilerde eksiklikleri olan, amaçsız tekrarlayan davranış kalıpları sergileyen ve zamirleri tersten kullanan çocuk ve ergenler için infantil OSB terimini kullanmıştır.[5,6] Hans Asperger tarafından 1944 yılında otistik psikopati teriminin kullanılması nedeni ile OSB uzun yıllar şizofreninin erken bir belirtisi olarak düşünülmüştür.[4] Rutter, OSB'ye 1978 yılında klinik bulguların 30 aydan önce başlaması, heterojen davranışlar, sosyal etkileşimde ve iletişimde bozukluk kriterle-

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SONUÇ

OSB yaşam boyu devam eden, klinik belirtilerin zaman içinde değişebildiği, erken tanı ve tedavi ile çocuğun ve ailesinin yaşam kalitesinin yükseltilebildiği, gelişimsel ve heterojen bir bozukluktur. Mümkün olan en erken zamanda OSB olan çocuklara özel eğitim fırsatı sağlanabilmesi amacıyla ve olası gecikmeleri engellemek için ailelerin OSB'nin erken dönemlerdeki belirtileri konusunda farkındalıklarının yüksek olması hayati bir önem taşımaktadır. Bu noktada, ailelerin "Çocuğum büyüdükçe açılır." düşüncesi oldukça yanlıştır. Çünkü gelişim üst üste konan basamaklar halinde ilerler ve beyin gelişimi açısından ilk üç yaş hayati öneme sahiptir. Ancak; OSB'nin erken fark edilmesi ve tanı konulması noktası kadar, bu tanının güvenilirliği de çok kritiktir. Aşırı tanısal değerlendirme yapılmasının da önüne geçilmelidir. Özellikle akraba evliliği ve ailesinde nörolojik hastalığı olan birey bulunan hastalar ile doğum öncesi, doğum sırası ve doğum sonrasında risk faktörleri olan çocuklar başta olmak üzere; etiyolojinin saptanması ve eşlik eden komorbid durumların tespit edilebilmesi için riskli tüm çocuklar bir hekim tarafından değerlendirilmelidir. Öncelikle tanı ve ayırıcı tanı açısından bir çocuk ve ergen psikiyatristi tarafından muayene edilmeli, sonrasında etiyoloji ve ilave nörolojik bozuklukların değerlendirilmesi için bir çocuk nöroloğu tarafından ayrıntılı olarak değerlendirilmelidirler. Tüm bu değerlendirmeler sonrasında da, OSB'li çocuklarda kanıta dayalı tek uygulama olan özel eğitim desteğine mümkün olan en erken zamanda başlanmalıdır.

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BÖLÜM 7

OTİZM SINIFLAMASI VE TANI KRİTERLERİ

Pınar ARICAN[1]

GİRİŞ

Otizm spektrum bozukluğu (OSB) tanı kriterleri, 1967 yılında uluslararası sınıflandırma sistemlerine dahil edilmesinden sonra 2013 yılında yayınlanan DSM-V (Diagnostic and Statistical Manual of Mental Disorders; Ruhsal Bozuklukların Tanısal ve İstatistiksel El Kitabı, beşinci baskı)'e kadar birçok kez değiştirilmiştir. Komite, DSM-V'in birincil hedefinin, klinisyenlerin hem yaşam boyu hem de bilişsel ve dil işlevlerinin tüm davranış aralığında OSB'yi teşhis etmek için mümkün olduğunca doğru bir şekilde yansıtan tanı kriterlerini sağlamak olduğuna karar vermiştir. DSM-V'e önerilen revizyonlar, klinisyenlerin tanı kategorileri içinde psikiyatrik ve ilgili semptomların hem varlığını hem de şiddetini derecelendirmesine olanak sağlamayı amaçlamıştır. Otizm spektrum bozukluğunun uygun destek ve tedavisi öncelikle doğru tanı ve sınıflandırmayı gerektirmektedir.[1-3] Bu nedenle tanı kriterlerinin ve sınıflandırma sistemlerinin güvenilirliği klinisyenler ve araştırmacılar açısından oldukça önemlidir.

Amerikan psikoloji derneği, 2013 yılında DSM-V'i yayınladığında, tanısal duyarlılığı korumak ve tanısal özgüllüğü geliştirmeye devam etmek amacıyla OSB tanı kriterlerinde önemli değişiklikler yapmıştır.[4] DSM-V tanı kriterlerindeki yapılan değişiklikler, OSB'nin tanısında önemli iki konuyu vurgulamaktadır. İlk konu, bu bozukluğun tanısına yardımcı olacak net bir nesnel tanı ölçüsünün olmamasıdır. Tanı kliniktir ve daha nesnel testler bile yorumlamada hala biraz özneldir. Belirli bir otizm tanısına yol açan tek bir gen, toksik maruziyet

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BÖLÜM 8

OTİZM OLGULARINA TANISAL YAKLAŞIM: PEDİATRİK VE NÖROLOJİK DEĞERLENDİRME

Elif DİDİNMEZ TAŞKIRDI [1]
Nihal OLGAÇ DÜNDAR [2]

GİRİŞ

Otizm spektrum bozukluğu (OSB), sosyal iletişim ve etkileşimde bozulmayla birlikte sınırlı ve tekrarlayıcı davranışlar, ilgi alanları ve/veya aktivitelerle karakterize, erken başlangıçlı bir nörogelişimsel bozukluktur. Klinik belirtiler hastalar arasında ve çocuğun gelişim süreci boyunca oldukça değişkenlik gösterebilir. Dil gecikmeleri ve alışılmadık sosyal beceriler genellikle 12 ila 24 ay arasında fark edilirken, garip ve tekrarlayıcı davranışlar genellikle yaşamın ikinci yılında belirgin hale gelir.[1] Kapsamlı otizm değerlendirmesi multidisipliner bir ekip tarafından yapılan değerlendirmeleri içerir. Değerlendirme ekibinde birden fazla uzmanın bulunması, teşhis sürecini hem kolaylaştırır hem de kapsamlı bir yönetim planının oluşturulmasına yardımcı olur. Tanı ayrıntılı gelişimsel öykü, klinik değerlendirme ve standart tanı araçlarının kullanımı temelinde konulur. Tanıyı doğrulayan herhangi kesin bir biyobelirteç bulunmamaktadır; tanı, **DSM-5-TR** kriterlerine dayanarak konur ve alternatif tanıların dikkatlice dışlanmasını gerektiren uzman değerlendirmesiyle kesinleştirilir. Bu süreçte, birinci basamak testler (örneğin, kromozomal mikrodizi analizi, erkekler için Frajil X sendromu DNA testi, odyoloji değerlendirmesi,vb.) yapılmalı ve erken müdahale hizmetleri başlatılmalıdır.[2,3] Amerikan Pediatri Akademisi, 18. ve 24.aylarda rutin tarama

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olarak işitme değerlendirmesi yapılmalıdır. Gerekli görüldüğünde uygun işitme cihazları sağlanmalıdır.[72, 73]

Genel popülasyondaki çocuklara kıyasla OSB'li çocuklarda kaba motor becerilerde ve koordinasyonda hafif gecikmeler yaşama olasılığı daha yüksektir ve erken motor gecikmeleri ile sonraki dil ve uyumsal gelişim arasındaki bir ilişki olduğu öne sürülmektedir.[74, 75] Genel tarama testleri veya uyumsal ölçümler, çocuk nöroloğu veya fizyoterapist tarafından yapılacak resmi bir değerlendirmeden fayda sağlayabilecek motor gecikmeleri gösterebilir.

Görsel olarak dikkatsiz olan, tekrarlayıcı davranışlar sergileyen (örneğin, gözlerini ovuşturma, kısma veya nesneleri aşırı yakından inceleme) ya da göz teması kurmayan çocukların ilk değerlendirmesinde görsel işlev de dikkate alınmalıdır. Azalmış görme keskinliği, bakışı etkileyebilir ve eğitim ortamında özel düzenlemeler gerektirebilir.[76] Görme bozukluğu olan çocuklar ayrıca tekrarlayıcı motor davranışlar da gösterebilirler.

Duyusal değerlendirme için yaygın olarak kullanılan değerlendirme araçları (Kısa Duyusal Profil gibi), ebeveynlerin çocuklarının koku, tat, görme, işitme ve dokunma duyularına ilişkin algısını ölçmeye yardımcı olur.[77] Bu tür anketler, duyusal rahatsızlık olarak kabul edilen durumları belirlemenin yanı sıra, motor hiperaktivite ve hipoaktiviteyi de duyusal arayış veya duyusal kaçınma davranışları şeklinde değerlendirebilir. Bu belirtiler, eş zamanlı olarak DEHB varlığına işaret edebilir. Duyusal semptomlar, genellikle daha küçük yaşlarda daha belirgindir ve OSB'nin alt tiplerini tanımlamada yardımcı olabilir.[78, 79]

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BÖLÜM 9

OTİZM OLGULARINA TANISAL YAKLAŞIM: PSİKİYATRİK DEĞERLENDİRME

Özlem ŞİRELİ [1]

GİRİŞ

Otizm spektrum bozukluğu (OSB) karşılıklı sosyal ilişki ve iletişim örüntülerinde niteliksel anormallikler, ilgi ve etkinliklerde kısıtlılık, tekrarlayan basmakalıp davranışlarla karakterize nörogelişimsel bir bozukluktur[1]. Epidemiyolojik çalışmalara göre OSB'nin yaygınlık oranı %1-2 olup güncel prevalans çalışmaları görülme sıklığının arttığına işaret etmektedir.[2,3] OSB'de çoğunlukla belirti ve bulgular yaşamın erken dönemlerinde ortaya çıkmakta ve yaşam boyu devam etmektedir. Erken tanı, tedavi müdahalelerin etkinliği açısından hayati öneme sahiptir.

OSB hem nedensel hem klinik görünüm açısından heterojen bir yapıya sahiptir. OSB'li bireyler bilişsel ve dil gelişiminde kısıtlılık, duygusal ve davranışsal sorunlar, uyku ve yeme bozuklukları; dikkat eksikliği, anksiyete, depresyon, kendine zarar verme, saldırganlık gibi eşlik eden psikiyatrik ve diğer tıbbi hastalıklar olmak üzere birçok alanda sorun yaşayabilirler.[4] Tanısal değerlendirmede bir çocuk ve ergen psikiyatri uzmanının yanı sıra bilişsel ve dil gelişimin ayrıntılı değerlendirilmesi için klinik psikolog, diğer tıbbi değerlendirmeler için ilgili pediatrist olmak üzere multidisipliner bir yaklaşım gereklidir.[4]

OSB'de tanısısal değerlendirme süreci, psikiyatrik muayene ve psikometrik değelendirmeler, gerekli diğer tıbbi incelemeleri kapsamaktadır. Tıbbi incelemeler, ayrıntılı gelişimsel ve tıbbi öykü, dismorfi, konjenital anomaliler açısından fizik muayene, motor beceriler, işitme ve görme muayenesi gibi temel tıbbi de-

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BÖLÜM 10

OTİZM OLGULARINDA TEMEL LABORATUVAR TESTLERİ

Turgay ÇOKYAMAN [1]

GİRİŞ

Otizm, kendi anlamına gelen İngilizce ‘’autism” kelimesinin çevirisidir. Otizmin karakteristik davranışsal özellikleri bilim insanları tarafından ilk kez 1943’te tanımlamıştır.[1] Ancak Ruhsal Bozuklukların Tanısal ve İstatistiksel El Kitabı-III (DSM-III)’te ayrı bir bozukluk olarak tanımlanması 1980’i bulmuştur.[2] En son 2013’te DSM-V’de “gelişimsel bozukluk spektrumu” terimi otizm spektrum bozukluğuna (OSB) değiştirildiğinde yeni tanı kriterleri önerilmiştir.[3] Günümüzde de adlandırma, tanı kriterleri ve olası etiyolojik mekanizmalar hakkında görüşler birtakım değişikliklere uğrayarak devam etmektedir.

OSB sosyal ve iletişim bozuklukları, dar ilgi alanları, basmakalıp ve tekrarlayıcı davranışlarla karakterize gelişimsel nöropsikiyatrik bir bozukluktur. OSB'nin yaygınlığı yalnızca Amerika Birleşik Devletleri’nde değil, aynı zamanda tüm dünyada da artmaktadır. Dolaysıyla OSB, tüm dünyada önemli bir halk sağlığı sorunu endişesi haline gelmiştir. OSB’nin etiyolojisi oldukça karmaşıktır ve çevresel, genetik ve birtakım nörolojik faktörler suçlanmaktadır.[4] OSB, sinir sisteminin gelişimsel bozukluklarının yanı sıra nörodejeneratif hastalıklarında da görülebilmektedir.

OSB konusunda farkındalığın artması ve toplumda daha fazla tarama testinin yapılması bu hastalığın görülme sıklığının arttığına dair görüşlerin doğmasına neden olmuştur. Ancak son yıllarda yapılan çalışmalar öncekilerle kıyaslandığında toplumdaki OSB sıklığının arttığına işaret etmektedir ve özellikle

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tanısı, önlenmesi veya tedavisinde yararlı olabilecek potansiyel biyobelirteçler olarak referans seviyelerinin hala netlik kazanmadığı görülmektedir.[57]

Diğer yandan bazı araştırmalarda OSB ve çölyak hastalığı arasında zayıfta olsa bir birliktelikten bahsedilmektedir. Ancak glutenin otizm semptomlarını ve yaşam kalitesini kötüleştirmede olumsuz bir etkiye sahip olmadığı gösterilmiştir. Glutenin OSB üzerinde olası olumsuz etkilerini göstermeye çalışan araştırmaların deneysel tasarım ve uygulamaları ve de sonuçları oldukça heterojendir. Dolaysıyla bu konuda hala genel bir yorum yapılması çok mümkün değildir. Diğer taraftan gluten kısıtlama diyetleri ebeveynlerinde desteği ile OSB'li çocuklara yaygın olarak uygulanmaktadır. Bu yönü ile bakıldığında glutensiz diyetin bu yüksek kabul görme oranı daha dikkatli ve titiz araştırmaları hak etmektedir.[58]

Günümüzde hızla çoğalan sosyal medya araçlarında bilimsel desteği olmayan vurgulu iddialar otizmin tedavi edilebilir bir nedenini bulma umuduyla birçok ebeveyni çeşitli laboratuvar testlerini yapmaya yönlendirmektedirler. Çölyak antikorları ve glutensiz diyet, immünolojik veya nörokimyasal anormallikler, vitamin seviyeleri gibi mikro besinler, saçtaki eser elementler, bağırsak geçirgenliği, dışkı analizi veya fekal transfer, idrar peptitleri gibi klinik testlerin yapılmasını destekleyen güçlü ve genelleşmiş kanıtlar yoktur.[59,60]

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BÖLÜM 11

OTİZM BİYOBELİRTEÇLERİ VE GÜNCEL GELİŞMELER

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GİRİŞ

Amerikan Pediatri Akademisi, 18 ve 24 aylık çocuklar için rutin otizm taraması önermektedir. Otizmin erken tanısında henüz sadece davranışsal özellikler değerlendirilmektedir fakat nesnel teşhis için biyobelirteçlerin varlığına ihtiyaç duyulmaktadır. Biyobelirteçler, otizm spektrum bozukluğu (OSB) için büyük bir potansiyel sunsa da bu alanda karşılaşılan metodolojik ve klinik zorluklar, biyobelirteçlerin güvenilirliğini ve klinik uygulanabilirliğini sınırlamaktadır. Bu sınırlılıklar arasında otizmin biyolojik ve klinik olarak çok heterojen bir spektruma sahip olması, tek bir biyobelirtecin tüm vakaları açıklamakta yetersiz kalması, biyobelirteçlerin farklı yaş gruplarında, kültürlerde ve ortamlarda tutarlı sonuçlar vermemesi, klinik olarak kullanılabilmesi için kolay, maliyet etkin ve yaygın erişilebilir olması sayılabilir. Mevcut biyobelirteçler genellikle karmaşık cihazlar veya spesifik uzmanlık gerektirir. Ayrıca, kullanım alanı biyobelirtecin hangi klinik bağlamda değerlendirileceğini belirleyen temel bir sorudur; tanı koyma, prognostik değerlendirme, tedavi yanıtını izleme, hastalık alt gruplarını belirleme (stratifikasyon), tedavi hedeflerini tanımlama (öngörü) ve risk değerlendirmesi (tarama) gibi farklı alanlardan hangileri için uygun olduğu belirlenmelidir.

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Biyobelirteç veritabanlarının artan kullanımı, OSB biyolojisinin daha iyi anlaşılmasını ve biyobelirteçlerin klinik doğrulama süreçlerinden geçerek teşhis ve tedavide rutin kullanıma sunulmasını hızlandırmaktadır. Çoklu-omik yaklaşımların ve büyük veri analizlerinin entegrasyonu, OSB biyobelirteç araştırmalarının gelecekteki yönünü şekillendirmekte ve daha hassas tanı araçlarının geliştirilmesine katkıda bulunmaktadır.

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BÖLÜM 12

OTİZM OLGULARINDA NÖROGÖRÜNTÜLEME BULGULARI

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GİRİŞ

Otizm spektrum bozukluğu (OSB), karmaşık bir nörogelişimsel bozukluktur. Sosyal etkileşimde zorluklar, tekrarlayıcı ve stereotipik davranışlar ile değişen düzeylerde bilişsel eksikliklerle karakterizedir. Epidemiyolojik araştırmalar, son birkaç on yılda OSB prevalansında dünya genelinde belirgin bir artış olduğunu göstermektedir. Amerika Birleşik Devletleri'nde her 54 çocuktan birinde OSB olduğu tahmin edilmektedir.[1] Yakın tarihli bir meta-analizde, OSB prevalansı Kuzey Amerika'da %1,01, Avrupa'da %0,73 ve Asya'da %0,41 olarak bildirilmiştir. En yüksek prevalans ABD (%1,12), İsveç (%0,90) ve Danimarka'da (%0,73); en düşük prevalans ise Tayvan (%0,11), Fransa (%0,32) ve Çin'de (%0,42) saptanmıştır. Küresel olarak OSB prevalansı, 1994–1999 yılları arasında %0,25 iken, 2015–2019 yılları arasında %0,99'a yükselmiştir.[2]

Otizm, yaşamın erken dönemlerinde başlar; sosyal ilişkiler ve iletişimdeki eksikliklerle birlikte gecikmiş bilişsel gelişim ile kendini gösterir ve yaşam boyu devam eder. OSB'nin temel semptomları genellikle 2 yaş civarında ortaya çıkar; bu süreçte beyin anatomisi, işlevi ve bağlantısındaki gelişimsel farklılıklar davranışları etkiler.[1] Otizm, yaklaşık yarım yüzyıl önce aile ve çevresel faktörlere bağlı bir bozukluk olarak tanımlanmışken, daha sonra zihinsel yetersizlik, epileptik bozukluklar ve EEG anormallikleriyle sık birlikteliği olduğu anlaşılmıştır.[4]

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Manyetik Rezonans Spektroskopisi

Otizmde zayıf yapısal ve işlevsel bağlantıya işaret eden verilerin birikmesi bağlamında, MRS gibi beyaz ve gri maddenin bütünlüğünün biyokimyasal belirteçlerini sağlayan tekniklerin bu popülasyonda yararlı olup olamayacağı sorusu ortaya çıkmıştır. MRS, bir dizi beyin metabolitinin kantifikasyonuna izin verir. Bu teknik, diğer nöropsikiyatrik bozukluklarda yararlı olmuştur, gri ve beyaz cevherin işlevsel bozukluğuna dair öngörüler sunar. Ek olarak, MRS ölçümleri altta yatan patolojilerin biyokimyasal profiline göre belirlendiği gri ve beyaz maddedeki anormalliklerin farklı mekanizmalarını yansıtabilir ve patogenezin biyokimyasal profilinin saptanmasına yardımcı olur. Bu nedenle MRS, otizmde gri ve beyaz maddenin incelenmesine bilgi sağlamak için iyi bir adaydır.[61]

En sık incelenen metabolitlerden biri olan N-asetil aspartat (NAA), nöronlar, aksonlar ve olgun oligodendrositlerde bulunur. Gri maddede NAA düzeylerinin nöronal yoğunluğu yansıttığı, beyaz maddede ise aksonal bütünlüğün bir göstergesi olduğu kabul edilir.[62] Gri maddede nöronal yoğunluk azalması, beyaz madde yollarındaki NAA düzeylerini de etkileyebilir. Otizmle ilişkili MRS çalışmalarında genellikle gri cevher hedef alınmış, burada NAA seviyelerinde düşüklük en sık raporlanan bulgu olmuştur.[63] Ancak bu durum, erken dönemde görülen beyin hacmi artışı ile çelişkili görünmektedir. Bu nedenle, sinaptik yoğunluk azalması, kortikal farklılaşma bozukluğu veya nöroinflamasyon gibi alternatif açıklamalar da gündeme gelmiştir.[64]

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BÖLÜM 13

OTİZM OLGULARINDA TEMEL GENETİK TESTLER VE SENDROMİK NEDENLER

Hakan ERÇELEBİ[1]

GİRİŞ

Otizm spektrum bozukluğu (OSB), heterojen klinik görünümü ve güçlü genetik temeli nedeniyle geniş bir genomik alanda araştırılan başlıca nörogelişimsel bozukluklardan biridir. Genetik araştırmalardaki ilerlemeler, OSB'nin sadece tek nükleotid varyantlarından değil, aynı zamanda daha büyük kromozomal yeniden düzenlemeler ve kopya sayısı varyasyonlarından (CNV) da etkilendiğini ortaya koymuştur. Yeni nesil genomik teknolojilerin (kromozomal mikroarray, trio-ekzom ve tüm genom dizileme) klinik uygulamaya girmesiyle, daha önce açıklanamayan OSB vakalarında moleküler tanı verimi önemli ölçüde artmış ve OSB'nin genetik yapısının çok daha yüksek çözünürlüklü bir karakterizasyonu mümkün hale gelmiştir. Bu gelişmeler, patojenik genomik yeniden düzenlemelerin OSB ve ilgili gelişimsel bozukluklara önemli katkısını ortaya koymuştur.[1]

2000'li yılların ortalarından bu yana, yüksek çözünürlüklü genomik teknolojilerin yaygın olarak benimsenmesi, OSB'nin genomik yapısına yeni bir bakış açısı getirmiştir. Kopya sayısı varyasyonlarının insan genomunda daha önce bilindiğinden çok daha yaygın olduğu gösterilmiştir; yapısal varyantlar, bireyler arası genomik varyasyonun yaklaşık %5-10'unu oluşturur ve bu varyantların bir alt kümesi OSB, zihinsel gelişim bozuklukları ve konjenital anomalilerle doğrudan ilişkilidir. Bu bulgular, OSB etyolojisinde hem tekrarlayan hem de bireye özgü (tekrarlanmayan) de novo CNV'lerin tanısal önemini vurgulamaktadır.[2]

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Tam penetranslı ve klinik olarak anlamlı duplikasyonlar arasında en yaygın olanı, OSB ile iyi bilinen genetik bir anomali olan 15q11.2–q13.3 bölgesindeki duplikasyondur; bunu OSB ile güçlü biçimde ilişkili 7q11.23 bölgesindeki artış (gain) izlemektedir. Eksik penetranslı duplikasyonlar ise 22q11.2, 1q21.1 ve 15q13.2–q13.3 bölgelerini içermektedir. OSB ile ilişkili en yaygın tekrarlayan CNV'ler, OSB'li bireylerin yaklaşık %1'inde tespit edilen, sırasıyla %0,42 ve %0,39 sıklıkta görülen 16p11.2 bölgesindeki mikrodelesyonlar ve mikroduplikasyonlardır. Ayrıca, sporadik OSB'li kişiler, kardeşleri OSB'li olan otistik vakalara göre nadir de novo CNV'lere sahip olma olasılıkları daha yüksektir.[28]

Sonuç olarak, OSB'nin genetik temeli, hem yüksek etkili monogenik bozuklukları hem de daha geniş bir genomik varyasyon yelpazesini içeren çok katmanlı bir yapıya sahiptir. Kopya sayısı değişikliklerinden de novo mutasyonlara ve poligenik risk modellerine kadar uzanan bu geniş genetik çeşitlilik, OSB'nin heterojen klinik görünümünü anlamada kritik bir rol oynamaktadır. Modern genomik teknolojiler tanısal verimi belirgin şekilde artırarak hem sendromik hem de sendromik olmayan olguların etyolojik aydınlatılmasına katkı sağlamaktadır. Bu ilerlemeler, yalnızca tanısal doğruluğu artırmakla kalmayıp, aynı zamanda bireye özgü izlem, tedavi ve danışmanlık stratejilerinin geliştirilmesine zemin hazırlamaktadır. Gelecekte, ileri dizileme teknikleri ve multi-omik yaklaşımların rutin pratiğe entegrasyonu ile OSB'nin genetik mimarisinin daha kapsamlı biçimde çözüleceği ve klinik yönetimin daha da kişiselleştirilebilir hale geleceği öngörülmektedir.

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BÖLÜM 14

RETT SENDROMU

Olcay GÜNGÖR [1]
Beste KİPÇAK YÜZBAŞI[2]

GİRİŞ

Rett sendromu (RS), olguların %96'dan fazlasında Xq28 bölgesinde yer alan MECP2 genindeki kayıp-fonksiyon varyantlarından kaynaklanan ağır bir nörogelişimsel bozukluktur.[1] Bugüne kadar 300'ü aşkın patojenik varyant tanımlanmış olup, olguların %60'ından fazlası yalnızca sekiz ortak "hotspot" mutasyonla açıklanır. Mutasyonların büyük bölümü de novo olup, erkeklerdeki MECP2 varyantları çoğunlukla ağır nörolojik fenotiplere ve sınırlı yaşam süresine yol açmaktadır. Buna karşın RS'li kızların yaklaşık %70'i erişkin yaşlara, hatta 50'li yaşlara kadar yaşayabilmektedir. MeCP2 proteini tüm dokularda bulunmakla birlikte özellikle beyinde yüksek düzeyde ifade edilir ve normal nörogelişim için kritiktir. Metillenmiş DNA'ya bağlanarak transkripsiyonel baskılama yapan bu protein; kromatin organizasyonu, alternatif kesim-birleştirme ve mikroRNA süreçleri gibi ek düzenleyici rollere de sahiptir.[2,3] 2010'lu yıllara kadar RS yönetimi büyük ölçüde semptomatik yaklaşımlara dayanırken, doğal seyir çalışmalarındaki ilerlemeler klinik bulguların ortaya çıkış zamanlarını daha iyi tanımlamış ve daha hedefli önleyici stratejiler geliştirilmesine olanak sağlamıştır.[4,5] Günümüzde kür sağlayan bir tedavi bulunmamakla birlikte, IGF-1 ilişkili bir bileşik olan trofinetide çoklu semptomlarda anlamlı iyileşme göstermiş ve RS için FDA onayı alan ilk tedavi olmuştur. Buna ek olarak farmakolojik ve gen temelli yeni tedavi yaklaşımlarının geliştirilmesi devam etmektedir.[6]

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rinde motor fonksiyon, solunum ve yaşam süresinde belirgin iyileşmeler gösterilmiş olup ilk insan klinik çalışmaları 2022–2023 yıllarında başlamıştır.[62,63]

B) X Kromozomu İnaktivasyonunun (XCI) Modülasyonu

Amaç, inaktif X üzerindeki sağlıklı MECP2 genini yeniden aktive etmektir. Xist RNA inhibisyonu ve CRISPR temelli epigenetik yeniden düzenleme çalışmaları preklinik aşamadadır.[64]

C) Antisens Oligonükleotidler (ASO)

ASO'lar mRNA düzeyinde hatalı MECP2 transkriptlerini düzeltmeyi veya normal proteinin üretimini artırmayı hedefler. Erken preklinik sonuçlar ümit vericidir.[63]

D) Protein stabilizasyonu ve şaperon tedavileri

Yanlış katlanan MeCP2 proteinlerinin stabilize edilmesi üzerine çalışmalar devam etmektedir.[65]

E) Hücresel Tedaviler

Astrosit veya mikroglia nakli gibi yaklaşımlar hayvan modellerinde denenmiş, ancak klinik aşamaya henüz geçmemiştir.[66]

SONUÇ

RS, nörogelişimsel bozukluklar içinde tedaviye en açık olanlardan biri kabul edilmektedir. MeCP2 biyolojisinin daha iyi anlaşılması, uygun klinik ölçütlerin geliştirilmesi ve gen tedavisi güvenlik parametrelerinin optimize edilmesi ile gelecekte daha etkili tedavilerin geliştirilmesi beklenmektedir.

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BÖLÜM 15

ASPERGER SENDROMU

Mustafa DİNÇER [1]
Müge AYANOĞLU [2]

GİRİŞ

Asperger Sendromu (AS), ilk kez DSM-IV'de; sosyal-duygusal gelişimde kısıtlılık ve farklılıklarla birlikte tekrarlayıcı davranışlar ve ilgi alanlarıyla seyreden bir bozukluktur şeklinde tanımlanmıştır. Asperger Sendromu, resmi tanımlama sistemleri olan ICD-10 (1993) ve DSM-IV'de (1994) ilk kez **"Asperger Bozukluğu"** olarak tanımlanmasından, DSM-V (2013) ve ICD-11'de (2022) ortadan kaldırılıp.[1,2] Otizm Spektrum Bozukluğu (OSB) kapsamına alınmasına kadar her zaman bilimsel ve klinik alanda büyük ilgi uyandırmış ve tartışma yaratmıştır.[1-6] Bugüne kadar, tanı sınıflaması, fenomenolojisi, tarihsel bağlamı, doğası ve birçok alanda süregelen tartışmalar devam etmekte olup terminoloji değişmeye devam etmektedir.

TANIM VE TARİHÇE

1944'de Hans Asperger, yaşları 6-11 arasında değişen dört erkek olguda; basmakalıp, yineleyici davranışlar, motor becerilerde zorluk/sakarlık, özel ilgi alanlarına aşırı yönelme ve sosyal izolasyon olduğunu gözlemlemiş ve **"otistik psikopati"** adını verdiği bu tabloyu kişilik bozukluğu olarak tanımlamıştır. Bu belirtilerin aileleri tarafından 3 yaşından sonra fark edildiğini, çocukların zeka-

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AS olsun ister YİO, sadece psikiyatrik tanılarıyla tanımlanmamalıdırlar. Bu bireylerin psikiyatrik değerlendirmesi yapıldıktan sonra durumun başvuran kişi veya ailesi ile paylaşılması gerekmektedir. Bu şekilde ailenin yapması gerekenler, çocukları ile ilgili beklentileri, çocuk/ergenin kendisi ile ilgili farkındalıkları ve beklentileri gerçekçi düzeye getirilir. Tanısal değerlendirme ve uygun bilgilendirme farkındalıklarını arttırmaya katkı sağlar. AS/ YİO 'lu bireylerde müdahale stratejileri hastanın yaşına, güçlü yanlarına, zayıf yanlarına ve ihtiyaçlarına göre değişir. Bazen aileler hatta ergenler de kendileri için okuyup, araştırıp gelerek "Asperger miyim?" sorusunun cevabını almak için bile başvurabilmektedirler. Ayrıntılı değerlendirme sonrası bireyin güçlü ve yetersiz olduğu alanlar tespit edilerek takip ve tedavi ona göre düzenlenmelidir. Erken yaşlar için uygun eğitsel programlara yönlendirmek gerekirken, daha büyük yaşlarda özellikle sosyal-iletişimsel ve uyum becerilerine göre terapötik yaklaşımlar gerekir. Okul seçimi, öğretmenler, ebeveyn ve sağlık profesyonellerinin iş birliği önemlidir. Bu bireylerin psikiyatrik takipte olmaları genel klinik gidişlerinin izleyerek uygun yönlendirmelerinin yapılmasını sağlar. Ayrıca AS/ YİO ile komorbid psikiyatrik bozukluklar sık gözlenmektedir. Bu durumlarda eş tanı ve tanıya uygun psikoterapötik müdahale önem taşımaktadır.

Son olarak, AS'nin mevcut ICD-11 ve DSM-5'te artık bir tanı kategorisi olmaması bu durumun var olmadığının göstergesi olamaz.[32] Bu bireylerin ve ailelerin semptomlarını adlandırıp tanı almaya, tedavi olmaya ve destek almaya ihtiyaçları vardır. Bu ihtiyaçları korumak sınıflandırma sistemlerinin kategorik yaklaşımla tanımladığı kriterlerden daha önemlidir.

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BÖLÜM 16

OTİZMDE TEDAVİNİN GENEL İLKELERİ

Begüm YULUĞ TAŞ [1]
Gonca ÖZYURT [2]

GİRİŞ

OSB (Otizm Spektrum Bozukluğu) tanısı alan bireylerde bulgular bir spektrum dahilinde birbirinden farklı seyreder. Bu sebeple bireyin tedavi programı kişinin bulgularına ve yetersizlik alanlarına bağlı yapılmalı, bireysel takip programı uygulanmalıdır. Tedavi ilkeleri bireyin gelişimsel özelliklerine, aile ve sosyal hayatta yaşadığı problemlere odaklanmalıdır. Tedavinin erken yaşta başlaması (<4 yaş), verilen tedavinin yoğunluğu ve kalitesi, tedavi öncesinde bireyin bilişsel kapasitesinin yeterliliği, özellikle ilk 6 yaştaki fiziksel ve tıbbi özellikleri, bireyin sosyal kaçınmasının olmaması ve aile özellikleri tedaviden faydalanımı artırdığı bilinmektedir.[1]

Otizm tedavi ilkelerine bakıldığında kanıtlanmış tek bir yöntem bulunmamakla birlikte, hakkında en çok kanıta dayalı bilgi bulunan yöntemin eğitsel yöntemler olduğu bilinmektedir.[2] Eğitsel yöntemler haricinde, bireyin bulgularına eşlik eden psikiyatrik semptomlara yönelik ilaç tedavileri ve alternatif yöntemler de bulunmaktadır. OSB çok yönlü tedavi edilmesi gereken bir nörogelişimsel bozukluk olup, bölümde tedavi yöntemleri anlatılmaya çalışılacaktır.

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Hiperbarik Oksijen Tedavisi: Hiperbarik oksijen tedavisinin beynin hipoksik kaldığı durumlarda uygulanması, otizmin etiyopatogenezi araştırılırken bir tedavi yöntemi olup olamayacağı hususunda tartışma yaratmıştır. Her iki durumun birarada görüldüğü durumlarda uygulanması hipoksik beyin bölgelerine iyi gelebilirken, hipoksinin eşlik etmediği otizmli çocuklar için faydadan çok zarar oluşturabilmektedir. Nöbetlerde artma, kulak ağrısı gibi yan etkiler görülebilmektedir. Araştırmalar otizm semptomları üzerinde etkili olmadığı yönünde kanıtlar sunmuştur.[61]

Neurofeedback: Bu yöntem farklı beyin dalgalarını egzersizle normale çevirmeyi kişiye öğretmeyi hedeflemektedir. Çocuğun beyin dalgaları, belirli noktalara yerleştirilen elektrotlar aracılığıyla uygun yazılıma sahip bir bilgisayara aktarılmaktadır. Bu program, beyin dalgalarını kullanıcının kolaylıkla algılayabileceği bir animasyona dönüştürmektedir. Kullanıcı, bilgisayar oyunu formatındaki bu animasyonu izlerken oyunu beyin aktivitesi ile kontrol edebilir. Dikkatini oyuna yoğunlaştırdığında, beyin uygun elektriksel aktiviteye geçtiğinden puan kazanmaya başlar; ancak dikkati dağıldığında oyun üzerindeki kontrolünü kaybeder. Ancak yapılan araştırmalar otizm semptomlarının yönetiminde kanıtlanabilir bir etkisinin bulunmadığını göstermiştir.[62]

Diğer Alternatif Yöntemler: Hayvan terapisi, müzik, spor, masaj gibi yöntemler yan etkisi düşük olan ve kısmen faydası olabilecek yöntemlerdir. Bu yöntemler otizm tedavisi olmayacağı ebeveynlere bildirilmelidir. Eşlik eden uyku problemleri, duyusal hassasiyet, hiperaktivite, göz kontağında kısıtlılık gibi bulgularda olumlu etkileri bulunmaktadır.

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BÖLÜM 17

OTİZMDE DAVRANIŞSAL VE EĞİTİMSEL MÜDAHALELER

Ayla UZUN ÇİÇEK [1]
Elif ABANOZ [2]
İlknur UCUZ [3]

GİRİŞ

Otizm spektrum bozukluğu (OSB) için önerilen müdahale programları çekirdek otizm belirtilerini ve birlikte ortaya çıkan ilişkili bozuklukları hafifletmeyi veya iyileştirmeyi, günlük işlevsel bağımsızlığı artırmayı, ailelere destek sağlamayı, yaşam kalitesini olumsuz etkileyen sorunlu davranışları azaltmayı ve sosyal ve toplumsal katılımı kolaylaştırmayı amaçlamaktadır. Ek olarak, bireylerin güçlü oldukları alanlarda potansiyellerini gerçekleştirmelerine yardımcı olunması hedeflenmektedir. OSB'li çocuklara yönelik müdahaleler eğitim uygulamaları, gelişimsel terapiler ve davranışsal müdahaleler aracılığıyla sağlanır.[1-3]

Müdahale programları teorik yaklaşım ve kapsamına (örneğin, odaklanmış ve hedefli veya kapsamlı) veya ortam ve uygulanma biçimine (örneğin, bireysel veya grup/sınıf, bir profesyonel tarafından okul ortamında veya eğitimli bir ebeveyn tarafından ev ortamında) göre kategorize edilebilir. Müdahale için kullanılan yaklaşımlar ise davranışsal yaklaşımlar, gelişimsel yaklaşımlar, bilişsel ve eğitsel yaklaşımlar ve sosyal-ilişkisel yaklaşımlar olarak sınıflanır. Bununla birlikte çoğu müdahale programında birden fazla yaklaşım bir arada kullanılır.[1-3]

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göre bireyselleştirilmesini, aile katılımını teşvik etmesini ve olabildiğince erken dönemde başlanmasını önermektedir.

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BÖLÜM 18

OTİZM SPEKTRUM BOZUKLUĞUNDA FARMAKOLOJİK TEDAVİLER

Esra DEMİRCİ [1]

GİRİŞ

Otizm spektrum bozukluğu (OSB)'nun küresel yaygınlığıyla ilgili yakın tarihli bir sistematik inceleme güncellemesine göre, dünya çapında yaklaşık 100 çocuktan 1'ine OSB teşhisi konmaktadır.[1] Yıllar içinde giderek artış gösteren sıklığına rağmen OSB'yi tedavi edebilecek, tüm çekirdek semptomlar üzerine etkili bir ilaç bulunmamaktadır. NICHD/National Institute of Child Health and Human Development, ABD Gıda ve İlaç Dairesi (FDA) tarafından otizm semptomlarını tedavi etmek için onay almamış hiçbir ilacın kullanımını desteklememektedir. Ancak bazı ilaçlar, özellikle belirli davranışlar olmak üzere, ASD ile ilişkili belirli semptomları ve eşlik eden durumları tedavi etmeye yardımcı olabilir. Çeşitli ilaçlar OSB semptomlarını hafifletmek için klinik denemelerden geçerken, yaygın olarak reçete edilen ilaçlar ise yeni nesil antipsikotikler, seçici serotonin geri alım inhibitörleri (SSRI'ler), stimülanlar ve alfa-2 adrenerjik agonistlerdir.[3] Risperidon ve aripiprazol FDA tarafından OSB ile ilişkili semptomlar için onaylanan iki farmakolojik ajan olup; çekirdek belirtilerden ziyade rahatsızlıkla ilişkilendirilen sinirliliği/irritabiliteyi hedef almaktadır.[4] OSB'nin temel semptomlarını tedavi eden ilaçlara dair çalışmalar devam etmektedir çünkü çok az ilaç bu semptomları etkili bir şekilde hafifletmekte ve şu anda kullanılan seçeneklerden henüz hiçbiri her bir birey için olumlu sonuç vermemektedir. Ayrıca, FDA OSB'nin temel çekirdek özelliklerini tedavi etmek için henüz bir ilacı onaylamamıştır.[4] Çalışmalar ilaçların davranışsal terapilerle birleştirildiğinde daha etkili olduğunu göstermiştir.

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analizde, oksitosinin sosyal işlevsellikte ve bazı temel ASD semptomlarında iyileşmelere yol açtığını bildirilmiştir.[113] 3-11 yaşlarındaki altmış çocuk ile yapılan bir çalışmada bumetanid ile Çocukluk Otizmi Derecelendirme Ölçeği puanlarında önemli ölçüde azalma raporlamıştır.[114] 91 çocuk üzerinde yapılan başka bir randomize kontrollü çalışmada ise, stereotipik davranışlarda azalma olduğu ancak bumetanid ile çekirdek semptomlarında önemli bir iyileşme olmadığı bildirilmiştir.[115] Çift kör, plasebo kontrollü bir çalışmada, on hafta boyunca kırk çocukta memantin tedavisinin etkilerini incelenmiş, sinirlilik, stereotipik davranış ve hiperaktivite alanlarında olumlu ilerlemeler gözlenmiştir.[116] 2022'de yapılan sistematik bir derlemede ise OSB ile ilişkili birincil veya ikincil sonuçlar için memantin ve plasebo arasında önemli bir fark bulunmamıştır.[117] Rivastigmin ile 12 hafta boyunca yürütülmüş bir çalışmada ifade edici konuşmada ve genel otistik davranışlarda önemli iyileşmeler gösterilmiştir.[118] Rastgele kontrollü bir çalışmada ise, 8-17 yaş aralığındaki 34 OSB'li çocukta donepezil ile plaseboyu karşılaştırılmış, iki grup arasında otizm semptomlarında anlamlı bir fark bulunmamıştır.[119] Genel olarak, bu farmakolojik ajanlar ile OSB tedavisine ilişkin kanıtlar kesin değildir ve daha fazla araştırma gerektirmektedir. Yine kannabidiol ile yapılan tedavilerin tekrarlayan davranışlar, sosyal etkileşim ve uyku bozuklukları gibi ilişkili komorbiditeleri iyileştirerek şiddetli OSB vakalarında fayda sağlayabileceğine dair çalışmalar.[120] bulunmakta birlikte bu alanda da daha fazla çalışmaya ihtiyaç duyulduğu aşikârdır.

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BÖLÜM 19

OTİZMDE DENEYSEL TERAPÖTİK YAKLAŞIMLAR

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GİRİŞ

Otizm spektrum bozukluğu (OSB) olan çocuklar genellikle sosyal etkileşim ve iletişim sorunları ile birlikte stereotipik davranış kalıpları gösterirler. Günümüzde, OSB tanısı konulan çocuk sayısı dünya genelinde önemli ölçüde artmaktadır. 2020'de Amerika Birleşik Devletleri'nde tahmini olarak 54 çocuktan 1'inde OSB vardı; bu, 2000'de bu tanıyı alan 150 çocuktan 1'ine göre yaklaşık %170'lik bir artıştır. Asya'da da OSB'li çocuk sayısında artış eğilimi vardır. Bu nedenle, OSB'li çocuklar için eğitim yaklaşımı ve davranış terapileri son on yılda giderek daha fazla ilgi görmüştür. Bununla birlikte eğitim ve davranış terapileri ve medikal tedavi ile aileler yeterli ve etkili tedavi aalamadıklarını düşünmekte ve tamamlayıcı, bütünleştirici ve diğer tedavi alternatifleri için arayış içine girdikleri görülmektedir. Ayrıca OSB'de etiyolojiyi temel alan bir tedavi yönteminin henüz olmaması, olası bir tedavi amacıyla tamamlayıcı ve alternatif tıp (TAT) uygulamalarının kullanılmasına yol açmaktadır. [1,2]

Tamamlayıcı ve Bütünleştirici Yaklaşımlar

OSB'li çocuklar arasında yaygın olarak kullanılan tamamlayıcı ve alternatif tıp uygulamaları arasında özel diyetler, besin takviyeleri, şifalı bitkiler, probiyotikler, müzik terapisi, sanat terapisi, masaj terapisi, kraniyosakral terapi, şelasyon,

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küçük ile orta düzeyde kalmaktadır. Dolayısıyla, bu bileşiklerin klinik kullanımda etkinlik ve güvenlik açısından daha kapsamlı ve güçlü çalışmalarla değerlendirilmesi gerekmektedir.

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BÖLÜM 20

TRANSKRANİYAL MANYETİK UYARIM (TMS)

Saban KARAYAĞIZ[1]

GİRİŞ

Transkraniyal Manyetik Uyarım (TMS), beyin korteksine manyetik darbeler göndererek sinir hücrelerini uyarmak için kullanılan non-invaziv bir nöromodülasyon tekniğidir. 1985 yılında Anthony Barker ve ekibi tarafından geliştirilen TMS, nörolojik ve psikiyatrik hastalıkların tedavisinde devrim niteliğinde bir yöntem olarak kabul edilmiştir.[1]

TMS 'nin Tanımı ve Tarihsel Gelişimi

Otizm Spektrum Bozukluğu (OSB), sosyal etkileşimlerde güçlük, tekrarlayıcı davranışlar ve sınırlı ilgi alanları gibi belirtilerle karakterize edilen nörogelişimsel bir bozukluktur.[1] Son yıllarda, OSB'nin nörobiyolojik temelini anlamaya yönelik çalışmalar, beyin bağlantısındaki anormalliklerin bu bozukluğun gelişiminde önemli bir rol oynadığını göstermiştir.[1] Bu bağlamda, Transkraniyal Manyetik Uyarım (TMS), beyin fonksiyonlarını modüle ederek OSB semptomlarını hafifletme potansiyeli nedeniyle dikkat çekmektedir.

TMS, elektromanyetik indüksiyon yoluyla beyin korteksine manyetik darbeler göndererek sinir hücrelerini uyarır. TMS'nin bu özellikleri, nörolojik ve psikiyatrik bozuklukların tedavisinde kullanılmasını mümkün kılmıştır. Özellikle, TMS'nin OSB'deki uygulamaları, sosyal etkileşimdeki güçlükleri ve tekrarlayıcı davranışları azaltma konusunda umut vadetmektedir.[1]

Tekrarlayan TMS (rTMS) yöntemi, belirli frekans ve yoğunluklarda manyetik darbeler göndererek belirli beyin bölgelerinde uyarım sağlamakta ve böylece

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Kombine tedavi yaklaşımları: TMS'nin davranışsal terapiler, farmakolojik tedaviler ve eğitim programlarıyla birlikte nasıl uygulanabileceğine dair daha fazla çalışma gereklidir.

Sonuç olarak TMS, OSB tedavisinde umut vaat eden bir yöntem olmakla birlikte, etkinliği konusunda hâlâ araştırılması gereken birçok nokta bulunmaktadır. TMS'nin bireysel farklılıklara göre uyarlanabilmesi, uzun vadeli etkilerinin netleştirilmesi ve diğer tedavi yöntemleriyle entegrasyonunun sağlanması, OSB tedavisinde daha başarılı sonuçlar elde edilmesini sağlayabilir. Gelecekte yapılacak çalışmalar, TMS'nin OSB'deki yerini daha sağlam bir şekilde belirleyecek ve klinik kullanımlarını optimize edecektir.

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BÖLÜM 21

OTİZM SPEKTRUM BOZUKLUĞU VE KÖK HÜCRE TEDAVİSİ

Mehmet CANPOLAT[1]

GİRİŞ

Otizm spektrum bozukluğu (OSB) günlük hasta pratiğinde hekimlerimizin sıklıkla karşılaştığı başlıca nörogelişimsel bozukluklardandır. Multifaktöryel etyolojiye sahiptir. Bu da her vakanın diğerlerinden farklı bir etiyolojik nedene bağlı olarak ortaya çıkabileceği anlamına gelir. Bu nedenle bu vakaların tanı, etiyolojik değerlendirme ve tedavi süreçlerinin yönetimi büyük bir önem arz eder.[1] Bu bölümde OSB tanımı, patofizyolojisi, tedavisi, kök hücre tanımı, kök hücre çeşitleri ve OSB olgularında hücresel tedavi güncel literatür [1-217] eşliğinde değerlendirilmiştir.

OTİZM SPEKTRUM BOZUKLUĞU (OSB)

OSB yaşamın erken dönemlerinde başlayan, sosyal iletişimde zorluklar, tekrarlayıcı davranışlar ve kısıtlı ilgi alanları ile karakterize karmaşık bir nörogelişimsel bozukluktur. *Ruhsal Bozuklukların Tanısal ve İstatistiksel El Kitabı*, Beşinci Baskı'ya (*DSM* -5) göre bir çocuğun OSB tanı kriterlerini karşılaması için; **a-** sosyal iletişim ve etkileşimin üç alanının her birinde kalıcı eksiklikleri ve **b-** dört tipteki kısıtlı, tekrarlayıcı davranışlardan en az ikisine sahip olması gerekir.[2-6] OSB, tanısı için henüz net bir biyobelirteç belirlenmediğinden DSM-V tanı kriterleri kullanılarak davranışsal değerlendirme yoluyla erken çocukluk döneminde teşhis edilebilir.[3,4,8,12,100]

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tedavisinin uzun vadeli güvenlik ve etkinliğinin değerlendirildiği daha kapsamlı çalışmalara gereksinim halen daha devam etmektedir.[1,59]

Önerilen Ek Okumalar

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BÖLÜM 22

OTİZM SPEKTRUM BOZUKLUĞUNDA GENETİK VE MOLEKÜLER TEMELLİ TEDAVİ YAKLAŞIMLARI

Elif Perihan ÖNCEL [1]
Pınar GENÇPINAR[2]

OTİZMİN GENETİK YÜZÜ VE TERAPÖTİK DÖNÜŞÜM

Otizm spektrum bozukluğu (OSB), son on yılda nörogelişimsel bozukluklar arasında en yoğun genetik araştırma alanlarından biri haline gelmiştir. Gelişmiş genomik teknolojilerin (ör. tüm ekzom/tüm genom dizileme, kromozom mikrodizi analizleri) klinik pratiğe girmesiyle hem sendromik hem de non-sendromik olgularda monogenik nedenler giderek daha sık tanımlanmaktadır. Bu bulgular, OSB'nin yalnızca davranışsal belirtilerle tanımlanan klinik bir sendrom değil, moleküler düzeyde heterojen bir biyolojik bozukluklar spektrumu olduğunu ortaya koymaktadır.[1]

Günümüzde CRISPR (Bacterial Clustered Regularly Interspaced Palindromic Repeats (CRISPR)/Cas) tabanlı gen düzenleme sistemleri, antisens oligonükleotid (ASO) tedavileri, epigenetik modülatörler ve metabolik yolaklara yönelik farmakolojik müdahaleler; OSB ile ilişkili spesifik genetik varyantları veya bozulmuş hücresel mekanizmaları hedef alabilen yeni nesil terapötik stratejiler olarak öne çıkmaktadır. Bu yaklaşım, semptom odaklı geleneksel tedavi anlayışından, genetik ve moleküler hedefi olan kişiselleştirilmiş tedavi paradigmasına geçişin temelini oluşturmaktadır. [2]

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- **Multidisipliner yaklaşım:** Etik kurullar, genetik danışmanlar, pediatrik nörologlar ve psikiyatristler iş birliğiyle hem güvenlik hem de klinik etkinlik sağlanmalıdır.

Araştırma ve Translasyonel Perspektif

- **Preklinikten kliniğe geçiş:** Fare ve insan hücre modellerinde elde edilen genetik ve epigenetik hedefli bulgular, kontrollü klinik çalışmalara taşınmalıdır.
- **Biyobelirteç tabanlı takip:** OSB'de tedavi yanıtının değerlendirilmesinde epigenetik, metabolik ve nörofizyolojik biyobelirteçler kullanılabilir.
- **Uzun dönem izlem:** Tedavinin etkinliği kadar, nörogelişimsel güvenlik, olası yan etkiler ve fenotip değişiklikleri izlenmelidir.

Gelecek Perspektifi

- **Hedefe yönelik tedavilerin yaygınlaşması:** Monogenik alt tipler ve genetik olarak belirlenmiş risk gruplarında terapötik müdahaleler, kişiselleştirilmiş OSB yönetimini mümkün kılacaktır.
- **Çevresel ve metabolik modülasyon:** Beslenme, mikrobiyota ve metabolik destek ile epigenetik ve sinaptik fonksiyonun optimize edilmesi hem semptomları azaltabilir hem de nörogelişimsel devrelerin sağlığını destekleyebilir.
- **Etik ve sosyal sorumluluk:** Biyoteknolojik müdahalelerin uygulanması sırasında toplumsal, etik ve hukuki boyutlar göz ardı edilmemelidir.

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BÖLÜM 23

OTİZM SPEKTRUM BOZUKLUĞU VE EPİLEPSİ

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EPİLEPSİ

Epilepsi, farklı nöbet tiplerinin görüldüğü ve her yaş grubunu etkileyen yaygın bir nörolojik hastalıktır.

Beyindeki anormal, aşırı veya eşzamanlı nöronal deşarjlar sonucunda ortaya çıkan geçici belirti ve bulgulara epileptik nöbet denir.[1] İlkinin üzerinden 24 saatten uzun zaman geçmiş, iki veya daha fazla tetiklenmemiş nöbet varlığı, epilepsi olarak tanımlanır. Bu tanım, Uluslararası Epilepsi ile Savaş Derneği'nin 2014 yılında yayınladığı raporda genişletilmiş; on yıl içinde tekrarlama olasılığı yüksek olan (>%60) tek tetiklenmemiş (ya da refleks) nöbet ve özgül bir epilepsi sendromu tanısı alan durumlar da bu tanıma eklenmiştir.[2]

Epilepsi Prevelansı

Epilepsi, anormal nöronal deşarjlar sonucunda oluşan ve tekrarlayan nöbetlerin görüldüğü sık rastlanan nörolojik bir hastalıktır. Görülme sıklığı çocuklar ve adolesanlarda yaklaşık olarak 20-124/100.000 civarındadır. Ayrıca, yirmi yaşına kadar olan popülasyonun %5'i en az bir nöbet geçirmektedir.[3]

Prevalans çalışmalarıyla elde edilen bulgular, özellikle halk sağlığı planlamalarına önemli katkılar sağladığından oldukça değerlidir. Günümüzde, tüm

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OTİZM SPEKTRUM BOZUKLUĞU VE DİKKAT EKSİKLİĞİ HİPERAKTİVİTE BOZUKLUĞU: TANI VE TEDAVİ

Ezgi KARAGÖZ TANIGÖR [1]
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TANI

Dikkat eksikliği/hiperaktivite bozukluğu (DEHB) ve otizm spektrum bozukluğu (OSB), genellikle çocukluk çağında başlayan nörogelişimsel bozukluklardır.

DSM-IV'e göre OSB olan bireye DEHB tanısı konulamamaktadır. DSM-5'te bu durum değiştirilmiş iki bozukluğun eş tanı olarak konulmasına izin verilmiştir. Güncel bilgilere göre DEHB/OSB sık görülen komorbid bozukluklardır. DEHB'li her 8 gençten yaklaşık 1'inin OSB'ye sahip olduğunu bildirmiştir.[1] DEHB, OSB'li çocuklarda en yaygın komorbid bozukluktur ve komorbidite oranları %40-70 aralığında yer almaktadır.[2] Bozuklukların temel semptomlarındaki farklılıklara rağmen, birçok çalışma DEHB tanısı almış çocuk ve ergenlerde otizm semptomların yüksek seviyelerde olduğunu bildirmiştir.[3]

DEHB ve OSB'de davranışsal, bilişsel ve nörobiyolojik açıdan benzerlikler olduğu görülmektedir.[4] İki bozuklukta da genetik faktörler önemli rol oynamaktadır. Dil gelişiminde gecikme, sosyal-iletişim becerileri zayıflığı, duyusal aşırı duyarlılık, emosyon regülasyonu, dikkat problemleri, karşı olma-karşı gelme davranışları gibi sorunlar DEHB ve OSB olan hastalarda ortak olarak görülebilen semptomlardır.[5] Ayrıca DEHB'li hastaların ailelerinde geniş otizm fenotipi bulgularının normal populasyondan daha sık olduğu belirtilmiştir.[6]

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tedavisi işlevselliği önemli ölçüde iyileştirmektedir.[25] DEHB-OSB komorbiditesinde rutin tedavi önerilmektedir. OSB-DEHB komorbiditesinde metilfenidat ilk sıra tercih olarak yer alsa da bir metaanaliz; OSB-DEHB komorbiditesinde, OSB'nin eşlik etmediği DEHB tedavisine göre metilfenidatın etki büyüklüğünün daha düşük olduğunu göstermiştir (sırasıyla ES=0.67 ve 1.03).[26] Bu olgularda metilfenidat etkinliğinin daha düşük, yan etkilerinin ise daha fazla olabileceği belirtilmiştir.[2, 27] OSB'de metilfenidat kullanımı sırasında sosyal geri çekilme, depresyon ve sinirlilik gibi daha yüksek oranda yan etkiler olduğu belirtilmiştir.[28]

Cochrane incelemesinde metilfenidatın, OSB'li gençlerde hiperaktivite ve dürtüselliği azalttığı, dikkat eksikliği üzerinde daha zayıf bir etkisinin olduğu ve temel OSB semptomlarını etkilemediği belirtilmektedir.[29] Orta dozlar, düşük dozlara kıyasla DEHB semptomlarında daha belirgin iyileşme sağlamaktadır. Klinik deneyimlere dayanarak, bu popülasyonda ilaçların düşük dozlarda başlatılması ve normalden daha dikkatli titre edilmesi gerektiği önerilmektedir.[25]

Metilfenidat birinci basamak tedavi olarak önerilirken, atomoksetin ve guanfasin de etkilidir. Atomoksetin uyku üzerinde nötr bir etkiye sahipken, uzatılmış salımlı guanfasin karşıt davranışlarda küçük bir azalma sağlasa da anksiyete ve uyku sorunları açısından fark yaratmaz.[30] Risperidon ve aripiprazolün bu popülasyonda hiperaktiviteyi kontrol etmede etkili olduğunu bildirilse de genel olarak psikostimülanlara göre daha büyük bir yan etki profiline (metabolik değişiklikler, kilo alımı) sahiptirler.[31]

Psikososyal müdahalenin ilaç tedavisine ek fayda sağlamadığına dair bazı veriler olsa da, genellikle ilaç ve psikososyal yaklaşımların birlikte kullanılması önerilmektedir.[32, 33]

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BÖLÜM 25

OTİZM VE UYKU BOZUKLUKLARI: TANI VE TEDAVİ

Taha ÖZÇELİK [1]
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GİRİŞ

Otizm spektrum bozuklukları (OSB), sosyal etkileşim ve iletişim bozuklukları, ilgi alanlarının azlığı ve tekrarlayıcı davranışlar ile karakterize nörogelişimsel bozukluklardır. OSB'li çocuklar, normal gelişim gösteren çocuklara kıyasla yüksek oranda uyku bozuklukları yaşarlar. OSB'li çocukların %80' inde uyku kalite ve süresi ile ilgili bozukluklar vardır. Uyku problemleri hem çocukların hem de ailelerinin yaşam kalitesini önemli ölçüde etkilemektedir.[1]

OSB'de uyku problemlerinin hem davranış hem de psikopatoloji ile ilişkili olduğu gösterilmiştir. Bu ilişki biyopsikososyal bir etkileşimin varlığını düşündürmektedir. OSB'de uyku problemleri, eşlik eden davranışsal bozukluklar (ör. sınırlı ve tekrarlayıcı davranışlar, kendine zarar verme, saldırganlık, stereotipi) ve psikopatoloji ile (ör. DEHB, anksiyete, depresyon) bağlantıları esas alınarak tanımlanmaktadır.

OSB'li çocuklarda uyku, en yaygın tıbbi takip nedenlerinden biridir. Hatta davranışsal bozukluklar veya saldırganlık nedeni ile yapılan başvurularda, öncelikli olarak uyku ile ilgili sorgulama iyi bir başlangıç noktasıdır. Uykusuzluk OSB'nin temel belirtilerinde artışa neden olur ve bu durum, OSB'li çocuklarda uyku bozukluklarını yönetmeyi zorlaştırır. OSB'nin temel belirtilerinin çoğu uykuyu olumsuz etkileyebilir ve kötü uyku, bu belirtileri daha da kötüleştirerek kısır bir döngü oluşturabilir.

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BÖLÜM 26

OTİZM VE ZİHİNSEL YETERSİZLİK: TANI VE TEDAVİ

Dilek ÇAVUŞOĞLU [1]

GİRİŞ

Zihinsel yetersizlik (ZY) ve otizm spektrum bozuklukları (OSB), batı ülkelerinde %2-3 iken genel popülasyonda %1 sıklığında görülen majör nörogelişimsel bozukluklardır.[1-3] Zihinsel yetersizlik (ZY), 18 yaşından önce hem zihinsel işlevlerde hem de adaptif davranışlarda önemli sınırlamalarla tanımlanır ve genellikle 70'in altında bir Zeka Bölümü (IQ) ile tanımlanır.[4,5] Otizm spektrum bozuklukları (OSB), iletişim ve sosyal etkileşimdeki eksiklikler, kısıtlı ve tekrarlayan davranışlar, ilgi alanları ve aktiviteler dahil olmak üzere bir dizi davranışsal fenotip için kullanılan kolektif bir terimdir(1). Zihinsel yetersizlik (ZY) ve OSB sıklıkla birlikte görülür; OSB hastalarının %70'inde ZY görülürken, ZY hastalarının ise %40'ında OSB saptandığı bildirilmiştir.[5,6]

Genetik olarak, hem ZY hem de OSB son derece heterojen bir grup olup içerisinde, moleküler yolaklar ve ağlar bulunmakta ve örtüşen fenotiplere sahip varyantları birbirine bağlamaktadır. Kromozomal mikrodizi analizi nedensel sapmaların yaklaşık %20'sini ve (üçlü) tüm ekzom dizilemesini yaklaşık %40'ını tespit etmekte ancak, ZY'nin önemli bir kısmı ve OSB hastalarının çoğunluğu genetik tanı almadan kalmaktadır. İkisinin birlikte olduğu genetik nedenlerin başında Frajil X sendromu ((OMIM # 300624), Angelman sendromu (OMIM #105830) ve Rett sendromu ((OMIM #312750) gelmektedir.[1]

Otizm spektrum bozukluğu (OSB) ve zihinsel yetersizliği (ZY) olan çocuklar, normal gelişim gösteren akranlarına kıyasla orantısız bir şekilde daha yüksek

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lanacağı ve ne zaman geri çekileceği, problemli davranışın nasıl engelleneceği ve yeniden yönlendirileceği ve diğer tedavi bileşenleri de içerir.

SONUÇ

Otizm Spektrum Bozukluğu (OSB) ve ZY olan çocuklarda sorunlu davranış, oldukça karmaşık ve heterojen bir durumdur. Gelişimsel bir engelin varlığına ek olarak, sorunlu davranışın ortaya çıkma ve sürdürülme riskini artıran çeşitli başka faktörler de vardır. Sorunlu davranış genellikle tıbbi veya psikiyatrik durumlar gibi biyolojik faktörlerin, operant öğrenme süreçleri aracılığıyla sorunlu davranışı güçlendiren deneyimlerle etkileşiminin ürünüdür. Araştırmalar, çoğu durumda problem davranışın sosyal pekiştirme koşulları tarafından sürdürüldüğünü, ancak uyarlanabilir davranış ve psikiyatrik koşullardaki eksikliklerin birçok durumda muhtemelen bir rol oynadığını göstermektedir. Nörodavranışsal bir bakım modeli, problem davranışın muhtemelen genetik anormallikler, psikiyatrik ve nörolojik işlev bozukluğu, pekiştirmenin mevcudiyeti gibi çevresel değişkenler ve sorunlu davranışı ortaya çıkarabilecek ve pekiştirebilecek sosyal etkileşimler gibi birden fazla belirleyiciye sahip olduğunu kabul eder. Bundan, değerlendirme sürecinin bu katkıda bulunan faktörlerin rolünü belirlemeye çalışması ve bu bilgiyi bireyselleştirilmiş müdahaleler tasarlamak için kullanması gerektiği sonucu çıkar. Özetle, sosyal ve çevresel değişkenlerden, sorunlu davranış için pekiştirme davranış geçmişlerini kapsayan bütünleştirici yaklaşım, beceri eksikliklerinden kaynaklanan sorunları ele almak için davranışsal müdahalelerin ve ayrıca nöropsikiyatrik işlev bozukluğundan kaynaklanan sorunları ele almak için farmakolojik ajanların kullanımı gerekmektedir.

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BÖLÜM 27

OTİZM SPEKTRUM BOZUKLUĞUNDA DİL VE İLETİŞİM BOZUKLUKLARI: TANI VE TEDAVİ

Yunus Emre DÖNMEZ [1]
Serkan KIRIK [2]

GİRİŞ

Otizm spektrum bozukluğu (OSB); sosyal ilişki, iletişim ve bilişsel gelişimde gecikme ya da sapma ile kendini gösteren ve genellikle yaşamın ilk yıllarında başlayan nöropsikiyatrik bir bozukluk olup dil ve iletişim becerilerindeki sorunlar hastalığın ana belirti kümesini oluşturmaktadır.[1]

Kavram olarak dil, iletişim kurulmasına olanak sağlayan kurallar ve semboller sistemidir.[2] İletişim ise en önemli unsurunu dil becerilerinin oluşturduğu, düşünceleri, duyguları ve fikirleri anlamada ve ifade etmede kullanılan tüm becerilerin koordineli kullanımını gerektiren bireyler arasındaki sosyal etkileşim biçimidir.[3, 4]

Sağlıklı çocuklarda 0-6 yaş aralığında dil gelişimi dört temel aşamada gelişmektedir.

1. Söz Öncesi/Konuşma Öncesi Dönem (0-12 ay): Bebeklerin başlarda refleks olarak sonrasında ise iletişim kurmak amacıyla çıkardıkları ilk temel seslerin olduğu dönemdir. Bu dönem kendi içerisinde yenidoğan dönemi (0-2 ay), gığıldama dönemi (2-4 ay), mırıldanma dönemi (4-6 ay), mırıldanmanın tekrarı dönemi (7-9 ay), başkalarının seslerini taklit dönemi (9-11 ay) ve ses-sözcükler dönemi (11-14 ay) olmak üzere sınıflandırılabilmektedir.
2. Konuşma Dönemi (12-24 ay): Sözcük üretmenin ve konuşmanın başladığı

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mektedir. Bu nedenle, çocukların daha zengin bir dil ortamına maruz kalması, daha iyi dil becerileri geliştirmelerine katkı sağlar.

OSB olan çocukların, kelime öğrenme ortamında tipik olarak mevcut olan sosyal-pragmatik ipuçlarını kullanma yetisinde ciddi şekilde zorlandığı bilinmektedir. Müdahale için bir yaklaşım, çocuğun dikkat ve motivasyon süreçlerini geliştirerek, sosyal ipuçlarını daha iyi kullanmasını sağlamak olabilir. Ancak sosyal-pragmatik yaklaşım, bu çocuklarda dil öğrenimini iyileştirmenin başka bir önemli yolunun çevreyi yeniden düzenleyerek, çocuğun erişebileceği sosyal ipuçlarını daha belirgin hale getirmek olduğunu öne sürer. Bu nedenle, müdahale araştırmalarının yalnızca çocuğa değil, onun içinde bulunduğu çevreye de odaklanması gerekir. Buradaki amaç, çocuğun öğrenmesini daha verimli destekleyen ince ayarlı etkileşimlerin nasıl sağlanabileceğini belirlemektir.

Bu tür müdahaleler, ebeveynlerin çocuklarının gelişen becerilerine sürekli olarak uyum sağlamasını öğretmeyi içerebilir. Örneğin, ebeveynler kelime anlamlarını öğrenmede giderek genişleyen bir sosyal-pragmatik ipucu yelpazesine odaklanarak çocuklarına rehberlik edebilirler.

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BÖLÜM 28

OTİZMDE DİYET VE BESLENME

Gamze YURTDAŞ DEPBOYLU [1]
Gülşah KANER [2]

GİRİŞ

Dünya Sağlık Örgütü'ne (DSÖ) göre otizm spektrum bozukluğu (OSB) yaklaşık olarak her 100 çocuktan 1'ini etkilemekte ve tipik olarak yaşamın ilk beş yılı içerisinde teşhis edilmektedir.[1] Günümüzde OSB'ye yönelik tedaviler temel olarak erken dönemde psikososyal müdahaleler ve farmakolojik müdahalelere odaklanmaktadır. Ancak, OSB'li çocukların erken gelişim dönemlerinde bu tedavilerle yoğun bir şekilde müdahale edilmesine rağmen, bazı semptomlar üzerindeki faydalı etkiler anlamlı değildir. Bu nedenle, aileler diyet müdahaleleri gibi alternatif tedaviler aramaktadır.[2]

OSB'li çocuklar arasında beslenme sorunları yaygındır. Bu çocuklar genellikle anormal yeme alışkanlıkları ile doku, renk, koku, kıvam ve tada dayalı seçicilik de dâhil olmak üzere besine karşı duyusal hassasiyet sergileyebilmektedir.[3] Bunun yanı sıra, OSB'li çocuklarda bağırsak geçirgenliğinde artış, değişmiş mikrobiyata, intestinal inflamasyon, mikrobiyal çoğalma, aminoasit dengesizliği, oksidatif stres, karbonhidrat sindirim enzimi aktivitesinin azlığı gibi gastrointestinal sisteme ilişkin sorunlar da bildirilmiştir.[4] Literatürde ketojenik diyet, glutensiz-kazeinsiz diyet, spesifik karbonhidrat diyeti, Feingold diyeti, Candida vücut ekoloji diyetinin yanı sıra probiyotikler, çoklu doymamış yağ asitleri, A, C, B6, B12 vitaminleri, magnezyum ve folat takviyelerinin OSB'nin yönetiminde

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ta-analizde omega-3 yağ asidinin 8 yaşında veya daha küçük OSB'li çocuklarda konuşma bozukluğu ve hiperaktiviteyi kontrol etmek için faydalı bir takviye olabileceğini ortaya koymuştur.[45] Genellikle yapılan çalışmalarda, omega-3 takviyesinin OSB'nin belirli davranışsal semptomlarını yönetmede umut vaat ettiği gösterilmiştir. Ancak, OSB'nin heterojenliği, omega-3 takviyesine farklı yanıtlar verilmesine katkıda bulunmakta ve fayda sağlama olasılığı en yüksek olan alt grupların belirlenmesini gerekli kılmaktadır. İdeal EPA/DHA oranı ve dozu belirsizliğini korumakta olup, çalışmalarda günde 300 mg ila 2000 mg arasında değişen dozlar kullanılmaktadır. Omega-3 yağ asitleri, OSB'nin belirli semptomlarını ele almak için güvenli ve erişilebilir bir müdahale olarak umut vaat etmektedir. Daha fazla yüksek kaliteli araştırma ile takviye, kişiselleştirilmiş tedavi stratejilerinin değerli bir bileşeni haline gelebilir.[38]

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BÖLÜM 29

OTİZM SPEKTRUM BOZUKLUĞU OLGULARINDA YAŞAM KALİTESİ

Fatma Duygu ÖZTÜRK ÖNSAL [1]
Nilüfer ELDEŞ HACIFAZLIOĞLU [2]
Şaziye Senem BAŞGÜL [3]

GİRİŞ

Yaşam kalitesi (YK) Yunan filozofları Platon ve Aristo'dan itibaren irdelenen bir olgudur ve toplumların ulaşmayı amaçladığı en önemli evrensel hedeflerden birisidir. Dünya Sağlık Örgütü (WHO) tarafından 'Bireyin yaşamdaki konumunu yaşadıkları kültür ve değer sistemleri bağlamında hedefleri, beklentileri ve endişelerine göre algılaması olarak" tanımlanmıştır.[1] YK kavramı, yalnızca bireyin refahını artırmaya yönelik bir rehber sunmakla kalmaz, aynı zamanda insanların olumlu değişimler yapmak için iş birliği yapmasını sağlayan ortak bir dil işlevi de görür.[2] YK fiziksel, psikolojik ve sosyal bileşenlerin, bireysel özellikler ve çevresel değişkenler tarafından etkilendiği çok boyutlu bir kavramdır. Bu nedenle bireylerin fiziksel sağlığı, psikolojik durumu, bağımsızlık düzeyi, sosyal ilişkileri, kişisel inançları ve çevrenin belirgin özellikleriyle olan ilişkileri YK'ini değerlendirirken dikkate alınmalıdır.[3]

OSB spektrum bozukluğu (OSB), sözel ya da sözel olmayan iletişimde zorluk, sosyal etkileşimde bozukluk ile tekrarlayıcı davranışlar ve kısıtlı ilgi alanı ile karakterize nörogelişimsel bir bozukluktur.[3,4] OSB'ye epilepsi nöbeti, dikkat eksikliği ve hiperaktivite, davranış, beslenme ve uyku bozuklukları eşlik edebilir.

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SONUÇ

''İyi bir YK herkes için temel bir hak olup gerçekçi ve ulaşılabilir bir hedeftir". Bu bireylerin yaşam kalitesini iyileştirmek için, YK üzerinde olumlu ve olumsuz etkisi olan faktörleri bilmemiz gerekmektedir. Ailelerin bilinçlendirilmesi, çocuklarının ihtiyaçlarını daha iyi anlamalarına ve onlara daha iyi destek olmalarına yardımcı olacaktır. Ebeveynlerin stres yönetimi ve başa çıkma mekanizmaları konusunda desteklenmesi, ailenin genel refahını artıracaktır OSB'li çocukların ve ailelerinin yaşam kalitesini artırmak için, bireysel ve toplumsal desteklerin güçlendirilmesi önemlidir. Okul, iş yeri ve sosyal alanlarda hem ebeveynlerin hem de çocukların refahını artıracak kapsayıcı politikalar ve destek sistemleri, bu ailelerin yaşamlarını daha sürdürülebilir hale getirebilir ve yaşam kalitelerini artırılabilir. Destek hizmetleri, farklı yaş seviyelerindeki değişen ihtiyaçlarını karşılayacak şekilde uyarlanmalıdır. Toplumların OSB konusunda bilinçlendirilmesi çocukların ev, okul ve sosyal yaşamda daha fazla kabul görmelerini ve sosyal hayata daha kolay uyum sağlamalarını destekleyerek OSB'li çocukların kendi potansiyellerini gerçekleştirmelerine, bağımsızlık kazanmalarına, sosyal becerilerini geliştirmelerine, kendilerinin ve ailelerinin yaşam kalitelerinin artmasına katkı sağlayacaktır. Tüm bunlarla birlikte toplumsal refahımız da artacaktır.

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BÖLÜM 30

OTİZMDE ADLİ SORUNLAR VE YÖNETİMİ

Elif AKÇAY [1]
Meryem Hilal ALTAŞ [2]
Nesrin CEYLAN [3]

GİRİŞ

Otizm Spektrum Bozukluğu (OSB), erken çocukluk döneminde başlayan ve yaşam boyu süren, sosyal iletişim ve etkileşimde kalıcı yetersizlikler ile sınırlı, tekrarlayıcı davranış örüntüleri ile karakterize edilen nörogelişimsel bir bozukluktur.[1, 2] Tanı genellikle sosyal iletişimde azalma, göz teması kuramama, ortak dikkat kurmakta yetersizlik, oyun becerilerinde kısıtlılık, duyusal farklılıklar (hipo- ya da hipersensitivite), tekrarlayıcı hareketler ve davranışlar gibi belirtilerin bir arada gözlemlenmesiyle konulur. Klinik yelpazesi oldukça geniş olan OSB, bireyler arasında belirgin şekilde farklılaşan bilişsel, dilsel ve davranışsal özellikler sergileyebilir; bu nedenle "spektrum" terimi, bozukluğun heterojen doğasını yansıtmaktadır.[3] Bu özellikler gelişimsel sürecin erken dönemlerinde fark edilebilmekle birlikte, bireyin yaşına, bilişsel kapasitesine ve çevresel etkileşimlerine göre farklı düzeylerde ortaya çıkabilir.[4] Ayrıca, OSB'ye sıklıkla dikkat eksikliği ve hiperaktivite bozukluğu (DEHB), anksiyete bozuklukları ve zihinsel yetersizlik gibi eş tanılar eşlik edebilmektedir.[5] Güncel verilere göre, OSB'nin küresel prevalansı yaklaşık %1 civarındadır.[6] Amerika Birleşik Devletleri'nde 2023 yılında *Centers for Disease Control and Prevention* (CDC) tarafından yayımlanan verilere göre, 8 yaşındaki her 31 çocuktan yaklaşık 1'inde (%3,2) OSB olduğu-

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BÖLÜM 31

OTİZMDE İLAÇ REHBERİ

Özlem ATEŞ YAMAN[1]
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İLAÇ ADI: ARİPİPRAZOL

FDA, 2009 yılında psikotropik bir ilaç olan aripiprazolü (Abilify, Bristol-Myers Squibb ve jenerikleri) 6-17 yaş arası OSB'li çocuklarda sinirlilik tedavisi için onaylamıştır.[1] Bu ilaç aynı zamanda şizofreni, bipolar I bozukluk, majör depresif bozukluk ve Tourette sendromu tedavisinde de kullanılmaktadır.

- **İlaç formu:** Ülkemizde 1 mililitresinde 1 mg aripiprazol içeren 150 ml'lik so-lüsyon formu, 5-10-15-20-30 mg'lık tablet formları, 5-10-15-30 mg'lık ağızda dağılan tablet formları ve 400 mg uzun salınımlı aripiprazol içeren enjektabl flakon formu bulunmaktadır.[2]
- **Endikasyonu:** FDA onayına göre aripirazolün endikasyonları:[3,4]
  - 13 yaş ve üzeri şizofreni tedavisi
  - 10 yaş ve üzeri mani ve mikst epizod tedavisi
  - 6 yaş ve üstünde otizm ile ilişkili agresyon tedavisi
- **Kontrendikasyonlar:** Aripiprazol veya ilacın herhangi bir bileşenine karşı bilinen aşırı duyarlılık durumunda kontrendikedir.
- **Mekanizma:** Etki mekanizması tam olarak bilinmemekle birlikte, dopamin tip 2 (D2) ve serotonin tip 1A (5-HT1A) reseptörlerinde kısmi agonist ak-

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