BÖLÜM 49

Karaciğer Bozukluklarında Psikofarmakolojik Tedavi Seçimleri

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GİRİŞ

Karaciğer metabolizmayı düzenleyen, organizmanın metabolizması için gerekli olan pek çok maddeyi üreten, depolayan ve salgılayan insan vücudundaki en büyük organdır (1). Biyoaktif maddelerin (hormon, ilaç vb), kimyasal dönüşümü ve metabolik faaliyetler sonucu oluşan bazı toksik maddelerin (amonyak vb.), daha az toksik hale dönüştürülmesi (üre, ürik asit vb.), karaciğer tarafından gerçekleştirilir (2). Karaciğer fonksiyon bozukluğu olan kişilerde nonspesifik nöropsikiyatrik belirtiler ortaya çıkabilmesi ile beraber karaciğer hastalığına ikincil gelişen psikiyatrik bozukluklar, sık görülen alkol ve madde kullanım bozukluğu birlikteliği, birincil psikiyatrik hastalıkların varlığı ve karaciğer hastalığının tedavisine ikincil gelişen psikiyatrik bozukluklar nedeniyle bu hasta grubunda psikiyatrik tedaviler yaygın olarak kullanılmaktadır.(3,4) Bu bölümde karaciğer fonksiyon bozukluğundaki değişiklikler, karaciğer hastalıklarında dikkat edilmesi gereken genel hususlar ve ruhsal bozukluklarda kullanılan ilaçların karaciğere etkileri incelenecektir.

KARACİĞER FONKSİYON BOZUKLUĞUNDA ORTAYA ÇIKAN DEĞİŞİKLİKLER

Metabolizma

Karaciğer ilaçlar üzerindeki metabolik etkisini ilaçların biyotransformasyonu ve/veya atılımlarını sağlayarak yerine getirir. Karaciğerde ilaç metabolizması iki fazdan oluşur. Faz 1 tepkimeleri (oksidasyon-redüksiyon/hidrolizasyon) CYP450 enzimleri aracılığı ile toksik bileşiklerin polarizasyonunu artırarak, vücuttan atılımlarını hızlandıran tepkimelerdir. Faz 2 tepkimeleri (transfer veya konjugasyon tepkimeleri) bileşiklerin detoksifikasyonunu sağlayan ve suda çözünürlüklerini artıran tepkimelerdir (5). Karaciğerin metabolik kapasitesinde azalma hepatik ensefalopati ve ilaçlarla dozla ilişkili yan etkilerde artma ile ilişkilidir (3).

Emilim

Karaciğer fonksiyon bozukluğuna eşlik eden portal hipertansiyon, karaciğer kan akımında azalma ve splanknik alanda vasküler konjesyonun bulunması ilaç emilimini azaltır (6). Ayrıca hepatik

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klordiazepoksit, klorazepat, klonazepam, flurazepam ve triazolam nadir görülen kolestatik karaciğer hasarı ile ilişkilendirilmiştir (98). Lorazepam, ağır karaciğer hastalığında en iyi tolere edilen ilaç olarak bilinir ve alkol yoksunluğunda çoğunlukla kullanılır (7). Ensefalopatiye neden olma riskinden dolayı kronik karaciğer yetmezliği olan hastalarda benzodiazepin kullanmaktan kaçınılmalıdır.

Z-İlaçlar

Karaciğerde metabolize edilirler, çoğunlukla kısa bir yarı ömre sahiptirler(1-7 saat). Hafif ila orta şiddette karaciğer fonksiyon bozukluklarında başlangıç dozlarının azaltılması, ağır karaciğer fonksiyon bozukluklarında ilacı kesmek önerilmektedir (7).

Zaleplon, kısa yarı ömürlüdür ve ilk geçiş metabolizmasına uğrar, zolpidem yüksek oranda plazma proteinlerine bağlanır ve karaciğer yetmezliğinde plazma seviyesi ve yarılanma ömrü artar; bu ilaçların dikkatli kullanılması önerilir (99). Zopiklon ve zaleplon hepatotoksisite ile ilişkilendirilmemiştir (7). Nadiren anormal KCFT bulguları ve zolpidem ile tek bir karaciğer hasarı vakası bildirilmiştir (100).

Melatonin

Melatonin büyük oranda karaciğerde metabolize edilir ve kısa yarı ömre sahiptir (101). Karaciğer yetmezliğinde melatoninin klirensi azalır ve yarı ömrü uzar, üretici firma karaciğer fonksiyon bozukluklarında kaçınılmasını önermektedir (7). Melatonin, karaciğer enzimlerinde yükselme ile ya da belirgin hepatik hasara sebep olmakla ilişkilendirilmemiştir (102).

SONUÇ

Psikofarmakolojik ajanların çoğu karaciğerde metabolize edilir. Karaciğer fonksiyonlarında bozulma nedeniyle ilaçların metabolizması, dağılımı, emilimi ve proteinlere bağlanma özelliklerinde değişim meydana gelir. Bu durum ilaçların kan düzeyinde ve etkinliğinde değişiklik oluşturur. Karaciğer fonksiyonu bir bütün olarak tüm sistemleri etkileyebilir. Gerek serum protein düzeylerinin azalması, gerekse hepatik kan akımının azalması, asit oluşumu ve ensefalopati oluşumu gibi durumlar nedeniyle ilaç kullanımında çok yönlü değerlendirme yapılmasını önemlidir. Ayrıca yetmezliğin düzeyi de ilaç seçim sürecinde kararlarımızı etkileyecektir. Kan düzeyi belli aralıkta bulunması gereken ilaçlar dikkatli takip edilmelidir. Özellikle konstipasyon ve belirgin sedasyon oluşturan ilaçlar ile antikolinerjik ve benzodiyazepinler, ensafalopati riskini artıracağı için tercih edilmemelidir. Uzun etkili ve depo ilaçlardan kaçınılmalıdır. Birçok ilacın asemptomatik, kendini sınırlayan, geçici transaminaz yüksekliği yapabileceği akılda tutulmalıdır. Karaciğer fonksiyon bozukluğu olan hastanın tedavisini ilgili branşlarla işbirliği içinde yönetmek önemlidir.

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