



BÖLÜM 5

Kronik Psikiyatrik Hastalıklarda Yeni Deneysel Psikofarmakolojik Çalışmalar

Cafer Çağrı KORUCU¹

GİRİŞ

Dünya Sağlık Örgütü (WHO), tedavi edilmeyen psikiyatrik bozuklukların toplam hastalık yükünün %13'ünü oluşturduğu belirtmiştir (1). Psikiyatride daha etkili tedavi seçeneklerinin azlığı, psikiyatrik bozuklukların biyolojik temelinin sınırlı anlaşılmasına bağlanmıştır. Ancak yapılan yeni çalışmalar, gelecekteki tedavi başarısı için karamsarlığın yersiz olabileceği göstermektedir (2).

MAJOR DEPRESYONDA YENİ DENEYSEL PSİKOFARMAKOLOJİK ÇALIŞMALAR

Major depresyon, oldukça yaygın görülen, kronik, tekrarlayan önemli bir psikiyatrik bozukluktur (3). Major depresyonda remisyon dönemlerinde de, kognitif fonksiyonlardaki bozulma sıklıkla tam düzelmemekte, antidepresanlar tarafından optimalin altında tedavi edilmektedir (4,5). Major depresyon tedavisi için yeni nöroprotektif ve prokognitif ajanların geliştirilmesi zorunlu bir ihtiyaç olmuştur (6). Anti-inflamatuar ajanların, major depresyon tedavisi için önemli sonuçlar sağlaması yeni terapötik tedavilerin öncüsü olarak değerlendirilmiştir (7,8). Minosiklin, mikrogial aktivasyonu önleyerek nöroprotektif etkiler sağlayan bir

ajandır (9). Psikotik özellikli major depresyonu olan hastalar (N=25) üzerinde 6 haftalık açık etiketli bir çalışmada minoksilinin major depresyonda etkin olduğu gösterilmiştir (10). Kırk major depresyon hastasında yapılan bir diğer çalışmada ise, selekoksib tedavisini takiben yanıtın (depresif semptom şiddetinde azalma) azalmış serum IL-6 seviyeleri ile ilişkili olduğunu bildirmiştir (11). Fonksiyonel nörogörüntüleme çalışmalarında, major depresyon hastalarında C-reaktif protein (CRP) artışı ile daha küçük hipokampal hacimler rapor edilmiştir (12). TNF- α antagonisti olan infliximabın antidepresan potansiyelini inceleyen bir çalışmada altmış hasta, başlangıçta, 2, 4 ve 6. haftalarda infliximab (5 mg/kg) uygulanmıştır. Yüksek duyarlılık (CRP seviyesi > 5mg/L) olan hastalarda depresyon şiddetini hafifletmede plasebodan üstün bulunmuştur (13). Ketamin, 1970 yılında anestezi tedavide kullanılmaya başlanan bir ilaçtır (14). Ketaminin son yıllarda yapılan çalışmalarda majör depresyonda suisid düşüncesini azalttığı belirlenmiştir (15,16,17,18). Anne yoksunluğu ile oluşturulan hayvan modelinde, tek bir doz ketamin uygulanmasından sonra depresif davranışları tersine çevirdiği ve oksidatif stresi azalttığı belirlenmiştir (19). Altmış yedi deneğin katıldığı ketamin ve midazolam ile karşılaştırıl-

¹ Uzm. Dr., Aydın Devlet Hastanesi, Ruh Sağlığı ve Hastalıkları Kliniği, korucu09@gmail.com

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