BÖLÜM 4

OBEZİTE VE İLAÇ FARMAKOLOJİSİ

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Giriş

Obezite hem ülkemiz hem de tüm dünyada ciddi ve artan bir sağlık sorunudur. Ülkemizde obezite oranı 2008'de %15,2 iken, 2019'da %21,1'e yükselmiştir. 55-64 yaş aralığında en yoğun olan obezite oranı kadınlarda erkeklere göre daha fazladır[1]. Onbeş yaş üstü yetişkinlerde durum bu iken, çocuklarda da her geçen gün obezite oranı yükselmektedir. Ülkemiz, obezite oranının Avrupa'da en yüksek olduğu ülke durumundadır ve dünyada ABD ve Suudi Arabistan'dan sonra 3. sırada yer almaktadır[2].

Dünya Sağlık Örgütü (DSÖ), VKİ'nin 30 kg/m^2'ye eşit veya daha yüksek olmasını obezite, 40 kg/m^2'ye eşit veya onun üzerinde olmasını da şiddetli (morbid) obezite olarak tanımlamaktadır (Tablo-1).

DSÖ verilerine göre 2016 yılında 18 yaş ve üzeri 1.9 milyar yetişkinin (dünya nüfusunun %39'u) aşırı kilolu olduğu ve bunların da 650 milyonunun obez olduğu görülmektedir. Dünyada obezite prevalansı 1975 ile 2016 yılları arasında 3 katına çıkmıştır. 2019 yılında 5 yaşın altındaki 38.2 milyon çocuğun aşırı kilolu veya obez olduğu tahmin edilmektedir. Yine 2016 yılında 5-19 yaş arası 340 milyondan fazla çocuk ve ergen aşırı kilolu veya obezdi[2].

Obezite Tip 2 diabetes mellitus (DM), kardiyovasküler hastalık, hipertansiyon, dislipidemi, kanser ve osteoartrit gibi birçok kronik hastalık riskini artırmakta ve yaşam kalitesini bozarak ortalama ömrü kısaltmaktadır [3]. Obez bireylerde kronik ağrı [4, 5] ve nozokomial enfeksiyon görülme oranları [6, 7] daha yüksek olarak bildirilmiştir.

Obez çocuklarda DM, hipertansiyon, uyku apnesi ve koroner arter hastalığı ve astım daha fazla görülmektedir [8]. Astımlı obez çocuklarda steroidlere yanıtta azalma olduğu bildirilmiştir[9].

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hastalıkların seyrinin kötüleşmesine yol açmaktadır. Bu etkiye ilave olarak, obezlerde kemoterapötiklerin FK'lerinin değişmesine bağlı olarak plazma konsantrasyonlarının obezlerde azalması enfeksiyon hastalıklarının kötüleşmesine katkıda bulunabilir [113]. Morbid obezitenin profobol FK'ni önemli ölçüde etkilediği ve muhtemelen ilaç tepkilerinin (FD) değişmesine neden olduğu bildirilmiştir [77]. Aksine yine profobol ile yapılan bir çalışmada, morbid obezlerde klirens ve ED_{50}'de azalma olmasına karşın, FD etkide azalma olmadığı, bunun beyinin profobole karşı artan duyarlığından kaynaklanabileceği öne sürülmüştür [86].

Nöromüsküler bloke edici ilaç olan atraküryum, obezlerde ve normal kilolu deneklerde benzer V_s, $t_{1/2}$, ve KL değerleri ve FD etkinlik göstermiştir. Ancak bu parametreler TVA'na göre düzeltildiğinde, obezlerde V_s, $t_{1/2}$, ve KL azalmış, plazma ilaç düzeyi artmış, ancak nöromüsküler blokajdan kurtulma süreleri değişmemiştir[114]. Daha sonra yapılan benzer çalışmalar atraküryum dozlarının IVA'na göre ayarlanması gerektiği bildirilmiştir[115]. Obez hastalarda triazolama duyarlıkta artma saptandı [116]. Obezitede gelişen insülin direnci ve DM'lu hastalarda insülin profilinde FK değişiklerden bağımsız olarak FD etkide değişikliğin olabileceği öne sürülmüştür [117, 118].

Adipositlerin aktive ettiği makrofajlar, karaciğer, damar endoteli ve trombositler gibi organ ve hücrelerin çoğunda inflamasyonu tetikleyen pproinflamatuvar sitokinlerin ve interlökinlerin salgılanmasını artırır. Endotelyal inflamasyon, koagülan mekanizmaların aktivasyonu ve antikoagülan mekanizmaların inhibisyonuna neden olur. Obezitede tromboza eğilim artar[119.] Obez hastalarda fraksiyone olmayan heparine yanıtlarda azalma ve gecikme olmuştur [120,121]. Yine, obez hastalardan alınan trombositlerde cAMP ve cGMP düzeylerinin düşük olduğu, bunun da aspirininin antitrombotik etkinliğindeki azalmaya yol açabileceği bildirilmiştir[122].

Metoprolol normal kilolulara kıyasla obez hastalarda daha fazla antihipertansif etki göstererken, isradipin normal kilolularda daha fazal etkinlik göstermiştir [123]

Sonuç olarak, obez hastalar için optimum ilaç dozlarının saptanması oldukça zordur ve tek bir vücut boyutu tanımlayıcısının kullanılması birçok durumda hatalı olabilir. İlaç düzeylerinin yakından izlenmesi (terapötik ilaç izlemi) ve hastanın ilaca yanıtlarının yakından takip edilmesi önemlidir. Obezitenin ilaçların FK ve FD parametreleri üzerindeki etkileri birçok faktöre bağlı olduğundan, ilaç grupları için kapsamlı çalışmaların yapılması gerekir. Ayrıca ilaç geliştirilmesi aşamasında obez popülasyonların da klinik araştırmalara dahil edilmesi optimal ilaç dozlamına katkıda bulunacaktır. Sağlıklı ve güvenilir veriler elde edilinceye kadar, klinisyenlerin obez hastalarda ilaç kullanırken daha dikkatli olmaları ve yakın izlem yapmaları önerilmektedir.

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