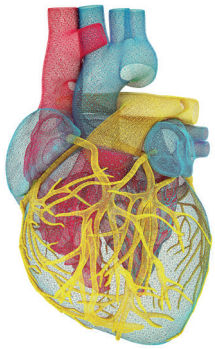

BÖLÜM **30**

İnsülinlerin Kardiyovasküler Hastalık, Kan Basıncı ve Kalp Yetersizliği Üzerine Etkileri

Himmet DURMAZ [1]

GİRİŞ

Dünya Diyabet Atlası'na göre 2030 yılında 643 milyon, 2045 yılında 783 milyon diyabetli birey olması öngörülmektedir (1). Artan diyabet sıklığı ile kardiyovasküler hastalık (KVH)'lar ve hipertansiyon da artış gösterecektir. 1922 yılında Dr. Banting ve Dr. Best diyabet tedavisinde çığır açan insülini keşfederek diyabet hastalarına umut olmuştur (2). Zamanla birçok antidiyabetik ilaç gelişimi olmuştur. İlaçların glisemik fayda sağlamasının yanında istenmeyen kardiak etkileri de görülmesi üzerine 2007 yılında Amerika İlaç Ajansı tüm yeni antidiyabetik ilaçların kardiyovasküler (KV) güvenlik çalışmasının olmasını zorunlu kılmıştır (3).

Tip 1 diyabetes mellitus (T1DM)'un tedavisi insülindir. Tip 2 diyabetes mellitus (T2DM) tedavisinde ise öncelik insülin dışı oral veya enjektabl antidiyabetik tedavidir. İnsülin tedavisine, insülin dışı antidiyabetik tedavi ile glisemik kontrol sağlanamayan, uzun süreli diyabet neticesinde endojen insülin rezervi azalmış hastalarda geçilmektedir. İnsülin tedavisine geçişte genel yaklaşım orta veya uzun etkili bazal insülin (insülin NPH, insülin detemir, insülin glarjin U100, insülin glarjin U300, insülin degludec) başlamaktır (4). Ama çoğu hasta bazal insüline ilave olarak postprandial glisemik hedeflere ulaşmak için insülin tedavisinin yoğunlaştırılmasına ihtiyaç duymaktadır. Tokluk kan şekerini kontrol etmeye yönelik olarak kısa etkili insülin analogları (insülin lispro, insülin aspart, insülin glulisin) tercih edilebilmektedir. Bazal plus, bazal bolus veya günde 2-3 defa uygulanan premiks insülin rejimleri kullanılmaktadır. Prandial insülinin ayrı uygulanması doz titrasyonu açısından daha fazla esneklik sağlamaktadır. Diğer alternatif yaklaşım ise premiks insülin kullanmaktır (5). Premiks insülinler, protamin insülin ve hızlı etkili insülin karışımlarından oluşan sabit doz formülasyonlarıdır. Premiks insülin kullanımı hastaların gün içinde daha az enjeksiyon uygulaması açısından kolaylık sağlarken sabit ko-formülasyondan dolayı bazal ve bolus dozları ayarlamakta zorluk olabilir. İnsülin degludek+insülin aspart koformülasyonu ise % 70 insülin degudek , % 30 insülin aspart içeren ilk 2 farklı insülinin hazır karışımıdır (6).

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vasküler inflamasyon ve ateroskleroz için başlatıcı faktör olabilir. Endotelyal disfonksiyonla vasküler permeabilite bozulur, lökosit-endotel etkilişimi bozulur, trombosit agregasyonu olur (91). Endotelyal disfonksiyon ve ateroskleroza bağlı DM hastalarında periferik arter hastalığı (PAH) sıklığı artar. Hba1c'de her % 1'lik artış PAH riskinde %28 artış yapar ve PAH şiddeti hiperglisemi süresiyle ilişkilidir (92). PAH, diyabetik hastalarda ekstremitede iskemi, ülser ve gangrene yol açarak ekstremite ampütasyon nedenlerinde başı çekmektedir. Ankle brakial index (ABI), PAH tanısında kullanılabilecek kolay bir ölçüm yöntemidir.

İnsülinin karmaşık KV etkileri nedeniyle, İD'nin ve sonuçta ortaya çıkan hiperinsülineminin damar sistemi üzerinde olumsuz etkileri olduğu bilgisi, yoğun diyabet müdahalesinin KV bir fayda göstermedeki başarısızlığı ve insülin tedavisinin KV güvenliği sorgulanmıştır. İnsülin, iskelet sistemindeki kas dokusunda vazodilatasyon yaparak vasküler rezistansı azaltır ve kan akımını arttırır (93). Farmakolojik dozda uygulanan insüline bağlı oluşabilecek hipoglisemi kontregülatuar hormon sistemlerine aktive ederek artan epinefrine bağlı vazokonstrüksiyona yol açabilir. İnsülinin diyabete bağlı hiperglisemiyi kontrol etmesine rağmen, makrofajlar tarafından proinflamatuar yanıtı artırabildiği ve sinyal iletim yollarının hormonal aktivasyonunu uyarabildiği, böylece endotel mediyatörlerinin sentezi ve salınımı arasındaki dengeyi bozarak aterogenezin ilerlemesini hızlandırdığı gösteren veriler de mevcuttur (94, 95). Araştırmalar, insülin tedavisinin artan trombosit agregasyonu ile ilişkili olduğunu, dolayısıyla insülin ile tedavi edilen hastalarda daha yüksek stent yeniden tromboz oranlarına katkıda bulunduğunu göstermektedir (96).

Sonuç olarak insülin vasküler sistem üzerindeki kompleks etkileriyle birlikte glisemik kontrolde iyileşme ve HbA1c düşüşü sağlayarak PAH riskinde azalma sağlayabilir. Ayrıca diğer KV risk faktörlerinin kontrolü ve PAH'ye spesifik tedavilerin uygulanması gerekmektedir.

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