

BÖLÜM 2



HİPERTANSİYON TEDAVİSİNDE RENİN ANJİOTENSİN ALDOSTERON SİSTEMİ BLOKERLERİ

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GİRİŞ

Kan basıncının antihipertansif ilaçlar ile düşürülmesi inme ve majör kardiyovasküler olaylarda önemli azalmaya neden olur. Anjiotensin dönüştürücü enzim (ACE) inhibitörleri, anjiyotensin II tip 1 (AT1) reseptör antagonistleri (ARB) ve mineralokortikoid reseptör (MR) antagonistlerinden oluşan renin-anjiotensin-aldosteron sistemi (RAAS) blokerleri hipertansiyon tedavisinin temel yapı taşlarını oluşturmaktadırlar. 1898'de Tigerstedt ve Bergman¹ tarafından renin keşfedildikten sonra çeşitli bilim insanlarının ortak çabalarıyla tüm kaskad aşamalı olarak ortaya çıkarılmıştır. Hipertansiyon tedavisinde kullanılan RAAS blokerlerinden ilki ACE inhibitörleridir. FDA tarafından onaylanan ilk ACE inhibitörü 1982 yılında kaptopril olmuştur.² Bir dekat sonra ise ARB'ler keşfedilmiştir ve losartan 1995'te FDA tarafından onaylanmıştır.³

ACE İNHİBİTÖRLERİ

Etki mekanizması;

Böbreklerin jukstaglomerular aparatından üretilen renin, karaciğerde üretilen anjiotensinojeni anjiotensin I'e dönüştürür. Anjiotensin I, ACE aracılığıyla Anjiotensin II'ye dönüştürülür. ACE inhibitörleri, anjiyotensin dönüştürücü enzimin aktivitesini bloke ederek, anjiyotensin I'in anjiyotensin II'ye dönüşümünü önler. ACE, büyük ve küçük damarların, kılcal damarların ve venüllerin endotel hücrelerinde ve pulmoner endotel hücrelerinde bulunur. Önemli olarak, ACE, akciğerlerdeki stratejik

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komasti ve impotansa yol açan androjen reseptörünün bir antagonisti olarak ve adet düzensizliklerine neden olan progesteron reseptörünün bir agonisti olarak görev yapar.³³ Eplerenon daha selektif olduğundan spironolakton gibi seksüel yan etkilere neden olmaz.

Klinik çalışmalar;

Randomize, çift kör, plasebo kontrollü 150 dirençli hipertansiyonu olan hastanın takip süresini tamamladığı ASPIRANT-EXT çalışmasında 8 hafta sonunda spironolakton ile gündüz, gece ve 24 saatlik ambulatuvar kan basıncında sistolik ve diastolik kan basıncında plaseboya kıyasla belirgin azalma olduğu saptanmıştır.³⁴ PATHWAY-2 çalışmasında ise spironolakton, doksazosin, bisoprolol ve plasebo karşılaştırılmış ve dirençli hipertansiyon tedavisinde eklenebilecek en etkili ilacın spironolakton olduğu saptanmıştır.³⁵ Eplerenonun arteriyel hipertansiyon tedavisindeki etkisi Weinberger ve ark. Tarafından araştırılmış ve eplerenonun ciddi yan etkiler olmaksızın plaseboya kıyasla kan basıncını önemli ölçüde azalttığı gösterilmiştir.³⁶ Antihipertansif etkinin doz bağımlı olduğu ve bununla eplerenonun kan basıncını düşürmede spironolaktondan daha az etkili olduğu görülmüştür.

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