5. Bölüm

ANJİYOTENSİN RESEPTÖR BLOKÖRLERİ (ARB)

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Renin-anjiyotensin-aldosteron sistemi (RAAS), akut ve kronik kalp yetmezliğinin patofizyolojisinde çok önemli bir rol oynamaktadır. Kalp yetmezliği için yapılan ultrafiltrasyon ve diürez gibi tedaviler ve diğer farmakoterapilerden çok fazla etkilenmektedir.

RAAS'NİN FİZYOLOJİSİ

Renin jukstaglomeruler cisimdeki özelleşmiş granüler hücreler tarafından sentezlenen bir enzimdir ve üç uyarıya sekonder olarak aferent arterioller tarafından dolaşıma verilir: 1) arteriolar damar duvarındaki baroreseptör hücreler tarafından algılanan arteryal kan basıncındaki azalma 2) Henle kulpunun sonundaki renal tübüllerde bulunan makula densa hücrelerinde azalmış intraselüler klorür düzeyleri ki bu potasyum azlığı tarafından da uyarılabilen bir süreçtir 3) sempatatik aktivasyon.(1) Yüksek sistemik kan basıncı ve volüm fazlalığı gibi durumlarda renal perfüzyon artar ve prorenin salınımı inhibe olur. Renin anjiyotensinojenden 10 aminoasidi kırar ve anjiyotensin I oluşturur, ki bu da ACE tarafından anjiyotensin II'ye dönüştürülür. Anjiyotensin I'i anjiyotensin II'ye dönüştüren proteaz kimaz adında başka bir alternatif yol daha vardır.(2) Anjiyotensin II adrenal bezden aldosteron salınımının çok güçlü bir uyarıcısıdır. RAAS'ın amacı kan basıncını, sıvı elektrolit dengesini ve sistemik vasküler direnci regüle etmektir.

Anjiyotensin II'nin Sistemik Etkileri

Anjiyotensin II primer olarak AT1 reseptörleri üzerinden etki eder ve çok sayıda kardiyovasküler ve renal olayı aktive eder:

a) Sistemik arteryal vazokonstrüksiyon
b) Renal arteriolar vazokonstrüksiyon
c) Renal tübüllerden sodyum ve suyun geri emilimini uyarır
d) Damar düz kaslarının kasılmasına yol açar
e) Adrenal bezlerden aldosteron salınımına yol açar

AT2 reseptörlerinin rolü ise tam anlaşılabilmiş değildir. KY'nde anjiyotensin II oluşumunun ilk sonucu sistemik kan basıncının devam ettirilmesidir. Daha sonra renal tübüler sodyum emiliminin artmasına bağlı olarak(direkt veya aldosterona bağlı olarak) plazma hacminde artış görülür. Böbrekte, renal perfüzyon azaldığında efferent arteriolar dirençteki artış glomerüler filtrasyon hızının (GFR)'ın korunmasını sağlar. Anjiyotensin II sistemik ve renal dolaşımda aşırı vazokonstrüksiyonu önleyen prostaglandinlerin salınımını da uyarır.(3)

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nostik öneme sahiptir. Normal EF varlığında bile, renal disfonksiyona bağlı gelişen volüm fazlalığı KY kliniğine neden olabilir.[59] Renal disfonksiyonlu volüm fazlalığı olan hastalarda KY'nin saptanması zordur. Ventriküler hipertrofi, diastolik disfonksiyon, KBY'li hastalarda volüm ve basınç fazlalığı, sol ventrikül disfonksiyonu olan hastalarda KY'nin görülmesi veya kötüleşmesine neden olabilir.[60] Son dönem böbrek yetmezliği hastalarının % 20'sinde KY'nin klinik bulguları mevcuttur.[61] Kardiyovasküler ve renal sistem arasındaki denge RAAS ve otonomik sinir sistemi tarafından sürdürülmektedir.[35]

Son American College of Cardiology Foundation/American Heart Association kılavuzuna göre, bir ACEİ ve beta-bloker tedavi almakta olan ve bir aldosteron antagonistinin endike olmadığı veya tolere edilemediği DEFKY'li hastalarda, bir ARB Klas IIa Düzey:A endikasyonla tedaviye eklenebilir.[13] Son European Society of Cardiology kılavuzuna göre, EF'si ≤ % 40 olan ve bir ACEİ ve beta-bloker tedavisine rağmen semptomları devam eden (NYHA sınıf II-IV) ve bir mineralokortikoid reseptör antagonistini tolere edemeyen hastalarda, Klas I Düzey:A endikasyonla tedaviye bir ARB eklenebilir.[40]

Özetleyecek olursak; ACEİ'leri DEFKY'li hastalarda KY'nin derecesine, sebebine ve semptomlara bakılmaksızın primer tedavi olarak verilmektedir. ARB'ler ise ACEİ'lerini tolere edemeyen hastalarda primer tedavi seçeneği olarak kullanılmaktadır. ACEİ ve ARB kombinasyonu ise, ACEİ'lerine bir aldosteron antagonisti eklenmesi daha iyi sonuç verdiği için pek uygun değildir.

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