

6.

BÖLÜM

KALSİYUM KANAL BLOKERLERİ

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GİRİŞ

Kalsiyum kanal blokerleri(KKB) uzun süredir antihipertansif, antianginal ve antiaritmik olarak yalnız başına veya kombinasyon şeklinde yaygın kullanılan heterojen bir ilaç grubudur. Kimyasal olarak non-dihidropiridin (NDHP) (diltiazem ve verapamil) ve dihidropiridin (DHP) (felodipine, nicardipine, nifedipine, nimodipine, nisoldipine gibi) ler olarak iki gruba ayrılmaktadır. Etkilerini hücre membranında bulunan voltaj bağımlı Ca^{+2} kanalları aracılığıyla gösterirler. Voltaj bağımlı kalsiyum kanalları hücre membranında heteromeric (farklı) yapılardan oluşmuştur. KKB leri alfa 1 subunitinde bulunan kalsiyum kanalları aracılığıyla farklı proteinler üzerinden etkilerini gösterirler. Alfa 1 subunitinde bulunan en az 5 tip kalsiyum kanalı vardır. Bu kanallar L, N, P/Q, R, T tipi kanallardır. L,N,P/Q,R tipi kanallar sinir sisteminde bulunurlar. Ayrıca L tipi kanallar miyokarda, vasküler düz kaslarda, atriyoventriküller nodta, sinüs nodunda ve adrenokortikal sistemde bulunmaktadır. T tipi kanallar ise miyokarda ve adrenokortikal sistemde daha yaygın görülmektedir. Böbrekte glomerül filtrasyon oranı (GFR) ve intraglomerüller basınç afferent ve efferent arteriyoller tarafından düzenlenmektedir. L tipi kanallar afferent arteriyollerin düz kaslarında mevcut olup efferent arteriyollerde bulunmamaktadır. T,P/Q ve N tipi kanallar ise hem afferent hemde efferent arteriyollerde bulunmaktadır. P/Q,N tipi kanallar hem afferent hemde efferent sinirleri innerve eden sempatik sinir uçlarında da mevcuttur.

L tipi KKB leri afferent arteriyollerde dilatasyona neden olmaktadır. Fakat efferent arteriyoller üzerinde vazodilatatör etkisi olmadığından intraglomerüller basınç artışına, GFR düşüşüne ve ayrıca renin angiyotensin aldosteron sisteminin (RAAS) devreye girmesine neden olmaktadır. Bunun sonucu olarak angiotensin2, aldosteron ve noradrenalin düzeyinde artışa neden olabilmektedir. Ancak N, T ve P/Q tipi KKB leri bunun tersine hem afferent hemde efferent arteriyollerde dilatasyona neden olup intraglomerüller basıncı azaltmakta ve RAAS sisteminin çalışmamasını

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renoprotektif etkileri açısından bir çok çalışmada nötür bulunmuştur ve amlodipin'in inme ve miyokard enfarktüsünden koruma etkileri ön plana çıkmıştır ve birçok RAAS blokajı ile beraber test edilmiştir.

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