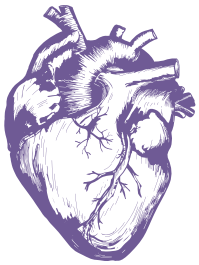

BÖLÜM 16

Sodyum Glukoz Ko-Transporter 2 İnhibitörlerinin Temel Farmakolojisi

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GİRİŞ

Sodyum Glukoz Ko-transporter 2 (SGLT2) İnhibitörleri Tip 2 Diyabetes Mellitus (DM) tedavisinde kullanılan oral ajanlar olup, böbreğin proksimal tübülünün S1-S2 segmentinde yer alan, glukoz ve sodyumun (Na) beraber geri emiliminden sorumlu SGLT2 kanallarını inhibe ederek etkilerini gösterirler (1). SGLT2 kanalları normalde filtre edilen glukozun %90'nın geri emiliminden sorumlu iken, kalan %10'luk kısım da proksimal tübülün S3 segmentinde yer alan SGLT1 kanalları tarafından gerçekleştirilir (1). SGLT2 inhibitörleri glukoz emilimini bloke ederek, insülin duyarlılığı ve sekresyonundan bağımsız olarak kan glukoz seviyesini düşürürler (2).

SGLT2 inhibitörlerinin kan glukoz düzeyini düşürmenin ötesinde çok sayıda faydalı etkisi bulunmaktadır. Yapılan çok sayıda büyük skala klinik çalışmada SGLT2 inhibitörlerinin kardiyovasküler mortalite, tüm sebeplere bağlı mortalite ve kronik böbrek hastalığında ilerlemeyi azalttığı, kalp yetersizliğine (KY) bağlı hastane yatışları ve aterosklerotik olaylarda azalma ile ilişkili olduğu gösterilmiştir (3-9). SGLT2 inhibitörlerin kardiyometabolik ve renoprotektif etkileri DM varlığından bağımsız olup multifaktöriyeldir (10). Bu yüzden güncel kılavuzlarda SGLT2 inhibitörleri DM varlığından bağımsız olarak düşük EF'li KY hastalarında Sınıf Ia endikasyon ile önerilmektedir (11,12).

SGLT TAŞIYICILARI VE SGLT2 İNHİBİTÖRLERİ

Normal fizyolojik koşullarda glomerüler filtrata günlük 180 gr. glukoz geçer ve bunun tamamı SGLT'ler tarafından geri emilir. Bunun %90'nı proksimal tübülün S1 ve S2 segmentinde olan SGLT2 taşıyıcıları tarafından, geri kalanı da proksimal tübülün S3 segmentinde olan SGLT1 tarafından gerçekleştirilir (1). SGLT 1 ve 2 SLCA5 gen ailesi tarafından kodlanırlar (13). SGLT2 yüksek kapasite/düşük afiniteli bir taşıyıcı iken, SGLT1 düşük kapasite/yüksek afiniteli bir taşıyıcıdır (14). SGLT2 proksimal tübül S1/S2 segmentinde yer alırken, SGLT1 taşıyıcıları gastrointestinal sistem, renal proksimal tübül S3 segmentinde, kalp, karaciğer ve akciğerde bulunurlar (15). (Tablo 1) Tip 2 DM hastalarında proksimal tübülde normalden daha çok sayıda SGLT2 taşıyıcısı bulunmaktadır. Bu da geri emilen glukoz miktarının artmasına ve hiperglisemiye neden olmaktadır. Plazma glukoz oranı sınır değeri aştığında (200-250 mg/100 ml) SGLT'ler satüre olmakta ve idrarda glukoz atılımı

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feksiyon riskini taşımadığı, korunmak için kişisel hijyene dikkat edilmesi gerektiği gösterilmiştir. Enfeksiyon durumlarında ilaca ara verilmesi, tekrar eden enfeksiyon durumlarında da ilaca devam edilmemesi önerilmektedir (71).

CANVAS (3) çalışmasında görülen artmış kemik fraktürü ve alt ekstremite amputasyon oranları, daha sonra SGLT2 inhibitörleri ile yapılan büyük popülasyonlu çalışmalarda saptanmamıştır (72).

SONUÇ

SGLT2 inhibitörlerinin kan glukoz düşürücü etkisinin ötesinde kardiyorenal koruyucu etkilerinin olduğu yapılan çalışmalarda gösterilmiştir. SGLT2 inhibitörlerinin bahsedilen tüm kardiyoprotektif etkileri ele alındığında, KY tedavisinde kullanılan RAS inhibitörleri, beta blokerler, mineralokortikoid reseptör antagonistleri, neprilisin inhibitörü gibi etkilerini nörohormonal antagonizma üzerinden gösteren ilaçlar gibi değerlendirilmesi gerekmektedir.

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