

Bölüm 15

PROTON POMPA İNHİBİTÖRLERİ YAN ETKİLERİ

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GİRİŞ

İlk olarak 1989'da onaylanan proton pompa inhibitörleri (PPI), dünyada en sık kullanılan ilaçlar arasındadır. Amerika Birleşik Devletleri Gıda ve İlaç İdaresi (FDA) tarafından PPI'lar, gastroözefajial reflü hastalığı ve Barrett özefagus semptomlarını kontrol etme ve önlemede, nonsteroid antiinflamatuvar ilaçlar ile ilişkili kanama profilaksisinde, peptik ülser hastalığında, aşırı mide asit salgısını kontrol etmek için Zollinger-Ellison sendromunda ve Helicobacter pylori (H. Pylori) eradikasyonunda onaylanmıştır. PPI'lar (omeprazol, lansoprazol, pantoprazol, rabeprazol, esomeprazol) benzimidazol türevleridir, gastrik pariyetal hücrelerde bulunan hidrojen/potasyum ATPaz (H⁺/K⁺-ATPaz) enzimine irreversibl olarak bağlanarak gastrik asit üretimini doz bağımlı olarak azaltırlar(1). PPI'lar hepatik sitokrom P450 enzim sisteminden CYP2C19 ve CYP3A4 tarafından metabolize olurlar. Rabeprazol, ağırlıklı olarak non-enzimatik yol ile ve az oranda da CYP 2C19 ve CYP3A4 ile metabolize olur (2). PPI metabolizmasında baskın role sahip CYP2C19 enzimi için iki inaktive edici mutasyon tanımlanmıştır ve mutasyona sahip bireylerde PPI'ların metabolizması gecikebilir (yavaş metabolizörler) (3). CYP2C19 enzimi yavaş metabolize edenlerde, standart doz PPI ile daha güçlü asit inhibisyonu elde edilirken, hızlı metabolize edenlerde asit inhibisyonu yapılamaz ve PPI'ların belirli aralıklarla yüksek doz verilmesi gerekir (2). PPI'ların hepatik sitokrom P450 enzimleri ile metabolize edilmesi bazı kişilerde spesifik ilaç etkileşimlerine yol açabilir. Son çalışmalar, PPI ilaçlarının uzun süreli kullanımı ile ilgili olumsuz etkileri olduğunu göstermiştir. PPI'lara bağlı minör yan etki riski yaklaşık %1-3 olup, klinik çalışmalarda yan etkiler nedeniyle ilacı bırakma oranı %1-2 olarak saptanmıştır ve yan etkiler açısından PPI'lar arasında fark bulunmamıştır (1). En sık görülen yan etkileri baş ağrısı, bulantı, ishal, kabızlık, baş dönmesi ve döküntüdür (3). PPI'lar genellikle iyi tolere edilir ve çoğu zaman uygun endikasyon yokluğunda uzun süreli, bazen yaşam boyu reçete edilmektedir. Ayrıca birçok hasta bu ilaçları tıbbi yardım ve reçete istemeden özgürce ve uzun süreli

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