BÖLÜM 17

POLİMİKSİNLERE VE FOSFOMİSİNE DİRENÇ MEKANİZMALARI

Duygu TEKİN[1]

Polimiksinlere direnç mekanizmaları

Giriş

1940'larda keşfedilen polimiksinler, *Bacillus polymyxa*'dan türetilen çoklu ilaca dirençli (ÇİD), gram negatif bakteriyel enfeksiyonların tedavisinde kullanılan polikatyonik antimikrobiyal peptitlerdir (1-4). Dış membrandaki lipopolisakkaritler (LPS) ve fosfolipitlerle etkileşime girerek hücre geçirgenliğini artırarak etki gösterirler. Polimiksinlerin ciddi nefrotoksisite ve nörotoksisite yan etkileri nedeniyle yerini aminoglikozidler gibi antibiyotikler almıştır (4,5). Bununla birlikte, 2000'lerin başından itibaren, ÇİD Gram-negatif bakterilerde artış ve polimiksine alternatif antimikrobiyal ajanların yokluğu nedeniyle son basamak tedavi olarak polimiksin kullanımı artırmıştır. Bu antibiyotiklerin artan klinik kullanımı direnç sorununu gündeme getirmiştir (6).

Klebsiella pneumoniae, *Pseudomonas aeruginosa* ve *Acinetobacter baumann*ii gibi bazı bakteriler, polimiksinlere karşı edinilmiş direnç geliştirirken, *Proteus* türleri, *Serratia* türleri ve *Burkholderia* türleri de doğal dirençlidir. Gram-negatif bakteriler polimiksine karşı çeşitli direnç mekanizmaları kullanır. Bu mekanizmalar efluks pompaları, lipid A›nın çeşitli modifikasyonları, kapsül varlığı ve dış membran proteininin aşırı ekspresyonudur (7).

Polimiksin etki mekanizması

Polimiksinin ana hedefi olan dış membran gram negatif bakterilere özgüdür. Çift sıralı fosfolipid tabaka ve proteinlerden oluşur, lipoproteinler aracılığı ile pep-

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rekli olmasına rağmen ilgili tek faktör değildir (94). Heterodirenç, MDR ve MDR olmayan *P. aeruginosa* suşlarında da tanımlanmıştır (95).

Fosfomisine in vitro yüksek direnç oranlarına rağmen klinik uygulamada direnç oranları düşüktür (66,76).

Çalışmalar fosfomisine dirençli suşların (FosA›nın varlığına bağlı olarak), evcil ve kümes hayvanlarından ve hayvansal gıdalardan yayıldığını göstermiştir (96).

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