BÖLÜM 18

GLİKOPEPTİTLERİN ETKİ SPEKTRUMU VE KULLANIM ALANLARI

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Giriş

Glikopeptitler özellikle gram pozitif bakterilerin neden olduğu pek çok enfeksiyonun tedavisinde ilk seçenek olarak tercih edilmektedir. Bu bölümde ülkemizde uzun süredir kullanımda olan vankomisin ve teikoplanin ile dünyanın bazı ülkelerinde belirli enfeksiyonların tedavisinde kullanılmak üzere onay alan fakat henüz ülkemizde kullanımda olmayan telavansin, dalbavansin ve oritavansin gibi antibiyotikler incelenecektir. Okuyucular bu yazıda glikopeptit grubu antibiyotiklerin kimyasal yapısı etki mekanizması ve spektrumu, farmakodinamik ve famakokinetik özellikleri, metabozması ve çeşitli klinik enfeksiyonlardaki kullanımına ilişkin bilgileri bulabileceklerdir.

Vankomisin

Kimyasal yapısı ve etki mekanizması

Vankomisin, trisiklik yapıyı oluşturan yedi üyeli bir peptit zincirinden ve amino şeker vankozamin ve glikozdan oluşan bağlı bir disakkaritten oluşan kompleks bir trisiklik glikopeptiddir. Molekül ağırlığı 1485.73 daltondur (Da), teikoplanin, daptomisin ve lipoglikopeptitler dışındaki diğer antimikrobiyal ajanlardan çok daha yüksektir. Glikopeptitlerin primer etkisi, bölünen bakterilerde hücre duvarı sentezinin geç aşamalarının inhibisyonudur.

Vankomisin, gram-pozitif mikroorganizmalara karşı geniş bir aktiviteye sahiptir. Stafilokoklar normalde vankomisine duyarlıdır, direnç durumu sonraki

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Antimikrobiyal etkinlik

Oritavansin, stafilokoklara (MRSA dahil), streptokoklara ve enterokoklara (VRE dahil) karşı in vitro aktiviteye sahiptir. *C. difficile*'ye karşı in vitro aktivite gösterir, hatta izolatların çoğuna etkinliği vankomisininkinden daha güçlüdür. Zaman öldürme eğrilerini içeren in vitro çalışmalar, oritavansinin sefazolin ve nafsilin ile kombine edildiğinde MRSA suşlarına karşı sinerjistik bir aktivite gösterdiğini göstermiştir. Oritavansin ile seftarolin kombinasyonu aynı zamanda MRSA'ya karşı sinerjistiktir ve test edilen MRSA, daptomisine duyarlı olmayan MRSA ve hVISA izolatlarına karşı en etkili kombinasyondur.

Klinik farmakokinetik ve farmakodinamik

Oritavansin, 3 saatte 1200 mg'lık tek bir doz olarak uygulanır. Hücre içinde karaciğerde, böbreklerde, dalakta, lenfoid dokuda ve akciğerlerde birikir ve buradan daha sonra salınır; uygulanan dozun sadece eser miktarları idrar ve dışkıda bulunur. Oritavansinin, plazma konsantrasyonunun yaklaşık %19'u kadar deri vezikül sıvısına yeterli penetrasyonu bildirilmiştir (52). Çeşitli gram-pozitif organizmalara karşı hızlı bir bakterisidal ve konsantrasyona bağlı aktivite gösterir. Tek bir tam doz oritavansin verildiğinde, fraksiyonlara ayrılmış dozlara kıyasla daha büyük bir bakterisidal etkinin görüldüğü de gözlemlenmiştir. Ayrıca in vitro olarak *S. aureus'un* durağan fazına ve biyofilm kültürüne karşı konsantrasyona bağlı bakterisidal aktivite sergiler (53).

Klinik kullanımlar

Oritavansin, komplike deri ve yumuşak doku enfeksiyonları olan hastalarla yapılan bir faz II çalışmasında (54) ve *S. aureus* bakteriyemili hastalarla yapılan başka bir çalışmada etkili bulunmuştur (55). DYDE'li yetişkin hastaların yer aldığı iki faz III randomize çalışmada, 1200 mg'lık tek doz olarak, 7 ila 10 günlük vankomisine benzer etkinlikte bulunmuştur (56,57). Bu sonuçlarla aşağıdaki gram-pozitif mikroorganizmaların duyarlı izolatlarının neden olduğu DYDE'li yetişkin hastaların tedavisi için onay almıştır; *S. aureus* (MRSA dahil), *S. pyogenes, S. agalactiae, Streptococcus disgalactiae,* S. *anginosus* grubu ve *E. faecalis* (yalnızca vankomisine duyarlı izolatlar).

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