BÖLÜM 4

OPİOİDLER

Ayfer ÜZÜM [1]

GİRİŞ

Opioid terimi opioid reseptörlere bağlanan ve agonist etkiler oluşturan bileşiklere verilen ortak bir isimdir. Bu terim opiumdan doğal olarak elde edilen morfin ve morfinden sentetik olarak türetilmiş tüm derivasyonları kapsar. Alkaloid yapıda olan opioidler papaversomniferum (haşhaş) isimli bir bitkinin tohumundan üretilmektedir. Opioid ismi Yunancadaki 'suyu' anlamına gelen 'opos' isminden türemiştir. Modern tıpta kullanımına izin verilmiş en potent ağrı kesicilerdir. Opiumun (afyon) tarihte ilaç olarak ilk kullanımı Sümer yazıtlarında MÖ 4000 lere dayanır. Alman farmakolog ve kimyager Friedrich Sertürner 1806 da opium (afyon) özütünden stabil bir kristal alkoloid sentezlemiş ve Yunan mitolojisindeki rüyalar tanrısı Morfeus tan esinlenerek bu bileşiği Morfin olarak isimlendirmiştir (1). 1920'lerde morfinin yapısı keşfedildikten sonra morfin benzeri sentetik opioidler türetilmiş ve yaygın olarak kullanılmaya başlanmıştır. Ancak ağrıları tedavi edilirken hastalar; baş dönmesi, ortostatik hipotansiyon, bulantı kusma, kabızlık, bağımlılık ve ölümcül olabilecek solunum depresyonu gibi yan etkilere maruz kalabilmektedir. Klinik anestezide istenen daha kısa etki başlangıç süresi, daha güvenli ve yan etkileri yönetilebilir opioid arayışları sentetik opioidlerin üretilmesine neden olmuş ancak yine de benzer yan etkiler görülmüştür. Yeni opioid agonistler elde etme çabaları farklı antagonist ve mikst agonist/antagonistlerin sentezlenmesine de olanak sağlamıştır. Günümüz anestezi pratiğinde opioidler perioperatif ve postoperatif yaygın olarak kullanılmaları yanı sıra kronik ağrı tedavisinde de kullanılmaktadır. Ayrıca postoperatif ağrı tedavisinde Hasta Kontrollü Analjezi (Patient Controlled Analgesia), perioperatif anestezi yönetiminde

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oidlerin yan etkilerini, sıklıkla solunum depresyonu etkilerini geri çevirmek amaçlı kullanılır. Bulantı-kusma, kaşıntı, üriner retansiyon, kas spazmı ve bilier spazmı geri çevirmek için de kullanılabilir (123). Etki başlangıç süresi 1-2 dk, yarılanma ömrü 30-60 dk'dır. Morfin gibi uzun etkili opioidlerin etkisini geri çevirdikten sonra renarkotizasyon görülebilir (3). Solunum etkilerini geri çevirmek için 1. 0-2. 0 μg/kg ile titre edilerek başlanır her 2-3 dakikada bir 0. 5-1. 0 μg/kg bolus dozlar verilir, yeterli spontan solunum geri gelinceye kadar bolus dozlara devam edilir (129). Naloksanın yan etkileri olarak kan basıncı ve nabız hızında artış, pulmoner ödem sayılabilir (130, 131).

Diğer Opioid Antagonistleri

Naltrekson Naloksana benzer olarak μ, δ ve K reseptör antagonistidir. Yarılanma ömrü 8-12 saat'tir. Nalmefen Naloksan ve naltreksona benzer şekilde μ, δ ve K reseptör antagonistidir. Yarılanma ömrü 8. 5 saattir. Metilnaltrekson kimyasal yapısı sebebiyle kan beyin bariyerini geçemez ancak opioidlerin periferal etkilerini geri çevirebilir.

OPİOİDLERİN İLAÇLAR İLE ETKİLEŞİMLERİ

Pentotal ve propofol gibi hipnotikler opioidlerin etkilerini artırmaktadır (132). Benzodiyazepinler ile opioid kombinasyonları opioid etkiyi güçlendirir (133, 134). Etomidat ve ketamin ile opioidlerin birlikte kullanılması kardiyovasküler stabilite sağlar (135). Opioidlerin oluşturduğu postoperatif hiperaljezi ve opioid toleransı, ketamin ile opioid kombine edildiğinde görülmemektedir. Antikonvülzan bir ilaç olan gabapentin ile morfin kombinasyonlarının analjezik etkiyi artırdığı bildirilmiştir (136).

N_2O ile opioid kombinasyonlarında genellikle kardiyaovasküler fonksiyonların korunduğu kabul ediliyor olsa da bu kombinasyonun kardiyak fonksiyonları bozduğu da rapor edilmiştir (137). İnhalasyon anestezikleri ile opioidler anestezi pratiğinde sıklıkla ve güvenle kullanılır. Pankuronyumun opioidler ile kombinasyonunda opioidlerin bradikardi yapıcı etkisinin pankuronyumun vagolitik etkisi tarafından azaltıldığı bildirilmiştir (138, 139). Vekuronyum ve opioidlerin kombinasyonu negatif inotrop ve kronotrop etki ile sonuçlanır (140, 141). Meperidinin MAOI ile kombinasyonu fatal etkiler ile sonuçlanabilir (142, 143). Hipertansiyon, hipotansiyon, koma, solunum arresti ile sonuçlanabilir. Bu etki artmış santral seratonerjik aktivite ile ilişkili olabilir. Opioidler Ca^{++} kanal aktivitesini inhibe etmektedir Ca kanal blokörleri ile kombinasyonları opioidlerin etkilerini artırabilir. Eritromisin tedavisi sırasında veya sonrasında azalmış sitokrom P-450 aktivasyonu sonucu alfentanilin etkileri uzayabilir, sufentanil ise etkilenmez (144, 145). Magnezyum sülfat'ın fentanil gereksinimini azalttığı gösterilmiştir (NMDA reseptörlerine olan etkisi). Nonsteroid antiinflamatuar ilaçların preoperatif veya postoperatif uygulanması opioidllere olan gereksinimi azaltır (146, 147). Difenhidramin ile opioidler kombine edildiğinde difenhidraminin opioidlerin neden olduğu CO_2 'e respiratuar duyarsızlığı önlediği bildirilmiştir (148).

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