

Bölüm 35

JİNEKOLOJİDE AROMATAZ İNİHİTÖRLERİNİN KULLANIMI

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GİRİŞ

Son yıllarda östrojen bağımlı hastalıkların tedavisinde östrojen blokajı yapan ilaçlar büyük ilgi görmektedir. Moleküler biyolojideki gelişmeler sayesinde östrojen reseptör proteini ve geni daha iyi anlaşılmıştır. Reseptör proteininde östrojene yüksek affinite gösteren ve DNA'ya yüksek affinite gösteren iki ayrı alan gözlemlenmiştir. Östrojenin reseptöre bağlanması ile mRNA üretimi artmakta ve dokularda proliferasyon sağlanmaktadır (1). Östrojen aktivitesinin blokajı için çeşitli yollar mevcuttur. Bunlardan ilk olarak bulunan östrojen reseptör antagonisti olan stilben derivativesi tamoksifendir (2). Östrojen reseptör antagonistleri reseptöre bağlanarak östrojenin bağlanmasını ve böylece biyoaktivitesini engeller. İkinci yaklaşım ise östrojen biyosentezini inhibe etmektir. Aromataz inhibitörleri ise östrojen biyosentezini aromataz enzim sistemi üzerinden etkileyerek bloke eder.

Aromataz İnhibitörleri

Aromataz enzimi iki polipeptidten oluşan, NADPH'ye bağlı bir redüktaz ile birlikte işlev gören (1) ve kromozom 15q 21 üzerinde lokalize CYP19 geninin ürünü olan sitokrom P450 ailesine ait mikrozomal bir enzimdir (2). Aromataz, östrojen üretiminde sınırlayıcı adım olan 19 karbonlu (C) androjenlerin (and-

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Amerikan Jinekoloji ve Obstetrik Derneği önerileri aşağıda belirtildiği gibidir:

- Meme kanseri tedavisinde uzun süreli aromataz inhibitörü kullanımında kemik dansitometri takibi önerilmektedir. Uzun dönem yan etkiler açısından kıyaslandığında tamoksifene göre daha düşük oranda tromboz, endometriyum kanseri ve vajinal kanama riski mevcuttur.
- Aromataz inhibitörleri ile yapılan ovulasyon indüksiyon yöntemi ile; polikistik over sendromu tanılı hastalarda yüksek canlı doğum oranları elde edildiği için tedavide ilk seçenek olabilir. Çalışmalarda özellikle BMI yüksek polikistik over hastalarında terci edilmektedir. Açıklanamayan infertilite tedavisinde de CC ile ovulasyon indüksiyonunu ile karşılaştırıldığında tedavi sonuçları açısından fark bulunmamıştır (42).
- Aromataz inhibitörleri endometriozise bağlı ağrı tedavide progesterinle kombine tedavisi bir seçenek olarak görülmektedir.
- Endometriyozis olgularında Aromataz İnhibitörleri GnRH tedavisine eklenecek yan etkiler azaltılıp daha uzun süreli kullanım sağlanabilir.

Sınırlı sayıda vakanın dahil edildiği bir çalışmada ise letrozol'ün ektopik gebelik tedavisinde başarılı bir şekilde kullanımı bildirilmiştir. Bu konuda daha geniş sayıda çalışmalara gereksinim vardır (42).

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