

BÖLÜM 28

GONADOTROPİN SALGILAYAN HORMON ANTAGONİSTLERİ

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GİRİŞ

Androjenlerin prostat kanseri gelişimindeki rolü 1941 yılında Huggins ve Hodges tarafından belirlenmiştir (1,2). Prostat kanseri hücreleri genellikle büyümek için testosteron gibi androjen hormonlarına ihtiyaç duyar. Bu bulgu androjen deprivasyon tedavisinin (ADT) gelişmesine yol açtı. Günümüzde ADT, metastatik prostat kanseri tedavisinin köşe taşıdır ve orta veya yüksek riskli lokalize hastalıkta da kullanılmaktadır (3). ADT, bilateral orşiektomi ile cerrahi olarak veya luteinizing hormone-releasing hormone (LHRH) agonistleri veya gonadotropin-releasing hormone (GnRH) antagonistleri kullanılarak medikal olarak elde edilebilir (4). FDA, üçüncü kuşak bir GnRH antagonisti olan degarelix'i 2008'de ve oral yoldan uygulanan ilk GnRH antagonisti olan relugolix'i 2020'de ileri evre prostat kanserinde onayladı (5,6).

ANDROJEN DEPRİVASYON TEDAVİSİ

ADT ile serum testosteronunu kastrasyon seviyelerine (<50 ng/dL; <1.7 nmol/L) düşürmek ve böylece androjen reseptörünün aktivasyonunu önlemek hedeflenmektedir. Androjenler androjen reseptörüne bağlandığında, hücre farklılaşmasını ve olgunlaşmasını kontrol eden gen transkripsiyonunu destekler (7). Son kanıtlar orşiektominin bir LHRH agonistinden daha güvenli olabileceğini düşündürse de, cerrahi kastrasyonun geri döndürülemez olması ve hasta üzerindeki önemli psikososyal etkileri nedeniyle medikal kastrasyon daha sık kullanılmaktadır (8).

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SONUÇ

ADT, metastatik prostat kanserinde temel tedavi yöntemidir. ADT, cerrahi veya medikal kastrasyon olarak uygulanabilir. LHRH agonistleri, medikal kastrasyon için yaygın olarak kullanılır, ancak ilişkili alevlenme fenomeni ve yetersiz testosteron kontrolü oluşabilir. GnRH antagonistleri, alevlenme fenomeni görülmeden testosteronu kastrasyon seviyelerine daha hızlı baskılar, bu nedenle antiandrojenlerin birlikte uygulanması gereksizdir. Degarelix, abarelix'in histamin aracılı reaksiyonlar nedeniyle kullanımdan kaldırılmasından bu yana en yaygın kullanılan GnRH antagonistidir. Relugolix, leuprolidden daha iyi kastrasyon seviyelerine ulaşabilen ve bunu sürdürebilen FDA onaylı ilk oral GnRH antagonistidir, ancak klinik deneyim şu anda sınırlıdır. GnRH antagonistleri kullanmanın yararı, kardiyovasküler komorbiditesi olan hastalarda daha belirgindir. GnRH antagonistleri ile tedavi için uygun hastalar, semptomatik veya eşlik eden kardiyovasküler komorbiditeleri olan ileri evre prostat kanseri hastalarıdır.

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