KANSER RİSKİNİ AZALTAN AJANLAR

58. BÖLÜM

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GİRİŞ

Kanser, karsinogenez için gerekli kritik moleküler olaylar olan hücresel proliferasyon, apopitoz, anjiogenez ve invazyonun kontrolünü sağlayan homeostatik mekanizmaların kademeli kaybı ile sonuçlanan uzun bir süreçtir[1]. Genellikle kemoprevensiyon olarak adlandırılan kanser riskini azaltma, invaziv kanser gelişimini önlemek, tersine çevirmek için ilaçlardan, izole diyet bileşenlerine, tüm diyet modülasyonlarına kadar bir dizi müdahalenin kullanılmasıdır[2]. Uzun karsinogenez sürecinin herhangi bir aşamasında kanser riskini azaltmak için müdahalede bulunulabilir. Karsinogenez sürecindeki bu latens dönem risk azaltmak için yapılacak müdahaleleri belirli maruziyetlere ya da risk profillerine göre uyarlama imkanı tanımaktadır. Kanser riskini azaltıcı ajanların etkili olduğunu anlamak için, bu ajanların kullanımında kanser insidansının ya da kansere bağlı mortalitenin azaldığını göstermek gerekmektedir[3]. Hanahan ve Weinberg'in tarif ettiği malign transformasyonun özellikleri; hücrenin büyümede kendi kendine yetebilirliği, büyüme karşıtı sinyallere duyarsızlık, apopitozdan kaçma, sınırsız replikasyon potansiyeli, sürekli anjiogenez, doku invazyonu ve metastaz yapabilmedir, bu özellikler hücresel sinyal kontrolünün kaybını yansıtır[4]. Malign transformasyona uğrayan hücrelerin ortak özellikleri ve olası önleyici müdahaleler Tablo 1'de gösterilmiştir[3].

Transformasyona neden olan moleküler hasar, kronik inflamasyon, oksidasyon, kalıtsal genetik mutasyonlar veya polimorfizmler ve eksojen çevresel maruziyetler gibi çok çeşitli genetik ve çevresel stres faktörleri tarafından tetiklenir. Sinyal ileti yolaklarının karmaşıklığı ve birbiri üstüne binmesi tek bir bölgeyi hedefleyen önleyici ya da tedavi edici müdahalelerin sınırlı etkisi olacağını düşündürmektedir. Karsinogenezi durdurmak ya da tersine çevirmek için birden çok moleküler yolağın hedeflenmesi gerekebilir[3].

MİKRONUTRİENTLER

Vitaminler ve mineraller gibi mikronutrientler çok küçük miktarlarda gerekli olan temel diyet öğeleri olarak tanımlanmaktadır[5]. Mikronutrietler, diyet ile alınan, normal insan biyolojisinde rol oynayan geniş ve farklı molekül grubunu içermektedir[3].

Retinoid

Hücre büyümesi, farklılaşma, apopitoz, bölünme ve morfogenez dahil olmak üzere hücre aktiviteleri üzerinde derin etkilere sahip olan A vitamini ve analogları toplu olarak retinoidler olarak adlandırılırlar[6]. Yüksek doz 13-cis-retinoik asid(50-100 mg/m^2/gün) ile yapılan ilk çalışmalarda lokal, rejyonel ya da uzak hastalık rekürrensi açısından anlamlı fark görülmemiştir ancak sekonder invaziv malignansi gelişim oranını anlamlı olarak azalttığı ve bu faydanın 5 yıl boyunca sürdüğü gösterilmiştir[7,8]. Retinoidlerin daha düşük dozlarının kullanıldığı sonraki çalışmalarda transformasyon riskini azaltmada başarı elde edilememiştir[9]. Hem retinil palmitatın denendiği EUROSCAN çalışmasında hem de 13-cis-retinoik asidin denendiği Lung Intergroup çalışmasında 2. primer akciğer kanseri gelişimi önlenememiş-

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