

BÖLÜM 12

PLATİN ANALOGLARININ ETKİ MEKANİZMALARI VE SINIFLANDIRILMASI

Abdülkadir KOÇANOĞLU¹

GİRİŞ

Dünyada yaygın olarak kanser tedavisinde kullanılan başlıca 3 platin analogu vardır. Bunlar sisplatin, karboplatin, oksaliplatin'dir. Ayrıca 4 tane daha platin analogu ulusal olarak onaylanmıştır. Heptaplatin Kore'de, lobaplatin Çin'de, miriplatin ve nedaplatin Japonya'da kullanılmaktadır.(1) Tüm platin analogları intravenöz yolla bolus yada yavaş infüzyon olarak uygulanır ve kanda bozunmadan taşındıkları düşünülmektedir. Serum proteinlerine ve özellikle albümine bağlanırlar.(2) Platin bazlı ilaçlar çeşitli mekanizmalarla hücre içine taşınır. Bunlar içerisinde en önemlileri bakır transport mekanizmaları ve özellikle yüksek afiniteli bakır transporter 1'dir.(3,4)

Hücre içine girdiklerinde düşük yoğunluklarda çözünürler ve labil grupları olan klorid ve karboksilat bazlı ligandlarını kaybederler. Hücre içerisinde bir defa çözündüklerinde oldukça reaktiftirler ve hücre içi biyomoleküllere bağlanabilirler.(5) Platin analogları hafif nükleofil özelliktedirler. Kükürtten zengin aminoasitler olan sistein ve metionin içeren peptit ve protein yapılarına kolayca bağlanırlar. Özellikle antioksidan etkisiyle bilinen bir peptit olan glutatyon ve nükleer DNA başlıca hedefleridir. Genellikle guanin'in N7 pozisyonuna bağlanır bazende adenozin rezüdülerine bağlanabilir.(5)

Platin analogları için direnç önemli bir problemdir. İlaç direnci kanser hücresi tarafından başlangıçta oluşabileceği gibi sonradan da kazanılabilir.(6) Sonradan kazanılan direnç 3 mekanizma ile gerçekleşir. Bu mekanizmalar etken madde nükleer DNA'ya ulaşmadan bozunması ve deaktive olması, etken maddenin hücre

¹ Uzm. Dr., Ankara Etlik Şehir Hastanesi, Tıbbi Onkoloji Bölümü kadirkoçanoğlu@hotmail.com

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