

## Bölüm 10

# İLAÇ VE TOKSİNLERE BAĞLI SARILIK

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### GİRİŞ

Reçeteli ya da reçetesiz birçok ilaç, bitkisel ürünler ve çevresel toksinler çeşitli mekanizmalarla hepatotoksositeye neden olur. Tanı koyabilmek için yüksek şüphe indeksi gerekmektedir.

İlaç kaynaklı karaciğer hasarı semptom olarak akut ve/veya kronik karaciğer hasarını taklit edebilir. Etiyolojide 1000 in üzerinde ilaç ve bitkisel ürün tanımlanmıştır (1). Yeni başlangıçlı sarılık ile başvuran hastaların %50 si ilaç, bitkisel ürün ve toksin kaynaklıdır (2).

### İlaç Metabolizmasında Karaciğerin Rolü

Karaciğer, vücuda giren birçok ilaç ve toksinin alımı, konsantrasyonu, metabolizması ve salınımından sorumludur. Bazı ilaçlar direkt hepatotoksite oluştururken, genellikle ilaç metabolitleri karaciğer hasarından sorumludur. Bu metabolitler, özellikle hepatosit endoplazmik retikulumuyla ilişkili membrana bağlı veya sitoplazmada çözülebilir serbest enzimlerce işlenir. Her ilacın, bu enzim sistemlerinden birini veya daha fazlasını içeren, kendine özgü yolları vardır (3).

Gastrointestinal sistemden emilen ilaçların çoğu, lipofiliktir ve suda çözünmez. Bunlar hepatik metabolizmayla suda çözünür hale getirilir ve böylece safraya daha kolay salınır veya böbreklerden süzülür. İlaçlar karaciğerde Faz 1 ve Faz 2 reaksiyonları ile metabolize olur. Daha sonra Faz 3 reaksiyonuyla kanaliküler veya sinüzodal membranlar üzerindeki taşıyıcılar yoluyla atılır (4).

**Faz 1 Reaksiyonları** – Faz 1 reaksiyonları; lipofilik molekülleri oksidasyon, redüksiyon veya hidroliz yoluyla daha polar, hidrofilik moleküllere dönüştürür. Bu reaksiyonlar membrana bağlı mikst fonksiyonlu oksidaz ailesinden sitokrom-P450

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**Koruma** – ilaca bağlı toksisitenin önlenmesi, hepatotoksik ilaç alan hastaların uygun doz ve diğer ilaçlarla, alkolle alınması durumunda gelişebilecek etkileşimler konusunda eğitilmelidir. Gelişebilecek semptom ve bulgular hakkında bilgi verilmelidir. İzoniazid ve metotreksat gibi şiddetli karaciğer hasarı yapan ilaçları hastalarda ALT düzeyleri izlenmelidir.

Sonuç olarak; ilaç alımından sonra ortaya çıkan nonspesifik semptomlar (bulantı, iştahsızlık, yorgunluk, sağ üst kadranda ağrısı veya kaşıntı) ilaç toksisitesini gösterir ve ilaca bağlı toksisite için değerlendirme ve ileri tetkik gerektirebilir. Tanı koymak zor olabilir ve karaciğer hasarı yapabilecek diğer nedenlerin ekartasyonuna bağlıdır. Primer tedavi ilacın veya toksinin uzaklaştırılması, kesilmesi ve karaciğer fonksiyon testlerinin normal sınırlara gelmesini sağlamaya yönelik izlemdir. Çoğu vakada ilaç kesildikten sonra iyileşme gerçekleşir.

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