BÖLÜM 90

HEPATİT B

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GİRİŞ

İlk olarak 1965 yılında tespit edilen, 1984 yılında aşısı geliştirilen ve takip eden yaklaşık 20 yıl içerisinde antiviral ilaçları üretilen Hepatit B virüsü (HBV) enfeksiyonu, küresel bir sağlık sorunu olmaya devam etmektedir (1).

HBV, akut ve kronik enfeksiyon yoluyla karaciğere zarar verir; hasta yükünün büyük kısmı, başta siroz ve hepatosellüler karsinom olmak üzere kronik enfeksiyonun uzun vadeli sonuçlarından kaynaklanır (2,3). Hastaların büyük bölümü asemptomatik olmakla birlikte uzun dönemde yaklaşık olarak %15-40 vakada siroz veya hepatosellüler kanser gelişmektedir (4).

EPİDEMİYOLOJİ VE HBV PREVALANSININ AZALTILMA ÇALIŞMALARI

Dünya nüfusunun yaklaşık üçte birinde geçirilmiş veya mevcut HBV enfeksiyonunun serolojik testleri pozitif bulunmaktadır. Kronik HBV enfeksiyonu, yani hepatit B yüzey antijeninin (HBsAg) altı ay veya daha uzun süre pozitif saptanması, dünya nüfusunun tahminen %3,7'sinde görülmektedir (5).

Dünya Sağlık Asamblesinde 2016 yılında toplum sağlığı tehdidi olarak viral hepatitlerle mücadele için "Dünya Sağlık Örgütü (DSÖ) Viral Hepatite İlişkin Küresel Sağlık Stratejisi" (WHO-GHSS) kabul edildi. 2015 yılına göre 2030 yılı için yeni vakada %95, ölümlerde %65 azalma, 5 yaşından küçük çocuklarda HBsAg prevalansının %0,1'den düşük olması hedefleri belirlendi (6). Bu hedeflerin DSÖ'nün 2024 yılında yayınlanan hedeflerinde de korunduğu kayda geçirildi (7). Bu hedeflere ulaşırken hepatit B bulaşını ve ilişkili hastalıkları engellemek için elimizde mevcut araç ve teknolojiler; aşılar, testler, antiviral tedaviler olarak sıralanabilir.

1992'de DSÖ'nün önerdiği ulusal aşılama programlarına hepatit B üç dozluk seri (HepB3) eklendi (8). 2009 da DSÖ tüm ülkelere aşılama programlarına eklemelerini önerdi (9). Yenidoğan aşılaması ve doğumdan sonraki ilk 24 saat içinde hepatit B immünoglobulin uygulanması ve uygun olduğunda hamile kadınlara antiviral ilaç uygulanması anneden çocuğa (vertikal) geçişi azalttı (10).

2019 yılında dünya genelinde tahminen 316 milyon kişide kronik HBV enfeksiyonu bulunuyordu. Tüm yaştaki küresel kronik HBV prevalansı

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Tablo 7. Hepatit B Tedavisinde Çeşitli Kılavuzlarda Tedavi Başlama Kriterleri (108,118,138,162)	
AASLD (Terrault 2018)	• **HBeAg-pozitif:** HBV-DNA > 20,000 IU/mL+ ALT > 2x ULN. • **HBeAg-negatif:** HBV-DNA > 2,000 IU/mL + ALT > 2x ULN. • **Siroz:** Sirozlu tüm hastalar, ALT veya HBV-DNA seviyelerinden bağımsız olarak tedavi edilmelidir. • **Bağışıklık-tolerant faz:** Genç hastalarda, normal ALT ve yüksek HBV-DNA varlığında tedavi önerilmez, ancak düzenli takip gereklidir.
APASL (Sarin 2016)	• Tüm hastalar: HBV-DNA tespit edilebilir ve orta ila ciddi inflamasyon veya anlamlı fibroz varsa • HBeAg(+): HBV-DNA >20,000 IU/mL+ ALT >2x ULN • HBeAg(-): HBV-DNA >2,000 IU/mL + ALT >2x ULN • Dekompanze karaciğer sirozu • Kompanze karaciğer sirozu + HBV-DNA>2,000 IU/mL (ALT düzeylerinden bağımsız)
FASL (EASL 2017)	• **HBeAg-negatif hastalarda HBV-DNA >2,000 IU/mL,** HBeAg-pozitif hastalarda HBV-DNA >20,000 IU/mL. • ALT > ULN veya karaciğer histolojisi/elastografide anlamlı fibroz/İnflamasyon varlığı. • **Sirozu olan tüm hastalar,** DNA veya ALT düzeylerinden bağımsız olarak
Belçika (Coüe 2007)	• HBeAg(+): HBV-DNA >20,000 IU/mL+ALT > 2xULN (veya biyopside orta/ciddi hepatit varsa) • HBeAg(-): HBV-DNA>2,000 IU/mL ve ALT yüksekse • Biyopsi düşünülen durumlar: Dalgalanan veya minimal düzeyde artmış ALT (özellikle 35-40 yaş üzerindekilerde)
Almanya (Cornberg 2011)	• HBV-DNA>2,000 IU/mL + minimal inflamasyon/düşük fibroz veya ALT yüksekliği

Tablo 8. Oral antivirallere direnç ve tedavi değişiklikleri (172)					
	Lamivudin	Adefovir	Entecavir	Telbivudin	TDF/TAF
Ters transkriptaz (rt) mutasyonları	rtL180M ± HM204V/I	İlA181V/T rtN236T	HL180M ± rtM204V/I HS2021 HM250V	rtL180M ±rtM204V/I	Bilinmiyor
Direnç oranı	1 yıl: %20 4-7 yıl: %75	1 yıl: %9 3 yıl: %30	1 yıl: %0 3 yıl: %1	1 yıl: %10 2 yıl: %25	1 yıl: %0 8 yıl: %0
Diğer ilaçlara direnç	Emtricitabine Telbivudin Entecavir	Tenofovir*	Lamivudin Emtricitabine Telbivudin	Lamivudin Telbivudin Entecavir	Yok
Değiştirilecek ilaç(lar)	TDF veya TAF	Entecavir, TDF veya TAF	TDF veya TAF	TDF veya TAF	Entecavir

** TDF'ye kısmi direnç., **2 yıl içinde TAF'a direnç bildirilmedi., TAF, tenofovir alafenamid; TDF, tenofovir disoproxil fumarat*

Küçük müdahale eden (interfering) RNA (siRNA), ile viral proteinlerin üretimine müdahale edilebilmektedir. HBsAg sentezini hedefleyen siRNA'lar ile anlamlı HBsAg düşüşü sağlanabilmektedir. HBsAg salınma inhibitörleri, bu antijenin neden olduğu T hücresi yorgunluğunun ve immün sistemden kaçışın engellenmesi amacı ile geliştirilmektedir. Ancak bu noktada yeterli klinik çalışma mevcut değildir (183,184).

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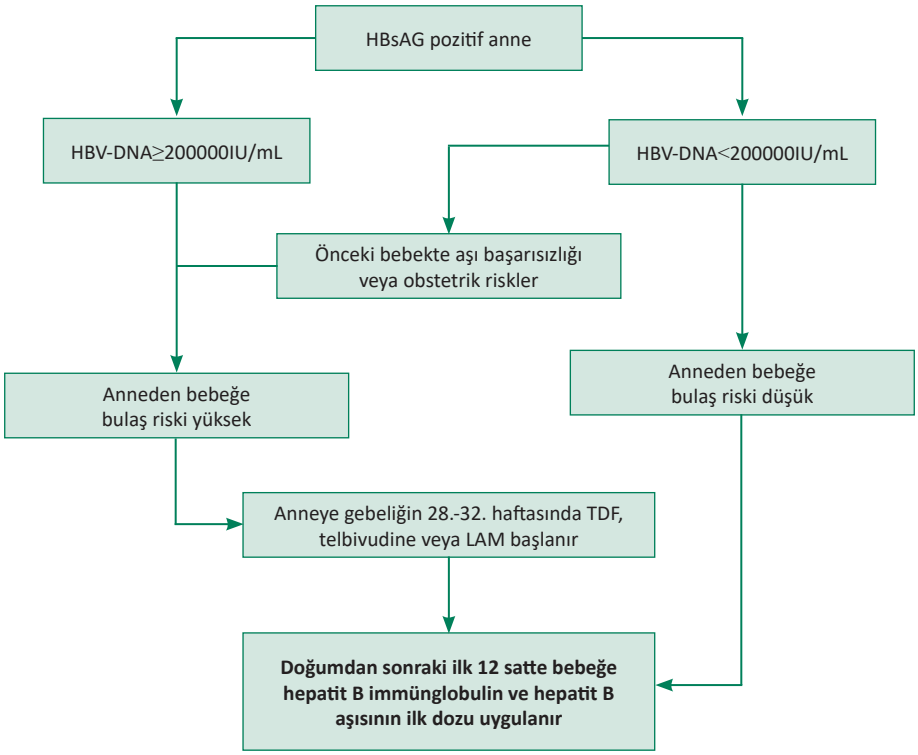

Şekil 2. *Gebelerde hepatit B tedavisi(172).*

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