

## BÖLÜM 8

### Viral Hepatitler

Şirin Zelal ŞAHİN TIRNOVA <sup>1</sup>

#### ÖZET

Viral hepatitler, hepatovirus ailesine ait beş adet virüsün neden olduğu, akut ve/veya kronik enfeksiyonlara yol açabilen, kronik enfeksiyonlarında uzun vadede karaciğer sirozu ve hepatoselüler kansere sebep olabilen, bazı türleri aşı ile önlenebilen küresel bir sağlık sorunudur. Tanısı ve tedavisi etkene göre değişmekle birlikte riskli popülasyonların taranması ve erken tedavi edilmesi, gerek mortal komplikasyonların gelişmesinin önlenmesi, gerekse sağlık harcamalarının azaltılması açısından kritik önem taşır.

#### Hepatit A Virüs Enfeksiyonu

##### Giriş ve Epidemiyoloji:

Hepatit A enfeksiyonu, picornaviridae ailesinin hepatovirus cinsi içerisinde yer alan hepatit A virüsün (HAV) sebep olduğu, sadece insanların kaynak olduğu, kendini sınırlayan ve kronikleşmeyen bir hepatit türüdür. Fulminan hepatit vakaların %1'inden azında görülür. Enfekte olan kişilerde ömür boyu bağışıklık oluşur ve hastalık aşı ile önlenir.

1947'de ilk olarak sadece iki tür hepatovirus tanımlanmıştır: Hepatit A ve B (1). Hepatit A virüse bağlı hepatit ise ilk kez 1973'te tanımlanmıştır (2).

Hepatit A tipik olarak fekal oral yolla (insandan insana veya kontamine su ve/veya gıdalla) bulaşır (3). Risk faktörleri arasında enfekte kişiyle aynı evde yaşamak, cinsel temas, pişmemiş kabuklu deniz ürünü ve sebze tüketmek, kan transfüzyonu ve yasadışı ilaç kullanımı sayılabilir. Maternal-fetal geçiş bildirilmemiştir. 50 yaş üstü ve altta yatan karaciğer hastalığı olanlarda fulminan hepatit gelişme riski daha fazla olmakla birlikte toplamda %1'in altındadır (4).

Hepatit A virüs enfeksiyonu tüm dünyada görülür ve her yıl tüm dünyada yaklaşık 1,4 milyon yeni vaka görülür (5). Sporadik veya epidemik olabilir. Hepatit salgınları kontamine su veya yi-

<sup>1</sup> Uzm. Dr. Şirin Zelal ŞAHİN TIRNOVA, Koç Üniversitesi Hastanesi İç Hastalıkları Bölümü ztirnova@kuh.ku.edu.tr

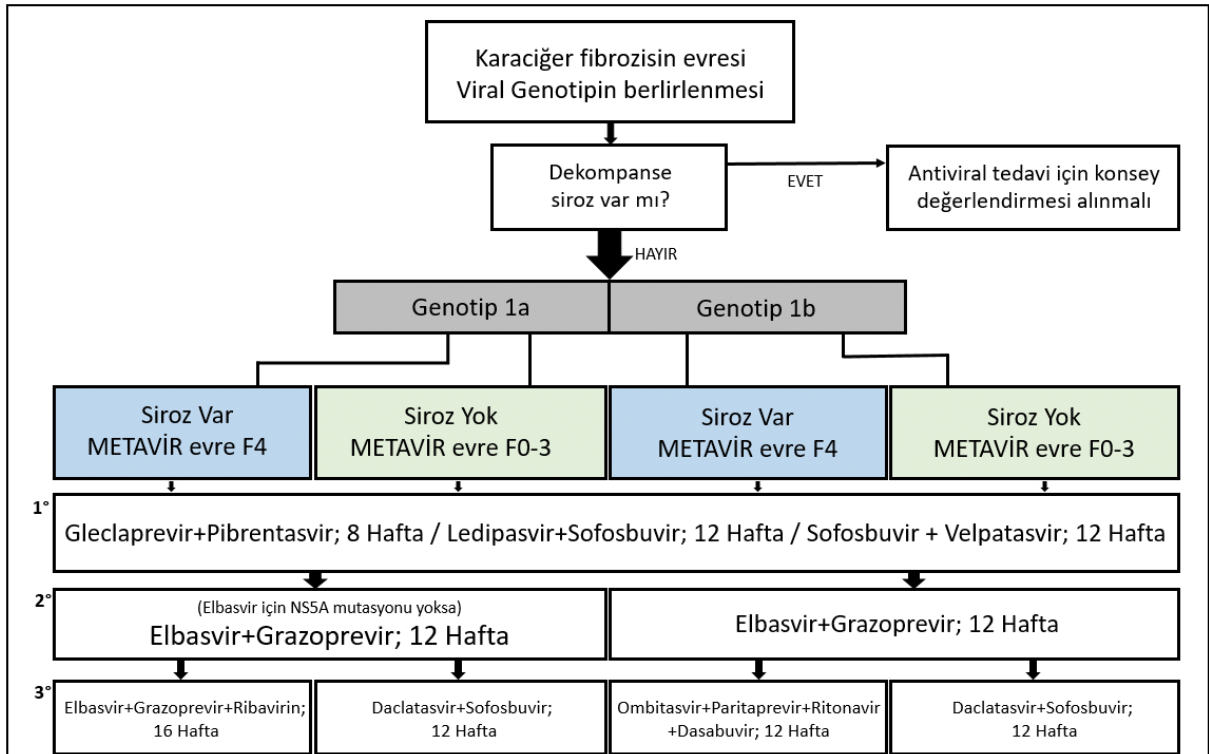
tasvir veya 12 haftalık Sofosbuvir+Velpatasvir+Voxilaprevir±Ribavirin tedavisi diğer seçenekler olacaktır.

**Genotip 4, 5 ve 6** grubu hastada 12 haftalık Sofosbuvir+Ledipasvir, Sofosbuvir+Velpatasvir, Glecaprevir+Pibrentasvir, Grazoprevir+Elbasvir gibi seçenekler kullanılabilir. Seçim ilacın ulaşılabilirliği ve maliyet gibi faktörlerle yapılmaktadır.

## KAYNAKLAR

1. MacCallum FO. Homologous serum jaundice. Lancet 1947; 2:691.
2. Feinstone SM, Kapikian AZ, Purceli RH. Hepatitis A: detection by immune electron microscopy of a virus-like antigen associated with acute illness. Science 1973; 182:1026.
3. Klevens RM, Miller JT, Iqbal K, et al. The evolving epidemiology of hepatitis a in the United States: incidence and molecular epidemiology from population-based surveillance, 2005-2007. Arch Intern Med 2010; 170:1811.
4. Centers for Disease Control and Prevention. Viral Hepatitis Surveillance:United States, 2013 US Department of Health and Human Services, Atlanta, GA 2016. (30.10.2021 tarihinde [https://www.cdc.gov/hepatitis/statistics/2014surveillance/pdfs/2014HepSurveillanceRpt\\_Rev2016-09-26.pdf](https://www.cdc.gov/hepatitis/statistics/2014surveillance/pdfs/2014HepSurveillanceRpt_Rev2016-09-26.pdf) adresinden ulaşılmıştır).

5. World Health Organization. Global Alert and Response (GAR): Hepatitis A. (30.10.2021 tarihinde <http://www.who.int/csr/disease/hepatitis/whocdscsredc2007/en/index4.html#estimated> adresinden ulaşılmıştır).
6. Centers for Disease Control and Prevention. Hepatitis A Questions and Answers for Health Professionals. (30.10.2021 tarihinde <http://www.cdc.gov/hepatitis/hav/havfaq.htm#general> adresinden ulaşılmıştır).
7. Wasley A, Samandari T, Bell BP. Incidence of hepatitis A in the United States in the era of vaccination. JAMA 2005; 294:194.
8. Vallbracht A, Fleischer B, Busch FW. Hepatitis A: hepatotropism and influence on myelopoiesis. Intervirology 1993; 35:133.
9. Lemon SM. Type A viral hepatitis. New developments in an old disease. N Engl J Med 1985; 313:1059.
10. Lednar WM, Lemon SM, Kirkpatrick JW, et al. Frequency of illness associated with epidemic hepatitis A virus infections in adults. Am J Epidemiol 1985; 122:226.
11. Tong MJ, el-Farra NS, Grew MI. Clinical manifestations of hepatitis A: recent experience in a community teaching hospital. J Infect Dis 1995; 171 Suppl 1:S15.
12. Koff RS. Clinical manifestations and diagnosis of hepatitis A virus infection. Vaccine 1992; 10 Suppl 1:S15.
13. Richardson M, Elliman D, Maguire H, et al. Evidence base of incubation periods, periods of infectiousness and exclusion policies for the control of communicable diseases in schools and preschools. Pediatr Infect Dis J 2001; 20:380.
14. Kemmer NM, Miskovsky EP. Hepatitis A. Infect Dis Clin North Am 2000; 14:605.



Şekil 5. Genotip 1 hastalarında birinci, ikinci ve üçüncü tedavi seçenekleri ve süreleri.

15. Gordon SC, Reddy KR, Schiff L, Schiff ER. Prolonged intrahepatic cholestasis secondary to acute hepatitis A. *Ann Intern Med* 1984; 101:635.
16. Glikson M, Galun E, Oren R, et al. Relapsing hepatitis A. Review of 14 cases and literature survey. *Medicine (Baltimore)* 1992; 71:14.
17. Centers for Disease Control and Prevention (CDC). Positive test results for acute hepatitis A virus infection among persons with no recent history of acute hepatitis--United States, 2002-2004. *MMWR Morb Mortal Wkly Rep* 2005; 54:453.
18. The World Health Organization. Global Hepatitis Report, 2017. (30.10.2021 tarihinde [https://apps.who.int/iris/bitstream/handle/10665/255016/9789241565455-eng.pdf;jsessionid=DC3616B5BDF94F\\_A8B6AC2FDB-C71E5B51?sequence=1](https://apps.who.int/iris/bitstream/handle/10665/255016/9789241565455-eng.pdf;jsessionid=DC3616B5BDF94F_A8B6AC2FDB-C71E5B51?sequence=1) adresinden ulařılmıştır).
19. Tassopoulos NC, Papaevangelou GJ, Sjogren MH, et al. Natural history of acute hepatitis B surface antigen-positive hepatitis in Greek adults. *Gastroenterology* 1987; 92:1844.
20. Centers for Disease Control. Surveillance for viral hepatitis – United States, 2013 (30.10.2021 tarihinde <http://www.cdc.gov/hepatitis/statistics/2013surveillance/commentary.htm#hepatitisB> adresinden ulařılmıştır).
21. World Health Organization. Guidelines on assessing donor suitability for blood donation. (30.10.2021 tarihinde [http://iacld.ir/DL/elm/whobloodonorselection-guidelinesonassessingdonorsuitability\\_forblooddonation.pdf](http://iacld.ir/DL/elm/whobloodonorselection-guidelinesonassessingdonorsuitability_forblooddonation.pdf) adresinden ulařılmıştır).
22. Liaw YF, Tsai SL, Sheen IS, et al. Clinical and virological course of chronic hepatitis B virus infection with hepatitis C and D virus markers. *Am J Gastroenterol* 1998; 93:354.
23. Garfein RS, Bower WA, Loney CM, et al. Factors associated with fulminant liver failure during an outbreak among injection drug users with acute hepatitis B. *Hepatology* 2004; 40:865.
24. Rehmann B, Ferrari C, Pasquinelli C, Chisari FV. The hepatitis B virus persists for decades after patients' recovery from acute viral hepatitis despite active maintenance of a cytotoxic T-lymphocyte response. *Nat Med* 1996; 2:1104.
25. Jeng WJ, Sheen IS, Liaw YF. Hepatitis B virus DNA level predicts hepatic decompensation in patients with acute exacerbation of chronic hepatitis B. *Clin Gastroenterol Hepatol* 2010; 8:541.
26. Lok AS, Lai CL. alpha-Fetoprotein monitoring in Chinese patients with chronic hepatitis B virus infection: role in the early detection of hepatocellular carcinoma. *Hepatology* 1989; 9:110.
27. Yan LB, Liao J, Han N, et al. Association between Hepatitis B Virus Infection and Metabolic Syndrome in Southwest China: A Cross-sectional Study. *Sci Rep* 2020; 10:6738.
28. Andreani T, Serfaty L, Mohand D, et al. Chronic hepatitis B virus carriers in the immunotolerant phase of infection: histologic findings and outcome. *Clin Gastroenterol Hepatol* 2007; 5:636
29. McMahan BJ, Holck P, Bulkow L, Snowball M. Serologic and clinical outcomes of 1536 Alaska Natives chronically infected with hepatitis B virus. *Ann Intern Med* 2001; 135:759.
30. Chu CM, Chen YC, Tai DI, Liaw YF. Level of hepatitis B virus DNA in inactive carriers with persistently normal levels of alanine aminotransferase. *Clin Gastroenterol Hepatol* 2010; 8:535.
31. Bonino F, Rosina F, Rizzetto M, et al. Chronic hepatitis in HBsAg carriers with serum HBV DNA and anti-HBe. *Gastroenterology* 1986; 90:1268.
32. Liu J, Yang HI, Lee MH, et al. Incidence and determinants of spontaneous hepatitis B surface antigen seroclearance: a community-based follow-up study. *Gastroenterology* 2010; 139:474.
33. Chen YC, Sheen IS, Chu CM, Liaw YF. Prognosis following spontaneous HBsAg seroclearance in chronic hepatitis B patients with or without concurrent infection. *Gastroenterology* 2002; 123:1084.
34. Lin CL, Tseng TC, Kao JH. What can we learn from hepatitis B virus clinical cohorts? *Liver Int* 2015; 35 Suppl 1:91.
35. The World Health Organization. Guidelines for the prevention, care, and treatment of persons with chronic hepatitis B infection. (30.10.2021 tarihinde [http://apps.who.int/iris/bitstream/10665/154590/1/9789241549059\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/154590/1/9789241549059_eng.pdf?ua=1) adresinden ulařılmıştır).
36. Lok AS, Lai CL, Wu PC. Prevalence of isolated antibody to hepatitis B core antigen in an area endemic for hepatitis B virus infection: implications in hepatitis B vaccination programs. *Hepatology* 1988; 8:766
37. Kleinman SH, Kuhns MC, Todd DS, et al. Frequency of HBV DNA detection in US blood donors testing positive for the presence of anti-HBc: implications for transfusion transmission and donor screening. *Transfusion* 2003; 43:696.
38. Carman WF, Jacyna MR, Hadziyannis S, et al. Mutation preventing formation of hepatitis B e antigen in patients with chronic hepatitis B infection. *Lancet* 1989; 2:588.
39. Martinot-Peignoux M, Boyer N, Colombat M, et al. Serum hepatitis B virus DNA levels and liver histology in inactive HBsAg carriers. *J Hepatol* 2002; 36:543.
40. Kumar M, Satapathy S, Monga R, et al. A randomized controlled trial of lamivudine to treat acute hepatitis B. *Hepatology* 2007; 45:97.
41. European Association for the Study of the Liver. Electronic address: [easloffice@easloffice.eu](mailto:easloffice@easloffice.eu), European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. *J Hepatol* 2017; 67:370
42. Yuan P, Chen P, Qian Y. Evaluation of Antiviral Therapy Performed after Curative Therapy in Patients with HBV-Related Hepatocellular Carcinoma: An Updated Meta-Analysis. *Can J Gastroenterol Hepatol* 2016; 2016:5234969.
43. Aragona M, Macagno S, Caredda F, et al. Serological response to the hepatitis delta virus in hepatitis D. *Lancet* 1987; 1:478.
44. Negro F, Bergmann KF, Baroudy BM, et al. Chronic hepatitis D virus (HDV) infection in hepatitis B virus carrier chimpanzees experimentally superinfected with HDV. *J Infect Dis* 1988; 158:151.
45. Terrault NA, Lok ASF, McMahan BJ, et al. Update on

- prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology* 2018; 67:1560.
46. Negro F, Shapiro M, Satterfield WC, et al. Reappearance of hepatitis D virus (HDV) replication in chronic hepatitis B virus carrier chimpanzees rechallenged with HDV. *J Infect Dis* 1989; 160:567.
  47. Longo DL, Fauci AS. (2013). *Harrison's Gastroenterology and Hepatology* (2nd Edition;357-385). USA, Mc Graw-Hill Education.
  48. World Health Organization. Web Annex B. WHO estimates of the prevalence and incidence of hepatitis C virus infection by WHO region, 2015. In: *Global hepatitis report 2017*. (30.10.2021 tarihinde <https://apps.who.int/iris/bitstream/handle/10665/277005/WHO-CDS-HIV-18.46-eng.pdf> adresinden ulaşılmıştır).
  49. Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, Degenhardt L. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. *Lancet*. 2011 Aug 13;378(9791):571-83. doi: 10.1016/S0140-6736(11)61097-0. Epub 2011 Jul 27. PMID: 21802134; PMCID: PMC3285467.
  50. Pereira BJ, Milford EL, Kirkman RL, Levey AS. Transmission of hepatitis C virus by organ transplantation. *N Engl J Med*. 1991 Aug 15;325(7):454-60. doi: 10.1056/NEJM199108153250702. PMID: 1649402.
  51. Roth D, Zucker K, Cirocco R, DeMattos A, Burke GW, Nery J, Esquenazi V, Babischkin S, Miller J. The impact of hepatitis C virus infection on renal allograft recipients. *Kidney Int*. 1994 Jan;45(1):238-44. doi: 10.1038/ki.1994.29. PMID: 7510350.
  52. Koike K, Tsutsumi T. The Oncogenic Role of Hepatitis C Virus. *Recent Results Cancer Res*. 2021;217:91-105. doi: 10.1007/978-3-030-57362-1\_5. PMID: 33200363.
  53. *Hepatit C Tedavi Kılavuzu Güncellemesi* (2019). (30.10.2021 tarihinde <https://www.vhsd.org/tr/hepatit-c-tedavi-kilavuzu-guncellemesi-a> adresinden ulaşılmıştır).
  54. Idilman R, Razavi H, Robbins-Scott S et al. A micro-elimination approach to addressing hepatitis C in Turkey. *BMC Health Serv Res*. 2020 Mar 24;20(1):249. doi: 10.1186/s12913-020-5019-8. PMID: 32209103; PMCID: PMC7093960.