

Chronic Hepatitis C in Elderly

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Introduction

Chronic hepatitis C (CHC) is an important cause of chronic liver disease (chronic hepatitis and cirrhosis) and hepatocellular carcinoma (HCC) in India. Around 15% of patients with cirrhosis liver and around 35% of patients with HCC seen in the liver clinic of Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh are related to CHC. The most prevalent genotype of hepatitis C virus (HCV) in India is genotype 3 followed by genotype 1, while the other genotypes are uncommon.

CHC in elderly patients is considered a special group because of the different epidemiology, clinical course, immunology and treatment in comparison to younger patients.

Epidemiology

Even though separate figures are not available in the elderly, prevalence of HCV infection is less than 1% in the general population in India. The prevalence of HCV in the elderly is variable as reported from United States and Europe. Risk factors for HCV infection in older individuals in US are blood product transfusions before 1992, military service, injection drug use, tattoos, hemodialysis, and employment as a health care worker. In India the screening for anti-HCV in blood banks became mandatory in the year 2001. Hence other than the risk factors already mentioned, history of blood transfusion before 2001 would be an important risk factor for all and for elderly population.

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Clinical Course

Adults older than 65 years of age more often present with complications of cirrhosis and HCC as initial manifestations of HCV infection compared with younger individuals. Older age at the time of initial infection is an important factor associated with more advanced fibrosis even after adjusting for other factors. Furthermore, progression to fibrosis may be more rapid when initial HCV infection occurs in older individuals, regardless of duration of infection.

Elderly individuals with HCV-RNA viremia are also more likely to have normal ALT levels than younger adults. Data on the utility of non-invasive serum markers and elastography for the assessment of hepatic fibrosis in elderly patients is sparse.

Immunological Aspects

When primary infection occurs in old age, it may be confronted with a reduction in both innate and induced specific immunologic responses. With aging, immunity to viral infections is affected by a decrease in T cell function, and a shift of T cell subsets from naive to activated and/or memory types. Additionally, repeated antigenic challenges to CD8+ T cells may lead to ultimate anergy, rather than to effective memory. Alterations in the cytokine profile that occur during aging may also affect the course of chronic liver disease in elderly persons.

Treatment

Treatment of patients with chronic hepatitis C (CHC) has changed significantly in last few years. Before the arrival of newer directly acting antiviral agents (DAA), pegylated interferon alfa (Peg-IFN) plus ribavirin (RBV) therapy had been the standard of care for these patients. However as per the recent recommendations by the American Association for

the study of Liver Diseases (AASLD), in collaboration with the Infectious Diseases Society of America, combination of oral drugs have replaced Peg-IFN plus RBV for the treatment of patients with CHC. Similar guidelines are available from the European Society of liver disease (EASL).

DAA's are costly in the Western world; hence the treatment of patients with CHC in those populations needs to be prioritized according to the disease severity. EASL recommends that treatment is not recommended in patients with limited life expectancy. Of the various DAA combinations recommended by the AASLD and EASL, only sofosbuvir has recently become available in India and is approved for the treatment of patients with CHC. The best combination for Indian patients with all types of genotypes thus are either the combination of Sofosbuvir plus RBV given for 24 weeks or the triple combination with Peg-IFN plus RBV plus Sofosbuvir given for 12 weeks in interferon eligible patients. Since the treatment is cheaper in India in comparison to US and Europe, the candidacy for treatment may differ in India. Since the sustained virological response with current drugs is very high, all patients eligible for treatment including elderly patients can be treated for HCV infection. Since the infection usually takes 10-15 years to significantly damage the liver, elderly patients with limited life expectancy, however may not be the candidates for treatment.

Typically, major clinical trials have excluded individuals older than 65 years predominantly because of the presence of various co-morbid conditions and presence of contraindications to anti-viral drugs. Even though, elderly individuals are less likely to have other barriers to anti-HCV therapy such as substance abuse and psychiatric disorders, overall, elderly patients with chronic HCV infection have been classified as a difficult-to-treat group, because of poor tolerance to interferon

based drugs, higher discontinuation of therapy or dose reductions. Even though the data is not available with newer oral directly acting anti-virals (DAAs), elderly patients have been found to have poorer response to pegylated interferon/RBV in comparison to younger patients. Elderly patients with CHC progressing to cirrhosis liver and HCC may not also be good candidates for liver transplantation if indicated.

References

1. Kumar A, Acharya SK, Singh SP, Saraswat VA, Arora A, Duseja A, et al. The INASL Task-Force on Hepatocellular Carcinoma. The Indian National Association for Study of the Liver (INASL) Consensus on Prevention, Diagnosis and Management of Hepatocellular Carcinoma in India: The Puri Recommendations. *J Clin Exp Hepatol*. 2014;4(Suppl 3):S3-S26.
2. Puri P, Anand AC, Saraswat VA, et al. Consensus statement of HCV Task Force of the Indian National Association for Study of the Liver (INASL). Part II: INASL recommendations for management of HCV in India. *J Clin Exper Hepatol*. 2014; 4: 117-140.
3. AASLD/IDSA HCV Guidance Panel. Hepatitis C guidance: AASLD-IDSA recommendations for testing, managing, and treating adults infected with hepatitis C virus. *Hepatology*. 2015; 62:932-54.
4. European Association for Study of Liver. EASL Recommendations on Treatment of Hepatitis C 2015. *J Hepatol*. 2015; 63:199-236.
5. Mindikoglu AL, Miller RR. Hepatitis C in the elderly: epidemiology, natural history, and treatment. *Clin Gastroenterol Hepatol*. 2009;7:128-34
6. Horsmans Y. Treatment of chronic hepatitis C in elderly patients. *Expert Opin Pharmacother*. 2010; 11:571-7.