New developments in the era of viral hepatitis vaccines

Viral hepatitis aşılarında yeni gelişmeler

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ABSTRACT
Chronic hepatitis B and hepatitis C infections are major health problems in the world. Therefore, prevention of the transmission of the viral infections gets higher priority. Development of hepatitis B vaccines by recombinant technology provide higher prevention rates. However, this success could not be achieved with hepatitis C vaccine. The present review discusses recent developments for hepatitis B and C vaccines.

Keywords: New vaccines, Hepatitis B, Hepatitis C

ÖZ

Anahtar kelimeler: Yeni aşılar, Hepatit B, Hepatit C

Introduction
Chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are the main etiologic factors of chronic liver diseases in the world. It is known that 400 million people are infected with HBV and 170 million people are infected with HCV infection worldwide [1,2]. Recent developments in HBV treatment provide sustained HBV infection suppression during on medication, however stopping the treatment causes increase in viral replication together with the flare up of the hepatitis. Treatment of chronic liver diseases and complications requires large amounts of costs, therefore prevention of these infections needs high priority in the control of these infectious diseases. In addition to reducing the routes of transmission, progression in the development of viral vaccines is also important for the control of the burden of HBV and HCV infections. After the isolation of HBV virus, development of HBV vaccines progressed rapidly and achieved 90% of prophylaxis after the vaccination. However, development of an effective vaccine against HCV still cannot be achieved. Yet, almost 100% cure rates are achieved in the era of new direct acting anti-viral (DAA) drugs. In this review, current situation and future directions will be discussed in relation to HBV and HCV vaccines.

Hepatitis B vaccines
Hepatitis B vaccines were firstly developed in France and USA through the deactivation of HBV from the serum of infected people by heating or treating with formaldehyde in 1981. However, by concerning the other viral transmission risks, usage of these vaccines mostly abandoned in all over the world. In 1986, recombinant technology was undertaken to produce HBs polypeptides from the yeast cells and second generation HBV vaccines were developed by replacing...
The aim of innovations in HBV vaccines is to increase the response rates to 100% for all individuals and immune deficiency patients, to make the application routes more comfortable such as oral or nasal routes instead of intramuscular or subcutaneous applications and to combine with the other vaccines [14]. One of the recently developed vaccine (HEPLISAV) which contains immune stimulant phosphorothioate oligodeoxyribonucleotide provides significantly higher response rates when compared with other third generation vaccines [15,16]. Also there are other studies by adding new adjuvants to HBV vaccine such as interferons, interleukins, etc. These adjuvant containing vaccines can be used in immune deficient patients to increase the immune response. The other vaccine developments are aimed to decrease the application quantities or the application routes such as only one injection vaccines are produced by capsulation of HBV surface antigen into the polymers which provides slow release of HBV surface antigen [17]. However, there are no human studies with those newly developed vaccines. There are also ongoing studies of oral, inhalation and intradermal applications of HBV vaccines as well [18-20]. Hepatitis B vaccine response is usually weak in chronic renal failure patients (CRF) so new adjuvant containing vaccines were also tested in those patients with good results, however these vaccines are not available in clinical practice right now. The other important subject is the use of adjuvant containing vaccines in chronic hepatitis B patients in order to increase the viral suppression. Products containing MPL and MF59 have prosperous results in phase 1 studies but needs further studies [21-26].

**Hepatitis C Vaccine**

Hepatitis C is a major health problem in all over the world and probably 2% of the world population is infected by HCV infection. Large prevalence study which was done by Turkish Association for the Study of Liver Disease (TASL) showed that 1% of Turkish population is infected by HCV infection [27]. During the last 5 years, enormous amount of progress has been done in the treatment of HCV infection, and almost 100% sustained virologic clearance is achieved by the recently developed oral drugs. However, these drugs are very expensive and small amount of infected people are aware of their infection. So primary prevention is still very important which includes HCV vaccination. However, although hopeful research and studies are conducted, until now there is no effective HCV vaccine in the market. One of the main factor is the variability of HCV RNA called as quasispecies which protects itself to the neutralizing antibodies. In the development of HCV vaccines, two major
genomic structure can be targeted which are E1/E2 proteins and non-structural proteins. Recently developed vaccine that consisted both E1/E2 proteins and MF59 as an adjuvant showed favorable results on chimpanzees and phase 1 studies are ongoing on humans [28,29]. The other point is to increase the T cell specific response to HCV virus by adding some kind of adjuvant molecules to the vaccine [30].

In conclusion, although large number of approaches have been pursued to develop HBV vaccines, same achievements could not be reached in HCV vaccines but by the new oral antiviral drugs HCV eradication is almost completely probable.

Key Points

- After the isolation of Hepatitis B, vaccine studies progressed rapidly and recombinant HBV vaccines achieved 9% of prophylaxis rates after the vaccination.
- Innovations in HBV vaccines are to increase the response rates to 100% for all individuals and immune deficiency patients, and to make the application routes more comfortable.
- Although hopeful research and studies are conducted, until now there is no effective HCV vaccine in the market.

References


