HEPATITIS B VACCINATION IN CKD: PROTOCOLS, CHALLENGES AND REALITY

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Despite stringent infection control practices and increased widespread use of erythropoietin and a concomitant reduction in the requirement for transfusions, hepatitis B virus (HBV) outbreaks occur in hemodialysis (HD) units.

The risk for HBV infection is significantly lower among vaccinated HD patients. Most HD patients can be protected from HBV by vaccination, and maintaining immunity among these patients reduces the frequency and costs of serologic screening. Immunization against HBV permits patient rehabilitation, holiday traveling and dialysis in host centres, while susceptible patients serve as potential HBV infection targets and transmitters of the disease back to home units.

Hepatitis B vaccine induces a protective anti-HBs response (defined as >10 milli-International Units [mIU]/mL) in 90%–95% of adults with normal immune status. However, patients with end-stage renal disease (ESRD) have an impaired immune response to many vaccines and that many patients fail to achieve an adequate immune response following HBV vaccination. Various approaches have been used to overcome the non-responsiveness of chronic uremic patients - intramuscular (IM) administration of multiple doses, or double doses co-administration of adjuvants, such as zinc supplements or immune modulators, such as γ-interferon, interleukin-2, thymopentin, levamisole, granulocyte-macrophage colony-stimulating factor (GM-CSF) and intradermal (ID) administration of HB vaccine. The use of recombinant erythropoietin, leading to an increase in the T-helper to T-suppressor cell ratio, as well as better dialysis biocompatibility can also improve the immune response to vaccination.

Two monovalent recombinant DNA hepatitis B vaccines are licensed in Canada: Recobbivax HB® (Merck Frosst Canada Ltd.) and Engerix-B® (GlaxoSmithKline Inc.). Recombivax HB contains 10–40 µg of HBsAg protein per mL, whereas Engerix-B® contains 20 µg/mL. Primary vaccination comprises three intramuscular doses of vaccine, with the second and third doses given 1 and 6 months, respectively, after the first. An alternative schedule of four doses given at 0, 1, 2, and 12 months to persons with normal immune status or at 0, 1, 2, and 6 months to hemodialysis patients has been approved for Engerix-B®.

Patients who develop an adequate antibody response should be given a booster dose of vaccine every five years. No data exist to indicate that additional doses would induce an antibody response in patients who remain non-responders after six doses of vaccine.

Seroconversion in response to HBV vaccination declines with age, as shown in the table below. End-stage renal disease (ESRD) further compromises the ability of an individual to mount an immune response to HBV, further decreasing seroconversion rates in older patients. Other host factors that contribute to decreased immunogenicity include smoking, obesity, and immune suppression. Chronic inflammation associated with renal failure, leads to impaired monokine production and decreased immunity. This impairment could be related to defective HLA-DRB7 02 expression on monocytes. Non-responders to Hepatitis B vaccination express increased levels of HLA class II alleles (T-cell immune response modulators) DRB1 01 (DR1) and DRB1 15 (DR15).

Patients with ESRD have an impaired immune response to vaccines. Consequently, many patients fail to achieve an adequate immune response following HBV immunization.

Table 1. Efficacy of HBV Vaccination in Adults*

Age Group (Years)	Seroconversion Rate (%)
20 – 29	95
30 – 39	90
40 – 49	86
50 – 59	71
>60	50 - 70

*Canadian Immunization Guide, 6th Edition, 2002

Among HD patients who respond to hepatitis B vaccine, protection against HBV is not maintained when antibody titres fall below protective levels. However, limited data exist to suggest that virtually all of these patients respond to a booster dose. Among persons with normal immune status who respond to the primary series of hepatitis B vaccine, protection against hepatitis B persists even when antibody titers become undetectable. However, among HD patients who respond to the vaccine, protection against hepatitis B is not maintained when antibody titers fall below protective levels. Regular antibody monitoring is required. Frequency is not quite defined.

References

1. Charest A et al. Am J Kidney Dis. 2003 Dec;42(6):1193-9
2. Charest A et al. Am J Kidney Dis 2000 Nov;36(5):976-82