How to Improve Anti-Hepatitis B Vaccination

See Chow et al., pp. c89–c93

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Hepatitis B virus (HBV) infection remains a concern in dialysis patients. Routine vaccination programs have been less successful than in the general population, as indicated by a lower seroconversion rate and a decreased ability to maintain protective antibody titer (≥ 10 IU/l) over time [1].

The impaired response has been attributed to a number of reasons, which contribute to a suppressed immunity: uremia, inadequate dialysis, malnutrition, anemia, diabetes mellitus, use of bioincompatible dialyzers, iron overload, obesity and old age. Various vaccination methods using increased dosages and schedules were used to improve patients' antibody production response. However, a question still remains: Which is the preferred method?

In this issue of *Nephron Clinical Practice*, Chow et al. [2] report a study which examined (a) the factors contributing to an impaired antibody response in these patients, and (b) the effect of an increased recombinant vaccine dose on antibody response in these patients. Sixty-four patients were vaccinated with intramuscular recombinant hepatitis B vaccine (Engerix B, GlaxoSmithKline) in a 3-dose schedule at 0, 1 and 6 months. They identified 3 historical cohorts of patients vaccinated with 20, 40, or 80 μ g per dose.

The patients were grouped according to seroprotective levels of anti-HB antibodies ≥ 10 IU/l, 1–3 months after the third dose. Older age, diabetes mellitus, obesity and

low Engerix-B dose were risk factors for an impaired antibody response by univariate analysis, confirming similar findings in previous studies. Vaccine dose was the only independent predictive factor for impaired antibody response by multivariate analysis. The 20- μ g dose proved to be inadequate. The most impressive finding is that although the 80- μ g dose did not lead to an increased antibody response rate compared to the 40- μ g dose, the antibody-protective level produced by it remained significantly higher than that of the 40- μ g dose, throughout the 6-year follow-up period.

The limitations of this study are: (a) it is a retrospective study, using historical controls; (b) there was a small number of patients in each group; (c) the patients in this study had a relative low hemoglobin level; a higher hemoglobin level or treatment with erythropoietin is associated with enhanced immune responses [3] and improved anti-HB antibody response following vaccination in dialysis patients [4, 5], and (d) nowadays, many centers use a 4-dose, rather than a 3-dose, intramuscular vaccination schedule of 40- μ g per dose at 0, 1, 2 and 6 months [6].

Several strategies may be used to enhance response to HBV vaccine in patients with chronic kidney disease (CKD): augmented dosing, as suggested by the Chow et al. study [2] and various reinforced schedules [6]; vaccination at an earlier stage of CKD [7]; the use of erythropoietin to increase hemoglobin levels [4, 5]; intradermal vaccination [8], and the use of other recombinant anti-

HB vaccine preparations, such as the adjuvanted vaccine HB-AS04 (Fendrix™, GlaxoSmithKline Biologicals), which are potentially more immunogenic than the current recombinant vaccine preparations. The adjuvant system is composed of an aluminum salt and 3-*O*-desacetyl-4'-monophosphoryl lipid A (MPL, Corixa, Seattle, Wash., USA). In a recent clinical study, which compared 4-dose schedules of Engerix with Fendrix, the adjuvanted vaccine was associated with an earlier seroconversion, a higher mean antibody geometrical concentration and a significantly higher rate of seroprotection (>10 IU/l) after 3 years of follow-up [9]. Another potentially more immunogenic anti-HB vaccine is the Bio-Hep-B (BioTechnology General, Rehovot, Israel), which expresses the S, pre-S1 and pre-S2 highly immunogenic antigenic viral pro-

tein components. A recent study with this preparation showed a high seroprotective antibody response with a high antibody level in patients with end-stage renal disease [10].

Additional controlled studies are needed to define the optimal vaccination method in CKD patients with regards to the dose, schedule and type of recombinant anti-HB vaccine. Today, the preferred method seems to be, a high 4-dose intramuscular vaccination schedule with an immunogenic recombinant vaccine given at the predialysis stage, followed by regular monitoring of antibody blood levels, with a booster vaccine, when antibody levels of the dialysis patient decrease below the seroprotective level.

References

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