Review: protective efficacy of hepatitis B vaccines in neonates

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Authors' objectives
To review the literature to date on the varying hepatitis B vaccine doses, with or without hepatitis B immune globulin (HBIG), and the schedules used; to determine how these factors influence the protective efficacy in neonates of mothers with hepatitis B e antigen (HbeAg).

Searching
An in-house SmithKline Beecham product literature database, which the authors described as 'containing all scientific publications on vaccines', was searched using the keywords 'immunisation', 'neonates', 'hepatitis B vaccines', 'vaccination' and 'immunogenicity'.

Study selection
Study designs of evaluations included in the review
The authors do not give a clear description of the included studies; some were prospective placebo-controlled studies, some used historical controls, and some calculated protective efficacy within a group of vaccinated neonates by assuming that 65% of untreated infants would become chronic carriers of hepatitis B.

Specific interventions included in the review
Vaccination with hepatitis B surface antigen, either plasma-derived or manufactured by recombinant DNA, given to neonates in a variety of doses according to different schedules, with or without concomitant administration of HBIG.

Participants included in the review
Neonates of mothers positive for HbeAg.

Outcomes assessed in the review
Protective efficacy of the vaccination schedule, based on the prevalence of chronic carriage (for over 6 months) of hepatitis B surface antigen. In some studies, prevalence of chronic carriage was estimated from point prevalence.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
Tables provide details of the dosing schedules, use of HBIG, number of recipients, nature of control group and protective efficacy for individual studies. A narrative synthesis is also provided.

How were differences between studies investigated?
No formal tests for heterogeneity were carried out. The authors set out to investigate the possible differential effects of
different vaccination dosing schedules, and the provision or not of HBIG. In their narrative synthesis, the authors concentrated on studies with placebo controls and comparisons made within the arms of a single study.

**Results of the review**

Studies of plasma derived vaccines: 8 papers reporting placebo-controlled studies; 6 papers reporting studies using historical controls; 8 papers using an assumed attack rate of 65%; and 2 papers in which the nature of the control group was unspecified. Studies of recombinant DNA vaccines: 2 papers reporting placebo-controlled studies; 3 papers reporting studies using historical controls; 2 papers using an assumed attack rate 65%; and 1 study in which the nature of the control group was unspecified.

The protective efficacy reported in individual studies ranged from 42 to 100% for the plasma-derived vaccines, and from 66 to 100% for the recombinant DNA vaccines. Lower doses of plasma-derived vaccines tended to give lower protective efficacy rates if no HBIG was provided. Seven studies showed the protective efficacy of low doses of plasma-derived vaccines was increased when HBIG was administered; this increase was not seen at doses of 10 microg or less of plasma-derived vaccines.

**Cost information**

None. However, it was noted that HBIG is becoming increasingly scarce and expensive.

**Authors' conclusions**

For infants at high risk of becoming chronic carriers of hepatitis B, it is clearly established that the administration of HBIG at birth has a significant (positive) effect on protective efficacy, particularly if lower-dose vaccines are used. Higher-dose vaccines can elicit high protective efficacy without HBIG.

**CRD commentary**

We have no means of ascertaining how comprehensive the in-house database used for the search was. The inclusion criteria and the procedures used to carry out this review were not clearly stated. Neither the possibility of adverse effects, nor the acceptability of the different vaccination schedules to parents, were considered. The authors note in their discussion that targeting high-risk groups only for hepatitis B vaccine has failed to significantly reduce the number of chronic carriers. They advocate universal vaccination of infants in countries where perinatal transmission is frequent. One author is employed by the pharmaceutical company SmithKline Beecham.

**Funding**

Funded in part by SmithKline Beecham.

**Bibliographic details**


**PubMedID**

7852954

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Dose-Response Relationship, Immunologic; Female; Hepatitis B/prevention & control/transmission; Hepatitis B Vaccines/administration & dosage/pharmacology; Humans; Immunization Schedule; Immunoglobulins/administration & dosage; Infant; Infant, Newborn; Infectious Disease Transmission, Vertical; Pregnancy
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.