Intradermal vaccination against hepatitis B in a group of medical students

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Summary

A prospective study of a low-dose (one-tenth) intradermal regimen using recombinant hepatitis B vaccine was undertaken during two consecutive years in 4th-year medical students. Eighty-one per cent of the vaccinees (123/152) seroconverted with anti-HBs levels of > 10 IU/l. The lower titre of hepatitis B surface antibodies compared with published studies on intramuscular immunisation, together with a seroconversion rate of only 81%, makes the intradermal method, in our opinion, a suboptimal form of hepatitis B immunisation.

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The prospect of administering a course of low-dose (one-tenth) hepatitis vaccine intradermally instead of a full dose intramuscularly is attractive in view of the potential cost saving. The immunogenicity of hepatitis B vaccine administered via the intradermal route has been demonstrated in several studies, with seroconversion rates varying from 83% to 92%.[1-3]

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One recent study[3] comparing intradermal and intramuscular hepatitis B vaccination in individuals matched for age and sex showed comparable seroconversion rates in both groups.

Since medical students form part of the health care team, they are occupationally exposed and should be immunised against hepatitis B. A major consideration in the administration of a hepatitis B vaccination is the cost of the vaccine.

Subjects and methods

Volunteers from two consecutive classes of 4th-year medical students were vaccinated with 2 μg (0,1 ml) of hepatitis B vaccine intradermally at 0, 1 and 6 months. Serum was obtained for the determination of hepatitis B surface antibody (anti-HBs) status before immunisation and 6 - 8 weeks after completion of the vaccination course. Informed consent was obtained from all participating students and it was indicated that a full dose (20 μg) of hepatitis vaccine would be given by intramuscular injection to non-responders. Vaccine was administered by medical practitioners and great care was taken to ensure that successful intradermal inoculation was achieved in all students.

A recombinant hepatitis B vaccine, Engerix B (Smith, Kline and French), was stored at 4°C.

Anti-HBs levels were determined by radio-immunoassay (Ausab, Abbot Laboratories, North Chicago). A linear correlation coefficient > 0,9 allowed extrapolation to international units per litre (IU/l). Seroconversion was defined as greater than 10 IU/l. Non-responders receiving 20 μg of hepatitis B

vaccine intramuscularly were tested for anti-HBs 1 month after receiving their intramuscular booster.

Results

A total of 165 students were immunised during 1988 and 1989. Thirteen (7,9%) were immune before vaccination and were therefore excluded from this analysis.

Seroconversion of greater than 10 IU/l was achieved in 123 students (81%). The non-responders received 20 μg of vaccine as an intramuscular booster. Post-booster serum was available from 12 students, 10 of whom subsequently seroconverted (83%).

Seventy-five students (49%) had antibody levels > 150 IU/l (Table I). No statistically significant differences were observed in the antibody responses of students vaccinated in 1988 and 1989.

TABLE I. ANTIBODY LEVELS FOLLOWING INTRADERMAL VACCINATION ($N = 152$)

	IU/l				
	< 10	10-49	50-99	100-149	> 150
1988	**17**	**13**	**9**	**7**	**42**
1989	**12**	**3**	**8**	**8**	**33**

No major side-effects were reported. Minor side-effects included an erythematous reaction, which appeared approximately 24 hours after vaccination and faded rapidly, although some reactions persisted to form pigmented macules approximately 3 mm in size. No increase in the severity and frequency of reaction was observed with the second and third doses of vaccine.

Discussion

The cost-saving advantage of hepatitis B vaccine administered intradermally must be weighed against the disadvantages of this route of vaccination.[4] The expertise required for intradermal inoculation is a major drawback in large immunisation programmes where individuals of varying training and skill will be responsible for vaccine administration.

Engerix B hepatitis B vaccine has been licensed for intramuscular use based on published studies on safety, immunogenicity and protective efficacy. Extreme caution must therefore be exercised if the recommended dosage and immunisation schedule are not adhered to. Administration of hepatitis B vaccine intramuscularly induces anti-HBs in more than 90% of healthy adults. Testing to determine seroconversion is therefore only necessary when an inadequate immune response is expected, e.g. in haemodialysis patients, and is not routinely recommended.[5] In our study we achieved an 81% seroconversion rate in volunteers from two consecutive 4th-year medical student classes using a reduced dose of hepatitis B vaccine intradermally. We feel, therefore, that routine post-immunisation testing to confirm a satisfactory immune response is essential. The cost of this additional testing, together with the cost of additional booster doses of hepatitis B vaccine, must be considered when evaluating the cost effectiveness of intradermal hepatitis B immunisation.

In addition, the peak anti-HBs levels following intradermal vaccination are generally lower. In a comparative study it was shown that the geometric mean titres of anti-HBs were considerably lower in subjects immunised via the intradermal route compared with those immunised intramuscularly (388 IU/l compared with 760 IU/l).[3] The duration of anti-HBs persistence is directly related to the peak antibody titre achieved after completion of immunisation.[6,7] Jilg *et al.*[6] proposed that subjects with anti-HBs levels < 100 IU/l after completion of the initial vaccine course should be given a fourth booster dose within 6 months. Therefore in our study 31% of students in 1988 and 21% in 1989 who achieved anti-HBs titres between 10 IU/l and 100 IU/l would require early boosting. If the non-seroconverters were included then a total of 46/88 (53%) of students in 1988 and 31/64 (48%) in 1989 would have required a booster of hepatitis B vaccination.

The lower titre of anti-HBs achieved in this study compared with published studies on intramuscular immunisation, together with a seroconversion rate of only 81%, makes intradermal hepatitis B immunisation a suboptimal form of hepatitis B immunisation. In our opinion, intradermal immunisation can only be recommended where the cost of intramuscular vaccination would preclude an individual at risk, for example a health care worker, from being immunised. In this case, intradermal immunisation would be preferable to no immunisation at all. The implications of not adhering to the manufacturer's recommendations should, however, be considered.

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