

# The Case for Intradermal Route Hepatitis-B Vaccination

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*Our argument in brief - The annual cost of hepatitis B immunization of all the newborns alone in India would be Rs. 250 crores, whereas the budget for TB control in India this year is only Rs. 105 crores. Given such a high cost, all options to reduce the cost of Hepatitis -B immunization need to be seriously considered in detail. This cost can be reduced to one-fifth if intradermal route is used. Majority of the published studies show that i.d. route is as effective as i.m./s.c. route and that acceptability by the people is not a problem.*

The Indian Academy of Pediatrics (IAP) has recommended universal immunization of the Under-fives in India for Hepatitis-B. Today, the cost of this vaccine is very high and the expenditure on the vaccine for 25 million newborn children would be Rs. 2500 million annually even if we assume that the vaccine-cost would be reduced to Rs.100/- per child, from the current cost of Rs. 210/-. Moreover, there are 110.4 and 196 million children in India in the 0- 4 and 5-14 age-group respectively. (1) The mere vaccine cost of immunizing these children would be Rs. 11,040 million and Rs. 19,600 million respectively. Spread over say 3 years, the annual cost of immunizing children in these age-groups would be to Rs. 3700 million and Rs. 6530 million respectively. Thus the total annual cost of the vaccine for this programme in the first three years would, respectively, be Rs.6200 million to Rs.12730 million, if 0-4 and 0-14 year age group is selected for immunization.

Compare these expenses with the current year's budget for malaria-control and TB control of Rs. 2904 and 1050 million respectively! (2).Using intradermal(i.d.) route would reduce the vaccine cost to one-fifth, as the dose of i.d. route is one fifth, that of i.m. route. But IAP has not recommended the i.d. route. We are not aware of any detailed analysis of this aspect by IAP. Since it is a matter concerning tens of millions of children and hundreds of crores of rupees of annual expenses, we feel that this option of i.d. vaccination requires a detailed consideration. We have briefly presented below a case for i.d. hep- B vaccination.

Perhaps IAP has doubts about its efficacy, perceived difficulty in giving intradermal injection and lastly, its acceptability by the people. However, published literature indicates that these fears are not well founded. Let us deal with these doubts sequentially.

## I) Protective Efficacy -

Many studies have compared the efficacy of intradermal, low dose (2 or 4 mcg) hep-B vaccination with the usual intramuscular vaccination with 20 mcg. As in case of many new areas of investigations, the results of these comparative studies have been somewhat divergent in some respects. Some studies in adults which employed a dose of 2 mcg for the i.d. route (10% of the adult i.m. dose) reported statistically significant, lower anti-HBs antibody titres compared with that after standard i.m. vaccination.(3-7) However other studies in adults which employed a 4 mcg i.d. dose (20% of the adult, i.m. dose) reported antibody titres as good as those with standard i.m. dose of 20mcg. (8,9). One study has reported such titres even with 10% of the i.m. dose (10). Similarly, studies for i.d. vaccination, have employed a similar higher dose, equivalent to 20% of the i.m. dose for that age, have reported antibody titres statistically significantly not different from that due to the i.m. dose. (11,12).

The higher initial titres of anti-HBs, after vaccination correlate with longer persistence of high antibody titres. However, since an antibody titre of more than 10 miu/ml is considered protective, the issue is say 3 to 5 years after primary vaccination, whether statistically significantly higher proportion of the im. Route-vaccinees have antibody titres higher than 10 miu/ml, as compared to the i.d.- route-vaccinees. Unfortunately most of these comparative studies have not followed up the vaccinees for 3 to 5 years. All three who have done a follow-up of 2-3 years of have reported no significant at difference in the persistence of antibodies after i.d. and i.m. vaccination (12-14). Through further studies with adequate follow up about adequate protective antibody levels the available data does indicate that 4 mcg i.d. dose is good enough required to settle this issue. Since protection lasts despite decline of the antibody levels to lower than 10 miu/ml, too much focus on the antibody titres, is perhaps unwarranted. Secondly, a

technically a little less efficacious measure may prove to be more effective, if it is considerably cheaper and hence is more widely used.

We conclude that the available data indicates that the protective efficacy of i.d. hep-B vaccination is as good as with i.m. vaccination, when a dose 20% of the standard i.m. dose for that age is used for i.d. vaccination. However, further studies are required to confirm these results, before policy decision can be taken.

The book 'Hepatitis-B in India' discusses in detail, various aspects of hep-B in India. The article in this book - Hepatitis-B vaccination, Indian experience, by V. A. Arankalle, also states that - "The studies by Elavia et al and Jaiswal et al have convincingly shown that intradermal immunization of low-dose plasma derived hepatitis-B vaccine in health care personnel produce desirable immune response".(15)

In this book, in the last section 'Summary, Recommendations and Issues : INSA-96,' S. K. Sarin has summarized the consensus of a one and half day long 'National Symposium on the Prevention of Hepatitis-B'. Here it is stated that "Subcutaneous intramuscular route is more acceptable than low dose intra-dermal route". (page 219) Though this statement is not backed up with any study, it may be noted here, that the acceptability and not the efficacy of the i.d. route has been questioned.

## **II) Side-effects -**

Intra-dermal vaccination leads to erythematous macular reactions in some vaccines. In the Indian study referred to above, such reactions were seen only in 17 out of 214 subjects. In two Western studies, 40 to 85% of subjects developed such reactions (16,17). This difference in reportage is probably because of difference in the skin-colour. In any case, these reactions are mild. The Indian study reports - "Side effects in the form of local reactions were seen among 17 of the 214 volunteers. In 10 volunteers, erythematous macules of 5-10 mm diameter were seen after 24-48 hours of the first dose which subsided after a few days leaving behind small hypersigmented macule. Among 5 subjects, the local reactions were seen after the second dose and there was itching at the site of the macule, associated with underlying small palpable cutaneous nodule persisting over 4 wk. In the remaining two, the local reactions were more marked after the third dose and the erythema was extended to about 4-5 cm and disappeared after a period of 4-6 wk. Besides these occasional local reactions the vaccine was well tolerated". (18)

Even in the white-skinned subjects, "most reactions consisted of mild-itching and an area of erythema less than 1 cm in diameter". (19) Secondly, when in one of these two studies, participants' perception of these side-effects were recorded, 96% of the 96 respondents opined that intradermal injection had no objectionable side-effects and 99% said, they would recommend this route of vaccination to other subjects". (20)

Thus the fear that this route of vaccination would be unacceptable to the people is unfounded. It must be borne in mind, that BCG vaccination with its papular, ulcerating lesion with a permanent scar has been accepted by people. With some educational effort, acceptance of i.d. vaccination would not be a problem.

## **III) Difficult technique of i.d. route -**

Its true that i.d. vaccination requires some skill and if the injection goes subcutaneous, the vaccination will be ineffective. We would point out that the paramedics have been giving intradermal BCG vaccination to tens of millions of children every year. Why can't they be trusted for Hep-B vaccination?

The option of using bifurcated needle, Heafgun, jet-injector should be explored to simplify the technique, reduce the cost and to eliminate the possibility of subcutaneous injection. Let us remember that hundreds of millions of people have been vaccinated against small-pox by i.d. route, with the help of simple bifurcated needle.

We conclude that doubts about i.d. Hep-B vaccination are not tenable. We should use i.d. route for universal immunization of our infants and save hundreds of crores out of the precious public money allocated for public health in India.

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