Indian J Med Res 65, 6, June 1977, pp. 756-759

Revaccination studies in children with graded potency of smallpox vaccines

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Received August 12, 1976; revised article received February 2, 1977.

Reactogenic and immunogenic response in young children aged five to sixteen years who were revaccinated with bifurcated needle employing graded potency (1×10^8; 5×10^7 and 1×10^7 PFU/ml.) of three different vaccines manufactured at Patwadangar in India, Moscow and Lister (England) revealed that major reaction produced by the three dilutions of the Patwadangar vaccine was comparatively higher than the Moscow and Lister vaccines. There was no appreciable rise in the haemagglutination-inhibition (HI) antibody titre in the post-vaccinial sera in comparison to the pre-vaccinial sera of most of the children exhibiting major/equivocal reaction following revaccination. However, 22·6 per cent children revaccinated with the graded potency of Patwadangar vaccine, 18·6 per cent with Lister vaccine and 6·4 per cent with Moscow vaccine did manifest four fold or more increase in the HI antibody titre in the post-vaccinial sera as compared to the pre-vaccinial sera.

Studies on reactogenicity and immunogenicity of three different vaccines manufactured at Patwadangar in (India), Moscow and Lister (England) under laboratory conditions have already been reported[1-3]. This paper deals with the revaccination studies in young children using three different strains of vaccinia virus of graded potency to evaluate the reactogenic and immunological response.

Material and Methods

Revaccination : Young children aged 5 to 16 years living in a few children's homes in Delhi were revaccinated in groups. The presence of vaccination scars was taken as an evidence of primary vaccination.

Three different freeze dried smallpox vaccines manufactured at Patwadangar (India), Moscow (USSR) and Lister, Elstree (England) were rehydrated in the reconstituting fluid (40 per cent glycerine McLvaine's buffer) in an appropriate volume so as to have an approximate graded potency titre of 1×10^7, 5×10^7 and 1×10^8 PFU/ml. of each vaccine. These titres were confirmed by checking the potency of the diluted vaccine on the chorioallantoic membrane of 12-day-old embryonated eggs after incubation at 35-36°C for 44 to 48 hours by the conventional methods.

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A particular vaccine in serial dilutions was inoculated in different groups of children on the forearm at two sites, 2·5 cm. apart, by making 20 insertions at each site with a sterile bifurcated needle which was changed every time.

Revaccinees were examined on 4, 7 and 14 days following vaccination and the reactions were recorded as per criteria laid down by the WHO Scientific Group[4].

Blood samples were collected, prior to and on 30 or 51 days following revaccination depending upon the availability of children for HI studies[5,6]. Micro HI test was conducted in U-shaped cups in microtitre lucite plates (Cooks Engineering Co., USA.) according to the technique described by Kempe and Vincent[7]. The antigen was always titrated prior to conducting the HI test and 2 HA units of the antigen were employed.

Results and Discussion

A total of 190 young boys were revaccinated with three different lyophilized vaccines of graded potency. This also included nine boys who were inoculated with placebo (the reconstituting fluid only) to serve as controls. The results have been summarised in the Table. Nine boys who were inoculated with placebo did not exhibit any reaction or change in HI antibody levels.

Though the object of this study was to evaluate the reaction and immunological response both in infants and older children following primary vaccination and revaccinations respectively, despite all efforts it was not possible to carry out primary vaccinations. The study was, therefore, confined to revaccination in young children who had previous vaccination scars.

The Patwadangar vaccine showed high rate of major reaction (40 per cent), followed by Lister vaccine (23·5 per cent) and the USSR vaccine (13·3 per cent), when vaccines having potency titre of 1×10^8 PFU/ml. were utilised for revaccination. With a potency of 5×10^7 PFU/ml. major reaction manifested by the Patwadangar vaccine was higher (16 per cent) as compared to the USSR (12·5 per cent) and Lister (9·5 per cent) vaccines. Boys revaccinated with vaccines having potency titre 1×10^7 PFU/ml. exhibited higher percentage of major reaction (40 per cent) with Patwadangar vaccine as compared to the Lister vaccine (4·8 per cent). There was no major reaction with the USSR vaccine in this titre.

Considering the three graded potencies of the three different vaccines together the overall rate of major reaction produced by the Patwadangar vaccine was significantly higher as compared to the Lister and USSR vaccines.

There was no appreciable increase in the HI antibody titre in the pre and post vaccination sera of majority of children showing either major or equivocal reaction following revaccination with the three graded dilutions of the three different vaccines.

Most of the revaccinees showed almost the same or less than four fold increase in the HI antibody titre in the post vaccinial sera as compared to the prevaccinial sera

TABLE. REACTOGENIC AND IMMUNOGENIC RESPONSE IN YOUNG CHILDREN FOLLOWING REVACCINATION WITH GRADED POTENCIES OF THREE DIFFERENT SMALLPOX VACCINES.

Vaccine strain and potency titre in PFU/ml.	No. of children revaccinated	Reaction		HI antibody titre in the post vaccinial sera as compared to the prevaccinial sera	
		Major	Equivocal	Less than 4-fold increase	More than 4-fold increase
Patwadangar					
1×10^8	25	10 (40·0%)	15	19	6
5×10^7	25	4 (16·0%)	21	19	6
1×10^7	25	10 (40·0%)	15	20	5
Total	75	24 (32·0%)	51 (68·0%)	58 (77·33%)	17 (22·67%)
EM-63 USSR					
1×10^8	15	2 (13·33%)	13	13	2
5×10^7	16	2 (12·50%)	14	15	1
1×10^7	16	0 (0%)	16	16	0
Total	47	4 (8·51%)	43 (91·49%)	44 (92·62%)	3 (6·38%)
Lister					
1×10^8	17	4 (23·53%)	13	13	4
5×10^7	21	2 (9·52%)	19	18	3
1×10^7	21	1 (4·76%)	20	17	4
Total	59	7 (11·86%)	52 (88·14%)	48 (81·36%)	11 (18·64%)

which is not considered significant. This is in conformity with the findings of other workers[8,9] who observed that revaccination may fail to induce increase in titre in haem-agglutination-inhibition and complement-fixing antibodies, though there may be a marked rise in neutralizing antibodies. However, only 17 (22·6 per cent) out of 75 boys revaccinated with Patwadangar vaccine, 11 (18·6 per cent) out of 59 boys inoculated with Lister vaccine and three (6·4 per cent) out of 47 boys revaccinated with USSR vaccine manifested more than four fold rise in the HI antibody titre of the post vaccinial sera when compared to the prevaccinial sera of the children showing major/equivocal reactions. The percentage of children showing more than four fold increase in HI titre in the post vaccinial sera was significantly higher with the Patwadangar and Lister vaccine as compared with the USSR vaccine. This is in conformity with earlier finding of Sehgal and co-workers[2] in rabbits, where the HI antibody titres in the post vaccinials sera were comparatively higher with the Patwadangar vaccine inoculated with bifurcated needle as compared to the other two vaccines *viz.* Lister and EM-63 from USSR.

Acknowledgment

This study was carried with financial support from the Indian Council of Medical Research, New Delhi.

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