COMPARISON OF IMMUNOGENIC1TY OF COMBINED DPT- INACTIVATED INJECTABLE POLIO VACCINE (OPT - IPV) AND ASSOCIATION OF DPI AND ATTENUATED ORAL POLIO VACCINE (DPI + OPV) IN PAKISTANI CHILDREN

Pages with reference to book, From 31 To 35

A. W. Qureshi (Present Address! Department of Paediatrics, Postgraduate Medical Institute and Lahore General Hospital, Lahore.)
I. Zulfiqar, A. Raza.N. Siddiqi (Department of Paediatrics, Rawalpindi General Hospital, Rawalpindi.)

Abstract

Two hundred children aged 2—24 months attending EPI Centre Rawalpindi General Hospital, were randomly assigned to two basic immunization schedules i.e. 3 doses of oral polio vaccine alongwith two doses of DPT (Conventional Schedule) and 2 doses of combined DPI — enhanced injectable polio vaccine (new simplified schedule). Comparison of the seroconversion results showed the presence of protective antibodies against all the 3 types of polio in 100% of the children in both the groups, but there was no statistical difference in the geometric mean antibody titre in the two immunization schedules. After two doses of DPT-IPV or DPT vaccine alone the results demonstrated antibody levels above the protective threshold in both the groups against Diphtheria, Pertussis and Tetanus(JPMA 39: 31 $ 1989).

INTRODUCFION

The success of poliomyelitis vaccination is one of the most remarkable events in medical history. The consequence of the implementation of immunization programme was a dramatic decrease of the incidence of polio within a few years. Thus, the effectiveness of the two vaccine, i.e., either oral (OPV) or injectable (IPV) is usually not questioned. Developed countries saw the virtual disappearance of the disease, but elimination is not achieved as yet. For instance, the USA reports an average of 10 cases annually, most of them OPV-associated.[1] In developing countries, poliomyelitis is still a major problem of public health and about 300,000 new cases are reported annually[2]. In these countries, because of the easy administration, OPV became popular and is extensively used, inspite of stringent cold-chain requirements which are difficult to achieve. It was soon recognized that OPV was irregularly immunogenic as evidenced by recent epidemics occurring despite satisfactory vaccine coverage and by an increasing number of cases in fully immunized children[3]. These facts led some health authorities (India, The Gambia) to modify their immunization schedule, recommending a fifth dose of OPV within the first year of life[4]. Pakistan has high prevalence rate of poliomyelitis. In 1975, there were 5052 cases with 20 deaths and 2024 cases with 42 deaths in 1979. This decrease correlates well with the successful implementation of the Expanded Programme of Immunization (EPI) since 1978. The coverage was recently assessed to be 80%, one of the best amongst the developing countries. However, 595 cases with 2 deaths were still reported in 1984[5]. 17% cases developed polio amongst the fully immunized children in Multan division (Personal communication). To improve upon the results of polio immunization programme, an alternative schedule, using inactivated polio vaccine combined with DPT, was evoked when a new enhanced potency IPV became available, making basic immunization simpler by giving only 2 shots. This schedule is now being applied in some developed and developing countries and has been found to be very effective. The aim of this study was to compare the antibody response to

two basic immunization schedules, i.e., 3 doses of oral polio vaccine associated with 2 doses of DPT (conventional schedule) and 2 doses of combined DPT-enhanced injectable polio vaccine (new simplified schedule).

MATERIALS AND METHODS

Population and Vaccination Schedule

Protocol is summarized in Table I.

TABLE I. Population and Study Schedule.

	Day 0	Day 30	Day 60	Day 90
Group 1 (DPT–IPV)	DPT-IPV		DPT–IPV	DPT
101 children	Blood sample		–	Blood sample
Group 2 (DPT+OPV)	DPT+OPV	OPV	DPT+OPV	DPT
104 children	Blood sample			Blood sample

Four hundred children, aged 2—24 months, free from previous DPI' and Polio immunization, who attended the Immunization Centre, Rawalpindi General Hospital, Rawalpindi, were randomly assigned to 2 groups: Group I children received two doses of the quadruple combined DPT—IPV vaccine (Imovax DPT—Polio) intramuscularly 2 months apart on Day 0 and Day 60. Group II children received 3 doses of oral polio vaccine 1 month apart on Day 0, Day 30 and Day 60. On Day 0 and Day 60, DPI' vaccine was given intramuscularly at the same time. In both groups, children were given an additional dose of DPI' on day 90 and immunization schedule completed accordingly. As soon as 105 children in each group completed the course of the protocol, the study was stopped.

Vaccines

Vaccines were prepared by Merieux Institute, France. Trivalent oral polio vaccine contained 10^6, 10^5, $10^{5.5}$ TCID50 per dose of poliovirus type 1 ,2 and 3 respectively. The DPT vaccine, adsorbed on aluminium hydroxide, contained Tetanus toxoid: 60 UI, Diphtheria toxoid: 30 UI, Bordetella Pertussis: 4 UI. Combined with DPT, the inactivated polio vaccine was formulated for the 3 poliovirus types as 40-8-32 D antigen units per dose.

Blood Specimens

In each group, blood specimens were collected with disposable syringes on Day 0 and on Day 90, one month after the completion of the basic course. Within 6 hours, the serum was separated at National Institute of Health (NIH), Islamabad and I ml put into 2 tubes of each sample with the same code number. One sample was tested at NIH Islamabad, and the other at Merieux Institute, France for

antibody response.

Serological Evaluation

Antibody to diphtheria and tetanus toxotos was measureu by racuoimmunoassay. Pertussis agglutinin titers were obtained by micro agglutination. Poliovirus antibody was measured by neutralisation. A serum was considered positive and therefore the child protected if its titer was equal to or greater than 10 mUI/ml for tetanus and diphtheria, 10 for pertussis and S for polio antibody.

RUSULTS

A total of 205 children completed the study (104 with the OPV and 101 with the DPT- IPV).

Polio Results

The results of the polio neutralisation tests are summarized in table II.

TABLE II. Serological Results for Polio Tests.

	GROUP I : DPT – IPV			GROUP 2:DPT+OPV		
	Polio 1	Polio 2	Polio 3	Polio 1	Polio 2	Polio 3
BEFORE VACCINATION						
Number of infants	100	100	100	101	101	101
% Protection	88.0	85.0	73.0	83.2	88.1	70.3
G.M.T.	92,98	146,21	89,72	120,51	160,34	89,98
AFTER VACCINATION						
All infants						
Number of infants	101	101	101	104	104	104
% Protection	100	100	100	100	100	100
G.M.T.	345,27	368,12	519,56	267,30	409,20	316,84
% 4 fold increase	59.0	54.0	71.0	55.4	52.5	63.4
Seronegative before						
Number of infants	12	15	27	17	12	30
% Seroconversion	100	100	100	100	100	100
G.M.T.	361,16	285,22	512,68	433,31	317,98	402,66

After completion of the schedule, i.e., after either 2 doses of IPV or 3 doses of OPV, all children evidenced antibody titres above the protective threshold for types 1,2 and 3 respectively. The geometric mean antibody titres after vaccination were not statistically different between the 2 groups for types I and 2, but for type 3, titres were significantly higher in DPT-IPV group compared with OPV group. All children who were seronegative before immunization, seroconverted in both groups. Titres of antibodies against polio types 1,2 & 3 checked in N.I.H (Islamabad) or Merieux Institute (France) showed good concordance and similarity. However DPT antibody titres were tested in France only. The results of the DPI' assays are summarized in Table III.

TABLE III. Serological Results for Tetanus, Diphtheria and Pertussis Tests.

	GROUP 1 : DPT–IPV			GROUP 2: DPT + OPV		
	Tetanus	Diphth.	Pertus.	Tetanus	Diphth.	Pertus.
BEFORE VACCINATION						
Number of infants	70	68	86	73	73	85
% Protection	64.3	52.9	45.3	61.6	53.4	47.1
G . M. T.	477,55	138,40	171,79	350,70	126,84	269,11
AFTER VACCINATION						
All Infants						
Number of infants	72	71	90	74	74	90
% Protection	98.6	98.6	95.6	100	98.6	93.3
G. M. T.	7742,74	438,30	855,13	6476,53	401,53	991,14
% 4 fold increase	76.8	67.2		84.1	73.9	73.7
SERONEGATIVE BEFORE						
Number of infants	24	31	43	27	33	39
% Seroconversion	100	100	93.0	100	97.0	89.7
G.M.T	6514,73	399,55	607,10	4827,04	310,18	720,75

After 2 doses of either DPT-IPV vaccine or DPT vaccine, respectively, 96 and 93% of the children developed pertussis anti-agglutinin titre above the protective threshold. The figures axe 99 and 100% for tetanus antibody and 99% in both groups for diphtheria antibody. No difference was seen between the two groups for seroprotection rate and geometric mean of antibody titre, both in all children and in seronegative before immunization.

DISCUSSION

This study demonstrates that 2 doses of DPT-IPV vaccine give a 100% protection rate against poliomyelitis when given 2 months apart to children 2-24 months old. This protection is similar to that offered by 3 doses of OPV although geometric mean antibody titre for type 3 (recently responsible for epidemics in Brazil) [6] is higher with IPV than with OPV. Several studies had already shown better immunogenicity of WV compared to OPV. Schatzmayr et al in Brazil found 99, 100 and 100% seroprotection rates after 2 doses of IPV for type 1,2 and 3 respectively when it was 77, 95 and 79% for OPV[7]. The geometric mean autibody titre observed after WV was always significantly higher than observed with OPV.. These figures were comparable with those observed in India with 100, 99 and 100% for IPV[8] and for OPV 73, 87 and 63% in infants[9], and in Mali with 100% for JPV and 49, 77 and 77% for OPV. [10] This good immunogenicity of IPV was recently confirmed. During an epidemic in Senegal in 1986, the vaccine efficacy of 2 doses of WV was evaluated as 89% (62-97%) which is higher than what is usually described for OPV in developing countries. [11] Concerning tetanus, diphtheria and pertussis, this study confirms that as early as one month after two shots of either DPT vaccine or combined DPT-Polio vaccine, more than 95% of the children are protected against these three diseases. Thus, children become protected from the age of 5 months, when maternal antibody related protection disappears. Persistence of antibody following immunization has been questioned. It was shown in Israel that a basic course of 2 doses of DPT-IPV, reinforced by a booster dose gives a good protection against poliomyelitis and pertussis for at least 5 years. [12] Herd immunity afforded by IPV was also a controversy. An answer can be given by the Netherlands and some provinces of Canada

where IPV is used exclusively and where there is no longer wild poliovirus circulation and where herd immunity due to IPV was good enough to prevent the spread to nonimmunized people of the polio epidemic that occurred in 1978-79 in religious sects. [13] One of the major problems faced by immunization programmes is the increasing rate of drop outs with each successive dose of vaccine. Therefore, recommending an additional dose of OPV to balance the irregular immunogenicity of this vaccine is not appropriate and simplifying the basic immunization schedule to only 2 shots could be very efficacious. This could be a reality with inactivated polio vaccine. IPV is now available, combined with DPT in ready to use syringe and basic immunization can be simplified to 2 injections of DPT-Polio. A booster dose is recommended. The thermostability of IPV allows its use under tropical conditions where OPV is usually difficult to use, accounting for a fair number of failures of oral vaccinations. Simplifying the basic vaccination course, DPT-IPV makes the dropout after the second dose to almost/nil and thus may significantly increase the vaccination coverage. Very effective and with no side effects, DPT-IPV can be used instead of DPT plus oral (Sabin) vaccine to prevent four of the most common childhood diseases in developing countries.

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