IMMUNOGENICITY AND FEASIBILITY OF PURIFIED CHICK EMBRYO CELL VACCINE

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ABSTRACT

Two hundred seventy-one children reported at the WHO Collaborative Centre for Rabies Epidemiology for South-East Asia at National Institute of Communicable Diseases, Delhi, for advice and antirabies antibody assessment after post-exposure prophylaxis with purified chick embryo cell (PCEC) antirabies vaccine from January 1986 to October 1992. Vaccine was very well tolerated by these children and only 7% complained about mild to moderate side reactions like pain, induration, fever or rash. On an average, every year 50-55 children had reported at this Centre after post-exposure vaccination with PCEC vaccine excepting years 1986 and 1987. One hundred and forty-four children underwent complete course of post-exposure prophylaxis, i.e., 5 or 6 doses on day 0, ' 3, 7, 14, 30 and 90 (optional) of PCEC vaccine were administered, forty-three (43) children received 4 doses on day 0, 7, 14 and 30 (day 3 dose was omitted) and eighty-four (84) children received 2 to 3 doses as the biting animals were alive for 10 days in these cases. Two hundred and twenty-nine children (84.5%) were bitten by dogs and in 10%, the dog was proven rabid by laboratory examination of dog brain. One hundred and forty-nine (55%) had Class III bite. Serological response, i.e., antirabies antibody titre in all these children were satisfactory (> 0.5IU/ml) with mean titre of 1.98 IU/ml irrespective of doses of PCEC vaccine administered. No vaccine failure was observed in this study.

Key words: *PCEC antirabies vaccine, Rabies, Post-exposure antirabies treatment.*

Nervous tissue vaccine produced in sheep brain is still in extensive use in India for post-exposure prophylaxis of rabies but its drawbacks are that a large number of painful inoculations with huge quantity has to be administered in abdominal wall and is associated with neuroparalytic complications(l). Development of vaccines of tissue culture origin(2) have provided safer and potent vaccine with reduced number of inoculations and quantum per dose. Among these human diploid cell strain (HDCS) vaccine(3) is the first generation tissue culture vaccine and its efficacy for post-exposure rabies prophylaxis was proved in our earlier study(4). Purified chick embryo cell (PCEC) (5) vaccine is one of the second generation vaccine available in this country. Our earlier studies(6,7) have shown the efficacy of PCEC vaccine in adults after pre-exposure and post exposure antirabies vaccination. The present study regarding the immunogenicity of PCEC vaccine in children after post-exposure prophylaxis was carried out in order to find out a safe and potent antirabies vaccine, which can be administered in children of all age-groups "since they are the most vulnerable group for animal bites with high rates of mortality due to severity of bites(8).

Material and Methods

Vaccine: Purified chick embryo cell

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(PCEC) antirabies vaccine is marketed as "RABIPUR" and it is readily available in India.

Study Cases: Two hundred and seventy-one children below 14 years of age reported at the WHO Collaborative Centre for Rabies Epidemiology for South-East Asia (Rabies Laboratory) at National Institute of Communicable Diseases, Delhi for antirabies antibody estimation in their serum after taking post-exposure prophylaxis with PCEC vaccine following clinically suspected or laboratory proved rabid animal bites were included in this study.

Study Period: The total study period was more than six years, *i.e.,* from January 1986 to October 1992.

Tolerance and Clinical Reactions: Clinical reactions like pain, fever, rash, erythema *etc.* after every dose of vaccine were noted.

Antirabies Antibody Assessment: 3 ml of venous blood samples were collected 10-15 days after the last dose of PCEC vaccine received to get the maximum antibody titre level in serum which was assessed for antirabies antibody titre by *in vitro* serum neutralization test (SNT) using a modified CIEP(9).

Laboratory Examination of Animals' Brain Specimen: Post-mortem diagnosis of rabies in animals (dog) brain specimens were done in the laboratory by Seller's staining method for Negri bodies and if negative then detection of virus antigen by Fluorescent Antibody Test (FAT)(10).

Results

A. *Tolerance and Clinical Reactions*

PCEC vaccine was very well tolerated in these children and there were a few mild post-vaccinal reactions. Ten children (3.7%) complained of mild to moderate pain and tenderness and five children (1.8%) had mild induration after first or second dose of vaccine which lasted for one or two days. Two children (0.74%) developed mild fever (99° to 100°F) after third or fourth injections. Two children developed mild rash over extremities and face after fifth dose which lasted for two days. In all nineteen (7%) children had some mild to moderate clinical reactions to PCEC vaccine.

B. *Age, Sex and Yearwise Distribution*

Of 271 children, 69 (25.5%) were female and rest 202 (74.5%) were male. The age distribution showed that 139 (51.3%) were in 6-10 year age group. Ninetyone (33.6%) in 1-5 year age group and 41 (15.1%) in 11-13 year age group with the mean age of 7 years (range 1-13 years).

The yearwise distribution of cases had shown that on an average 50-55 children had attended rabies laboratory for post-exposure anti-rabies antibody titre estimation except for the years 1986 and 1987.

C. *Distribution of Cases According to Biting Animal and Status of Biting Animal*

The distribution showed that 84.5% children were bitten by dogs and 14.4% by monkeys. Other animals involved were cat and mangoose. One hundred and thirty three (49.1%) children were bitten by stray animals which were untraceable. Twenty seven children (10%) were bitten by laboratory proven (brain of the animal was positive for rabies virus) rabid dogs.

D .*Distribution of Cases According to Doses of PCEC Vaccine and Class of Bite*

As shown in *Table I,* 144 (53.1%) children had received full course of post-exposure PCEC vaccination, *i.e.,* 5 to 6 doses on days 0,3,7,14,30 and 90 (optional), 84 (31.0%)

TABLE 1- *Post-Exposure Antirabies Treatment with PCEC Vaccine: Distribution of Cases According to Doses of PCEC Vaccine Given and Class of Bite (Children upto 13 Years)*

Class of bite	Number of PCEC Doses						
	2	3	4	5	6	Total	(%)
I	4	30	3	10	-	47	(17.3)
II	I	45	20	8	1	75	(27.7)
III	-	4	20	114	11	149	(55.0)
Total	5	79	43	132	12	235	
(%)	(1.8)	(29.2)	(15.9)	(48.7)	(4.4)	(100)	

(From January 1986 to October 1992).

children received 2 to 3 doses of vaccine as the biting animals *(i.e.,* dogs) were alive for 10 days in these cases and 43 (15.9%) received 4 doses on day 0, 7, 14 and 30, as they did not receive day 3 dose. One hundred and forty nine (55%) children had Class-Ill bite, 27.7% had Class-II and the rest 17.3% Class-I bite. One hundred and twenty five of 149 children with Class-Ill bite had received full course of anti-rabies vaccination, *i.e.,* 5 to 6 doses. Seventy five (27.7%) children with Class-I and Class-II bite received three doses of PCEC vaccine.

E. *Serological results*

Antirabies antibody titre in these children is depicted in *Table II.* Irrespective of doses of PCEC vaccine administered, every child had satisfactory level of antibody titre with a mean titre of 1.98 IU/ml. As mentioned in our earlier studies(6,7), base-line titre is taken as 0.5 IU/ml, *i.e.,* any titre below this level is taken as negative and titre of $\geq$0.5 IU/ml is taken as satisfactory or protective. The correlation between doses of PCEC vaccine given and subsequent antibody titre level showed that out of 132

TABLE II- *Post-Exposure Antirabies Treatment with PCEC Vaccine: Distribution of Antirabies Antibody Titre and Doses of PCEC Vaccine Administered*

Antibody titre	Number of PCEC Doses						
(IU /mI)	2	3	4	5	6	Total	(%)
0.59	5	13	-	-	-	18	(6.6)
1.18	-	60	22	20	4	106	(39.1)
2.36	-	5	18	98	8	129	(47.6)
4.72	-	1	2	13	-	16	(5.9)
9.44	-	-	1	1	-	2	(0.7)
Total	5	79	43	132	12	271	(100)

Mean Antibody Titre - 1.981U / ml.

(From January 1980 to October 1992).

children who had received 5 doses of vaccine, 98 children had antibody titre of 2.36 IU/ml and 13 had titre of 4.72 IU/ml. Out of 79 children who had received 3 doses of PCEC vaccine, 60 had titre of 1.18 IU/ml and 13 children had antibody titre of 0.59 IU/ml only. In five children who had received 2 doses of vaccine, the antibody titre was only up to 0.59 IU/ml. There were no cases of vaccine failure and no non-seroconverter reported in this study.

Discussion

Rabies is perhaps the most dreadful of all zoonotic diseases as there is invariably a fatal outcome once the disease has manifested clinically. However, due to its long incubation period, it can be prevented by timely immunizing the victim after animal bites. In our country nervous tissue vaccine still now forms the mainstay of post-exposure prophylaxis; however, since the last one-and-a-half decade considerable advances have been made in the field of anti-rabies vaccines of tissue culture origin. At present in India, tissue culture vaccines which are available, are human diploid cell strain (HDCS) vaccine, purified chick embryo cell (PCEC) vaccine and purified vero cell (PRVR) vaccine.

PCEC vaccine compares well with HDCS vaccine in terms of immunogenecity(11). Moreover, our earlier studies(6,7) although conducted in adults had shown satisfactory antibody response in both pre-exposure and post-exposure groups. There is hardly any longitudinal study conducted on the efficacy of PCEC vaccine in children although this vaccine is extensively used in children for post-exposure antirabies prophylaxis.

The results of our present study demonstrated the safety and immunogenicity of rabies vaccine cultured on purified chick embryo cell, when given after post-exposure to 271 children upto 13 years of age over a period of more than six years. All the children tolerated the vaccine well with very few, (7%) minor side-effects. All of them had satisfactory level of antibodies with a mean titre of 1.98 IU/ml. The results of our present study compare well with the results of studies conducted in children with HDCS vaccine(12-14). During this period there were no vaccine failures. Moreover, 27 children who were bitten by laboratory proven rabid dogs (rabies was diagnosed in dog brains either by Seller's staining method or by immunofluroscence test), were also fully protected by post-exposure prophylaxis with PCEC vaccine.

Thus, the immunogenicity of PCEC vaccine compares well with HDCS vaccine in children for post-exposure anti-rabies prophylaxis and this vaccine can be safely administered in children of all age-groups.

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