Clinical Study to Assess the safety and Immunogenecity of vero cell culture inactivated Rabies Vaccine

G.Sampath*, P. Sangram[1], N. Ananda Murthy[2], and
Y. Udaya Bhaskara Rao[3], C. Palaniappan[3], V. Suhasini Reddy[1],
1: Institute of Preventive Medicine, Narayangupta, Hyderabad 2: Moosa Seit Complex Commercial Road, Udhagamandalam 3: Pasteur, Coonoor
* Author for correspondence

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INTRODUCTION

Fatality and dreadful nature of the disease makes rabies as one of the major dramatic diseases of humans. The incidence of animal bite cases is directly related to the population of stray dogs[1]. Human suffering will continue until & unless concerted efforts from all sections of the society are applied to control the stray dog bite. Even today neural tissue vaccine (NTV) is used extensively in India for post exposure treatment (PET) of animal bites. Inspite of neurological reactions associated with NTV, it is widely used in India because of its affordability and availability. WHO recommended usage of tissue culture vaccine for PET considering the various aspects of safety, potency and sero-conversion[2]. The safety and immunogenicaty of tissue culture rabies vaccine derived from vero cell line is well established[3]. The present study was conducted to assess the safety and immunogenicity of purified vero cell culture inacitivated rabies vaccine (Abhayrab) produced by Human Biologicals Institute, Ooty, a Division of the Indian Immunologicals Limited.

Subjects and Methodology :

Human volunteers : 60 volunteers (Group I) without previous rabies vaccination history and 32 volunteers (Group II) with previous rabies vaccination history in the age group 20-55 years were enrolled in the study.

Patients : 28 patients in the age group of 6-40 years with a history of rabid animal bite attending the Rabies Clinic, Institute of Preventive Medicine, Narayanguda, Hyderabad enrolled in the study for PET. Patients with Class ii and Class III type of exposure were taken in the study.

Vaccine and Vaccination : Abhayrab, purified vero cell culture inactivated rabies vaccine in freeze dried form is diluted in 0.5 ml. of diluent and inoculated intramuscularly in the deltoid region.

Regimen for prophylaxis : All the volunteers of Group I were vaccinated on 0, 7 & 28th day. The volunteers of Group II were given one dose of vaccine on day 0.

Post-exposure treatment : The patients were administered with Abhayrab on days 0, 3, 7, 14, 30 & 90 (WHO Essen regimen). Equine rabies immunoglobulin (ERIG) was administered as indicated in WHO protocol.

Post-vaccinal reactions : Standard format was used to record post vaccinal reactions of volunteers and patients in the study.

Serum Samples : Blood samples on 0, 14, & 35 days post-vaccination were collected from all the volunteers of Group I & II. Blood samples from the patients were collected on 0, 14, 30 & 90 days post-vaccination. Serum samples were separated from all the blood samples and sent to Pasteur Institute, Coonoor for serum antibody assay.

Serum antibody assay : The titration of serum antibodies was performed by Rapid Fluorescent Focus Inhibition Test (RFFIT) described earlier[4]. The results are expressed as IU/ml.

Results :

The observations of post-vaccinal reactions are furnished in Table 1. In Group I, 5 volunteers showed mild pain at the site of inoculation during first and second dose of vaccination. In Group II, 2 volunteers have expressed mild pain at the site of injection. Eight patients have shown pain at the site of injection, one patient reported itching and one patient reported mild fever. No medication was advised.

The results of serum antibody assay are shown in Table 2. For the Group I, the '0' day mean antibody titre was <0.5 IU and the mean antibody titres of 12.69 and 18.19 were recorded on 14 & 35 dpv respectively. In Group II, the mean antibody titres prior to vaccination were 8.33 and 38.85 and 22.14 noticed on 14 & 35 dpv respectively. The mean antibody titres of patients on day 0 were <0.25 IU/ml. The mean antibody titres on 14, 30 and 90 days were 9.42, 13.85 and 5.29 IU/ml. respectively.

Table-1 : Summary of reactions noticed in volunteers and patients vaccinated with Abhayrab

Reactogenicity		Group 1 '3' doses			Group 2	Patients - 6 doses					
		1	2	3	Single Dose	1	2	3	4	5	6
Local reaction at the site of injection :											
a) Pain	Mild	5	5	-	2	2	-	4	2	-	-
	Moderate	-	-	-	-	-	-	-	-	-	-
	Severe	-	-	-	-	-	-	-	-	-	-
b) Irritation		-	-	-	-	1	-	-	-	-	-
c) Redness		-	-	-	-	-	-	-	-	-	-
Systemic Reactions :											
a) Fatigue		-	-	-	-	-	-	-	-	-	-
b) Dizziness		-	-	-	-	-	-	-	-	-	-
c) Headache		-	-	-	-	-	-	-	-	-	-
d) Lymphadenopathy		-	-	-	-	-	-	-	-	-	-
e) Pyreixa		-	-	-	-	-	-	-	-	-	-
Allergic reactions		-	-	-	-	-	-	-	-	-	-
Neurological reactions if any		-	-	-	-	-	-	-	-	-	-

Table II - Serological response of the volunteers and patients vaccinated with Abhayrab

Sl. No.	Group	Mean antibody titres IU/ml.				
		0	14	30	35	90
1.	I	<0.5	12.69 ±16.30	ND	18.19 ±9.28	ND
2.	II	8.33 ±10.07	38.85 ±21.64	ND	22.14 ±15.12	ND
3.	Patients	<0.25	9.42 ±5.73	13.85 ±8.92	ND	5.29 ±3.66

ND = NOT DONE

Discussion :

The vaccine was well tolerated by the two groups of volunteers under study except minor symptoms such as mild pain at the site of inoculation. No serious untoward local or systemic reactions were noticed. Similar observations were made with HDC vaccine[5] and purified vero cell culture rabies vaccine[3]. The results of serum antibodies of group I all the volunteers have shown that 100% sero-conversion with first two doses of vaccine and the serum antibody titres on 14 days were well above the protective titre level of 0.5 IU/ml. The subjects have shown substantially higher mean antibody titres on 35 dpv. when compared to 14 dpv with third vaccination. The data correspond to the earlier findings[6]. It was observed that all Group II subjects were having protective antibody titres before first vaccination and all the volunteers have shown an amnestic response as observed 14 days mean serum antibody titres. The results of prophylactic vaccination indicate that the vaccine under study is safe and immunogenic.

The analysis of adverse reactions in patients who have undergone PET revealed local symptoms such as pain and systemic reactions of mild fever. The symptoms were of short duration and in no case made it necessary to seek medical intervention. Similar type of reactions were recorded when HDC vaccine is used in patients earlier[7]. The PET consisted of six injections of Abhayrab and ERIG for patients of Class III bite category. The patients showed steep rise in antibody titres during short period with three inoculations who had no antibody titres prior to first immunization. The passive immunisation did not interfere with active immunization as shown in the results of sero-conversion studies of patients on 14 and 30 dpv. 100% sero-conversion was observed on 14 dpv. The results accomplish the observations made earlier with purified vero cell culture vaccine[5]. All the patients tolerated PET and the immunogenecity of the vaccine was established by serological assay performed on serum samples collected on different days during PET course.

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