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RESEARCH ARTICLE

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CLINICAL SAFETY OF INTRA DERMAL RABIES VACCINATION (IDRV) WITH PURIFIED VERO CELL RABIES VACCINE (PVRV)

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ABSTRACT

To study the clinical efficacy and side effects of Intra Dermal Rabies Vaccination (IDRV) using Purified Vero Cell Rabies Vaccine (PVRV) in the post exposure treatment of animal bites; a cross sectional, non-comparative, hospital based study was carried out among 123 patients attending the Anti Rabies Clinic (ARC) of a tertiary-care teaching hospital at Brahmapur in Orissa. All the 123 cases were treated with Inj. Verorab (manufactured by sanofi pasteur) by Thai Red cross (TRC) Regimen.

Though all the patients complained of some type of local side effects, but these symptoms were relieved by simple administration of paracetamol and cetrizine orally for 3 days. The side effects (local symptoms) noted are local itch (47.9%), local pain (34.9%), fever (5.6%) and the local signs noted are local induration (87.8%), local erythema (15.4%). In 12.2% of the cases there were no signs and symptoms.

All the patients were followed up to 1 year and found to be healthy & alive. Thus, this cost effective way of treating the animal bite cases using PVRV (Inj. Verorab) by TRC regime is recommended to reduce the burden of Rabies in India.

KEYWORDS

Rabies, Post Exposure Prophylaxis for animal bite, Intra Dermal Rabies Vaccination, Purified Vero cell Rabies Vaccine, Safety of IDRV, Side effects of IDRV

INTRODUCTION

Rabies is a 100% fatal disease. The disease is entirely preventable, provided complete post-exposure prophylaxis is implemented promptly. Globally, rabies is the tenth leading cause of death due to infection in humans. [1].

The WHO in 1994 had recommended withdrawing NTV for active immunization. The production and use of this reactogenic vaccine have been stopped since December 2004 in our country. [2]

In 1992, WHO recommended the multi-site intra-dermal method for post-exposure treatment i.e. Intra Dermal Rabies Vaccination (IDRV). [3] The vaccines recommended by WHO for IDRV were the PVRV (Inj. VERORAB) by Sanofi Pasteur and PCECV (Inj. RABIPUR) by Novartis. By this method, two doses of vaccine are administered at two sites intra-dermally on days 0, 3, 7 and no dose is administered on day 14. Subsequently one dose of vaccine is administered at a single site on days 28 and 90 ("2, 2, 2, 0, 1, 1" or Thai Red Cross regimen). For PVRV while using ID route, 0.1 ml is given per site which is deposited in the layers of the skin at multiple sites. The antigen is directly presented to the antigen presenting cells (without circulation/ dilution in blood) at multiple sites triggering a stronger immune response.

Studies have showed a good antibody production on using intradermal doses of both PVRV and PCECV. [4-7] To determine the Clinical safety of post-exposure treatment by Intra Dermal Rabies Vaccination, a prospective randomized trial was conducted using the Thai Red Cross regimen in patients with Category-III animal bite exposures.

MATERIAL AND METHODS

The Anti Rabies Clinic (ARC) of Department of Community Medicine, MKCG Medical College, Brahmapur, Orissa registers nearly 5000 cases every year for Anti Rabies Treatment. After withdrawn of the supply of NTV,the State Govt. began to supply Purified Duck Embryo Rabies Vaccine (PDEV) to be used as Post-exposure vaccination by Essen Regime. However the supply was very inadequate and highly irregular. The daily average new case registration in the ARC is about 10-15 and the daily requirement of Anti Rabies Vaccine (ARV) to be given by Essen Regime is about 50 doses. As the ARC usually had no supply of ARV during that period, the patients were advised to procure the same for administration. The high cost of the vaccine prevented many to express their inability to procure the same and they waited for days together patiently and anxiously for the free Govt. supplied vaccine. Review of literature had shown that IDRV with Inj. PVRV (Inj. VERORAB) by TRC regime is a cost effective method for active immunization against rabies. Therefore, to avoid drop out, delay in treatment or irregular treatment, the cases were advised for this cost-effective mode of Active Immunization i.e. IDRV.

Detailed explanation of this situation was done to the cases and after taking verbal consent, a total of 123 cases were put on IDRV by TRC Regime. The vaccine prescribed was Inj. Verorab, manufactured by sanofi pasteur with a total reconstitution volume of 0.5 ml. The TRC Regime was used for which 0.1 ml vaccine was given per site on two sites on days 0, 3 & 7. No vaccination was done on Day 14 and on Days 28 & 90, only one site was administered. As all the cases had Category-III exposures, Equine Rabies Immunoglobulin (ERIG) was administered to all the cases after skin test at a dose of 40 IU/Kg body weight.

RESULTS

All the 123 patients enrolled in the study presented for post-exposure rabies treatment for Category-III animal bites at the ARC of MKCG Medical College Hospital, Berhampur, Orissa, between April 2004 and May 2005. The demographics of the patients are listed in Table-I.

Table – I
Patient population demographics

Age in Years	Rural			Urban			Total
	M	F	T	M	F	T	
<14	31	9	40	9	6	15	55 (44.7%)
15-45	26	12	38	7	2	9	47 (38.2%)
46-60	8	4	12	2	0	2	14 (11.3%)
>60	5	0	5	1	1	2	7 (5.6%)
Total	70	25	95 (77.2%)	19	9	28 (22.8%)	123 (100%)

89 patients were males and 95 patients were from rural areas. Children less than 14 years of age were 44.7% and adults in the socio-economic productive age group of 15-45 years were 38.2%.

Table – II
Type of Animal

Type of Animal		Number (%)
Stray Dogs	Provoked	35 (28.4%)
	Unprovoked	22 (17.8%)
	Abnormal	10 (8.1%)
	Killed	26 (21.1%)
Cat		5 (4.06%)
Jackal		8 (6.5%)
Monkey		17 (13.8%)

In majority (75.6%) of the cases dog was the responsible animal, among which 10 showed abnormal behaviour and 26 were killed because of abnormal behaviour. During the study 8 cases reported because of Jackal bite. Provoked stray dog bites (35) outnumbered the unprovoked nature of dog bites.

Table – III
Distribution of Bite Sites

	Total Bites	
	No.	%
Head/Neck	10	8.1%
Face	5	4.06%
Hand	7	5.69%
Trunk	9	7.31%
Leg	37	30%
Ankle/ Foot	29	23.5%
Multiple sites	26	21.13%

26 patients had bites over multiple sites, 5 had bites over face (all children <14 years), and 7 patients had lacerated bites over hand. Majority (53.6%) of the bites were over the lower limbs.

Table – IV
Side effects of IDRV (PVRV)

Symptoms	
Local Pain	43 (34.9%)
Local itch	59 (47.9%)
Headache	3 (2.4%)
Fever	7 (5.69%)
Generalized Itch	2 (1.6%)
Signs	
Local erythema	19 (15.4%)
Local induration	108 (87.8%)
Lymphadenopathy	0
Rash	0
No signs and symptoms	15 (12.2%)

In 108 patients local induration was observed. The other common side effects of intradermal PVRV administration were local pain, itch and local erythema (Table-IV). 7 cases had fever which subsided by paracetamol tablets given for three days. 3 patients complained of headache and in another 3 cases generalized pruritus was noticed. Systematic treatment was done for the cases and all were relieved by this procedure.

All the patients were followed up to 1 year and found to be healthy and alive.

Lack of financial resources acted as a hindrance to estimate the antibody titre in all the cases. However with contribution from the investigators, the antibody titre was done in four randomly selected cases exposed to animals showing abnormal behavior. The antibody titre was done at the end of 180 days and it was found to be 1.98±0.5 IU/ml.

DISCUSSION

In the present study 80% of the patients were bitten on the limbs and only 12% over face, head and neck. Chutivongse et al [8] in their study among 100 patients found, 18 patients had multiple bites and on the basis of historical controls, about 14 patients would have been expected to die if untreated.

In Thailand the TRC-ID PVRV regimen (2, 2, 2, 0, 1, 1) represents a saving of 68% over an intramuscular 5-dose schedule with the same vaccine. Previous studies have shown that the TRC-ID regimen resulted in detectable cell-mediated immunoreactivity by day 7 in a substantial number of patients. [9]

In our study the most common side effects of intradermal administration of PVRV (Inj. Verorab) were mainly local symptoms like pain, itch, induration and erythema which were alleviated by oral administration of antihistamines and analgesics. Chutivangse S et al found the side effects of intradermal PVRV as mild regional adenopathy, transient fever and malaise and which did not differ significantly from those they found with the standard intramuscular post-exposure schedule [8, 10].

DJ Briggs et al reported adverse reactions more frequently in patients who received intradermal injections of PCECV (48%) or PVRV (51%) compared to patients who received intramuscular injections of PCECV (33%). The adverse reactions they reported in decreasing order of frequency occurrence are: erythema, pain and/or swelling at the site of injection, and fever. There was no significant difference between the number of adverse reactions reported by patients who received PCECV and PVRV intradermally[5].

Jaiiaroensup W et al in their study in Thailand reported pruritus at injection sites was the only significant local reaction and

low-grade fever, the only significant adverse systemic event was more common (in 8% of all subjects) in intramuscular groups than intradermal groups. [4]

In a Thai study of 319 patients with rabies in whom the incubation period was known, 96% of patients developed symptoms within 1 year and 97% within 2 years. [11] In the present study, all the 123 patients were followed-up during the first year and were found to healthy and alive.

In conclusion, our study showed that administration of PVRV by intradermal route by TRC regimen according to the WHO recommendations for postexposure treatment of patients with WHO category-III rabies exposure along with ERIG is quite safe. The side effects reported are common to other studies and can be resolved by oral administration of antihistamines and analgesics.

REFERENCE

1. Rabies & Envenomings, A neglected public health issue, report of a consultative meeting, WHO, Geneva, 2007.
2. National Guidelines for Rabies Prophylaxis and Intra-dermal Administration of cell culture Rabies Vaccines, NICD, DGHS, Ministry of H&FW, Govt. of India, New Delhi, 2007.
3. Eighth Report of the WHO Expert Committee on Rabies, Geneva, WHO, 1992, 24-25 (WHO TRS No. 824).
4. Jaiiaroensup W, Lang J, Thipkong P, Wimalaratne O, Samranwataya P, Saikasem A, Chareonwai S, et al, Safety and efficacy of purified Vero cell rabies vaccine given intramuscularly and intradermally. (Results of a prospective randomized trial), Vaccine, 1998 Oct; 16(16): 1559-62.
5. D.J. Briggs, A. Banzhoff, U. Nicolay, S. Sirikwin, B. Dumavibhat, S. Tongswas, & C. Wasi, Antibody response of patients after postexposure rabies vaccination with small intra-dermal doses of purified chick embryo cell vaccine or purified Vero cell rabies vaccine, Bulletin of the World Health Organization, 2000, 78 (5): 693-698.
6. Persistence of Antibodies in Children after Intra-dermal or Intramuscular administration of Pre-exposure primary and Booster Immunization with Purified Vero Cell Rabies Vaccine ; Pediatric Infect Dis J. 1998 Nov; 17 (11) : 1001-7.
7. Immunogenecity and safety of Low-Dose Intra-dermal Rabies Vaccination given during an expanded Programme on Immunization Session in Vietnam: Results of a Comparative Randomized Trial - Trans R Soc Trop Med Hyg., 1999 Mar-Apr; 93 (2) : 208-13.
8. Supawat Chutivongse, Henry Wilde, Chalida Supich, George M. Baer, Daniel B. Fishbein, Postexposure prophylaxis for rabies with antiserum and intradermal vaccination, The Lancet April 14, 1990, 896-898.
9. Phanuphak P, Khawplod P, Sirivichayakul S, Siriprasomsub W, Ubol S, Thaweepathomwat M. Humoral and cell-mediated immune responses to various economical regimens of purified Vero cell rabies vaccine. Asian Pac J Allergy Immunol 1987; 5: 33-37.
10. Chutivongse S, Supich C, Wilde H. Acceptability and efficacy of purified vero-cell rabies vaccine in Thai children exposed to rabies. Asia Pac J Public Hlth 1988; 2: 179-84.
11. Vibulbandhitkij S. Work report. Data from the rabies patients at Bamrasnaradura Hospital between 1971 and 1977. In: Thongcharoen P. ed. Rabies. Bangkok: Aksarasamai, 1980: 235-51.