CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1298678

Available online at: http://www.iajps.com Research Article

A DESCRIPTIVE CROSS-SECTIONAL RESEARCH ON POST-VACCINATION SERO-CONVERSION BY INTRADERMAL (ID) ROUTE FOR POST EXPOSURE PROPHYLAXIS IN ANIMAL BITE CASES

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Abstract:
Objective: *Our research was aimed at the determination of seroconversion following the vaccination of the rabies by intradermal route in the animal bite cases specifically for post exposure prophylaxis.*
Study Design: *Descriptive Cross-sectional research.*
Place and Duration*: Research was carried out at Nishtar Hospital, Faisalabad (Department of Microbiology) from March to September, 2017.*
Patients and Methods: *We included the all age cases presented in the time duration of twenty-four to seventy-two hours. We included Category II & III patients and used PVRV (Purified Vero Cell Vaccine) having an antigenic content (> 2.5 ml) as per the regimen of Thai Red Cross that is (2 – 2 – 2 – 0 – 2). Every animal bite case was managed with (0.1 ml) on every deltoid an intradermal dose on 1st, 3rd, 7th and 28th day and blood samples were drained on 1st, 14th and 35th day. Estimation antibody titers of the titers were made through ELISA Kit.*
Results: *Our sample was of 50 animal bite cases including twenty children and male to female proportion was four to one. On fourteenth day an optimum seroconversion was noticed as (> 0.5 IU / ml). There was a further increase in the antibody levels on 35th day in almost 92% of the animal bite cases as (> 4 IU / ml). On 14th and 35th day the geometric mean titers were observed respectively as (3.2 IU/ml) and (6.2 IU / ml).*
Conclusion: *Intradermal route is considered as safe and effective for culturing of rabies vaccine cell for animal bite cases postexposure prophylaxis. Small vaccine dose is affordable by all the patients as and when referred.*
Key words: *Intradermal Vaccine, Rabies, Thai Red Cross Regime, (PVCV) Purified Vero Cell Vaccine.*

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Please cite this article in press Muhammad Abubakar et al., ***A Descriptive Cross-Sectional Research on Post-Vaccination Sero-Conversion by Intradermal (ID) Route for Post Exposure Prophylaxis in Animal Bite Cases,*** *Indo Am. J. P. Sci, 2018; 05(06).*

INTRODUCTION:

Rabies is among the zoonotic disease which is fatal and it is caused by animal bite specially by the bite of an infected one, neurotropic virus is its causative agent which present in the rabid animal saliva causing death of 55000 souls per year globally in the under developed countries [1 – 3]. It is mainly an unreported disease and community based statistical data is scarce in Pakistan with very few research work and alarming rise in the animal bite cases [4 – 7]. WHO (2010) reports that incidence of dog bite was above 97 thousand just in Pakistan [8].

Nervous tissue vaccine replacement is recommended by WHO for even safer and effective culturing of the tissue/cell vaccines PEP (Post Exposure Prophylaxis) as less immunogenic and excessively reaction is reported in nervous tissue vaccines but their use is still large all over the country as TCV are expensive and unaffordable by a number of affected cases [7, 9, 10].

In the limited resources WHO recommends an intradermal regimen in addition to cell culturing vaccines in case of affordability and availability issues also suggested for PEP [9 – 11]. WHO recommends Oxford regimen used with HDCV (Human diploid cell vaccine) and Purified Chick Embryo Cell Vaccine (PCECV) respectively having (8 – 0 – 4 – 0 – 1 – 1) and (2 – 2 – 2 – 0 – 1 – 1) schedules [11, 12]. Thai Red Cross regimen constitutes of (0.1 ml) intradermal injection of PCECV or PVRV administered at two different locations on each upper deltoid (one inch) on 1st, 3rd, 7th, 28th and 90th day, these vaccines are recommended by WHO [12, 13]. Regional research studies have also proved and safety and immunogenicity of these interventions [16 – 20]. The administration of cell culture vaccines was first used on the intramuscular route also known as Essen regimen few years back but they were expensive and few used them [13, 14]. A number of cases were managed with NTV; whereas, TCV is recent vaccines. Our research was aimed at the determination of seroconversion following the vaccination of the rabies by intradermal route in the animal bite cases specifically for post exposure prophylaxis.

MATERIALS AND METHODS:

We included all age cases presented in the time duration of twenty-four to seventy-two hours. We included Category II & III patients and used PVRV (Purified Vero Cell Vaccine) having an antigenic content (> 2.5 ml) as per the regimen of Thai Red Cross that is (2 – 2 – 2 – 0 – 2). Every animal bite case was managed with (0.1 ml) on every deltoid an intradermal dose on 1st, 3rd, 7th and 28th day and blood samples were drained on 1st, 14th and 35th day. Estimation antibody titers of the titers was made through ELISA Kit. We did not include previous rabies and pregnant cases including acute infectious illness cases, immune globulins or immune suppressive therapy cases. Every patient was briefed about the research protocols. We also collected information about body weight, gender, age, animal exposure duration and animal status whether alive or killed.

We washed the sounds with water and soap, market purchased PVRV was used with antigen content of (> 2.5 unit / 0.5 ml). We reconstructed vaccines using a diluent (0.5 ml) and used this reconstruction in the time span of 6 hours whereas it was stored at a temperature of (4°C). A trained nurse administered the vaccine according to Modified Thai Red Cross regimen. Same schedule has been applied by another author [15]. Single dose of intradermal vaccine (PVRV, 0.1 ml) is one fifth of the (0.5 ml) reconstituted vaccine. With this approach of two PVRV vials were sufficient for the five patients; whereas, one required two doses one per day. We injected children through anterolateral thigh. Cat-II cases were also prescribed RIG.

Blood was drained for sampling as mentioned earlier and follow-up was also instructed to patients, detailed analysis of the serums was carried out. Safe level titers were observed on first day so few of the patients were excluded; whereas, total research sample was restricted to fifty cases.

An indirect immunized method helped in the detection of virus of rabies (anti glycoprotein antibodies) with the help of ELISA Kit. Positive and negative controls were run on OD (optical density). Curve construction was used for quantitative analysis which also helped in the calculation of unknown sera of titers.

RESULTS:

We categorized the total sample population on the basis of their age such as (3 – 15 years) children, (16 – 50 years) adults and older age group as (> 50 years) [5]. Male to female strength was respectively forty males and ten females. Cat-II cases were 29 (58%); whereas, 21 Cat-III cases (42%) as shown in Table – I. Dogs were mostly involved in the animal bite cases (80%). However, other animals included cats, donkey, horse, monkeys and cows. Titers were developed in all the cases on fourteenth day as (above 0.5 IU / ml).

Table – I: Patient demographics and wound Category

Group	Age (Years)	Victims	Ratio		Wound Category	
			Male	Female	II	III
Children	**3 - 15**	20	17	3	11	9
Adults	**16 - 50**	25	18	7	14	11
Older Age Group	**Above 50**	5	5	0	4	1
Total		50	40	10	29	21

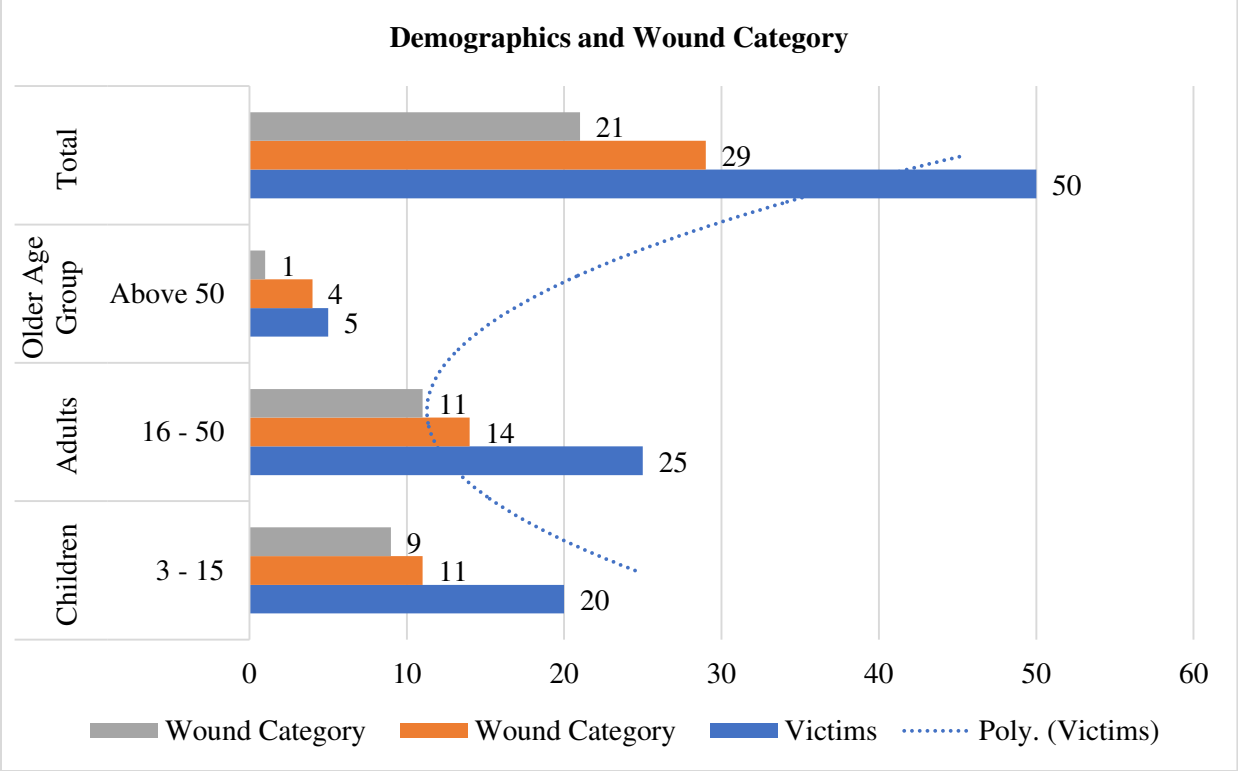


Table – II: Anti rabies antibody titers on various days in study cases

Anti-rabies Antibody Titer (IU/ml)	1st Day		14th Day		35th Day	
	Number	Percent	Number	Percent	Number	Percent
< 0.5	50	100	0	0	0	0
0.5 – 0.9	0	0	6	12	0	0
1 – 3.9	0	0	36	72	4	8
4 and above	0	0	8	16	46	92

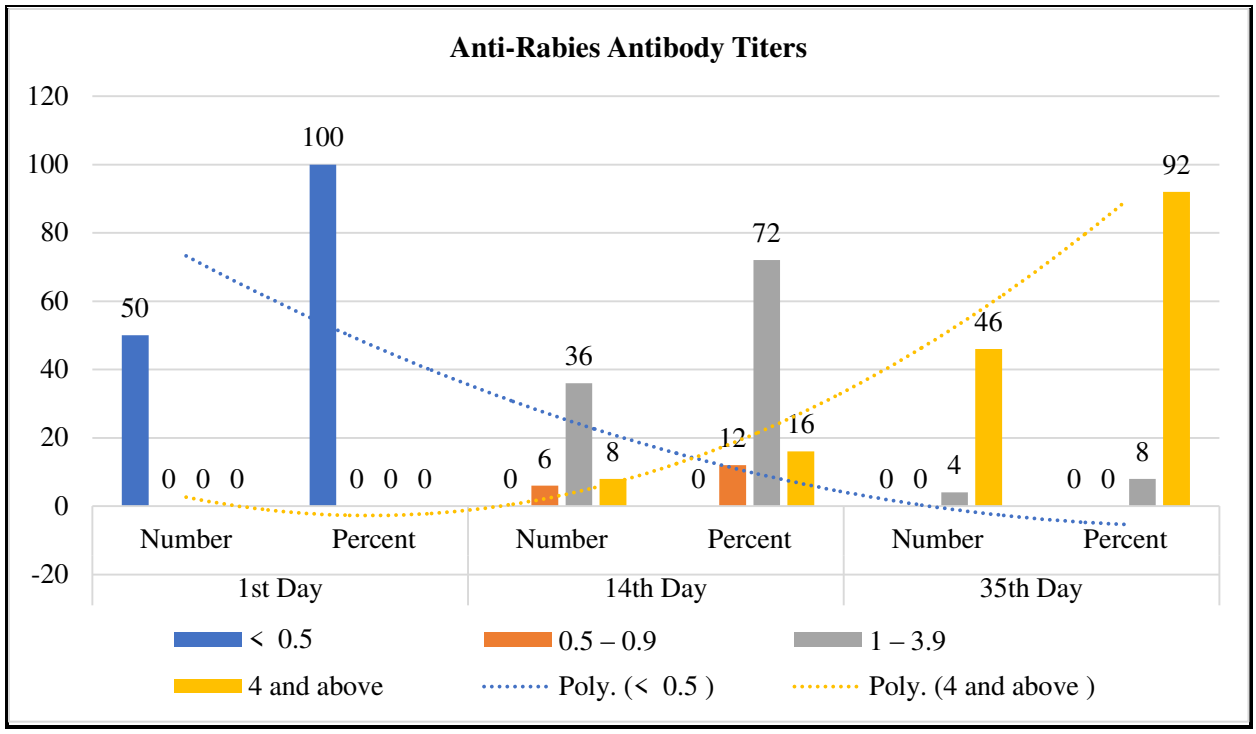
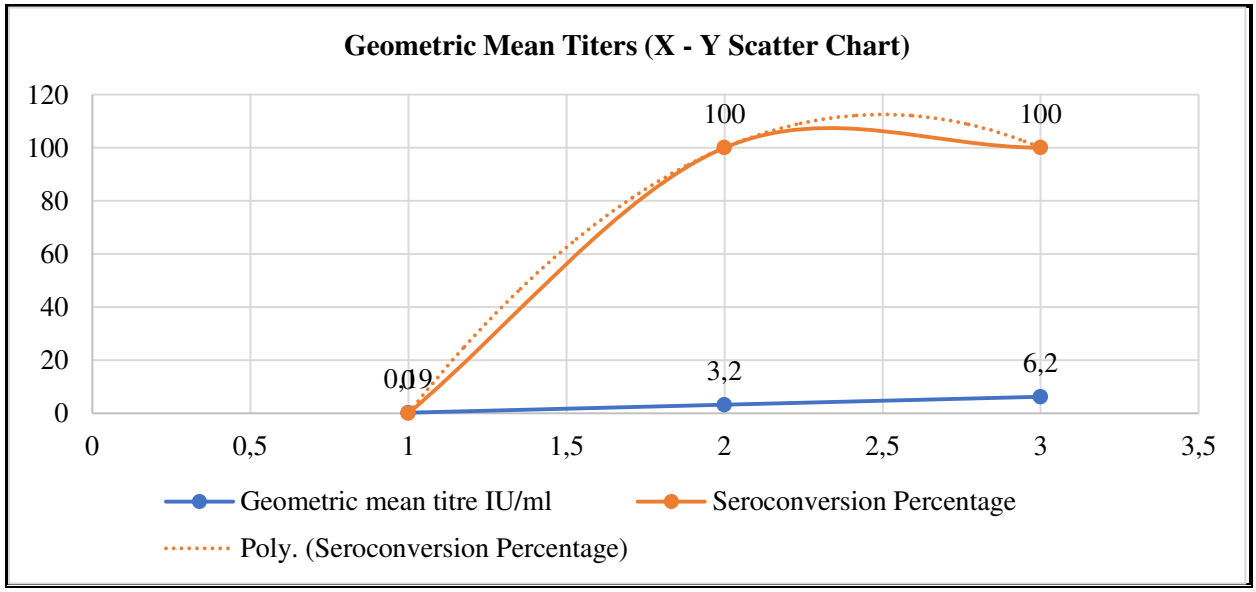


Table – III: Geometric mean titers of rabies antibodies

Day	Geometric mean titer IU/ml	Seroconversion Percentage
1st	0.19	0
14th	3.2	100
35th	6.2	100



Further titers improvement was observed after the antibodies detection on 35th day as shown in Table – II. Table – III reflects the geometric mean of the titers day wise. Five cases were observed with an adverse reaction (Erythema) and four cases (induration) in the first three days. Cat-III was advised with RIG; whereas, nine cases were treated with RIG. Non-affordability was the reason behind noon-administration of RIG in twelve cases. Three months follow-up was also carried out, every animal bite case was healthy.

DISCUSSION:

An adequate level of (≥ 0.5 IU / ml) is recognized by WHO in order to neutralize the virus at 14th day after being vaccinated [13]. In this particular research patients were given (PVRV, 0.1 ml) which gained the level of antibody titers on day fourteen (above 0.5 IU / ml) with an increase as observed on 35th day; this can be compared with earlier research outcomes. Chutivongese assessed the proved rabid animal bites through PVRV (Thai Red Cross intradermal PET schedule). Ten patients were observed on fourteenth day about seroconversion. Every case was followed for one complete year after the exposure.

Cent percent regimen efficacy was confirmed as no patient died. According to Briggs anti body titer on day 14 was (> 0.5 IU) with TRC, PVRV administered intradermally [14]. An adequate neutralizing was also reported by Khwaplod with two and eight site regimens on fourteenth day [18]. Safe titers can be acquired by any of the techniques but no titers were observed on 5th and 7th day. It was also suggested that on first day RIG administration was also an important component in case of severely exposed cases. Various schedules and antibody levels have been reported by various authors in various settings of research studies with respects to days and dose [21 – 23].

RIG was given to nine out of twenty-one patients of Cat-III wound cases. Low antibody titers were observed in these cases than fourteenth day sera which was in the range of safe limit, it can also be compared with the outcomes of Briggs et al [17].

ELISA test was employed for the evaluation of sera and titers can be compared with the outcomes of Mala et al [20]. Mala also reported TRC immunogenicity post exposure vaccine regimen with the help of PCECV by using ELISA [20]. According to Welch there is a low variability degree between RFFIT (Rapid Fluorescent Focus Inhibition Test) and ELISA assay with an exception of high values of RIFFAT [25]. Lower titers were observed by Simani through ELISA and comparison was made with ELISA [26]. Gold standard consideration is given to RIFFIT and FAVN (Fluorescent Antibody Virus Neutralization) with skilled staff and specialized clinical facilities.

It is economical because two PVRV (intradermal) vials are sufficient for one patient against five PET (intramuscular) vials. Same has been proposed by WHO for intradermal vaccinations [17, 19, 20]. PEP cost is reduced up to sixty percent through ID route, which become affordable for the animal bite cases who belong to low income class. Against the rabies cases the use of intradermal regimen is effective which provides ample titers antibody protection in postexposure prophylaxis. Small doses are economical and affordable for under developed countries as the incidence of animal bite is higher in these countries. On the grounds of research outcomes, we may conclude that ID route culture vaccines may be used instead of nervous tissue vaccine at national level referral centers with better and effective management of the dogs to control the dog bite cases.

CONCLUSION:

Intradermal route is considered as safe and effective for culturing of rabies vaccine cell for animal bite cases postexposure prophylaxis. Small vaccine dose is affordable by all the patients as and when referred.

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