

Clinical Safety and Side Effects of Intra Dermal regimen of Tissue culture Anti-rabies Vaccine

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Abstract—Rabies is 100% fatal but preventable disease. WHO recommends Tissue culture Anti-rabies Vaccines for post exposure treatment but this prophylaxis becomes expensive. So for reducing the 1/6th cost of this prophylaxis intradermal ARV regime was also recommended. But again there is a question mark for balance between cost effectiveness and safty so this cross sectional study was carried out in year 2013 on 654 recipients of Purified Chick Embryo Cell Vaccine (PCECV) anti-rabis vaccine (ARV) at Anti Rabies Clinic (ARC) of a tertiary-care teaching hospital (SMS) at Jaipur, Rajasthan. Side effects were observed during the follow up visits on days 3, 7 and 28. Though all the recipients complained of local side effects at site of inoculation but these symptoms were relieved by simple administration of paracetamol and ceterizine orally. The side effects (local symptoms) noted on First dose were local itch (4%), local pain (3.8%), low grade fever (2.1%) and the local signs noted are local induration (22.3%), local erythema (1.2%). Same pattern of sign and symptoms were observed in D3 and D7 dose of injection but in decreased frequency. None of the cases had anaphylaxis or regional lymphadenopathy. Thus, this cost effective way of treating the animal bite cases using PCECV in Intra Dermal Rabies Vaccination (IDRV) is recommended to deal with the burden of animal bite cases for the prevention of Rabies in India.

Keywords— Animal bite, Rabies, ARV, PCECV and Intra Dermal Rabies Vaccination.

1. Introduction

Rabies is a zoonotic disease with 100% fatality.¹ Nearly 95% of all human infections are due to exposure to rabid dogs. The disease is preventable, provided complete post exposure prophylaxis is implemented promptly with potent rabies vaccines as per WHO guideline. Globally, rabies is the tenth leading cause of death due to infection in humans. The WHO (1994) had recommended withdrawing NTV for rabies prophylaxis and it is to be replaced by TCV.² Production and use of this NTV vaccine have been stopped since December 2004 in our country. In 1992, WHO recommended the multisite intra-dermal method for post-exposure treatment i.e. Intra Dermal Rabies Vaccination (IDRV).³

In developing countries, rabies is an endemic disease and the use of intra-dermal rabies vaccination (IDRV) is cost effective. Many countries in Asia including India are now using IDRV for rabies prophylaxis. In this regime, antigen is directly presented to the antigen presenting cells (without circulation/ dilution in blood) at multiple sites triggering a stronger immune response.² Studies have showed a good antibody production on using intradermal doses of PCECV.^{4,5}

Intradermal rabies vaccination (IDRV) is a recent (2006) development in India which was intended to provide an ethical, efficient and cost effective alternative. ID is safe, effective, and well tolerated. Technique of ID can be learned easily. Universal ID with 1 ml is the ethical solution, which is easy to administer and monitor, economical, effective, and imparts early immunity (Five E's).⁶ Realizing the significance of implementing this IDRV, Rajasthan Government has decided to provide IDRV free

of cost to all animal-bite recipients as per “Mukhay Mantri Nishulk Dawa Yojana, Launched by the Health Department of the State Government from October 2, 2011. So this study was undertaken to find out clinical safety and side effects of post-exposure prophylaxis by Intra Dermal Rabies Vaccination.

2. Methodology

This hospital based cross sectional observational study conducted on 654 Category-II and III new victims of animal bite enrolled at the Anti-Rabies Clinic, SMS Hospital, Jaipur, Rajasthan between June 2013 to 30 Sept. 2013 (4 months). Recipients who did not give consent were excluded from the study. These victims under study were given Purified chick embryo Cell culture Rabies Vaccine (PCECV) supplied by free of cost Government of Rajasthan injected by updated Thai Red cross (TRC) Regimen(2-2-2-0-2) as recommended by WHO. It requires four visits to the clinic on 0, 3rd, 7th, and 28th days. On each visit 0.1 ml of vaccine is given per site which is deposited in the dermal layer of the skin at multiple (2) sites. All the subjects were observed for half an hour following the first dose of vaccination (on day 0) for possible immediate adverse events (AEs). At the end of half an hour, AE was recorded after soliciting from the subjects as well as physical examination of the subjects. All subjects were given a reminder slip indicating the date of the next dose of vaccination and blood sampling. Adverse events were again recorded during their follow up visit for subsequent vaccinations on days 3, 7 and 28. Data regarding outcome variables were studied along with socio-demographic factors, characteristics of the exposure, animal causing the bite, side effects after IDRV of the recipients were collected using a semi-structured questionnaire and by the direct interview method. Bivariate analysis of qualitative variables was done using chi-square test.

3. Results

Present study observed that out of total studied 654 PCRCV recipients 492 (75.2%) were males and 162 (24.8 %) were females having M:F ratio 3:1. Likewise urban and rural recipients were 85% and 15% respectively. Maximum recipients were i.e. 50.92% were adults followed by 33.49% children of <14 years with mean age 25.54 ± 17.9 years.

Maximum recipients were exposed to Dog bite (79.7%) consisting 85.4% stray dog. Majority of bites were over Lower Extremities (65.56%) . Majority of 370 (56.6%) bites were unprovoked bite was Almost equal amount of cases were observed in grade 2 and grade 3 i.e. 350(53.3%) and 304(46.5%) respectively. In grade 3, there were 51 (7.8%) lacerated wound.

When side effects observed with 1st dose of IDRV in the present study, among symptoms Local Itch (4%) was maximum followed by Local Pain (3.8%) and Low Grade Fever (2.1%) and the signs observed. And the most frequent sign with 1st dose of IDRV was Fever (34.8%) followed by local Indurations (22.3%) , Erythema (2.1%), Anaphylaxis or lymphadenopathy were not observed in ant of recipient. These local side effects decreased gradually with the progress of time by its own or with the use of medication like antihistamines & analgesics, on day 3, 7 & 28.

Same pattern of sign and symptoms were observed in D3 and D7 dose of IDRV but in decreased frequency. Generalized symptoms reported (<1%) were headache, dizziness, weakness, abscess and flu like illness. However, none of the recipients delayed the regimen due to side effects. None of the recipients dropped out of study due to side effects.

When association of these side effects with socio-demographic factors like location, sex, age groups, provoked status, fate of animal site of bite, were observed it was not found significant ($P > 0.05$ NS) in any of these studied factors.

4. Discussion:

Present study observed that out of total of 654 animal bite victims included in the study maximum were 558 (85%) of urban background. In the present study maximum recipients were i.e. 50.92% were adults followed by 33.49% children of <14 years with mean age 25.54 ± 17.9 years and M:F ratio 3:1. In this study, adults & children were mainly affected because of their outdoor activities. Similar findings were made in other studies also like Mohd Junaid⁷(2012) who reported 31.5 % in 21 - 30 years age-group and 48.4% below 25 years of age.

As in this study most (75.2%) of the animal bite victims were males with M:F 3:1. Mohd Junaid⁷(2012), Venu⁸(2012) had shown similar result in their study this can be explanation with the higher outdoor activity of males. Main biting animal was dog (79.7%) of whom 85.4% were stray dog in this study which is similar to other studies too.⁵⁻⁸ D.J. Briggs et al,(2000), Durga⁹(2011), Mathew (2012, Mohd Junaid⁷(2012), Venu⁸(2012).

In this study majority of bites were unprovoked may be because of the reason that study period (June to Sept.) is used to be considered as breeding seasons of dogs. Other authors like Anita¹⁰(2003) and Mohd Junaid⁷(2012) have also reported similar observations in their study.

In this study, 202 (63.1%) had category III exposure which can be attributed to the fact that the study centre is a tertiary care hospital so more serious victims visit this centre if they were referred from other clinics and nursing homes. Mohd Junaid (2012)⁷ %, and Mathew⁶ (2012) has also reported the almost similar observations.

Majority of bites in this study were over legs 37.31% followed by hand and foot (both) 181 (27.7%) these observations were also in agreement with other authors.^{2,5,10,11}

When the side effects with IDRV is concerned, D.J. Briggs et al⁵(2000) reported adverse reactions in 48% which were in decreasing order of frequency occurrence included were erythema, pain/swelling at the site of injection, fever. Another author Pratap AK¹²(2010) found Local Indurations as the most common (91.8%) local side effect followed by Erythema (43.1%), pruritus (29.8%) and pain (19.9%) in recipients of IDRV. Whereas in the present study these side effects were quite low; may be because of the reason that with the time advancement in techniques and increased resistance of the recipients. This is further supported with reports of National Rabies Guidelines 2013, who also reports that adverse events may include mild itching, erythema, rarely body ache and fever that are usually self-limiting. Sometimes symptomatic management using analgesics and antihistamines may be needed.

CONCLUSIONS

The study revealed that IDRV is quite safe as it is associated with minor side effects which can be taken care by symptomatic therapy and counseling if given with vaccination. These IDRV regime is also cost effective than intra-muscular regime, it's a well known fact. So this IDRV regime may be recommended.

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