SHORT ARTICLE
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A Study of Adverse Effects Following Administration of Anti-Rabies Vaccination - A Hospital Based Study

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ABSTRACT

Rabies is an acute viral zoonotic disease that affects all warm-blooded animals including mammals and occurs in more than 150 countries and territories. Although rabies is a 100% fatal disease, it can be prevented by the use of potent anti-rabies vaccines (ARV). The present study was a hospital based descriptive longitudinal study conducted during February 2019 to July 2020 amongst the animal bite patients attending the Anti -Rabies clinic (ARC) of Vardhman Mahavir Medical College and Safdarjung Hospital (VMMC & SJH), New Delhi, to study the adverse events (vaccine reactions) if any following administration of the ARV. The age of the study participants ranged from 2 to 65 years and the mean age was (29.3±15.2) years. No severe or serious adverse events were reported. Of the minor reactions, the most commonly reported symptom was pain at the injection site (34; 9.4%) followed by occurrence of tingling sensation (29; 8.1%), headache (22; 6.1%) and itching at the injection site (19; 5.3%). These findings corroborate with those found in previous studies in the literature. It was concluded that although there are possible local or mild or systemic adverse reactions to rabies vaccination, but once initiated, rabies prophylaxis should not be interrupted or discontinued.

Keywords: Rabies, Anti-rabies vaccine, Adverse effect following immunisation, post-exposure prophylaxis

INTRODUCTION

Rabies is an acute viral zoonotic disease that affects all warm-blooded animals including mammals and occurs in more than 150 countries and territories.[1] The etiological agents of rabies encephalitis belong to the Mononegavirales order, the Rhabdoviridae family and the Lyssavirus genus.[2,3,4]

Although rabies is a 100% fatal disease, it can be prevented by the use of potent anti-rabies vaccines (ARV) like cell cultured vaccine (CCV), embryonated egg-based vaccine (EEV), rabies immunoglobulin (RIG) if indicated; coupled with local treatments as part of its post exposure prophylaxis (PEP). Intradermal rabies vaccination (IDRV) using selected CCVs has been established to be an efficacious and economic alternative to the standard intramuscular regimens. [5] Rabies is the only disease where prophylaxis can be started after the patient has been exposed. This is because of the long incubation period of the virus which gives enough time for the patient to take preventive measures. [6] The present study was done amongst the animal bite patients attending the Anti -Rabies clinic (ARC) of Vardhman Mahavir Medical College and Safdarjung Hospital (VMMC & SJH) and aimed to study the adverse events (vaccine reactions) if any following administration of the ARV.

MATERIALS AND METHODS

This was a hospital based descriptive longitudinal study conducted at the Anti-Rabies Clinic (ARC) of Vardhman Mahavir Medical College (VMMC) and Safdarjung Hospital, New Delhi, in the period February 2019 to July 2020. The study participants for the purpose of this study were the animal bite patients attending the ARC of VMMC & Safdarjung Hospital. Since the present study is a part of a larger study, which was done to assess the compliance to full

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course of ARV among the animal bite patients. Therefore, taking the compliance to full course of ARV as 55.2% as per the study conducted by Nikhil et al at the Anti-rabies vaccination OPD in a tertiary care hospital in Mumbai [7] the sample size was calculated using the formula, $n = z^2_{1-\alpha/_2} * p\ (1-p)/\varepsilon^2$

Where, n is sample size, $z_{1-\alpha//2}$ is the constant 1.96 for 95% confidence limits, P is anticipated population proportion, and Ɛ is relative precision.

The sample size was calculated to be 321. After adding 10% as loss to follow up, the sample size was calculated to be 360.

Patients with Category-II and III animal bite wounds coming to the ARC, for administration of Anti Rabies Vaccine (ARV) were included in the study. The categorisation of wounds was done as per the classification of animal bite wounds for post-exposure prophylaxis based on WHO recommendations.[2,8]

The vaccine which was used during the study period was Abhayrab which is a Purified vero cell rabies vaccine. The regimen being followed at VMMC and Safdarjung Hospital, New Delhi is **2-2-2-0-2** (updated Thai Red Cross Schedule) which involves injection of 0.1 ml of reconstituted vaccine per ID (intradermal) site and on two sites per visit (one on each deltoid area, an inch above the insertion of deltoid muscle) on days 0, 3, 7 and 28, where the day 0 is the date of first dose administration of anti-rabies vaccine which may not necessarily be the date of rabies exposure/animal bite.

A non-probability convenient sampling method was used to select the study participants and achieve the required sample size. The importance of the study was explained to the animal bite patients or to the accompanying guardians for those who were less than 18 years. Those who were willing to participate were included after obtaining written informed consent / assent. Information regarding their socio-demographic profile and history of animal bite exposure were collected using a pre-designed, pre-tested, structured questionnaire which was administered by interview. An attempt was made to call all the study participants after the administration of 1st dose to ask about any adverse event following immunization.

All the data were coded and entered into a master sheet on MS Office Excel and later transferred to SPSS (IBM SPSS Statistics 21.0) for analysis. Data validation checks were performed at regular intervals for data entered into the worksheet of MS Excel. The results obtained were expressed in terms of percentages and proportions and depicted as tables and graphs. Ethical clearance was obtained from the Institute Ethics Committee of VMMC and Safdarjung Hospital, New Delhi.

An adverse event following immunization (AEFI) is any untoward medical occurrence which follows immunization and does not necessarily have a causal relationship with usage of the vaccine. The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom or disease.[9]

Minor reactions are usually occurred within a few hours of injection, resolve after short period of time and pose little danger. They can be local i.e., restricted or limited to a specific body part or region (includes pain, swelling or redness at the site of injection) or systemic relating to a system, or affecting the entire body or an entire organism (e.g., fever) (includes fever, malaise, muscle pain, headache or loss of appetite). **Severe reactions** are those which usually do not result in long-term problems, but they can be disabling although they are rarely life threatening. They may include seizures and allergic reactions caused by the body's reaction to a particular component in a vaccine. [9]

RESULTS

The study was conducted among 360 animal bite patients who attended the anti-rabies clinic of VMMC and Safdarjung Hospital following the incident of animal bite. The clinic-social profile of the study participants has been discussed in Table 1.

The age of the study participants ranged from 2 to 65 years and the mean age was (29.3±15.2) years. The median age (interquartile range) of the study participants was 26 (18-40) years.

Table 1: Clinico-social profile of animal bite patients (N=360)

Variable	Cases (%)
Age (years)	
0-20	112 (31.1)
21-59	237 (65.8)
≥ 60	11 (3.1)
Gender	
Male	266 (73.9)
Female	94 (26.1)
Occupation	
Employed / Working	212 (58.9)
Student	99 (27.5)
Housewife	33 (9.2)
Unemployed	9 (2.5)
Retired	7 (1.9)
Literacy status	
Literate	298 (82.8)
Illiterate	62 (17.2)
Type of animal	
Dog	317 (88.1)
Cat	22 (6.1)
Monkey	16 (4.4)
Rat	5 (1.4)
Category of wound	
Category – II	69 (19.2)
Category – III	291 (80.8)
Site of bite	
Lower limb	238 (66.1)
Upper limb	81 (22.5)
Trunk	19 (5.3)
Multiple sites	13 (3.6)
Head and neck	9 (2.5)

Table 2: Distribution of study participants reporting any adverse events following immunization* (N=360)

Types of adverse events	Cases* (%)
Pain at injection site	34 (9.4)
Occurrence of tingling sensation	29 (8.1)
Headache after vaccination	22 (6.1)
Itching at injection site	19 (5.3)
Redness at injection site	16 (4.4)
Fever after vaccination	11 (3.1)

*Multiple response possible

About three-fourth (266; 73.9%) of the study participants were males while one-fourth (94; 26.1%) were females. Majority (298; 82.8%) of the study participants were literate. Majority (317; 88.1%) of the bites were caused due to dogs. Almost 4/5th (298; 82.8%) of the study participants were bitten by stray animals whereas (53; 14.7%) were bitten by pet dogs. Majority (291; 80.8%) of the study participants had Category-III wounds as per the classification of animal bite wounds for post-exposure prophylaxis based on WHO recommendations. (Table 1) A larger proportion (238; 66.1%) of participants reported to have been bitten in their lower limb followed by upper limb (81; 22.5%).

Most of the events reported were minor reactions. No severe or serious adverse events were reported. Of the minor reactions, the most commonly reported symptom was pain at the injection site (34; 9.4%) followed by occurrence of tingling sensation (29; 8.1%), headache (22; 6.1%) and itching at the injection site (19; 5.3%). (Table 2)

DISCUSSION

In the present study, no severe or serious adverse events were reported by any of the study participants. Most of the events reported were minor reactions, and amongst them the most commonly reported symptoms were pain at the site of injection (34; 9.4%) followed by tingling sensation at the injection site (29; 8.1%).

Most reported adverse events following immunization with rabies vaccine in the previous literature have been reported to be local reactions such as pain at the injection site, swelling, redness, and induration. According to the US Centres for Disease Control and Prevention, local reactions are more common following HDCV (human diploid cell vaccine) as compared with PCECV (purified chick embryo cell vaccine).[10]

Shankaraiah, et al, in their study, conducted at municipal corporation hospitals in Bangalore, India reported no adverse reactions to anti-rabies vaccines.[11]

A multi-centric, health facility-based survey conducted by Ravish et al among animal bite victims reported that 14.2% of the study participants had pain, numbness, itching, redness, rash, body ache, malaise, nausea, and fever following administration of anti-rabies vaccination.[12]

As per the study findings of Diallo et al, in a survey to assess the human rabies post exposure prophylaxis at the Pasteur Institute of Dakar, few patients reported adverse effects after administration of anti-rabies vaccine. Adverse events were reported by 6% of the patients after first two doses and by 3% of the patients after the third dose. Amongst those who reported the adverse events, most commonly reported symptoms were headache, fever and pain at the injection site which occurred on the same day of the vaccine injection .[13]

Our findings corroborate with those found in previous studies in the literature. Although there are possible local or mild or systemic adverse reactions to rabies vaccination, but once initiated, rabies prophylaxis should not be interrupted or discontinued. Minor adverse events do not contraindicate future doses,[14] because if rabies vaccination is not completed, rabies is almost always fatal.[18,19,20] Rabies vaccination should be monitored appropriately, adverse reactions or events should be reported timely and reduced as far as possible.[14,18] Patients who have adverse reactions should be offered prompt treatment, and symptoms should be controlled and alleviated effectively.[19,20]

From all the past research and studies, it has been known that patients with adverse reactions to vaccination, including rabies vaccination, could be treated effectively, and their symptoms could be controlled and alleviated effectively.[14,15,16] Studies have shown that hypersensitive reaction following rabies vaccination is rare, with the overall incidence reported to be 11 per 10,000 vaccines (0.11%), and serious anaphylactic reactions at a rate of approximately 1 per million doses. [17]

CONCLUSION

In the present study it was concluded there were very few incidences of adverse reaction following administration of anti-rabies vaccination and those were mostly mild reactions which subsided with analgesics and anti-allergic medications.

Health education messages should be designed in the context that the local or mild adverse reactions following vaccination should not be a deterrent in completing the recommended regimen of ARV, which will help in improving the knowledge and bursting the myths regarding anti-rabies vaccination among the common people, thus reducing the burden of mortality due to Rabies and help in achieving the target of zero deaths due to Rabies by 2030 in the long run.

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