

Original Research Article

Clinical safety profile of Premi-Rab a new indigenous equine rabies immunoglobulin for cat III animal bite victims at anti rabies clinic of a tertiary care hospital, Karnataka

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ABSTRACT

Background: WHO guidelines recommend for treating Cat III animal bite victims with local infiltration of Equine Rabies Immunoglobulin (ERIG) into and around animal bite wounds followed by anti-rabies vaccine (ARV). The main reason for non-use of ERIGs by medical profession is the fear of anaphylaxis and laborious process. The present study was taken up with the objectives to assess the clinical safety of a new ERIG, describe sociodemographic profile of ERIG recipients and compliance to Intra Dermal Rabies Vaccine (IDRV), who reported to Anti Rabies Clinic (ARC) of Mandya Institute of Medical Sciences (MIMS), Mandya.

Methods: Descriptive study at ARC, MIMS, Mandya for a period of one year. The data was collected using structured questionnaire. The data was entered into Microsoft excel and results were expressed using descriptive statistics.

Results: The study revealed that cat III animal bite victims were 3400 (56.3%), of these only 545 (16.0%) opted for the new ERIG. Skin Sensitivity Test (SST) showed positive results in 17 (3.1%) cases. Among the ERIG recipients 28 (5.1%) had mild adverse reaction to ERIG. The compliance rate was 49.2% for all 4 doses of IDRV.

Conclusions: 3.1% showed positive result to SST. 5.1% had mild adverse reaction to ERIG.

Keywords: Safety profile, New equine rabies immunoglobulin, Category III animal bite, Compliance to IDRV

INTRODUCTION

Rabies-an acute viral disease, causes fatal encephalitis that can affect virtually all the warm blooded animals including man. The transmission of virus to other animals and humans occurs through the saliva of the infected animal following bite, scratches, licks on broken skin and mucous membrane.¹

The dog mediated rabies is estimated to cause 59,000 human deaths globally with an associated loss of 3.7 million DALYs (Disability Adjusted Life Years). It is estimated that Asia (59.6%) accounts for majority of the

deaths followed by Africa (36.4%). In Asia it is estimated that 35,172 human deaths occur every year due to dog-mediated rabies with an associated loss of 2.2 million DALYs.

Most deaths in Asia (59.9% of human rabies deaths) and globally (35% of human rabies deaths) occurs in India. Annually 17.4 million animal bite cases occur in India and 20,847 deaths occur due to human rabies.^{2,3} Categorization of animal bites are based on World Health Organization (WHO) guidelines for initiation of post exposure prophylaxis. According to WHO guidelines, any bite or scratch with a single drop of blood from the

bite wound is classified as cat III.⁴ The treatment of cat III animal bite victims requires administration of Anti Rabies Vaccine (ARV) and Rabies Immunoglobulin (RIG). RIG inactivates the residual virus present at the site of bite, thus it is life saving. The WHO current recommendation is to administer maximum amount of RIG in and around the wound depending on anatomical feasibility and remaining amount by intramuscular route. WHO- APCRI (association for Prevention and Control of Rabies In India). Indian rabies survey has revealed that the use of RIG is as low as 2% in India. Among those health care facilities using RIG, majority of them use Equine Rabies Immunoglobulin (ERIG) due to cost considerations when compared to Human Rabies Immunoglobulin (HRIG). The main reason for non-use of ERIG by medical professionals is the fear of anaphylaxis and laborious process. The presently available ERIG in our country is highly safe for use as it is purified with low protein content and highly enzyme refined. There are many brands available in the market. The present study was taken up to observe the clinical safety of a new indigenous ERIG with the following objectives,

1. To assess the clinical safety profile of a new ERIG among the cat III animal bite victims receiving it.
2. To describe their socio-demographic profile.
3. To assess compliance to IDRV among them.

METHODS

This was a record based descriptive study done at ARC, MIMS, Mandya from 1st April 2016 to 31st March 2017. Permission was obtained from Institutional Ethics Committee and head of the institution. The medical records of ARC were accessed for collection of data. The information regarding socio-demographic characteristics, circumstances of animal bite, anatomical distribution of the bite wound, post exposure prophylaxis and adverse reaction to immunoglobulin was compiled from all cat III animal bite victims, who received the new ERIG (PREMI-RAB) from 1st April 2016 to 31st March 2017. All animal bite victims who had received new ERIG during the study period were included for the study. The collected data was entered into Microsoft excel and results were expressed using descriptive statistics.

RESULTS

During the study period, the total number of animal bite victims reported to ARC was 6034. The cat III bite cases were 3400 (56.3%), of these only 545 (16.0%) received the new ERIG.

There were more males i.e., 375 (68.8%) compared to females i.e., 170 (31.2%). Children aged less than 15 years i.e., 212 (38.9%) constituted the largest. 365 (67.0%) were from rural area and 502 (92.1%) were from low socioeconomic class.

Among the cat III bites, dog was the most common animal involved in 514 (94.3%) of the exposures followed by cat in 20 (3.7%) cases. In 214 (39.2%), it was provoked bite and in 345 (63.3%) by a stray animal (Table 1). Majority i.e., 162 (29.7%) had bite mark in lower limb and 121 (22.3%) had multiple bites at different anatomical sites.

Table 1: Distribution according to type of animal and type of bite (n=545).

Type of animal	Type of bite		Total
	Provoked (%)	Unprovoked (%)	
Pet animal	120 (56.1)	80 (24.2)	200 (36.7)
Stray	94 (43.9)	251 (75.8)	345 (63.3)
Total	214 (39.2)	331 (60.8)	545

The wound was immediately washed with soap and water as a first aid measure in 431 (79.1%) cases and 30 (5.5%) cases had applied irritants like chilli powder paste, jackfruit sap and some had tied copper coin.

Of the people who received ERIG, 360 (66.1%) received ERIG within 24 hours and 185 (33.9%) received between one to seven days after exposure to animal bite. SST was done before administration of the full dose of ERIG. SST showed positive results in 17 (3.1%) cases. In those cases which showed reaction to the SST, H1 and H2 blockers were given before administration of the full dose. The mean quantity of ERIG administered locally was 4.57 ± 2.73 ml and systemic was 5.57 ± 2.12 ml and in 270 (49.5%) the whole amount of ERIG was administered locally.

For assessing the adverse reaction among the cases who received ERIG (545), follow up was done by telephonic interview and during the follow up visit for vaccination at the centre (time period 7-9 days), among them 28 (5.1%) cases has mild adverse reaction to ERIG. Pain was seen in all cases, swelling was seen in 25 (89.2%) and 9 (32.1%) complained of fever (Table 2) and all the cases were treated symptomatically. Anaphylaxis was not seen in any case and serum sickness was also not reported by any of the victims who received ERIG.

Table 2: Shows different adverse reaction to ERIG (n=28).

Adverse reaction	Number*	Percentage
Pain	28	100
Swelling	25	89.2
Redness	19	57.8
Itching	13	46.4
Fever and malaise	09	32.1

*Multiple response.

Among 545 ERIG recipients receiving vaccination for PEP by intradermal route, 268 (49.2%) received all 4 doses of IDRV (i.e., on days 0, 3, 7, 28) (Table 3).

Table 3: The compliance to IDRV among ERIG recipients (n=545).

IDRV	Number	Percentage
All 4 doses	268	49.2
3 doses	375	68.8
2 doses	452	82.9
1 dose	545	100.0

DISCUSSION

Rabies immunoglobulin is lifesaving immunobiological. It neutralizes the virus at the site of bite and is a must for all category III exposures. RIG is more effective when infiltrated immediately or within 24 hours of animal bite along with the first dose of vaccine; whereas, if vaccine alone was started, then RIG can be given up to 7 days after starting first dose of vaccine as this will not interfere with the vaccine effect.

ERIG presently available are highly purified, safe and affordable. But still the number receiving ERIG is low, which may be due to fear of anaphylaxis and ignorance of importance of ERIG in post exposure prophylaxis (PEP).

In our study only 16% of category III animal bite victims received ERIG, the reason could be that the victims have to pay a nominal fee, even though it is a government hospital. 5.1% of them had Adverse reaction to ERIG was seen in 5.1% which is less than that seen in a study on safety of ERIG in children done by Ravish et al, skin sensitivity was positive in 8% which may be due to the difference in age group of study subjects.⁶

In our study, among those who had reactions to ERIG, everyone (100%) had pain, 89.2% swelling, 57.8% redness, 46.4% itching at the site of administration of ERIG and 32.1% had fever and malaise which was higher when compared to Tapas et al study, where pain was present in 53.8%, induration 67.1%, and pruritus in 29.2%.⁷ Systemic side effects such as low-grade fever were observed in 12.3%. In our study none of them had anaphylaxis and serum sickness which is similar to the study done by Sathpathy et al, and Chavan et al.^{8,9}

Compliance to vaccine among category III animal bite victims was 49.2% in our study which is similar to study by Vinay et al, which was 47.5% and less when compared to observations done by Shankaraiah study, where compliance was 77%, this can be explained by the fact that majority of animal bite victims coming to our center are from rural area and lower socioeconomic class.^{10,11} Also, the animal bite victims may have completed the PEP course in other centers in the periphery.

CONCLUSION

3.1% showed positive result to SST. 5.1% had adverse reaction to ERIG, the common ones were pain, swelling, redness and itching. None had severe adverse reactions like anaphylaxis or serum sickness.

Recommendations

The new indigenous equine rabies immunoglobulin PREMI-RAB is clinically safe and can be used for all category III animal bite victims.

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