Title: # RETROSPECTIVE EVALUATION OF THE SAFETY AND EFFICACY OF ANTI- RABIES SERUM IN PIMPRI CHANCHWAD MUNICIPAL CORPORATION HOSPITALS

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Keywords Rabies, Equine rabbies immunoglobulin, ERIC, adverse events, Inj, Premirab, dog bites

Abstract To evaluate the safety of efficacy of Equine Rabies Immunoglobulin (ERIG) used in rabies clinic in the Pimpri Chanchwad Municipal Corporation area over 1 year

Original Article:

RETROSPECTIVE EVALUATION OF THE SAFETY AND EFFICACY OF ANTI-RABIES SERUM IN PIMPRI CHINCHWAD MUNICIPAL CORPORATION HOSPITALS

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ABSTRACT:

Objective: To evaluate the safety and efficacy of Equine Rabies Immunoglobulin (ERIG) used in rabies clinics in the Pimpri Chinchwad Municipal Corporation (PCMC) area over 1 year

Materials and methods: Retrospective data was collated from the records for all dog bite cases attending the clinics under PCMC administration. Between February 15 and January 16, there were 9628 cases of dog bite of which 3375 (35.05 %) required post exposure prophylaxis with the standard protocol of wound toilet, ERIG and a course of rabies vaccine administered intradermally. Local and intramuscular ERIG was administered following a test dose. After observation on the first day, patient followed up on day 3, 7 14 and 30. Incidence of adverse reactions was recorded.

Results : Only 66 patients (1.96%) had adverse effects. 62 of 66 had skin redness/flare at the site of test. 1 case suffered from skin rash, and 3 complained of itching swelling giddiness and vomiting.

Conclusion: We conclude that the ERIG used from this particular vendor (Inj Premirab) is safe for long term use.

Keywords : Rabies, Equine rabies immunoglobulin, ERIG, adverse events, Inj. Premirab, dog bites

INTRODUCTION

A recent study estimates that globally, canine rabies causes approximately 59,000 human deaths, over 3.7 million disability-adjusted life years (DALYs) and 8.6 billion USD economic losses annually[1] As per Baxter JM, based on available evidence, a fair estimate of rabies burden in India is 2.74 rabies cases per 100 000 people annually. The annual estimated number of dog bites in India is 17.4 million, leading to estimated 18 000 20 000 cases of human rabies per year[2]

Indian national guidelines as well as WHO,[3,4] recommend that for all category III exposures, rabies immunoglobulin should be infiltrated in the depth of and around the wound(s) to neutralize the locally present virus. This is in tandem with a full course of antirabies vaccine.

The anti-rabies serum/Rabies Immunoglobulin (RIG) provides passive immunity in the form of ready-made anti-rabies antibodies, to tide over the initial phase of the infection before it is physiologically possible for the patient to begin producing his/her own antibodies following antirabies vaccination. Anti-rabies serum or RIG has the property of binding with the rabies virus, thereby resulting in neutralization and thus loss of infectivity of the virus and hence it is most logical to infiltrate RIG locally at the site of exposure.[3]

RIG of both human and equine origin are available but the equine immunoglobulins being more economical are widely used. Since ERIG is of heterologous origin, it has the potential to cause anaphylaxis, serum sickness and other allergic reactions. This retrospective evaluation was conducted to confirm the safety and efficacy of ERIG from a new vendor, for the Pimpri Chinchwad municipal Corporation

MATERIALS AND METHODS

Pimpri Chinchwad Municipal Corporation (PCMC) is situated in Pune District of Maharashtra State. It covers an area of 181 Sq.Km. and has a population of 20 lacs. PCMC has 8 hospitals and 23 dispensaries. PCMC also has high number of dog bite cases every year.

Post-exposure prophylaxis against Rabies includes local treatment of wound, antirabies vaccination and rabies immunoglobulin administration. A pilot project for the intradermal vaccination for rabies was introduced in the year 2009 in PCMC. It was during this period that Anti-Rabies Serum/ Rabies Immunoglobulin (RIG) treatment was introduced in the protocol for dog/animal bite cases. As per WHO, all transdermal bites or scratches are category III bites and at PCMC hospitals all Category III bite cases are given ARS after performing skin test and it is injected into the wound as per protocol.

Since the initiation of RIG treatment PCMC were procuring Equine Rabies Immunoglobulin (ERIG) from a particular company. Due to a sudden disruption of supply in 2015, it was decided to procure ARS from another manufacturer, Premium Serums & Vaccines Pvt.Ltd. (PSVPL), Narayangaon, Dist.-Pune. As this new product was being used for the first time, it was decided to conduct a retrospective study of its safety and

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efficacy at the various clinics and hospitals under PCMC. Rabies Antiserum, I.P. supplied by PSVPL is a sterile solution containing enzyme refined anti rabies equine immunoglobulin F(ab')2 fragments (ERIG).

Rabies antiserum was administered at recommended dose of 40 IU/kg. As much of the calculated dose, as anatomically feasible, was infiltrated into and around the wounds. The rest of the dose was given intramuscularly as a single dose in the gluteal region followed by a complete course of vaccination. If calculated dose was insufficient to infiltrate all wounds, it was diluted in normal saline 2-3 folds. The first dose of vaccine was given at the same time as the immunoglobulin, but in a different part of the body.

The skin sensitivity test was performed as follows-

1. 0.1 ml Rabies Antiserum diluted 1:10 in physiological saline was injected intra-dermally into the flexor surface of the forearm to raise a bleb of about 3-4 mm in diameter.
2. An equal amount of normal saline was injected intradermally as a negative control on the flexor surface of the other forearm.
3. After 15 minutes an increase in diameter to >10 mm of induration surrounded by redness/ flare, itching was taken as positive skin test, provided the reaction on the saline test was negative.
4. An increase or abrupt fall in blood pressure, syncope, hurried breathing, palpitation and any other systemic manifestation was also taken as positive test.
5. All patients showing positive skin test on Day 0, were administered ARS after a prophylactic dose of antihistamines, observed for 8 hours and discharged if found stable. Some who could afford were administered HIG Safety was evaluated in the clinics during the visits for vaccine on days 3, 7, and 28. They were classified as those occurring on the first day like hypotension, dyspnea, urticaria or anaphylaxis, and those reported during later visits like delayed reactions. Absence of any symptoms, signs of rabies during these 30 days was a measure of efficacy.

RESULTS:

Following table gives the details of total number of dog bite cases and reactions seen during the 1 year period from 1st February 2015 to 31st January 2016, at various hospitals/clinics under PCMC.

Table 1:
Number of dog bite cases per location, number administered ARS and the number and percentage Of adverse reactions

No	Name/ location of Hospital	Total no. of dog bite cases	Total no. of cases given ARS	Total Reactions (%)
1	Akurdi	1330	443	26 (5.87)
2	Bhosari	1931	284	1 (0.35)
3	Jijamata	982	695	6 (0.86)
4	Talera	844	293	6 (2.05)
5	Thergaon	754	296	0 (0)
6	Sangvi	301	114	1(0.8)
7	Yamuna Nagar	706	322	15 (4.66)
8	YCMH	2780	928	11 (1.19)
	TOTAL	**9628**	**3375**	**66 (1.96)**

9628 dog bite cases reported for treatment during the year, of which 3375 (35.05%) were category III bites requiring ARS treatment. Out of these 3375 patients, 66 patients (1.96 %) showed adverse reactions. 62 of 66 had skin redness/flare at the site of test. 1 case suffered from skin rash, and 3 complained of itching swelling giddiness and vomiting. All the patients were monitored for 28 days and none of them complained of delayed or late adverse reactions. None of the cases showed any signs and symptoms of rabies during the follow up period.

DISCUSSION:

It is an accepted fact that the adverse reactions to ERIG are dependent upon the manufacturing process and the extent of purification. The 1st WHO expert series report mentions that unlike the original unpurified rabies antisera which resulted in adverse reactions in as many as 40% of recipients, the adverse-reaction rate of patients receiving highly purified ERIGs has been reduced to <12%.[5] The extent of purification could vary between manufacturers; hence this would justify the retrospective analysis of the ERIG supplied by a new manufacturer.

Literature supports that there is no scientific ground for performing a skin test prior to administering ERIG because testing does not predict reactions, and ERIG should be given irrespective of the result of the test[3] Yet in public hospitals like those in PCMC the skin test is conducted as a matter of abundant precaution, so that one can be better prepared in cases who have tested positive.

The national guidelines quote a figure of 1 in 150,000 cases for true anaphylaxis due to ERIG. In other cases there may be transient tenderness at the injection site and a brief rise in body temperature that does not require any treatment.

In our study only 1.96 % cases reported a reaction, which is in keeping with the WHO estimate. Almost all cases had local redness and swelling. One case had skin rashes and 3 cases complained of itching giddiness and vomiting. These 4 cases could be considered to be mild anaphylactoid reactions. There were no reports of delayed side effects. During the followup period no case presented with signs and symptoms suggestive of rabies. It is fair to conclude that the ERIG, Premirab is safe and effective in this retrospective evaluation

CONCLUSION:

Based on the majority of local reactions observed over the study period and no reported cases of rabies, we conclude that Anti rabies serum, Premirab is safe for use on a mass scale.

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