SPECIAL ARTICLE

Clinical Safety of Rabies Monoclonal Antibodies: A Follow up study conducted at ARC, VIMSAR, Burla

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Abstract

Background - As ERIG was not available in The Anti-Rabies Clinic of VSS Institute of Medical Science & Research, Burla, Sambalpur, Odisha in November 2017, patients were counselled regarding R'Mab (Rabies Monoclonal Antibodies), which is available in Indian Market recently and was prescribed to patients with category III animal bite to study its clinical safety. **Objective -** To study the clinical safety of injection R'Mab. **Methods -** A prospective follow up study on 53 cases having Category III animal bite, who were able to purchase R'Mab available in Market were administered at Anti-Rabies Clinic, Dept. of Community Medicine, Veer Surendra Sai Institute of Medical Science & research, Burla, Sambalpur, Odisha, India and these cases were followed of for both local & systemic side effects on Day 3, 7, 14, 28, 45, 60, 90, 180 from December 2017 to August 2018. **Results -** 62.2% were Male and 54.3% were children. Out of the total 53 animal bite cases, 72% were due to dog bite and rest 38% were due to Monkey bite, Cat bite, and Pig bite respectively. Most of the bites are in lower limb (35.8%) followed by upperlimb (20.7%). Only 6 persons (11.32%) complained about local pain at the site of R'Mab administration whereas 2 (3.77%) persons presented with local site induration on day 3. Most common Systemic side effects were malaise & fever which was observed in only 2 cases (3.77%) as on Day 3 . No serious side effect like anaphylaxis was present. **Conclusion -** Out of 53 patients administered R'Mab only 15.09% shows local adverse effects whereas only 3% complained of systemic effects like malaise & fever which decreases with progress of time without any additional medication and no side effects (local and systemic) were reported after 7th followed up days.

Key words - Rabies, Rabies Monoclonal Antibody (R'Mab), Adverse Reaction, Safety

Introduction

Rabies, a zoonotic viral infection commonly transmitted by saliva through the bite of an infected animal, is a fatal disease to humans if not treated immediately.1 Each year, it is estimated that at least 60,000 people die from rabies and more than 10,000,000 receive post-exposure vaccination against rabies.2 The World Health Organization (WHO) recommends post-exposure prophylaxis (PEP) for different categories of animal bite or non-

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bite exposures which consist of a combination of wound cleaning, active immunization with a tissue culture rabies vaccine and passive immunization with Immunoglobulin. Three classes of biological product are available for passive immunization: human rabies immunoglobulin, equine rabies immunoglobulin and Rabies Monoclonal Antibody. WHO has recommended use of MAb "cocktails" containing at least two antibodies against RABV, as alternatives for RIGs in PEP3. Several human MAbs have been tested against rabies. The first (a single MAb) was recently licensed by the Serum Institute of India4. Studies so far show the equivalence of its performance to human RIG. The availability of this MAb could fill critical public health gaps. As it is made by recombinant technology, it will be less prone to problems such as availability, safety and purity. It should be recommended for use in public health programmes, depending on the epidemiological and geographical setting, with monitoring of its safety and efficacy (clinical outcomes) during post-marketing use. Thus, the aim of this study is to evaluate the clinical safety of Rabies Monoclonal antibody (R'Mab) alternative to RIG, so that access to appropriate treatment in the India can be improved.

Objective

To study the Clinical safety of Injection Rabies Monoclonal Antibody

Material & Methods

It was a prospective observational study done from December 2017-August 2018 at the Anti Rabies clinic (ARC) Of Department of Community Medicine, at VSS Institute of Medical Science & Research, Burla, Sambalpur, Odisha. All the patients having category III animal bite were counselled regarding ERIG, HRIG &R'Mab. As R'Mab was not supplied by government and keeping in mind the cost factor only 53 out of687 patients (Enrolled Category III patients from December 2017 to February 2018) agreed to purchase R'Mab and gave written consent to participate in the study. Amount of Inj.R'Mab required was calculated as 3.3 IU/Kg body weight. The volume of R'Mab injected locally depended upon the site of bite and rest was administered intramuscularly on anterolateral aspect of thigh. Simultaneous active immunisation with modern cell culture vaccines was also administered. The patients were then followed upregarding local & systemic side effects during their subsequent visit at ARC OPD for active immunisation.After completion of vaccine course that is after 28 days patients were telephonically followed up on Day 45, 60, 90, 180 regarding any side effects.

Results

Table 1: Age & Sex wise distribution of patients

Age	Male		Female		Total
	N	%	N	%	N(%)
< 18 yrs	18	34	11	20.7	29(54.3)
> 18 yrs	15	28.2	9	17.1	24(45.7)
Total	**33**	**62.2**	**20**	**37.8**	**53(100)**

Total 53 patients with Category III animal bite were give consent to participate in the study. Out of which 29 (54.3%) were <18 yrs. of age and rest 24(45.7%) were above 18 yrs. of age. 33 (62.2%) out of total 53 were male and rest 20(37.8%) were female. Male and female children constitute 18(34%), 11(20.7%) of total study population respectively.

Table 2: Distribution of Site of Bite

Site	Number	Percentage
Upper Limb	11	20.7
Lower Limb	19	35.8
Trunk	6	11.3
Head & Neck	9	17
Multiple Sites	8	15.2
Total	**53**	**100**

Highest number i.e. 19(35.8%) of bite reported in the lower extremities followed by 11(20.7%) in the upper extremities. 9(17%) cases presented with bite over face & head. 8(15.2%) cases presented with bites over multiple site who were most commonly children.

Table 3: Type of Animal Bite

Type of Animal	Number	Percentage
Dog	38	71.70%
Monkey	8	15.09%
Cat	5	9.43%
Pig	2	3.77%
Total	**53**	**100**

Whereas 38(71.7%) of the cases reported were dog bite cases, monkey bite, cat bite and pig bite cases were 8(15.09%), 5(9.43%) and 2(3.77%) respectively.

Table 4: Local reaction after administration of Injection R'Mab(Day wise)

Adverse Reaction	Day 0	Day 3	Day 7	Day 14	Day 28	Day 45	Day 60	Day 90	Day 180
Local Edema & Induration	0	2(3.7%)	0	0	0	0	0	0	0
Local Pruritus	0	0	0	0	0	0	0	0	0
Local Pain	0	6 (11.32%)	0	0	0	0	0	0	0

Out of 53 cases, 2(3.7%) cases were presented with local edema & induration on day 3 which subsided naturally without any medication. 6(11.32%) cases had complained of pain at the site of R'Mab administration on day 3 which was relieved by taking analgesic. None of the person received R'Mab complained about any local side effects like edema, induration, pruritus, pain at the site of R'Mab administration on Day 7, 14, 28, 45, 60, 90, 180.

Table 5 : Systemic reaction after administration of Injection R'Mab (Day wise)

Adverse Reaction	Day 0	Day 3	Day 7	Day 14	Day 28	Day 45	Day 60	Day 90	Day 180
Generalised Pruritus	0	0	0	0	0	0	0	0	0
Fever& Malaise	0	2 (3.77%)	0	0	0	0	0	0	0
Rashes	0	0	0	0	0	0	0	0	0

Fever more than 390C & Malaise were reported by 2(3.77%) case on Day 3. None of the cases reported rashes at the site of R'Mab administration or at any other sites. No systemic reaction reported on Day 7, 14, 28, 45, 60, 90, 180.

Discussion

The WHO Guidelines define category 3 exposure as single or multiple transdermal bite/scratches and the patient should receive both passive and active immunization.More and more international manufacturers are discontinuing ERIG production and Human RIG is available in confidential quantities on specific markets and is too expensive for most people. Monoclonal antibodies (MAbs) capable of neutralizing a diverse range of rabies isolates could offer a solution to address the cost, supply and safety issues associated with blood derived Rabies Immunoglobulin (RIG). The advantages of human MAbsareminimalallogenic reactions; better compartmentalisation; longer in vivo half-life; improved ability to interact with human Fc receptors.

The present study conducted in 53 cases of whom 72% were dog bite and 35.8% of cases presented with bite over lower limb. The amount of R'Mab administered, as per the calculated body weight (3.3IU/Kg body weight) as much as anatomically feasible and rest were injected over thigh. In a study done by **Kaware a et al**[5], dog was the most common (93%) biting animal and 44.35% bites were on the lower limb which were similar to our study.

In our present study local pain, edema at the site of R'MAB administration and induration was present in 11.32% and 3.77% of patients respectively, where as local pain, induration and edema were observed in 95.8% of cases on day of ERIG administration followed by pruritus in a study by **Behera T R et al**[6]. In another study by **Verma R K et al**[7]local swelling was found in as high as 41.5% of the subjects. In the present study all these side effects gradually decrease and no local side effect reported on day 7, 14, 28,45,60,90,180.

Systemic reaction like malaise & fever was present in 3.77% of cases which were relieved after taking analgesic (T. Paracetamol). In a study by **Behera T R et al**[6], the systemic side effects of patients receiving ERIG like low grade fever and malaise were 42.86% and 49.77% respectively. These figures were much higher than our study.

Conclusion

The present study enlightensthe scope of using the newly available Rabies Monoclonal antibody and can be used against ERIG or HRIG at an affordable cost in all Category III cases with minimal adverse events.

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