

**Title:** A CLINICAL EVALUATION OF USAGE OF RABIES IMMUNOGLOBULINS

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## Keywords

**Abstract** World Health Organization (WHO) recommends infiltration of rabies immunoglobulins into animal bite wounds as a life saving measure in all severe or category III exposures. In Case of animal bite victims with less number of wounds after infiltration of all wounds an remaining rabies immunoglobulin is administered intramuscular or systematically at a site away from the site of vaccine administration as per the recommendations of WHO.

## A Clinical Evaluation of Usage of Rabies Immunoglobulins

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### ABSTRACT

**Background.** World Health Organization (WHO) recommends infiltration of rabies immunoglobulins into animal bite wounds as a life saving measure in all severe or category III exposures. In case of animal bite victims with less number of wounds, after infiltration of all wounds any remaining rabies immunoglobulin is administered intramuscular or systemically at a site away from the site of vaccine administration as per the recommendations of WHO. Hence, this study was done to identify the ratio of volume of RIGs injected into or around the wound (s) and intramuscular (IM) or systemic at a site distant from the site of vaccine administration.

**Methods.** A case record analysis of persons treated following exposure to rabies during June, 2008 to August, 2009 in anti-rabies clinic of KIMS Hospital, Bangalore revealed that out of 1270 cases treated with rabies immunoglobulin, 31 (2.4%) patients had severe / WHO category III confirmed rabid exposures.

**Results.** Majority were males (81%), aged 3 to 60 years and the body weight ranged from 13 to 81 Kgs. The biting animal was mostly dog (74.2%) and wounds were abrasions & lacerations (35%) and on lower limbs (45 %). Equine RIGs (87 %) was injected in undiluted form and the wastage factor/ ratio i.e. volume of RIGs (in mL) injected into and around wound(s) to volume injected IM/systemic was about 1: 0.8.

**Conclusion.** In more than 87 % of subjects, RIGs in an undiluted form was injected systemically in those who have fewer animal bite wounds and usage to wastage factor was calculated to be 1: 0.8. The study recommends evaluation of the benefit or otherwise of systemic/IM injection of RIGs.

### Introduction :

Rabies Immunoglobulins (RIGs) are life saving in severe or category III exposures to rabies. In an individual not previously immunized against rabies, there are at least ten critical days after starting rabies vaccine before blood and tissue rabies virus neutralizing antibodies (RVNA) levels are sufficient to inactivate any residual virus in the wound(s). It is to cover this window period of vulnerability that injection of RIGs into the wound(s) is important (1). The RIGs inactivate any residual virus present in the wound(s). The current recommendation of World Health Organization (WHO) state that the dose for human RIGs is 20 IU / kg body weight and for equine RIG and F (ab)<sup>1</sup>2 products is 40 IU / kg body weight. All of the RIG or as much as anatomically possible (Cave Compartment Syndrome) should be administered into or around the wound site(s). Any remaining RIG should be injected intramuscularly at a site distant from the site of vaccine administration (2). Animal bite wounds inflicted can be severe and multiple, especially in small children. In these circumstances, it is advisable to dilute the passive immunoglobulin product in normal saline to a sufficient volume to be able to inject into all wounds (3). However, some experts consider the volume of RIGs injected intramuscularly at sites other than bite wounds as wasted (1). The recent WHO expert consultation on rabies held from October 7-9, 2009 at Annecy, France was inconclusive on this issue. Incidentally, this paper was one of the working documents of this meeting.

The objective of this study was to identify the ratio of volume of RIGs injected into or around the wounds and intramuscular (IM) or systemic at a site distant from the site of vaccine administration.

### Subjects and Methods :

The Kempegowda Institute of Medical Sciences (KIMS) Hospital, Bangalore, India runs an anti rabies clinic, which receives animal bite victims particularly referred for administration of RIGs. A retrospective case records analysis of animal bite victims/ rabies exposures treated in this clinic during the period of June, 2008 to August, 2009 (15 months) was done.

### Results :

- 1. Profile of subjects and exposure to rabies.** A total of 1270 cases were treated with RIGs of which 31 (2.4%) belonged to severe or category III confirmed rabies exposures. Majority were males (81%), ages ranging from 3 to 60 years and body weight from 13 Kgs to 81 Kgs. The biting animal/ exposure to rabies included dog (74.2%), cat (3.2%) and others (22.6%).
- 2. Description of wounds (Table-1).** In 31 individuals who had confirmed rabies exposures, 20 (64%) had animal bite wounds and in 16 (52%) these were countable. The wounds were mostly on lower limbs

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**Table 1:**  
Description of wounds in animal bite victims

Sl. No	Wounds	Number	
1	Distribution / site of wounds (n=20)	Head & neck	Nil
		Trunk	2
		Upper limb	5
		Lower limb	9
		Multiple sites	4
2	Type of wounds (n=20)	Abrasions	7
		Puncture wounds	3
		Lacerations	7
		Mixed wounds	3
3	Number of wounds (n=16)	1 no	6
		2 nos	5
		3 nos	2
		4 nos	1
		5 nos	1
		7 nos	1

n= Number of subjects

(45%), abrasions and lacerations (35%) and had one (37%) and two (31%) wounds.

3. **Administration of RIGs** (Table-2). The equine RIGs were used in the majority of cases (87%) and in undiluted form. In 14 (87%) individuals the volume (in ml) of RIGs was injected into 26 wounds and the left over quantity injected systemic/IM was 48.4: 37.5 or 1: 0.8. In 2 individuals who had more wounds (12 numbers) the RIG was diluted with sterile normal saline to a volume sufficient to infiltrate all wounds and no systemic injection was given.

#### Discussion :

RIGs are life saving biologicals, scarce and expensive especially human RIGs. Worldwide less than 3% of at risk dog bite cases receive RIGs and it is often still not injected into wounds (1, 4). The present study conducted in an antirabies clinic which meticulously practices the recommendations of WHO revealed that about 80% of RIGs, in an undiluted form is injected systemic in those who have fewer animal bite wounds. This is as a result of calculating the dosage of RIGs based on body weight of the patient as advocated by WHO.

**Table 2:**  
Details of administration of rabies immunoglobulins

Sl. No.	Rabies immunoglobulins	Numbers (s) / ratio
1.	<b>Type of RIGs administered</b>	
	• ERIGs + • HRIGs **	14 2
2.	<b>Nature of RIGs administered</b>	
	• Undiluted • Diluted	14 2
3.	<b>Undiluted RIGs injected (few wounds) [n=14 ; w=26]</b>	
	• Total volume injected	85.9 mL
	• Volume injected into the wounds	48.4 mL
	• Volume injected systemic	37.5 mL
	• Wastage factor / ratio***	48.4 : 37.5 or 1 : 0.774 or 0.8
4.	<b>Diluted RIGs injected (more wounds) [n=2; w=12]</b>	
	• Total volume injected into the wounds	16.0 mL
	• Total volume injected systemic/IM	NIL
	• Wastage factor / ratio***	1.33 : NIL

+ ERIGs (300 IU/mL) = Equirab, India (11) & Abhayrig, India (3)

\*\* HRIGs (150 IU/mL) = Kemrab, Israel

\*\*\* Wastage factor/ratio = Volume of RIGs [in mL] injected into wounds: Volume of RIGs [in mL] injected systemic/IM

n= number of patients  
w = number of wounds

**Hence, it is recommended that the potential benefit or otherwise of possible wastage of injecting RIGs systemic/IM route may be reassessed through studies, using animal models and appropriate clinical evaluations. Till such time new clinical evidence becomes available, it is inevitable and advisable to continue with the existing practice of administration of RIGs, the dosage of which is calculated on the body weight of the patient and based on the recommendations of WHO.**

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