ORIGINAL ARTICLE

New Technical Device for Rabies Immunoglobulin infiltration for category III animal exposures in anti rabies clinic

Dr. Sumit Poddar*, Dr. Snehamay Chaudhuri**

*MBBS, MBA, Ph.D, FRSTM & H (UK), MACCP, MIPHA; Senior Critical Care and Anti-rabies Consultant Institute of Animal Bite Management

**MD,DNB Associate Professor of OBG, Midnapur Medical college and Hospital West Bengal

Abstract

Background: Wound infiltration of rabies immunoglobulin (RIG)/ rabies monoclonal antibodies (RMAb) in all category III exposures is to neutralize the virus at the wound site. It has to be infiltrated thoroughly into all bite wounds with minimal damage of the surrounding tissues.

Objective: To find out the usefulness and safety of new technical device/ injection needle for Rabies Immunoglobulin infiltration with minimum injury to the surrounding tissues.

Methodology: A cross-sectional study was conducted from January 2012 to December 2018 at a renowned anti rabies clinic in Kolkata. 45 patients with category III bites were included in the study. The data was collected using proforma consisting of socio-demographic characteristics and characteristics of animal exposure. The study compared the mechanism of action and safety of conventional single bore needle of 20-24 size with that of the multi-bore needle of same size.

Results: Majority of the patients were bitten by dog (71.11%) followed by cat (22.22%) and others. It was observed that RIG/ RMAb infiltration in the tissue by using the new device spreads uniformly into the tissue in and around wound and the technique is less cumbersome with only 1 prick as compared to 2-3 pricks from conventional needle and was less painful.

Conclusion: The multi-bore needle can be used to uniformly administer the RIG/ RMAb without the need for painful multiple pricks, as an alternative to conventional needle.

Key Words: animal bites, post exposure prophylaxis, technical device, RIG infiltration, category III exposures

Introduction

Rabies is one of the dreadful Zoonotic disease that occurs in many countries including India and poses a potential threat to more than 3.3 billion people worldwide.1 The virus is found in domestic animals and wild animal and is transmitted to other animals and to humans through their saliva (i.e. bites, scratches, licks on broken skin and

Corresponding Author: Dr. Sumit Poddar MBBS, MBA, PhD (Lincoln University), FRSTM & H (UK), MACCP, MIPHA. 56H, Beliaghata Main Road, Kolkata – 700010. Email: drsumitpoddar@gmail.com, Phone No. - 9830059468, 9830599468

mucous membrane). In India, the disease is mainly transmitted by dogs, which is responsible for 95% of animal bite cases and it is the source of >99% of human rabies infections.2 There are reported cases of treatment failures following treatment with IDRV or non-administration of RIG or inadequate infiltration of RIG to all sites of the wounds.[3,4]

Rabies can be prevented by timely and correct post exposure prophylaxis (PEP) after exposure to the virus.[5.6] The consequence of an exposure to RABV depends on several factors including the severity of the wound, the location of the bite on the body, the quantity and variant (genotype) of virus inoculated into the wound(s) and the

timeliness of post-exposure prophylaxis (PEP).[7] PEP consists of thorough wound washing with soap or detergent and water and/or virucidal agents to reduce the viral inoculum at the wound site; post-exposure vaccination to induce antibodies which lower the risk of RABV entering peripheral nerves after a bite from a rabid animal and timely administration of RIG/ RMAb to all category III exposures to neutralize the virus at the wound site.[8,9]

In many of the category III exposures, RIG/ RMAb are not infiltrated because of the fear to adverse drug reactions (ADRs) or for its cumbersome procedure such as multiple pricks from different sides of the wound or turning the needle inside the wound to infiltrate in different directions, which may damage the surrounding tissues and cause more pain for the patient. In this background, the corresponding author of the present study devised a new technical device/ needle for thorough infiltration of animal bite wounds with single prick and minimal damage of the surrounding tissues. Thereby, making it more friendly for both the anti rabies clinic physician and the patient; so that, on both the sides, it increases the acceptance and proper usage of RIG/ RMAb. Wound infiltration of RIG/ RMAb is one of the most important step in PEP and has to be provided to all category III exposures to control and finally eliminate rabies by 2030.[10,11]

Objectives

General: To initiate use of new technical device for infiltration of Rabies Immunoglobulin in case of animal bite wound. Other objectives are to identify the types and nature of wound due to animal bite, to assess the antibody response on the patient of critical animal bite cases, to suggest the preventive and control measure for rabies, to assess the knowledge and practice of animal bite victims and to assess the morbidity and mortality due to critical animal bite

Methodology

Study type: Cross sectional prospective.

Study population: 45 patients of category III bites in a renowned anti rabies treatment centre at Kolkata.

Inclusion criteria: All patients of category III presenting with dog, cat, mongoose, rabid cow, fox bites and consented for study.

Exclusion criteria: Immuno compromised individuals, rodent bites, patients with pre exposure schedule, and all those who did not give verbal or written consent for the study.

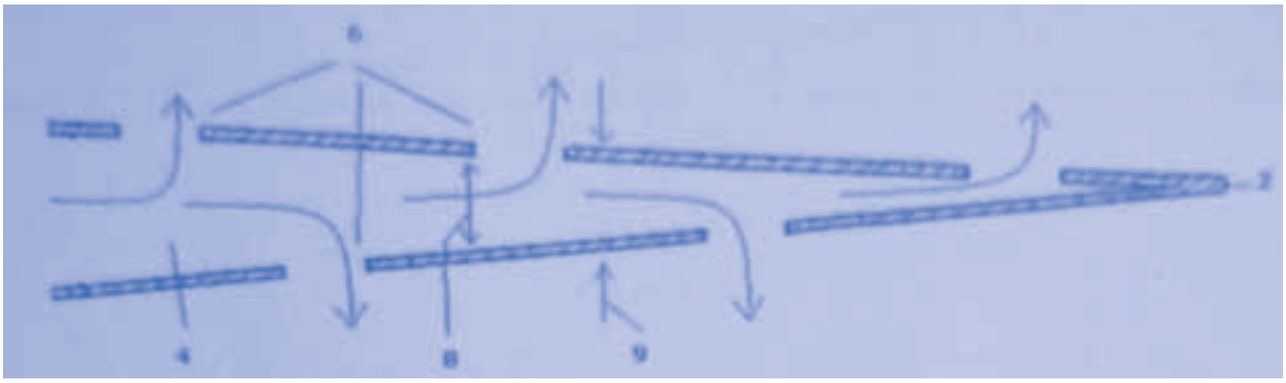
Materials and Methods:

A cross-sectional study was conducted from January 2012 to December 2018 at a renowned anti rabies clinic in Kolkata. 45 patients who came to the centre for PEP with category III bites were included in the study. Informed consent was obtained from each study subject and the data was collected using proforma consisting of socio-demographic characteristics (e.g. age, gender, SES, etc.), characteristics of animal exposure (e.g. bites, type of animal, etc.) and actions taken by the exposed victim following an exposure.

All the subjects were provided complete PEP as per WHO recommendation, by the corresponding author who is an expert in the field for > 20 years. As a part of PEP, all the study subjects were provided RIG/ RMAb by using

different kinds of needles i.e., conventional single bore needle of 20-24 size or multi-bore needle with 6-10 holes of same size and compared the mechanism of action and safety of different technical device/ needle for wound infiltration of RIG/ RMAb.

Fig. 1: Cross-section of the proffered embodiment of injecting needle 20-24 size



All the collected details were compiled in an Excel sheet and analysed using descriptive statistics like frequency and percentages.

Results:

The study included 45 animal bite cases; among whom 44.4% were < 20 years, 33.3% from 20-40 years and 22.2% were > 40 years. Majority (66.6%) of the bite victims were males and most of them are from above poverty line (66.6%) and were from urban areas (71.1%). Dog was the biting animal for most of the patients (71.1%); followed by cat (22.2%), fox (4.4%) and 1 case of exposure to mongoose.

Among the study subjects, majority of the bites were on leg (53.3%) and forearm (26.6%) followed by face (11.1%), neck (4.4%) and abdomen (4.4%). Most of the wounds were measuring 5-10 cms (40%) followed by < 5cms (31.1%) and > 10 cms (28.8%). Most of the study subjects (80%) reported to the health care facility within 48 hours after exposure.

The following table shows the details of the needles used for the study and the amount of RIG/ RMAb infiltration.

Table – 1 : Distribution of patients according to site of animal bite. (n=45)

Site of animal bite	Number	Percentage (%)
Leg	24	53.33
Fore arm	12	26.66
Neck	02	04.44
Face	05	11.11
Anterior abdominal wall	02	04.44
Total	**45**	**100**

Table 1 reveals that majority of the site of the animal bite was leg (53.33%) followed by fore arm (26.66%) and face (11.11).

Table – 2: Distribution of patients according to measurement of wound. (n=45)

Measurement of wound	Number	Percentage (%)
< 5 cm	14	31.11
> 5 – 10 cm	18	40.00
> 10 cm and above	13	28.88
Total	**45**	**100**

Table 2 reveals that majority of the measurement of wound was > 5-10 cm (40%) followed by < 5 cm (31.1%).

Table – 3: Distribution of patients according to reporting of animal bite cases in the centre. (n=45)

Reporting of animal bite cases	Number	Percentage (%)
Early Reporting (within 48 hrs)	36	80.00
Late reporting (after 48 hours)	09	20.00
Total	**45**	**100**

Table 3 reveals that majority of the respondents reported within 48 hours after animal bite (80%).

Table – 4: Distribution of patients according to primary wound toilet. (n=45)

Primary wound toilet	Number	Percentage (%)
Adequate	04	08.88
Inadequate	41	91.11
Total	**45**	**100**

Table 4 reveals that 91.11% of the respondents toilet their wound inadequately.

Table 5: Distribution of condition of biting animals. (n=45).

Condition of biting animals	Number	Percentage (%)
Living	15	33.33
Dead	14	31.11
Untraced	16	35.55
Total	**45**	**100**

Table 5 reveals that majority of biting animals were untraced (35.55%) followed by dead (31.11%) and living (33.33%).

Table 6: Details of the needles used for the study and the amount of RIG/ RMAb infiltration

Particulars	Conventional single bore needle 20-24 size	Needle with open front end and side holes in single plane of the needle 20-24 size	Needle with side hole according to the presently developed needle 20-24 size
Subjects (n=15)	Subjects (n=15)	Subjects (n=15)	Subjects (n=15)
Hole size	0.2-0.5 mm	0.2-0.5 mm	0.2-0.5 mm
No. of hole	1	6-10	6-10
Average Amount of RIG/ RMAb infiltrated	6 ml	6 ml	6 ml
No. of needle prick a. Single wound			
<3.5 cm	1.5*	1*	1*
>3.5-4 cm	3*	2.5*	2*
b. multiple wounds	4.5*	3*	1*
Coverage of total area	Disproportionate, more in front of the needle	Inadequate and disproportionate	Substantially uniform coverage of wound area
Area covered by Infiltration	2.25cm*	2.75 cm*	> 4 cm*

*Mean Value

Fig. 2: Illustration of a conventional single bore 20-24 needle

Figure 3: Releasing of the injectate from the fluid/ medicament injecting needle 20-24 size of the new multi-bore needle.

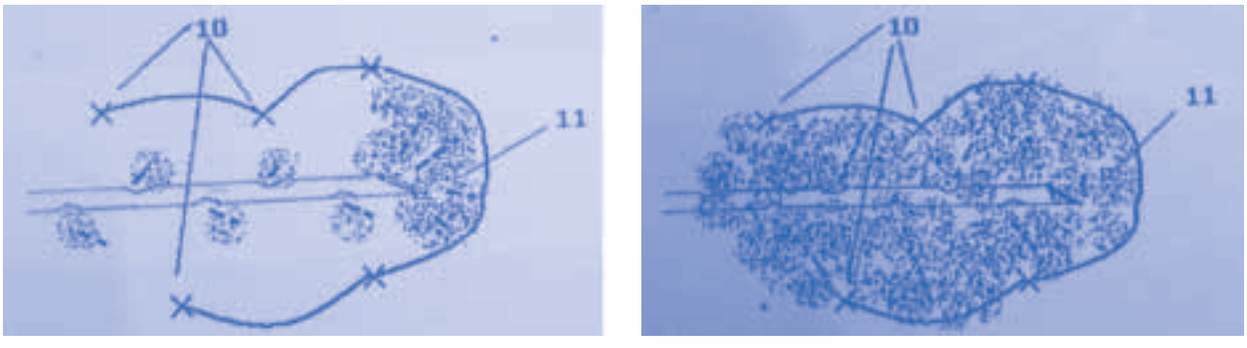


Figure 4: Type of delivery of RIG/ RMAb into the wound using different needles

All the study subjects experienced less pain and redness after using newly developed multi-bore needle when compared to conventional needle. All the study subjects were followed up for 6 months from the administration of PEP and all were found to be healthy and alive.

Result related to objective to initiate use of new technical device for infiltration of Rabies Immunoglobulin in case of animal bite wound.

Thus while traditional needles do continue to serve the basic purpose of injecting drugs/actives for treating various conditions, there are certain conditions / requirements especially where some urgent localized and uniform distribution of the drug/active is required, injecting of actives through such conventional needles with single hole is found to be not only not effective for the purposes of desired drug delivery in localized regions but also is found to lead to loss of expensive drug / active since by the time it may reach the region of treatment in an around the spot of the needle piercing the body, the desired effect may either be not achieved with in the stipulated time or may be lost in transit through the body.

It is to be noted that in cases where the uniform distribution of drug is desired involving such single bore needle the attending physician has to go for multiple pricks/ injections in various locations surrounding the wound area to totally cover the affected region. Such multiple prick/ injections not only seriously aggravates the pain of the subject being administered with the drug/actives but more importantly, such multiple pricks in an around the wound region expose the subject to further infection which can have very fatal consequences due to an increased risk of viral entry through many pores.

The advantage of the present invention is specially directed to needles for injections for delivering drug/ medicaments such as hypodermic needles with very fine internal dimensions such as the 20-24 no. needles which

would enable efficient administration of local anaesthesia ensuring that the same does not expose the subject to unwanted additional pain avoiding possibilities of multiple pricks and also not to expose the subject during injection of actives/drugs to further unwanted infections.

Table 9: The specification different needles

Variable	Conventional single bore needle	Needle with open front end and side holes disposed in a single plane of the needle cannula	Needle with open endand side holes disposed in diametrically opposite sides (not in same plane) of the needle cannula along.	Needle of the present invention: closed front end and side holes disposed diametrically opposite sides (not in same plane) of cannula along.
Size (gauze)	20-24	20-24	20-24	20-24
Hole size	0.2-0.5 mm	0.2-0.5 mm	0.2-0.5 mm	0.2-0.5 mm
No. of hole	1	6-16	6-16	6-16
Length	26-38 mm	26-38 mm	26-38 mm	26-38 mm
Position of holes	Tip of the needle	Parallel both sides	Criss-cross	Criss-cross
Distance between two consecutive side holes	N.A.	4-6 mm	4-6 mm	4-6 mm
Shape	Round-body	Round-body	Round-body	Round-body
Tip	Open and pointed	Open and pointed	Open and pointed	Closed and pointed
Chance of breaking	Minimum	Brittle can break within tissue	Minimum	Minimum
Pressure	Maximum in front of the needle	Inadequate	Disproportionate	Substantially uniform
Purpose of use	Injecting drugs	Not suitable for RIG administration	Not suitable for RIG administration	Perfectively suitable for RIG administration
Coverage of total area	Disproportionate, more in front of the needle	Inadequate and disproportionate	Disproportionate	Substantially uniform coverage of wound area
Uniformity of distribution of fluid	More in front	Non uniform	Non uniform	Symmetric around the needle

It has also been found that the stated selective criss-cross disposition of the holes with blocked front tip needles also improvesthe rigidity to the construction of the needle and makes it safe for administration of drugs unlike other randomly created holes or other configurations which render such needles brittle and prone to breakage and thus unsafe for use.

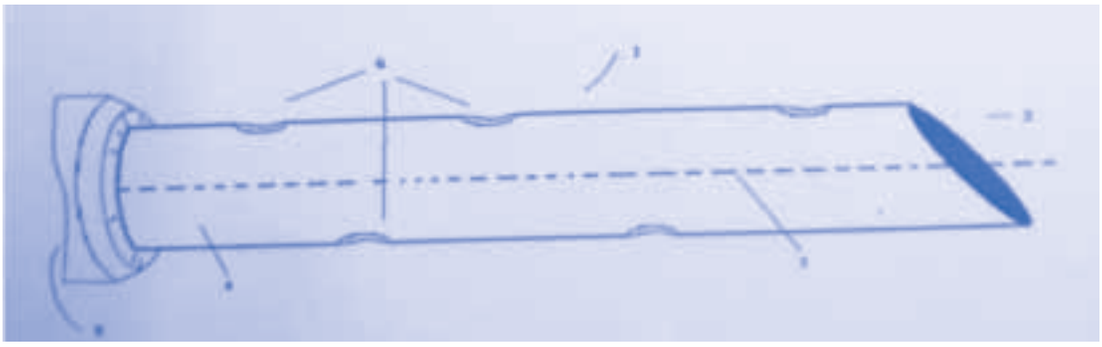


Figure 5: Illustration of a preferred embodiment of fluid/medicament injecting needle 20-24 size selectively disposed side holes

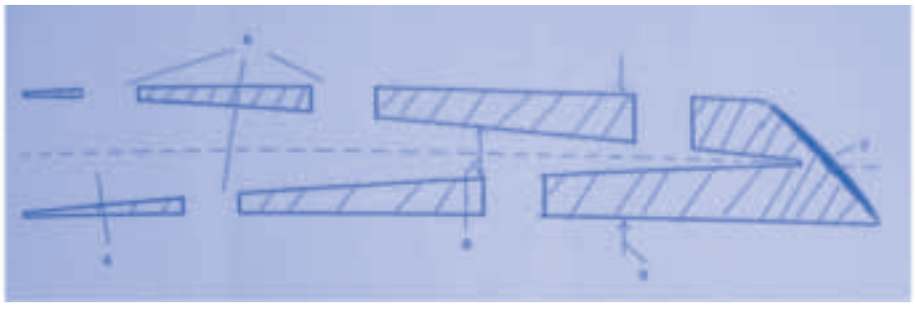


Figure 6: Cross sectional view of the preferred embodiment of fluid/medicament injecting needle 20-24 size

Figure 7: Benefit of the closed front end of the needle 20-24 size of the invention which favours unwanted loss of fluids

Figure 8: Irregular distribution of RIG in the base of the wound through single bore needle with front open

Figure 9: Benefit of the closed front end of the needle 20-24 size of the invention which favours unwanted loss of fluids

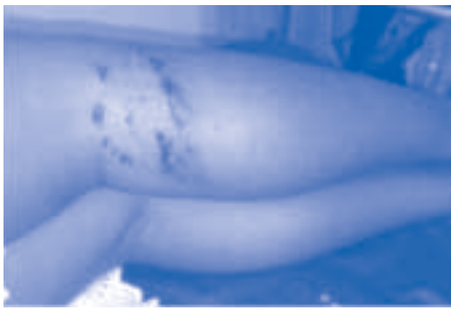


Figure 10

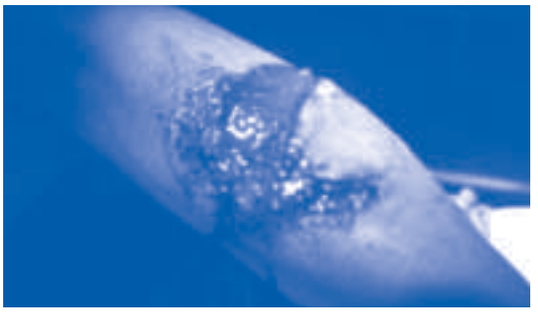


Figure 11

Dog bite treated with vaccination and RIG infiltration through Poddar Multi Bore Needle

Figure 12: Showing the technique of RIG administration using PMBN with uniform distribution of RIG through the base of wound

Discussion:

In India, where an approximated 17.4 million bites occur every year; with majority of them being category III exposures; RIG/ RMAb infiltration to all such wounds are necessary to prevent rabies in the exposed individuals.12 RIG/ RMAb are readymade antibodies, which provide passive immunity and helps in tiding of the initial phase, since any modern cell culture vaccine takes a minimum of 7-14 days to elicit required antibody titre to protect against rabies.

Therefore, providing RIG/ RMAb for all category III exposures is important for completing PEP. The present study was conducted to ease the administration of RIG/ RMAb in a more acceptable way and, in particularly, improved needles for injections to infiltrate localized regions effectively and efficiently.

The uniform delivery of the drug/medicaments over a spread region in the tissue by involving the newly developed needle, enable efficient administration of RIG/ RMAb ensuring uniform distribution of the drug/medicaments in the region of its intended application without involving multiple pricks and consequently avoiding possible contamination/virus infiltration in wound / affected /treatment area. It has also been found that the stated selective criss-cross disposition of the holes with such fine dimensions also favour required rigidity to the construction and is safe for administration of drug unlike other randomly created holes or other configurations which render such needles brittle and prone to breakage and thus unsafe for use.

Conclusion:

The multi-bore needle can be used to uniformly administer the RIG/ RMAb without the need for painful multiple pricks. It may be recommended for RIG infiltration which allows better distribution and absorption

It would be apparent from the above results that the needle of the present invention achieved the desired end attributes for safe, patient friendly administration of the drug with least number of pricks. The combination of diametrically opposite disposed side holes withblocked tip provided for the desired back pressure to facilitate the above advantages of administration involving the needle of the invention. Such an arrangement of holes is found to be special and not only improves efficacy of administration but also makes the needle rigid and unbreakable during administration.

References

1. *World Health Organization. Weekly Epidemiological Record. Rabies vaccines: WHO position paper No. 16. 2018;93:201–20.*
2. *National Rabies Control Programme. National guidelines for rabies prophylaxis, National Centre for Diseases Control, Ministry of Health and Family Welfare, New Delhi, India. 2015. p. 7-12.*
3. *T R Behera, P K Kar, M R Jena, Failure of Antibody Production to Intra Dermal Rabies Vaccination in Management of Category III Animal Bite: A Case Report; Journal of Communicable Diseases 2016;48(4):36-40.*
4. *T R Behera, Failure of antibody production to intra dermal rabies vaccination in the management of category III animal bite: an unusual case report; APCRI Journal 2016; 12(2):12-15.*
5. *WHO Expert Consultation on Rabies. Third report. Technical Report Series No. 1012. Geneva: World Health Organization; 2018.*
6. *WHO fact sheet on rabies. Available at http://www.who.int /mediacentre /factsheets / fs099/en/ accessed in May 2018.*
7. *Rabies vaccines and immunoglobulins: WHO position, World Heatlh Organization, 2018*
8. *Sudarshan MK, Madhusudana SN, Mahendra BJ, Rao NSN, Ashwath Narayana DH, Abdul Rahman, et al. Assessing the burden of human rabies in India: results of a national multi-center epidemiological survey. Int J Infect Dis. 2007;11(1):29-35.*
9. *Ravish HS, Rupsa Banerjee, DH Ashwath Narayana, Rachana Annadani. Safety of Equine rabies immunoglobulin in children. APCRI Journal 2014;16(1):7-9.*
10. *World Health Organization. New global strategic plan to eliminate dog-mediated rabies by 2030, 2018. Available from http:// www.who.int/news-room/new-global-strategic-plan-to-eliminate-dog-mediated-rabies-by-2030.Accessed on 15.10.2018.*
11. *Zero by 30: The global strategic plan to end human deaths from dog mediated rabies by 2030. Food and Agriculture Organization of the United Nations; World Organisation for Animal Health; World Health Organization and Global Alliance for Rabies Control Geneva, 2018*
12. *Sudarshan MK, Mahendra BJ, Madhusudana SN, Ashwath Narayana DH, Abdul Rahman, Rao NSN, et al. An epidemiological study of animal bites in India: results of a WHO sponsored national multi-centric rabies survey. J Commun Dis 2006;38(1):32-9.*

Acknowledgments:

The author's are grateful to Mrs. Dipali Poddar, Director, HP Poddar Memorial Clinic and Nursing home and Institute of Animal Bite Management for allowing us to do the relevant study.

The author's are grateful to Dr. Sourav Sanyal, GDMM, PGDM Management and Data science consultant, Kolkata.

Thanks to Mr. Jitendra Singh, Mr. Arijit Basak, Mr. Pintu Saha, Mr. Tirthankar Das and Mr. Shyamal Kumar Mitra for the support in preparing this article.

Reviewer:

Prof. Dr. H. S. Ravish, MD Prof. Community Medicine, KIMS Hospitasl, Bengaluru

Prof. Dr. Santanu Munshi, MD DM, Head, Dept. of Pharmacology, Calcutta National Medical College & Hospital, Kolkata