ORIGINAL ARTICLE

Intradermal administration of Rabies Vaccine at an affordable cost: Experience from tertiary care hospital in Jammu

Deepika Dewan[1], Suresh Kotwal[2], Abroo Bashir[3], Dinesh Kumar[4]

[1]Medical officer, Post Graduate Department of Community Medicine, Government Medical College, Jammu; [2]Senior Resident, Post Graduate Department of Community Medicine, Government Medical College, Jammu, [3]Senior Resident, Post Graduate Department of Community Medicine, Government Medical College, Srinagar; [4]Professor & Head, Post Graduate Department of Community Medicine, Government Medical College Jammu.

Abstract | Introduction | Methodology | Results | Conclusion | References | Citation | Tables / Figures

Corresponding Author

Address for Correspondence: Dr Dinesh Kumar, Professor & Head, Department of Community Medicine, Government Medical College, Jammu
E Mail ID: kumardineshpsm@gmail.com

Citation

Dewan D, Kotwal S, Bashir A, Kumar D. Intradermal administration of Rabies Vaccine at an affordable cost: Experience from tertiary care hospital in Jammu. Indian J Comm Health. 2018; 30, 3: 213-218.

Source of Funding: Nil **Conflict of Interest:** None declared

Article Cycle

Received: 02/07/2018; **Revision:** 19/08/2018; **Accepted:**24/09/2018; **Published:**30/09/2018

Abstract

Background: Rabies continue to be a major public health challenge in India. It can certainly be prevented by timely and appropriate administration of WHO recommended pre and post exposure prophylaxis. Intradermal regimen is running successfully and beneficial both in monetary as well as non-monetary terms. **Aim& Objective:**To evaluate the reduction in direct cost incurred with the use of intradermal regimen as compared to intramuscular regimen. **Settings and Design**: The present cross-sectional study was conducted in Government Medical College Jammu, a tertiary care centre. **Methods and Material**: A total of 17535 patients attending Anti Rabies Section of GMC Jammu were studied from Jan 2015 to September 2017.The patients belonging to Category II and III received 0.1 ml 2 site ID purified vero cell culture vaccine (PVCCV) on days 0, 3, 7 and 28 (2-2-2-0-2) and Rabies Immunoglobulin (RIG)(Category III only). Cost borne per patient receiving intradermal regimen was calculated and compared with cost borne in case Intramuscular regimen would have been used. **Statistical analysis:** Results were presented in descriptive manner using percentages and proportions. **Conclusions**: Intradermal regimen reduces the direct cost as compared to intramuscular regimen.

Keywords

Intradermal regimen; Rabies; Rabies vaccine; Post exposure prophylaxis

Introduction

Rabies still remains an under-reported neglected zoonosis with a case-fatality rate of almost 100% in humans and animals. Worldwide, it claims an estimated 59,000 human lives annually, mostly among underserved populations in Africa and Asia (1) Dog mediated rabies accounts for about 99% of human rabies cases.

In India, rabies is a major public health problem with annual incidence of deaths to be around 18,000 to 20,000. (2) However, the true burden of Rabies in India is not known and we can say that the reported incidence is probably an underestimation due to poor surveillance and reporting system. Worst affected section of the society affected are poor and underserved as they are less aware, cannot afford

treatment, transport and poor access to health care facility.

Cell culture vaccines administered through intramuscular route as pre/post exposure prophylaxis are costly thus limiting its wide spread use. The regimen approved by the WHO/DCGI India is the Intradermal (ID) Updated Thai Red Cross Regimen (TRC), which was later modified as 2 sites ID on Day 0,3 and 7. (3) Use of Intradermal regimen is less costly as compared to 5 dose Essen intramuscular regimen. It also reduces the volume of vaccine required thus reducing the vaccine cost by 60-80%. (4) Intradermal regimen elicits equivalent immune response as the 5-dose intramuscular Essen or 4-dose Zagreb regimens. (5) Considering it more useful in low resource settings, the present study was conceptualized to document the reduction in direct cost with the use of intradermal regimen in government settings.

Aims & Objectives

To evaluate the reduction in direct cost incurred with the use of intradermal regimen as compared to intramuscular regimen

Material & Methods

Study Design: The present study design was cross sectional. **Study Population**: The study participants were the persons attending antirabies OPD of Post Graduate Department of Community Medicine in GMC Jammu during the time period of Jan 2015 to Sep 2017. **Ethical Approval**: Prior approval from Institutional Ethics Committee Government Medical College Jammu (IECGMCJ) was obtained before commencing the study. All the new cases of animal bites/exposures reported during the period were included in the study.

Consent: After explaining the purpose of study and obtaining verbal informed consent from the patients attending Anti Rabies OPD, all patients were interviewed with the aid of preformed structured questionnaire. Data was collected in clinic up to the end of study period. All the patients were enquired about sociodemographic profile, type of bites including site, duration, category of exposure, contact with saliva, wound toilet, treatment including both active and passive immunization. The cases of animal bites/exposure were classified as per guidelines given by World Health Organization (WHO) (6). Patients received WHO recommended Post exposure prophylaxis as per category of exposure. Wound cleansing for at least fifteen minutes with soap or detergent and copius amount of water, followed by topical application of an iodine containing or similar virucidal to the wound was practised. All category 2 wounds were treated with WHO pre-qualified Purified Vero cell culture Rabies Vaccine (PVCCV 1 ml vial) having proven safety and immunogenicity, approved for intradermal injection. RIG was administered for severe category III exposures. Wounds that require suturing were sutured loosely and only after RIG infiltration. 0.1 mL of reconstituted vaccine per each of two ID sites (usually deltoid of both arms) per visit on days 0, 3, 7 and 28 (2-2-2-0-2) since our study ended before April 2018. Day 0 was the day of first dose administration of vaccine, and may not be the day of animal bite. The patient or his/her attendant was informed about the next dates of vaccine dosage and importance of completing the vaccination regimen. In case of a bite on the arm, the vaccine was given by the ID route on either thigh or on supra-scapular areas. GMC Jammu being government hospital is providing intradermal vaccines free of cost to all patients. However, Rabies Immunoglobulin (RIG) has to be purchased by patients themselves. The cost of vaccine supplied by government for intradermal use was noted from the supplies and purchase department of the hospital during the study period. It was around Rs 200 per vial for Government supply as compared to market price of Rs 400. The benefit in terms of expenditure to government was calculated in case if intramuscular regimen was used. Direct Cost per patient in seeking post exposure prophylaxis was also recorded. Data was entered in Microsoft Excel and results were presented descriptively in the form of percentages and proportions.

Results

We came across 17535 persons attending Anti rabies OPD of GMC Jammu during the period from January 2015 to September 2017. Maximum patients belonged to age group of 21-30 years followed by 11-20 years. (Table 1) Males were more in no. as compared to females. There were 75% males and nearly 25% females in our study. Patients were categorized as per WHO guidelines of risk exposure. Maximum patients belonged to category III (78%) followed by category II (21.5%) and Category I (13.2%). (Table 2)

Majority of patients 12438 (71%) reported to Anti Rabies section within first two days of bite/exposure. Only 5% of patients reported after 7 days. (Table 3)

Maximum patients had bites on lower extremities followed by patients having bites at multiple sites. (Table 4) Stray dog and pet dog bites accounted for majority cases of exposures followed by monkey bites However stray dog bites were almost double as compared to pet dog bites. Patients also reported exposures to rabid cattle, bear, mongoose, cats and squirrel. 67 patients had history of consumption of unboiled milk. (Table 5) Out of 17535 patients, 17504 patients received intradermal Purified vero cell culture vaccine .(Table 6) .Since each vial of 1 ml was used for average 5 patients, for 17504 patients ,approximately 14005 vials were used for completing entire course of intradermal regimen.(accounting for wastage as well).

Each vial costed around Rs 400 in the market. So, the total cost borne for providing intradermal regimen calculated was around Rs 5602000 and cost per patient was Rs 320 in case patient had to purchase vaccine for intradermal use from market.

Rabies Immunoglobulin (RIG) was given to 13464 patients. Out of them, 13455 received ERIG (Equine Rabies Immunoglobulin) and 9 patients received Human Rabies Immunoglobulin (HRIG.) Among patients receiving ERIG, 8886 received 2 vials per patient and 4569 received 1 vial per patient (as per thier body weight) and cost per patient was Rs 900 and Rs 450 respectively. (Each vial of ERIG costed around Rs 450 and HRIG (monoclonal) costed around Rs 1800). (Table 7)

But since in our setup government is supplying free intradermal vaccination to all patients and each vial in supply costed around Rs 200, the total cost borne by government for providing intradermal regimen calculated was around Rs 2801000 and cost per patient was Rs 160. If patients were to be administered full course of post exposure Prophylaxis using Essen Intramuscular regimen the cost borne would have been Rs 2000 per patient as compared to Rs 160 per patient in case of intradermal regimen. Percent reduction in cost for full course of vaccination using intradermal regimen came out to be 92%. (Table 8)

Discussion

As rabies is nearly 100% fatal disease, there is no contraindication to PEP. Pregnancy, lactation, infancy, old age and concurrent illness are no contraindications for rabies PEP in the event of an exposure. It is recommended that complete PEP should be given depending on the category of the exposure. Following WHO recommendations, results of clinical trials and international experience, Drug Controller General of India (DCGI) approved the use of safe, efficacious and feasible ID route of administration of Cell Culture Vaccines from February 2006 (4). Intradermal regimen for administration of Vaccine has been implemented in Anti Rabies Section since 2012. The present study highlights the economic advantages of using ID regimen.

Regarding demographic characteristics, more persons in the age group of 11 to 30 years could be due to the reason that young population is more involved in handling animal population as compared to older age groups. Children get unintentional exposure while playing or passing nearby, moreover they are also unaware of severity of animal bites making them more vulnerable. Males were more exposed as compared to females in the present study. Similar results were also described in various studies. (7) It has been usually seen that males are more involved in handling and managing animals both pets and wild whether they domestic or organizations. Nearly 84% patients reported within first three days of exposure and only 5% of patients reported for the first time 7 days after exposure. This indicated that awareness among general masses in timely approaching health care facility in case of exposure has been relatively good. However, we cannot make generalization regarding awareness levels on whole as we can comment only on patients attending health care facility. Proportion of population not seeking medical care in case of exposures also needs to be accounted for stray dog bites were the reason for maximum exposure among population which corroborates with the scenario in other developing countries as well. WHO recommendation of immunizing 70% of dog population to stop circulation of virus at the source (8) is the need of hour. Maximum bites were seen in lower extremities (Thigh, ankle, leg and foot). This could be due the fact that in most cases animals attack from the back and lower extremities are within their easy reach in standing position of person. The present study also reinforced the WHO recommendation of using intradermal regimen in developing countries where intramuscular regimen is less affordable and beyond reach of many. As we demonstrated, 92% reduction in cost in administering full course of vaccination using intradermal regimen as compared to scenario if

intramuscular regimen would have been used. Intradermal administration of these vaccine requires only 1–2 vials of vaccine to complete a full course of PEP, thereby reducing the volume used and the direct cost of vaccine by at least 60% compared with standard intramuscular vaccination as demonstrated in various studies.(9) Since theoretically only 0.8 mL of vaccine is needed for each patient, resulting in the use of ≈1 vial/patient considering wastage factor of vaccine 20% as opposed to five vials/patient that receive PEP using the IM route.

Corroborating results have been documented by other authors as well. Verma R also established that the ID route is ideal in terms of economic benefits, safety and efficacy. It reduces the cost of vaccination by about 68%.(10)

In a study done in Government setting in Pakistan, TRC-id regimen reduced the cost of vaccine to 1/5th of Essen regimen and was strongly recommended for institutions with large throughout.(11)

There is no evidence that intradermal administration requires vaccines with a potency higher than that recommended for intramuscularly administered rabies vaccines. (12) In 2015, WHO Member States and key partners set a global goal to achieve zero human deaths from dog transmitted rabies by 2030.(13)

Unfortunately, awareness of rabies prevention in most developing countries of the world including India is unsatisfactory. Most patients with exposure history do not report to a health center nor do they wash the bite wound with soap and adequate amount of water. Application of Chilli paste, surma, leaves, mud etc is still a prevalent practice in many parts of our country including our area. People resort to superstitions and visit quacks, traditional faith healers. Our Study on Knowledge, Attitude and Practices Regarding Management of Animal Bites Jammu published elsewhere also gave similar picture. (14) Adding more, the peripheral health centres do not assess wound severity correctly. Even in some larger health care centres, scenario is same. With the use of intradermal technique in low resource but high burden settings, atleast we are able to reduce the direct as well as indirect cost involved in monetary terms as well as travel time and expenses for patient visit. This is an attempt to increase compliance of patients towards Rabies treatment and prophylaxis. More IEC activities are required to make people more aware about this deadly disease.

Conclusion

Intradermal regimen reduces direct cost as compared to Intramuscular regimen.

Recommendation

In developing countries where the rabies load is high and resources are limited i.e. vaccine and money are in short supply, the ID route is ideal and should be practiced

Limitation of the study

Present study being cross sectional is prone to various biases. Patients attending health care facility are generally more aware and comparatively have better socioeconomic status. Generalizations should only be made keeping these factors in mind. Patients usually presented on day 2 or day 3 of bites so information retrieved from them is prone to recall bias. Only the direct cost borne by government in implementing intradermal PEP has been documented. Indirect Costs and Out of Pocket expenditure cost borne by patient, travel time, loss of wages could not be calculated due to limited resources, limited time and heavy patient burden

Relevance of the study

The study demonstrated that number of patients with varying degree of animal exposures presenting in tertiary care centre is high and pre/post exposure prophylaxis using WHO recommended vaccines using Intradermal regimen is more promising

Authors Contribution

DD: preparation of research study, data collection tools, data analysis, and interpretation; SK: data collection, analysis; AB: data collection, analysis; DK: approval of final research study, data analysis and interpretation

References

1. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, Barrat J, Blanton JD, Briggs DJ, Cleaveland S, Costa P, Freuling CM, Hiby E, Knopf L, Leanes F, Meslin FX, Metlin A, Miranda ME, Müller T, Nel LH, Recuenco S, Rupprecht CE, Schumacher C, Taylor L, Vigilato MA, Zinsstag J, Dushoff J; Global Alliance for Rabies Control Partners for Rabies Prevention. Estimating the global burden of endemic canine rabies. PLoS Negl Trop Dis. 2015 Apr 16;9(4):e0003709. doi: 10.1371/journal.pntd.0003709. eCollection 2015 Apr. Erratum in: PLoS Negl Trop Dis. 2015 May;9(5):e0003786. PubMed PMID: 25881058; PubMed Central PMCID: PMC4400070.[PubMed].
2. WHO. Eliminating rabies in India through awareness, treatment and vaccination. (2016). Available at :www.who.int/mediacentre/factsheet/fs099/en. Rabies vaccines and immunoglobulins: WHO position April 2018.

Available at www.who.int/rabies/resources/who_cds_ntd_nzd_2018.04/en/. Accessed 11/06/ 18.
3. Rabies vaccines and immunoglobulins: WHO position April 2018. Available at www.who.int/rabies/resources/who_cds_ntd_nzd_2018.04/en/. Accessed 11/06/ 18.
4. National Guidelines for Rabies Prophylaxis and Intra-dermal Administration of Cell Culture Rabies Vaccines. NICD 2007.
5. Hampson K, Cleaveland S, Briggs D (2011) Evaluation of cost-effective strategies for rabies post-exposure vaccination in low-income countries. Available at: PLoSNegl Trop Dis 5: e982. doi: 10.1371/journal.pntd. 0000982 PMID: 21408121. Accessed 11/06/ 18.
6. WHO Guide for Rabies Pre and Post Exposure Prophylaxis in Humans.Updated 2014. World Health Organization.Available at :www.who.int/rabies/PEP_Prophylaxis_guideline_15_12_2014.pdf. Accessed 11/06/ 18 .
7. MK Sudershan,SN Madhusudana.BJ Mahendra,N.S.NRao.DHAshwath, Narayana S, Abdul Rahman. Assessing the burden of human rabies in India: results of a national multi-center epidemiological survey. International Journal of Infectious diseases.2007;11(1):29-35.
8. World Health Oragnisation. Rabies Fact Sheet September 2010.Available at: http://www.who.int/mediacentre/factsheets/fs099/en/index.html. Accessed 11/06/ 18.
9. Chhabra M, Ichhpujani RL, Bhardwaj M, Tiwari KN, Panda RC, Lal S. Safety and immunogenicity of the intradermal Thai red cross (2-2-2-0-1-1) post exposure vaccination regimen in the Indian population using purified chick embryo cell rabies vaccine. Indian J Med Microbiol. 2005 Jan;23(1):24-8. PubMed PMID: 15928417.[PubMed].
10. Ramesh Verma, Pardeep Khanna, Shankar Prinja & Meena Rajput . Intra-dermal administration of rabies vaccines in developing countries: At an affordable cost, Human Vaccines.2011; 7:7, 792-794, DOI: 10.4161/hv.7.7.15410 Accessed 11/06/ 18.
11. Salahuddin N, Gohar MA, Baig-Ansari N. Reducing Cost of Rabies Post Exposure Prophylaxis: Experience of a Tertiary Care Hospital in Pakistan. PLoS Negl Trop Dis. 2016 Feb 26;10(2):e0004448. doi: 10.1371/journal.pntd.0004448. eCollection 2016 Feb. PubMed PMID: 26919606; PubMed Central PMCID: PMC4769324.[PubMed].
12. WHO position paper on rabies vaccines . Weekly Epidemiological Record, 2010, 85:309-320.
13. Global Elimination of rabies. The time is now. (2015). Available at:http://apps.who.int/iris/bitstream/10665/204621/1/WHO_HTM_NTD_NZD_2016.02_eng. pdf?ua=1. Accessed 11/06/ 18.
14. Sangral R, Lachala K, Kumar D, Shora TN, Dewan D, Sangra S. To Study the Knowledge, Attitude and Practices Regarding Management of Animal Bites Among General Population in A Rural Area of Jammu – A Community Based Cross-Sectional Study.Ind J of Research.2015;4(3):6-8

Tables

TABLE 1 AGE WISE DISTRIBUTION OF PATIENTS ATTENDING ANTI RABIES OPD

Age in Years	TOTALN(%)
<1 year	36 (0.20)
1-10	2554(14.6)
11-20	3300(18.8)
21-30	3794(21.6)
31-40	2798(15.9)
41-50	2358(13.4)
51-60	1552(8.9)
61-70	838(4.8)
71-80	247(1.4)
81-90	51(0.29)
91-100	7(0.03)
Total	17535(100)

TABLE 2 PROFILE OF PATIENTS ATTENDING ANTI RABIES OPD

Gender	TOTALN=17535
Male	13182(75.2%)
Female	4353(24.8%)
Category of Bite	
I	23(13.2%)
II	3778(21.5%)
III	13734(78.3%)

TABLE 3 DISTRIBUTION OF PATIENTS ACCORDING TO DAY OF REPORTING

Day of reporting	TOTAL
D1	5022
D2	7416
D3	2207
D4	985
D5	484
D6	240
D7	309
More than 7 days	872
Total	17535

TABLE 4 DISTRIBUTION OF PATIENTS ACCORDING TO SITE OF BITE

Site of Bite		Total
Upper Extremity	Head and Neck (Forehead, Head, Face, Neck)	236
	(Shoulder, Arm, Forearm, Hand, Finger)	3314
Chest / Trunk		174
Abdomen		94
Lower Extremity	(Thigh, Leg, Foot, Ankle)	8426
Back		520
Gluteal Region		468
Multiple Sites		4390
		17622

 # Each patient can have bite at one or more than one site.

TABLE 5 DISTRIBUTION OF PATIENTS ACCORDING SOURCE OF BITE

Source of Bite	Total
Stray Dog	9879
Pet Dog	5005
Rabid Dog	147
Rabid cattle	540
Monkey bite	754
Bear Bite	21
Rat bite	52
Mongoose	56
Squirrel bite	4
Cat bite	424
Any other animal	346
Other Sources of Exposure	
Consumption of unboiled milk	67
Contact with saliva	217
Total	17512

TABLE 6 DISTRIBUTION OF PATIENTS ACCORDING TO TREATMENT RECEIVED

Treatment received	Total
No Treatment required	11
TT only	12
TT and Anti rabies Vaccine	3778
TT, Antirabies Vaccine and Anti rabies serum	13734
Total	17535

TABLE 7 CONSUMPTION OF ANTI RABIES VACCINE AND RABIES IMMUNOGLOBULIN

	Type	No. of patients		No. of patients	No. of vials consumed	Total cost of vials (Rs)	Cost/patient (Rs)
Rabies Vaccine (Intradermal)	PVCCV	17504			14005	2801000	160
RIG (Rabies Immunoglobulin)	ERIG	13464	Requires 2 vials	8886	17772	7997400	900
			Require 1 vial	4569	4569	2056050	450
	HRIG	9	Requires 2 vials	4	8	14400	3600
			Require 1 vial	5	5	9000	1800

TABLE 8 COST SAVINGS OF VACCINE USING TRC-ID REGIMEN FOR 17504 PATIENTS

Regimen	Visit Schedule (No. of visits)	No. of vials consumed	Total Cost (Rs)	Cost per patient for full course of vaccination (Rs)	Cost Saving (Rs)	% reduction in cost for full course of vaccination
Essen Regimen	0,3,7, 14,28(5)	87520 (0.5 ml vial)	35008000	2000		100
TRC ID	0,3,7&28(4)	14005 (1 ml vial)	2801000	160	32207000	92