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Medical Science

COST ANALYSIS OF POST EXPOSURE PROPHYLAXIS OF RABIES AND FACTORS ASSOCIATED WITH DELAY IN ANTIRABIES VACCINATION IN A TERTIARY CARE CENTRE OF PATNA, BIHAR

KEY WORDS: Anti rabies vaccine, cost effective analysis, Post exposure prophylaxis

Dr. Rajesh Ranjan Sinha Associate Professor Department of Community Medicine, Patna Medical College, Patna

Dr. Ajay Krishna* Assistant Professor Department of Community Medicine, Patna Medical College, Patna *Corresponding Author

Dr. Khalid Anwar Junior Resident Department of Community Medicine, Patna Medical College, Patna

Dr. Dhananjay Kumar Tutor Department of Community Medicine, Patna Medical College, Patna

Dr Rashmi Singh Professor & Head, Department of Community Medicine, Patna Medical College, Patna

ABSTRACT

Objectives: The present study was conducted to analyse the direct and indirect cost of the post exposure prophylaxis of rabies vaccine using intramuscular route and Intradermal route and to find the factors associated with delay in taking anti rabies vaccine.

Material and Methods: We conducted a retrospective analysis of case records of a period from January 2016 to June 2018 at Immunization and Preventive clinic (IPC) of Patna Medical College Hospital (PMCH). The benefit in terms of expenditure to the Government and indirect cost of patient was calculated if ID regimen had been used in all these cases.

Results: Total 55026 cases of animal bite registered which include 52309 vials consumed during study period. By using Intradermal regimen less than 1 vial/patient is needed as compared to 5 vials /patient that receive PEP using IM route. Indirect costs involved in terms of man hour cost, travel time and expenses for that visit, can also be reduced. Rural locality and lower socio-economic class were main factors responsible for delayed antirabies vaccination in animal bite victims.

Conclusion: ID route reduces the cost of vaccination by about 30% and hence is ideal in terms of economic benefits, safety and efficacy.

INTRODUCTION

Number of incidences of human rabies is estimated to be between 30,000- 70,000 on annual basis, throughout the world. Among these, more than 90% of cases are reported from developing countries. This contributes to 20,000 deaths related to Rabies and 17.4 million cases of animal bites per annum. India and Philippines are the countries where the highest numbers of human deaths are observed due to rabies, wherein India accounts for 36% of the Global and 65% of the Asian rabies related deaths. [1] A nationwide survey reported that annual incidence of animal bites was 1.7% (2003) in India, more common in rural areas, among children and low income groups. [2]

In spite of this disease burden, rabies is a neglected infectious disease in India. Stray Dogs are the main biting animals followed by the cats. [2] To avert the rabies only effective pre- exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP) are used. [3] PEP includes anti-rabies vaccine administration, and for severe categories of exposure, infiltration of purified rabies immunoglobulin (RIG) in and around the wound. [4] RIG is rarely used in low and middle income countries, as it is very expensive and not regularly available[5-8]. Hence, in patients affected with animal bites only post exposure vaccination is provided. In the year 2007, out of all animal bite cases, 50% received PEP in India. Out of this almost 40% got nerve tissue vaccine (NTV) due to its low cost and free availability.[9]

In the year 2004 Government of India (GOI) banned use of NTV, and so patients of animal bites have only the option to purchase Tissue Culture Vaccine (TCV). Since Non-availability or irregular supply in public health system and high cost of TCV contributed to significant out-of-pocket expenditure (OOP) in the range of 1500-1800 Indian Rupees (Rs) for five doses under PEP. Therefore in 1997, World Health Organization (WHO) recommended intra-dermal (ID) TCV administration in resource-poor setting [10]. Immunological response and effectiveness of PEP via intra-dermal route has been found to be similar to other intra-muscular regimens [11]. In the year 2006, GOI recommended use of ID TCV administration under PEP [12]. Although some Indian states provide TCV free of cost through few public health facilities, irregular supply reduces its utilization. Loss of wages due to required multiple visits to the health facility has been incriminated in poor compliance to PEP. This has been also identified as a reason for increased rabies deaths especially in rural areas [12]. In many states of India intradermal administration of PEP is given but in some states like Bihar still intra muscular route administration of PEP is provided.

The present study was carried out with an objective to analyse the direct and indirect cost of the post exposure prophylaxis of rabies vaccine using intramuscular route and Intradermal route and to find the factors associated with delay in taking anti rabies vaccine of animal bite cases attending Immunization & preventive clinic at Patna Medical College Hospital (PMCH) Patna.

METHODOLOGY

This was a hospital based cross-sectional study of animal bite victims attending Immunization & Preventive Clinic, Patna Medical College & Hospital, Patna. Immunization & Preventive clinic runs under the Department of Community Medicine. We collected the data from the register maintained at rabies clinic, PMCH from the period January 2016 to June 2018 for the assessment of ARV vials consumed and to calculate the direct and indirect cost during this period. The cost of ARV for this period was calculated and compared with intradermal regimen (modified Thai schedule). It was noted that during this period purified Vero cell vaccine (PVCV) supplied by the hospital was used which cost about Rs 260/vial in the market. The benefit in terms of expenditure to the Government and indirect cost to patient and daily wages loss was calculated, if ID regimen had been used in all these cases.

We also interviewed patients who visited the clinic for vaccination in month of June 2018 to assess the biting pattern of animal and to assess the factors for delayed vaccination with ARV, if any. In the present study total 1759 Animals bite victims attended the immunization and preventive clinic at PMCH during the month of June 2018 in which 613 cases were new and 1146 were old cases. All new cases were selected for study, in which selection was random and only who gave consent to participate in study. 132 victims were selected and data were collected by personal interview of animal bite victims during visit for vaccination using pretested structured questionnaire.

Techniques applied were to interview and clinical examination of study subject. Pre tested semi structured Performa was used to collect interview data. Personnel interview of patient and clinical

examination was done for those clients who were selected. In case of children (<15 years) information were obtained from their attendants. Classification of animal bites, Appropriateness of wound management & post-exposure prophylaxis were as per WHO guidelines. Inclusion criteria of client were:-

(1.) All new patients attending IPC clinic, PMCH, who have been bitten by an animal likely to cause rabies,
(2.) Who are willing to participate in the study and to give consent.

Sites and Dose for Intradermal and Intramuscular Regimen

The regimen approved by the WHO/ DCGI India is the Updated Thai Red Cross Regimen involving injection of 0.1 mL of reconstituted vaccine per each of two ID sites per visit on days 0, 3, 7 and 28 (2-2-2-0-2). Day 0 is the day of first dose administration of IDRV, and may not be the day of animal bite. Only four visits are needed for complete immunization. In the intramuscular regimen which is being practised at IPV clinic 0.5 ml of vaccine is given intramuscularly on 0, 3, 7, 14 and 28 day. In the ID regimen, day 14 is skipped as compared to the IM regimen. [13, 14, 15]

The Data was entered in Microsoft Excel. Frequency tables were made for each identified outcome variables and chi square test used for showing association between study variables and delay for receiving ARV by Using IBM SPSS software version 21. The informed consent was obtained from the participants and their guardians in case of minor.

RESULTS

The data of vaccine consumed in terms of vial and total expenditure on this process from January 2016 to June 2018 was analysed. Total cases of animal bites were 55026 and total vials consumed for intramuscular vaccination were 52309 from January 2016 to June 2018. (Table 1)

Table 1: Total registered cases and vials used from Year 2016 to June 2018 at immunization and preventive clinic PMCH, Patna

Year	New cases	Old cases	Total	Total no of vial consumed
2016	6497	12763	19260	18435
2017	7423	15643	23066	21784
2018 (till june)	3955	8745	12700	12090
TOTAL	17875	37151	55026	52309

For intramuscular 1 ml ARV/ person is required hence one vial is used for one person. Since cost of one vial is about Rs 260, so cost of total vial for intramuscular vaccination is about 52309 x 260= Rs.1,36,00,340. In case of intradermal vaccine schedule only 0.1ml of vaccine per dose is required, hence in one vial about 4 persons will be vaccinated .Therefore total vial consumption in case of intradermal vaccination will be reduced to 13756 from 52309. So, cost of vaccination in case of intradermal route will also be reduced to 13756 x 260=Rs35,76,560 from Rs1,36,00,340. Hence on comparing total cost of intradermal vaccine with intramuscular vaccine we find that there is reduction in total cost about Rs 1,00,23,780 (around 1 crore rupees) which is more cost effective. Indirect costs involved in terms of man hour cost, travel time and expenses for that visit, can also be reduced. Taking minimum daily wages as Rs 257 per day [16] the total indirect cost of patient/ attendant also reduces from Rs 7,07,08,410 to Rs 5,65,66,728 in intradermal regimen i.e. around 1.4 crore rupees. So total direct and indirect saving would be approx Rs.2.5 crores for this period. (Table 2)

Table 2: Comparison between cost of intramuscular and intrade r mal vaccine

Variables	Intramuscular Route	Intradermal Route	Difference
No. Of visits	5 (5ml)	4 (0.8ml)	1
No of vials	52,309	13,756	38,553
Total cost of vaccines (A)(Rs.260/Vial)	1,36,00,340 (1.36 crore)	35,76,560 (35 lakhs)	1,00,23,780 (1 crore)
Cost of syringes (B) @ RS 4/-	2,09,236 (2 lakhs)	55,024 (55 thousand)	1,54,212 (1.5 lakhs)
Daily wages loss@RS 257/day.* (C)	7,07,08,410 (7 crore)	5,65,66,728 (5.65 crore)	1,41,41,682 (1.4 crore)
Total expenditure in Rs.(A+B+C)	8,45,17,986 (8.4 crore)	6,01,98,312 (6.01 crore)	2,43,19,674 (2.4 crore)

Out of 132 participants who were interviewed, 102 (77.3%) were male and 30 (22.7%) were female. 93(70.5%) subjects belonged to urban locality while 39 (29.5%) subjects belonged to rural locality. Children below 15 years were 46(34.8%) while above 45 years age group were 20 (15.2%). 13(9.8%) study subjects belonged to upper socio-economic class, 25(56.8%) belonged to middle class while 44(33.3%) belonged to lower socioeconomic status. Majority of animal bite cases were dog bite (90.9%) followed by monkey (7.6%) and cat 2(1.5%). 104(78.8%) cases were bitten by street animal while 28(21.2%) from pet animal. Maximum cases i.e 60.6% had category III bite, then category I (22.7%) and category II (16.7%) bite. Out of 132 participant 55.3% received ARV within 24 hr while 59(44.7%) received after 24 hr. (Table 3)

Table 3: ocio demographic profile of study participants and Biting Pattern of Animals in patients attending Immunization and preventive clinic

Variable		Frequency	Percentage
Gender	Male	102	77.3
	Female	30	22.7
Age group (in yrs)	0-14	46	34.8
	15-29	42	31.8
	30-45	24	18.2
	>45	20	15.2
Locality	Rural	39	29.5
	Urban	93	70.5
Literacy	Illiterate	20	15.2
	Primary	57	43.2
	High school and above	55	41.7
Socioeconomic	Upper	13	9.8
	Middle	75	56.8
	Lower	44	33.3
Biting animal	Dog	120	90.9
	Monkey	10	7.6
	Cat	2	1.5
	Others	0	0
Pet vs Street dog	Pet	28	21.2
	Street	104	78.8
Category of bite	I	30	22.7
	II	22	16.7
	III	80	60.6
Time Gap For receiving ARV (in Hrs.)	0-24	73	55.3
	>24	59	44.7

After studying the factor association with delays for receiving the vaccination, 58(56.9%) male received ARV within 24 hour while 44 (43.1%) male received after 24 hours. 15(50.0%) female received ARV within 24 hour while 15 (15.0%) female received after 24 hours. 14(35.9%) Cases from rural area received ARV within 24 hour while 25 (64.1%) after 24 hour. 59 cases (63.4%) from urban area received ARV within 24 hour while 34 (36.6%) after 24 hour and the association was statistically significant (P =.004). Upper (53.8%) and Middle class (64.0%) of socioeconomic status victims received early ARV as compared to lower socio-economic class (40.9%) and the association was statically significant (p=0.05). Others factors like Sex, Literacy, Categories of bite, type of animals and age group was not statistically association with time gap. (Table 4)

Table 4: Association between time gaps for receiving ARV with various factors

Variable		Time Gap		X^2 Value	P-Value
Locality		<24 hour	>24 hour	8.433	.004
	Rural	14(35.9)	25(64.1)		
	Urban	59(63.4)	34(36.6)		

Sex	Male	58(56.9)	44(43.1)	.442	.506
	Female	15(50.0)	15(50.0)		
Age group(in yr)	0-14	25(54.3)	21(45.7)	1.056	.788
	15-29	23(54.8)	19(45.2)		
	30-45	12(50.0)	12(50.0)		
	>45	13(65.0)	7(35.0)		
Socioeconomic	Upper	7(53.8)	6(46.2)	5.994	.050
	Middle	48(64.0)	27(36.0)		
	Lower	18(40.9)	26(59.1)		
Literacy	Illiterate	13(65)	7(35)	2.703	.259
	Primary	27(47.4)	30(52.6)		
	High School and above	33(60.0)	22(40.0)		
Category of Bite	I	20(66.7)	10(33.3)	2.104	.349
	II	12(54.5)	10(45.5)		
	III	41(51.2)	39(48.8)		
Type of Animals	Pet	18(64.3)	10(35.7)	1.160	.281
	Street	55(52.9)	49(47.1)		

(the figures in parenthesis denotes percentage)

DISCUSSION

In the present study we tried to find the cost effectiveness of intradermal ARV regimen in comparison to intramuscular route administration at a tertiary care hospital of Bihar i.e. Patna Medical College, Patna.

Intradermal ARV regimen is well compliant and more volume and cost-saving than intramuscular one. In ID regimen 0.1 ml vaccine per dose is used while in i.m. regimen 0.5ml per dose is used. In case of ID regimen 4 day visit to health facility is required while in i.m. regimen 5 day visit is required. Hence in ID regimen less than 1 vial/patient is needed as compared to 5 vials /patient in IM regimen. Vaccine shortage is a common problem in clinics and also in most Government hospitals. Most of those who turn up for treatment cannot afford to buy the complete schedule of vaccines as each dose ranging from Rs 260 to Rs300. So, by using ID regimen, we will be able to reduce the direct as well as indirect costs such as man-hour cost, travel time and expenses per visit. 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 5 vials/patient that receive PEP using the IM route. [15]

During the study, it was observed that majority of victims were male (77.3%) as compared to female (22.7%). Men are more prone than women because their involvement in outdoor activities, other studies also reported more number of male cases than female. Cases less than 15 year age group (34.8%) were more affected as compared to more than 45 year age group (15.2%). This shows that young adults are more prone for getting animal bite cases due to more exposure to outdoor activities. Behera et al. also noted that 46.4% of the victims of animal bite were from economically productive age group of 15 to 45 years. Children's are also more prone due to involvement of playful activities and lack of judgement about how to deal with dogs and other pet animals and their inability to fend off an attack, may put them their additional risk. [17, 18]

Maximum victims attending the IPC clinic at PMCH belonged from urban area that is 93 (70.5%). Cases from rural area have more delay than urban area. This could be due to easy accessibility of urban population to health care facility since maximum population covered by IPC clinic is urban area.

The victims of upper and middle socio-economic class received early ARV as compared to lower (40.9%) socioeconomic class. Knowledge, Awareness, litracy about rabies is low in lower socioeconomic class. Dog was the commonest animal for exposure i.e 90.9% cases. In India 96% of the rabies is due to bite from dogs. Sudarshan MK et al also found dog as the main biting animal(91.5%). [2,19] 55.3% victims received first dose of ARV within 24 hr while 44.7% received after 24hr. Almost similar finding was reported in a study where 68% received the first dose of ARV within 24 hr of the exposure. [20]

CONCLUSION

Data from preventive clinic PMCH shows that patients attending the clinic and ARV used is increasing year by year, adding financial burden for the purchase of ARVs. ID route administration will reduce the cost of vaccination by about 30% and hence is ideal in terms of economic benefits, safety and efficacy. ID administration requires some amount of technical skills which may be imparted by training health personnel and staff nurses.

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