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Research Article

Post-Exposure Prophylaxis in Animals: Insight on Biting Animals, Nature of Bites and Comparative Cost Analysis of Intradermal and Intramuscular Routes of Administration

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A B S T R A C T

Introduction: Rabies is an almost 100% fatal zoonosis and is only preventable through proper vaccination. Dogs are considered the main reservoirs (97%) of this disease. Vaccine supply for dogs is a global concern.

Methods: A comparative cross-sectional observational study analyzed the costs involved in the Rabies Control Programme in the Rampur Bushahr area, with intradermal (ID) immunization as an alternative to the standard intramuscular (IM) route for post-exposure prophylaxis (PEP).

Results: The study suggested achieving a similar immunogenicity and efficacy with five times less dosage compared to previous studies. This reduces the expenses of dog owners on vaccination costs by 5 times compared to intramuscular rabies vaccination (IMRV). Other miscellaneous and one-time expenses remain the same for intradermal rabies vaccination (IDRV) and IMRV regimens. It was seen that animal-to-animal bites are mainly through dogs (92.5%), followed by leopards, monkeys, and other wild animals, with lacerated wounds being the most common type (68.5%), followed by multiple wounds, abrasions, and puncture wounds.

Conclusion: The total cost incurred for PEP in the IDRV group was 13.6% less compared to the IMRV group.

Keywords: Cost Comparison, Intradermal Vaccination, Intramuscular Vaccination, Animal Rabies, Rabies Vaccination

Introduction

Animal bites are a major public health nuisance in most of the developing countries. With special reference to dog bites, rabies is transmitted to other animals as well as human beings.[1] Commonly, rabies is transmitted following the bite of a rabid dog (97%), cat (2%), and other animals (1%), i.e. mongoose, fox, wolf, jackal, and other wild animals.[2] Considering the seriousness of dog-mediated rabies, it is targeted for elimination from India by 2030. The high cost of vaccines and funding problems are the major concerns that personnel associated with the control of rabies in India are experiencing. In the Southeast Asia region, there are more animal exposures than in any other part of the world; by virtue of large human and dog populations living in congested habitat areas.[3] More than 1.4 billion people in this region are at risk of contracting rabies. Therefore, it continues to be a major public health and economic problem in most countries throughout the region.[4,5] There are 24.74 million dogs in India out of which 9.43 million are owned and 15.31 million are stray as per the 20th livestock census report[6] but now stray dog population rise has been considered to be approximately between 35–60 million dogs in India.[7] Mass dog vaccination needs a huge amount of 9 billion INR/ 120 million USD alone for rabies vaccinations annually.

In Himachal Pradesh, 89.97% of the land area is covered under rural settings,[8] and most people residing here are marginal farmers who can't afford costly treatment for themselves, let alone treating animals. Furthermore, rabies is not prioritized in the National Animal Disease Control Programme (NADCP) of the Department of Animal Husbandry[9] so that animals could get the free vaccines; this might again be due to the budgetary issue but has been covered under the National Action Plan for Rabies Elimination (NAPRE) by National Centre for Disease Control (NCDC, New Delhi), Ministry of Health & Family Welfare, Government of India[10]. The type of anti-rabies vaccine (ARV) and route of administration as well as the type of rabies immunoglobulin (RIG) used, significantly influence the cost of treatment/ vaccination. Sub-cutaneous and intramuscular (IM) routes are mainly used in animals for rabies vaccination, the intradermal (ID) route has also been proven to be equally effective with 10–20% dosage only.[11-13] With a collaborative One Health approach cutting down the cost of vaccination in animals is possible by using intradermal rabies vaccination (IDRV) instead of sub-cutaneous rabies vaccination (SCRV) and intramuscular rabies vaccination (IMRV) for both pre- and post-bite prophylaxis. Using one health approach, we may cut down the cost of mass dog vaccination (MDV) as well as PEP in animals by 80%. By this, 5 times less expenditure will be incurred in MDV and PEP in animals.

For animal bite victims, there is a promising PEP study that shows that 0.2 mL IDRV (middle of the neck) has more immunogenicity than 1 mL IMRV in domestic bovines for PrEP, as well as PEP, and local wound infiltration with eRIG is a life-saving treatment approach for bovines and equines.[12] Along similar lines, we have designed a PEP protocol for dogs too, using local wound infiltration of eRIG in the bite wound along with anti-rabies vaccination on days 0, 3, 7, 14, and 28.

Methods

Study Design

The study was conducted according to ARRIVE guidelines.[14] The economic analysis relied on data from a prospective observational study. The analysis was conducted with a societal perspective, including direct medical and non-medical costs, as well as indirect costs in terms of loss of wages, and it was conducted in accordance with methods for economic evaluation of healthcare programs.

Study Sites

The study was conducted at the Veterinary Polyclinic (VPC) in Rampur Bushahr Town, Shimla District, Himachal Pradesh, India (latitude 31.450926 and longitude 77.630768), as part of the implementation of an ongoing Rabies Control Program conducted by the Department of Animal Husbandry. The program focuses on advocacy, animal health promotion, and vaccination of the stray dog population, as well as the management of routine animal bite cases in the area.

Participants

The intervention group consisted of animals with animal bites presented by their owners at VPC-Rampur, with category III animal exposures, and were available for follow-up. All category II animal exposures and re-exposure cases visiting for PEP were excluded.

Intervention

For all dogs and other animals with category III bites, rabies vaccine was administered using both traditional IM and ID routes (0.2 mL in the pre-scapular site in dogs and middle of the neck in cows). All animals presented for PEP to the clinic were considered according to guidelines provided by the Department of Animal Husbandry, Himachal Pradesh.

PEP is not recommended by WHO for animals, but due to socio-economic reasons in India, PEP is practiced. PEP in animals follows a regimen similar to the human regimen of giving anti-rabies vaccine (ARV) on days 0, 3, 7, 14, and 28, known as the Essen regimen. The PEP schedule followed was in line with the One Health approach recommended by WHO for human beings.[15,16]

Implementation of Programme

The study was conducted as part of an ongoing Rabies

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Control Programme in Rampur Bushahr block of District Shimla, Himachal Pradesh state, India. The programme conducts mass dog vaccination for all stray and owned dogs, animal birth control programme, and rabies post-exposure prophylaxis in animal-bitten victims presented to Veterinary Polyclinic Rampur as per ARRIVE guidelines of animal experiments.[14] In any suspected rabid dog bite case in the Rampur Subdivision area, local bodies, non-government organizations, or locals are contacted in that area, and proper contact tracing was conducted for any animal-bitten victims. The animal owners were made aware of the future consequences of rabid dog bites to their animals and were advised to take proper anti-rabies prophylaxis after the incident.

Local representatives of Gram Panchayat were made aware of the seriousness of the matter and were further informed to make other people aware of it so that no animal victim goes unnoticed.

We have also designed a mobile application for recording rabies surveillance, vaccination data and animal birth control surgeries in collaboration with Mission Rabies NGO named WVS-Data collection application customized for District Shimla on a pilot basis. We have mapped all the talukas and veterinary institutions under district Shimla in the application for precise data collection as shown in Figure 1.

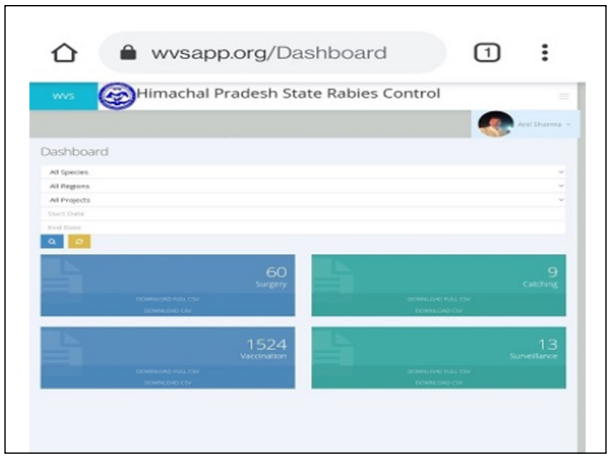

Figure 1.Himachal Pradesh Rabies Control Project, WVS-Data Collection Application

Sample Size

The size of the sample represented in the study was derived from the number of stray/ pet dogs and other animals presenting for PEP at Veterinary Polyclinic–Rampur Bushahr. Those reporting during the period December 2021 to May 2023 (98 dogs and 23 cows) were included in the study.

Outcome Measures

The outcomes of interest for the cost analysis of the implementation study were the total costs on average per animal receiving ID or IM route of PEP or vaccination.

Total Costs

Details regarding socio-demographic characteristics, characteristics of biting animals, details of animal exposure, and out-of-pocket expenditure for PEP and mass vaccination were collected. Direct costs, which include the amount spent on drugs and hospital charges, whereas indirect costs like loss of wages, travel of patients, and owners of pets, were also considered.

The cost of the anti-rabies vaccine used, i.e., inj. Raksharab 1 mL, is Rs. 150. The cost of vaccination by IM and ID routes was calculated based on the per mL price of the vaccine. The cost of equine rabies immunoglobulin (eRIG) per 5 mL was Rs. 500 per vial. We considered the average eRIG volume to be 1 mL per animal, so the tentative cost of eRIG per animal is Rs. 100.

Administrative charges include a registration fee of Re. 1 for the first visit on day 0 only; no administrative charges or other fees were taken for follow-ups.

Stepwise Post-Exposure Prophylaxis

Identification of the number of wounds (large, small, and punctuated): Proper shaving around the wounds/ bite sites is a crucial aspect to be performed,[17] which makes the identification of even punctuated wounds easier. The skin of animals is covered with hair, and we need to identify the bite sites by exploring the skin under the hair by shaving around the bite sites (Figure 2).

Figure 2.Shaving of the Bite Site, Showing the Bite Wounds

Sometimes, small wounds can go unnoticed, and if no local infiltration of these small punctuated wounds is done with eRIG, the animal can develop rabies. Wounds in areas like the oral cavity and nasal planum region should also be explored, as these are the most neglected regions where dog bites commonly occur, including regions above the neck.

In one instance, a dog presented with 2 bite wounds (one

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on the ear and another on the forelimb). When shaved and explored for the number of bites, there were 23 bite wounds in total, including 3 on the ear, 5 on the face, 4 on the neck, 5 on the limbs, and 6 in the oral cavity (Figures 3a and 3b).

In another case, a goat kid was presented with a history of 5 bite marks on its leg, but when properly shaved, there were 25 small bite wounds present on its leg (Figures 4a and 4b). Each wound was later infiltrated with eRIG in both cases, and the animals survived.

Figure 3a.Exploring the Bite Wounds in Oral Cavity

Figure 3b.Local Wound Infiltration in the Bite Wound Inside the Oral Cavity

Figure 4a.Hind Leg of Goat Kid Bitten by Suspected Rabid Dog

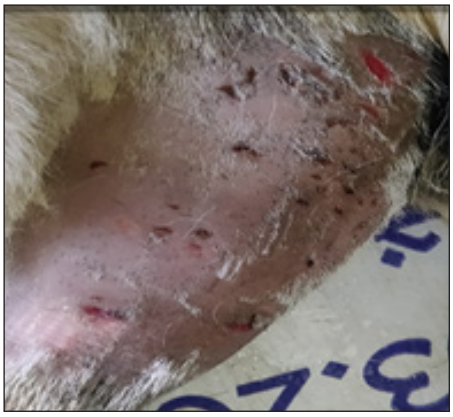

Figure 4b.Multiple Bite Wounds in a Goat Kid Visible Only After Shaving the Hairs

Wound washing: Wounds were properly washed after shaving and exploring every single bite wound. Wound washing should be done in running water with soap (preferably cloth washing soap) for about 15 min (Figure 5).

Figure 5.Wound Washing with Soap and Water for 10–15 Minutes

If it is a category III bite as per WHO standards, the bite wound was properly infiltrated with eRIG so that virus neutralization occurs immediately. We prefer to infiltrate eRIG on the bite wound within 24 hours, but it can be done up to 7 days if the first dose of vaccine is not administered. RIG is infiltrated superficially as well as deep into the bite wound to cover the whole length of the wound and every possibility to neutralize the rabies virus (Figure 6).

Figure 6.Infiltration of Bite Wound Sites with Equine Rabies Immunoglobulins (eRIG)

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The vaccination schedule for PEP followed was on days 0, 3, 7, 14, and 28. In one group, ID rabies vaccination was performed near the prescapular region with a 0.2 mL volume using an insulin syringe. A round bleb formed at the site of vaccination indicates successful vaccine delivery (Figure 7). We chose the prescapular region because there is a cluster of lymph nodes in that area, and the immune response generated will be comparatively prompt compared to other sites. This idea of administering the vaccine in the prescapular region is something we conceived and performed for the first time.[13]

In another group, we administered the vaccine by the IM route in the biceps femoris muscle with a 1 mL volume of vaccine (Figure 8), which is five times more than the volume used in the ID route of vaccine administration.

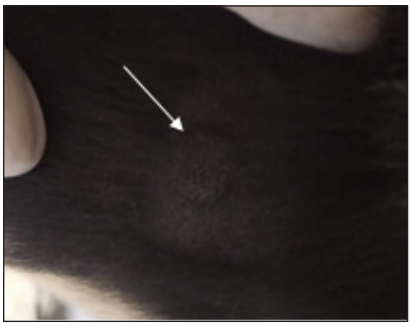

Figure 7.Bleb Formation after Intradermal Vaccination, Depicting Successful Vaccine Delivery

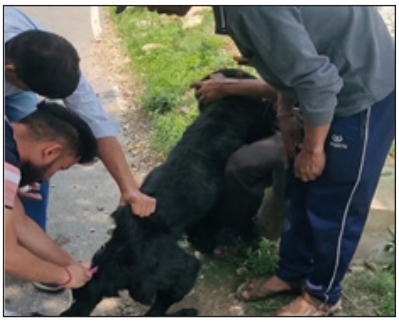

Figure 8.Injecting Anti-Rabies Vaccine via Intramuscular Route in Biceps Femoris Muscle

We conducted the Rabies Fluorescent Foci Inhibition Test (RFFIT) for rabies virus neutralization titer estimation on days 0 and 14. It was found that RFFIT titres were adequate (> 0.5 IU/mL) on day 14 in both the IM and ID groups. However, in one case administered with the IM vaccine, RFFIT titres were < 0.5 IU/mL on day 14.[13]

Tentatively, the cost of wound dressing per animal was approximately Rs. 70. The average cost of antibiotics, usually broad-spectrum antibiotic inj. ceftriaxone was Rs. 400 for each animal. The average cost of transportation per animal to a veterinary facility for each visit was Rs. 300, by hiring a private vehicle, auto, or public transport, for to-and-fro movement. Miscellaneous expenses included food cost, syringe and needle cost etc. and were calculated to be on average Rs. 100 per animal. Wage losses were calculated at Rs. 212 per day in reference to the Mahatma Gandhi National Rural Employment Guarantee Act scheme (MGNAREGA).[18]

Ethics Statement

The study was approved by the Institutional Animal Ethics Committee of DGCN, COVAS, CSKHPKV, vide approval No. CSKHPKV/COVAS/IAEC/13, dated 18/12/2021.

Results

The study included 98 dogs and 23 cows presented for post-exposure prophylaxis at the Veterinary Polyclinic in Rampur Bushahr. Out of 121 animals bitten by rabies-suspected and some bitten by rabies-confirmed dogs or other animals, 51 were given 0.2 mL of intradermal rabies vaccine near the prescapular region on days 0, 3, 7, 14, and 28, while 70 bitten dogs were given 1 mL of intramuscular rabies vaccine on the biceps femoris muscle on days 0, 3, 7, 14, and 28. Local wound infiltration was done for all category III bite wounds with equine rabies immunoglobulin (eRIG).

Table 1.Characteristics of Biting Animals

Characteristics of Biting Animal		IMRV (n = 70)	IDRV (n = 51)	Total (N = 121)	Percentage (%)
Biting animal	Dog	65	47	112	92.50
	Cat	-	1	1	0.82
	Monkey	-	1	1	0.82
	Leopard	3	2	5	4.10
	Bear	-	-	-	-
	Other wild animal	1	-	1	0.82
	Cow-to-cow saliva mixing	1	-	1	0.82
Vaccination status of biting animal	Vaccinated	6	8	14	11.50
	Unvaccinated	3	2	5	4.10
	Don't know	61	41	102	84.30

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Vaccination history of bitten animal	Vaccinated	15	7	22	18.20
	Unvaccinated	50	39	89	73.60
	Don't know	5	5	10	8.30
Fate of biting animal	Healthy	-	-	-	-
	Sick	-	-	-	-
	Died	5	5	10	8.30
	Killed	1	1	2	1.70
	Not traceable/ unknown	64	45	109	90.00

Table 2.Characteristics of Exposures

Characteristics of Exposure		IMRV (n = 70)	IDRV (n = 51)	Total (N = 121)	Percentage (%)
Place of bite	Home	3	2	5	4.13
	Outside home	67	49	116	95.87
Type of exposure	Abrasion	6	5	11	9.00
	Laceration	50	33	83	68.60
	Puncture wound	2	4	6	4.90
	Multiple wounds	12	9	21	17.40
Site of exposure	Forelimbs	14	12	26	21.50
	Hind limb	21	11	32	26.40
	Head, neck and face	20	20	40	33.00
	Abdominal region and genitals	9	5	14	11.50
	Multiple sites	6	2	8	6.60
Circumstance of bite	Provoked	14	11	25	20.70
	Unprovoked	52	35	87	71.90
	Unknown	4	5	9	7.40

Table 3.Cost Incurred for Post-Exposure Prophylaxis by Intramuscular Route and IDRV and Local Wound Infiltration with eRIG

Type of Cost (Rs.)	Day 0		Day 3		Day 7		Day 14		Day 28		Total	
Direct medical cost (Rs.)	IM	ID	IM	ID	IM	ID	IM	ID	IM	ID	IM	ID
Cost of ARV (Rs.)	150	30	150	30	150	30	150	30	150	30	750	30

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Average cost of eRIG (Rs.)	100	100	0	0	0	0	0	0	0	0	100	100
Administration charges (Rs.)	1	1	0	0	0	0	0	0	0	0	1	1
Cost of pre-medication (including shaving, washing, and antiseptic dressing of wound) (Rs.)	70	70	0	0	0	0	0	0	0	0	70	70
Cost of TT vaccination (Rs.)	10	10	0	0	0	0	0	0	0	0	10	10
Cost of antibiotics and anti-inflammatories (Rs.)	400	400	0	0	0	0	0	0	0	0	400	400
Total medical cost (Rs.)	731	601	150	30	150	30	150	30	150	30	1331	721
Direct non-medical cost (Rs.)												
Travel expenses for owner and animal (Rs.)	300	300	300	300	300	300	300	300	300	300	1500	1500
Other miscellaneous expenses (syringe, food, etc) (Rs.)	100	100	100	100	100	100	100	100	100	100	500	500
Total direct non-medical cost (Rs.)	400	400	400	400	400	400	400	400	400	400	400	400
Total direct cost (Rs.)	1131	1011	550	430	550	430	550	430	550	430	3331	2731
Indirect cost (Rs.)												
Loss of wages[a] (Rs.)	212	212	212	212	212	212	212	212	212	212	1060	1060
Total cost (Rs.)	1343	1223	862	642	862	642	862	642	862	642	4391	3791

[a]Indirect cost incurred included loss of wages and the same was calculated as per Mahatma Gandhi National Rural Employment Guarantee Act (MGNAREGA).[18]

Discussion

In India and some other countries, studies have examined providing PEP to animals. PEP in livestock animals is practiced in India due to socio-cultural and economic reasons that are unavoidable under given circumstances. In India, 49% of all veterinary rabies vaccine doses used are for pre-exposure vaccinations, 32% towards PEP in animals for economic reasons (mostly applied to cattle and buffaloes), and 19% to dogs due to emotional reasons. As mentioned above, religious sentiments and cultural aspects influence the decisions to practice PEP in animals.[19,20]

In this study, we provided PEP to dogs, cats, monkeys, cattle, and other domestic animals presented to us with a history of a dog/ cat bite or a wild animal bite. As shown in Table 1, it is evident that in 92.5% of cases, the biting animals were dogs, followed by leopards (4.13%), monkeys, other wild animals, and cows. Only 11.5% of biting animals were vaccinated against rabies, 4.1% were unvaccinated, and in 84.3%, the vaccination status was not known. Among the biting animals, 90% were not traceable, 1.7% were killed, and 8.3% died naturally.

In Table 2, it has been observed that most of the animal

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exposures took place while the animal victims were outside the home (95.8%), and in the majority of cases, the circumstances of the bite were unprovoked (71.9%). Lacerations were the most common type of wound (68.6%), followed by multiple wounds (17.4%), abrasions (9%), and puncture wounds (5%).

All bitten animals were provided with PEP, which included shaving around the bite site, thorough wound washing, applying equine rabies immunoglobulin on the bite site, and administering anti-rabies vaccination on days 0, 3, 7, 14, and 28. The cost of PEP with IMRV (n = 70) and IDRV (n = 51) groups was assessed among bitten animals.

Table 3 depicts that the cost of ARV for IDRV is five times less than for IMRV, but the direct medical cost incurred is 45.8% less in the IDRV group than in the IMRV group per dog. The direct non-medical cost is the same for both groups. The total direct cost incurred in the IDRV group is 18% less than in the IMRV group. Indirect costs include the loss of wages for animal attendants for visiting the veterinary facility, i.e., Rs. 212, which is the same for both groups.

The total cost incurred per animal per post-exposure in the IDRV group was Rs. 3991, and for the IMRV group, it was Rs. 4391. This shows that the total cost incurred for complete PEP in the IDRV group was 13.6% less than in the IMRV group.

Conclusion

In this study, we conclude that there were 4 steps to be followed for PEP in animals, i.e., shaving the hair near the bite site, washing the wound for about 15 minutes under running water with soap, local infiltration of eRIG, and anti-rabies vaccination.

Earlier studies have reported that rabies is mainly spread to human beings through dogs, accounting for 97–99% of bites. However, these reports pertained only to bites in human beings. In our study, we considered only animal-to-animal bites. It was observed that dogs were the main biting animals, responsible for 92.5% of bites in o ther animals, followed by leopards (4.13%), monkeys, and other wild animals. We also observed that lacerated wounds were the major type of wounds in animal-to-animal bites. For PEP in animals, intradermal rabies vaccination (IDRV) was found to be cost-effective, with 13.6% less expense in total compared to intramuscular rabies vaccination (IMRV).

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Conflict of Interest: None

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