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A cost evalauation analysis of treatment strategy in re-exposure animal bite cases

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Abstract
Background: The occurrence of repeat exposures to animal bite is quite common. Economic evaluations of such interventions are important tools for informing health policy.
Objective: A cost analysis was carried out to compare the re-exposure booster vaccination with serological test strategies with full Essen PEP treatment in re-exposure cases.
Methods: This retrospective study had been based on the data of last 10 years of an antirabies clinic.
Statistical Analysis: Frequency distribution with percentage proportion
Results: Overall, 2684(8.19%) out of 32735 cases had evidence of Re exposure of dog bite and in 962 (35.84%) cases, dog survived more than 10 days. Additional Re-exposure cases taking complete anti rabies vaccines were 626(27.4%). Cost benefit 495 per case if all Re exposure cases are treating as first exposure
Conclusion: Using the example of cost benefit analysis (CBA) of re-exposure animal bite case treatment by booster doses after RFFIT testing or as a PEP treatment (first exposure) we demonstrate that the PEP treatment in all animal bite cases have certainly cost evaluation with perspectives of covering total risk.
Implication: "Better and safer to over treat than under treat" in view of risk benefit analysis of rabies death in endemic India.

Keywords: Dog bite, Re-Exposure, treatment strategy

Introduction
Rabies is a viral zoonosis that occurs in more than 100 countries and territories in the world. It is transmitted to humans and other animals through close contact with saliva from infected animals, i.e., through bite, scratches, and licks on broken skin and mucus membranes. Although a number of carnivorous animals serve as natural reservoirs, dogs are the main source of human infections and pose a potential threat to more than 3.3 billion people.[1]
According to World Health Organization animal bites are a public health problem and an estimated 17.4 million animal bites occur annually, 30,000 persons die of rabies in India which constitutes 60% of the global report of 50,000 deaths[1]. One of the reasons for these deaths is the improper, inadequate and incomplete post exposure rabies prophylaxis by medical professionals[2]. This is attributed to low level of awareness about anti-rabies treatment amongst medical doctors more so for WHO recommendations on modern rabies prophylaxis[3]. In India, annually, on an average 1.7% of the population gets bitten by an animal, or suffer from a confirmed or suspected rabies exposure and some of these exposures are repeat exposures.[1] In rabies endemic areas like India, re-exposure to rabies is common with an incidence up to 15%.[4] Many of these repeat exposures occur in persons who have received PEP against rabies. However, the real burden of re-exposure in our country is not precisely known. Re-exposure to rabies is a short form of repeat exposure, or repeated exposure. In cases of re-exposure, the patient, in the past has suffered at least one for which the constitution is sought. [4] The medical doctors, particularly the general practitioners / family physicians who treat the majority of dog bites are often unclear and confused and hence provide inappropriate advice or treatment, which has sometimes resulted in development of rabies an death of the patients[5,] In this background a cost-minimization analysis was carried out to compare the re-exposure booster vaccination with serological test strategies and full Essen PEP treatment also in re-exposure as first exposure and The author has developed a clinical algorithm as a 3 steps "Decision chart" for rabies prophylaxis for use by medical practitioners in India. An effort has been made in this article to review the salient cost benefit and cost effective features in the field of rabies re exposure vaccination prophylaxis.

Methodology

This retrospective study was initiated after clearance from the institutional ethics committee of G.R. Medical College & JA Group of hospital, Gwalior, India. The author based on his experience of running an Institutional anti-rabies clinic for over 20 years had been collected animal bite cases and analyzed data of last 10 years of antirabies clinic of JA Group of Hospitals, Gwalior. We compared 2 strategies in the cost-evaluation Analysis. The first strategy was that re-exposure animal bite cases were treated as re-exposure case and alternate strategy was that all re-exposure animal bite cases were treated as first exposure and given them PEP treatment. In both strategy guidelines was taken as advised by WHO. Further has been calculated the cost of RFFIT antibody tire test plus two booster dose of ARV vaccination in first strategy. Cost-evaluation analysis using strategy full course treatment as PEP in all re-exposure cases marking to all as first exposure by providing 5 IM ARV in class II & III and RIG in class III bites.Statistical analysis was made by Frequency distribution with percentage proportion.

Result

Total cases of animal bite 32735 were collected in last ten years of 2005-2010. Out of them 2684(8.2%) of re-exposure cases total Victims 2282(85%)of re-exposure dog bite eligible for two dose of booster after diagnostic of sera antibody titre by RIFFT in which 402(15%) victims of class I category and 1718(64%), 564(21%) of Class II and III respectively. Out of 2282 re-exposure cases only 962(35.8%) re-exposure cases have PEP treatment history. In all re-exposure cases 894(33.3%) culprit dogs were survived more than 10 days. Total number of re-exposure cases 1946(90.5%) were taken complete PEP treatment from 2149(94.1%) re-exposure cases those initiated treatment while the expectation of taking complete treatment according to re-exposure booster dose treatment was 1320 (57.8%. it means 626 (27.4%) re-exposure cases had been taken additional anti rabies vaccines as complete PEP treatment. (Table 1)

We estimated the cost of treatment of each re-exposure case according to WHO criteria to be 2250INR, almost evenly split between the cost of Antibody titer test (RFFIT) [1600INR] and the two Booster dose of ARV vaccine (650INR. This compares reasonably well with the estimated average cost of PEP full course treatment of all re-exposure animal bite cases (1761 INR) (Fig 1).

Cost Comparison and Cost-Effectiveness

Considering direct costs only, booster vaccination and RFFIT testing results in incremental costs of 5.134 million INR of all 2282 re-exposure cases and 1.131 million INR for Costs for additional cases to take complete Anti Rabies Treatment and comparing in both strategies by cost every victims of dog bite could be able to save 495 INR in average by taking complete PEP treatment in place of two booster doses after RFFIT testing with more safety satisfaction. We consider the full treatment as first exposure to each re-exposure animal bite case to be economically attractive because the costs per event averted seem reasonable, this strategy remained dominant from a societal perspective and retained a still-attractive cost-effectiveness ratio of 100:80 using the per patient payer perspective.

For a theoretically equivalent immunogenicity for rabies virus, the cost of the alternative strategy (treated all re-exposure cases as first exposure) ranged from 20-25% lower than that of the two booster recommendations after confirmation of antibody titer by RFFIT.

Discussion

The occurrences of repeat exposures to animals are quite common and in many cases the second exposure is more serious in nature than the first, the second exposure may be caused by a confirmed rabid animal. This may lead to death of the patient due to rabies if the anamnestic response, depending on which the secondary exposure case is to be managed, is not strong enough, due to the altered state of the patient's immune system.[6]

Re-exposure to rabies is a short form of repeat exposure, or repeated exposure. In cases of re-exposure, the patient, in the past has suffered at least one for which the constitution is sought. In those cases where no post-exposure prophylaxis has been taken previously, the situation is treated similar to those with first exposure.[5]

This guideline of WHO do not specify the duration of protection provided by previous vaccination i.e. pre-exposure (PrEP) or post exposure prophylaxis. The WHO TRS 931, also mentions that Persons previously vaccinated with a potent and effective rabies vaccine (that meets WHO criteria) and have adequate document of antibody titer testing (after testing with RFFIT) should receive a two booster series consisting of one 1M or ID dose on day o and, another on day 3. [7]

The review of the Medical Literature on the topic of Boosters for re-exposure reveals that there are a lot of grey areas. There is a possibility of poor immune responders in more than 25% of the population. Patients do not come to their doctors, with labels about their immune status attached, to them. There is every possibility of poor immune responders succumbing to Rabies in a re-exposure case if not provided full PEP treatment.[8]

The results of our analysis strongly support the economic attractiveness of complete PEP vaccination of all first exposure as well as re-exposure animal bite cases. In geographic regions with a high burden of rabies virus infection and vaccination costs lower to those prescribed in re-exposure treatment program. The extent to which the results of this analysis are generalizable to other geographic regions depends largely on 3 factors: the incidence rate of re-exposure, vaccination costs, and antibody titer test RFFIT facility and its cost of treating rabies virus-related re-exposure illness.

Our analysis suggests that vaccinating all animal bite cases by complete Essen schedule IM/ID with RIG who remains at risk for rabies infection is cost-effective, because cost of antibody titer test (RFFIT) and fatalness of disease may alter the attractiveness of this re-exposure strategy of giving only two booster doses. Compared with re-exposure animal bite two booster dose models, validated prognostic model of complete PEP treatment even to re-exposure animal bite case may have a higher degree of Clinical fidelity and prognostic accuracy.

Thus there is a need for development of simple cost benefit strategy which can be performed without conflict and complications.

Recommendation

All cases of re exposure in which dogs are stray & unable to observe 10 days treated as first exposure will certainly cost

benefit as well as cost effective in place of re exposure booster dose

Implication of study

"Better and safer to over treat than under treat" in view of risk benefit analysis of safer modern vaccines vis-à-vis the risk of rabies death in endemic India.

Till then simple and inexpensive test for evaluation of antibody titre develop, can be performed in any laboratory especially for developing countries i.e., India adopting simple 3 step approach enable physician to make best decisions for post exposure rabies prophylaxis.

- Firstly, to examine & treat the wounds and decide category of bite. (step – 1)
- Secondly, to ascertain some details of biting animals (traceable or stray and was available/not available for 10 days observation (mostly the dog or cat). (step – 2).
- Thirdly, if a dog and cat available for observation prescribed pre-exposure prophylaxis schedule and if stray and not available for observation then to offer post exposure rabies prophylaxis (Essen schedule of 5 IM doses or ID schedule) with RIG in III category(code plan) (Step-3).

Abbreviation

1. RFFIT Rapid Fluorescent focus inhibition test
2. WHO World Health Organization
3. PEP Post Exposure Prophylaxis
4. INR Cost in Indian Rupees
5. IU International Unit
6. RIG Rabies Immunoglobulin

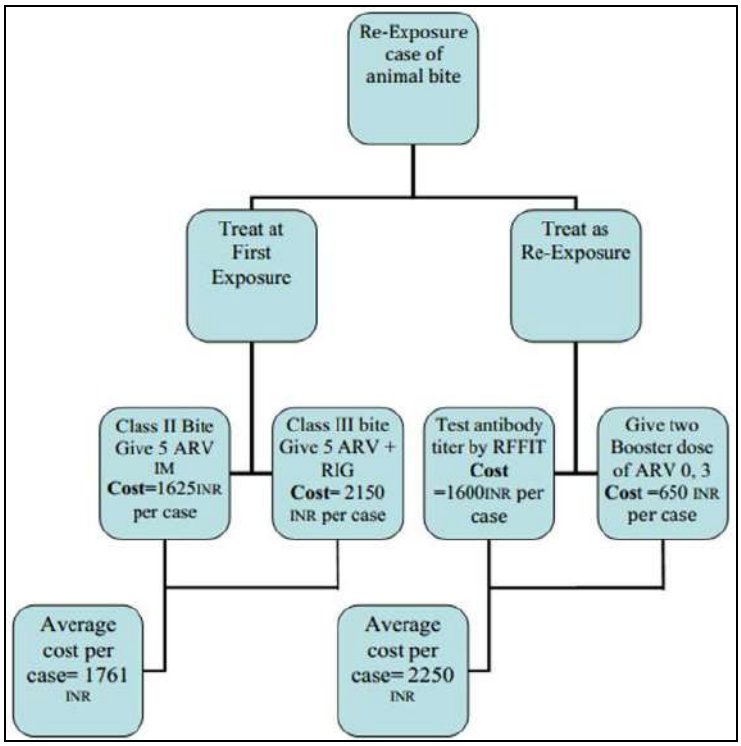

Fig 1: Decision model and cost benefit analysis for re-exposure of animal bite case

Table 1: Statistics of Dog bite, Re-exposure cases and Treatment status

Duration (1)	**2005-2015**		
Total No. of dog bite cases (2)	**32735**		
Total no. of re-exposure (2684) [8.19%:95%CI;7.2,9.2] (3**)**	Degree of bite		
	I No. (%)	II No. (%)	III No. (%)
	402 (14.9)	1718 (64.0)	564 (21.01)
Total Victims of re-exposure dog bite eligible for two dose of booster + after diagnostic of sera antibody titre by RIFFT (4)	II + III = 2282 (85.02%:95%CI;83.7,86.3)		
Complete previous PEP history in re-exposure cases (5)	962 (35.84%:CI;34.1,37.6)		
Total no of dog survived >10days in re-exposure cases (6)	894 (33.31%:CI;31.6,35.0)		
Total no of cases initiated ARV after re-exposure (2149, 94.17%) (7)	Degree of bite		
	I No. (%)	II No. (%)	III No. (%)
	0	1613 (93.8%: CI;92.9,94.7)	536(95.03%: CI;94.2,95.8)
Total no. of re-exposure cases taken complete PEP ***** (8)	1946(90.55%:95:CI;89.9,91.1)		
Expected re-exposure cases of Class II & III bite to take complete PEP (9)[4-5]	1320(57.84%:95%CI;57.0,58.6)		
Additional Re-exposure cases taking complete anti rabies vaccines 10(8-9)	626(27.4%:95%CI;26.7,28.1)		
***** ESSEN schedule of 5IM doses viz., 0,3,7,14, 28 days			

Table 2: Cost analysis of re-exposure treatment and first exposure (PEP) treatment of re-exposure dog bite cases

Costs for diagnostic of sera antibody titre in all re-exposure cases(class II & III=2282) and two doses of booster (2282×1600)** + (2282×650)***[4th column of Table 1]	5.134million
Costs for additional cases[Column 10th & column 7th of Table 1] to take complete Anti Rabies Treatment (626×1625 for ARV)+(536[III] × 525@ for RIG) =	1.313 Million
Cost benefit per case when treating all re exposure cases as first exposure.	495 INR per case
Rs. 1600/ Minimum Average price of RFFIT test(recommended by WHO TRS 931[7]) * Rs. 650 for 2 booster doses of tissue culture vaccine (Taking consideration Rs. 325/vial in retail price after averaging of 5 brand ARV @ Rs. 525/5ml vial (1500IU) retail price after averaging of 4 brands available in mkt.	

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