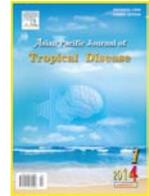




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Epidemiology and prevention of animal bite and human rabies in a rural community—One health experiment

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PEER REVIEW

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Comments

This is a good study in which the authors have come out with a novel idea and demonstrate the success of the one health experiment.
Details on Page S490

ABSTRACT

Objective: To estimate the incidence of human rabies and animal bite/exposure; to describe the post exposure prophylaxis received by animal bite/exposure cases; to assess the safety and immunogenicity of rabies vaccine (purified chick embryo cell vaccine) administered as pre-exposure vaccination for school children and risk groups by intradermal route in the rural community and to demonstrate a decrease in the incidence of human rabies and animal bite/exposures through implementation of one health experiment.

Methods: This prospective interventional study was conducted over a period of 2 years (December 2009–November 2011) in a rural area near Bangalore, Karnataka, South India and consisted of six villages (project villages), three villages were identified as study villages with active interventions (Implementation of rabies awareness activities, post exposure prophylaxis, pre-exposure intradermal rabies vaccine) and three villages as control villages without any active interventions.

Results: A majority of the animal bite cases were category III exposures and all of them had received rabies immunoglobulin and anti-rabies vaccine as per WHO recommendation. A majority received 3 to 5 doses of vaccine. Three hundred and sixty eight subjects had received pre-exposure intradermal rabies vaccination thrice on days 0, 7 and 28 d.

Conclusions: No human rabies case was reported during the study period and there was 30% decrease in animal bite/exposure cases in study villages after the one health experiment project was implemented. Pre-exposure vaccination was safe and immunogenic.

KEYWORDS

Animal bite, Incidence, Post exposure prophylaxis, Intradermal rabies vaccine, Pre-exposure prophylaxis

1. Introduction

There are no global estimates of dog-bite incidence, however studies suggest that dog-bites account for tens of millions of injuries annually[1]. An estimated 55000 people die annually from rabies, and bites from rabid dogs account for the vast majority of these deaths[2]. About 20000 human rabies deaths and 17.4 million animal bite cases occur in India annually which corresponds to an incidence rate of 1.7%. Ninety five percent of human rabies deaths are due

to dog bites[2]. Majority of human rabies victims are from rural areas and belong to lower socio-economic status. Two thirds of Indian population live in rural areas and are at risk of dog bites and rabies[2].

However when one looks at the prevention and control measures available for human and animal rabies in the country, it was observed that the different stake holders like medical, veterinary and animal welfare activist all work independent of each other and have not integrated their work at any level of the organization setup.

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In this background, the medical, veterinary and animal welfare professionals in a joint effort had come together in a novel project for the prevention and control of rabies and demonstrate a decrease in incidence of animal bite in a rural community with the concept of one health experiment[2]. The objective of this paper is to estimate the incidence of human rabies and animal bite/exposures, to describe the post exposure prophylaxis received by animal bite/exposure cases, to assess the safety and immunogenicity of rabies vaccine (purified chick embryo cell vaccine) (PCECV) administered as pre-exposure vaccination for school children and risk groups by intradermal route in the rural community, and to demonstrate a decrease in the incidence of human rabies and animal bite/exposure through implementation of one health experiment.

2. Materials and methods

This prospective interventional study was conducted over a period of two years (01 December 2009 to 30 November 2011) in a rural area. The project area was situated 25 km away from Bangalore city, Karnataka, India and consisted of six villages (project villages), three villages were identified as study villages with active interventions (Implementation of rabies awareness activities, post exposure prophylaxis, pre-exposure intradermal rabies vaccine) and three villages as control villages without any active interventions. These villages were selected for the reasons that two human rabies death was reported in the last eight years and animal rabies was enzootic in this area. All the people residing in these villages were the study subjects.

For the purpose of estimation of animal bite/exposure incidence 20% of the population was selected in each village by probability proportionate to size sampling technique. The first household was selected randomly and subsequently every fifth household in the village was surveyed by systematic random sampling technique. The institution ethical clearance was obtained before the start of the project. Informed consent from vaccinees and parent/guardian of children was taken for administration of pre-exposure rabies vaccination.

From the households selected an baseline survey (Beginning of the project) information on animal bite/exposure in the study subjects was obtained from an adult responsible respondent in the family aged between 18 to 60 years using pre-tested structured questionnaire in local language (Kannada) by interview technique. Subsequently based on the results available from the base line survey a series of socio-culturally acceptable rabies and animal bite behavior change and communication materials were developed which included outdoor wall painting having messages on rabies and animal bite prevention, post exposure prophylaxis, *etc*; posters on rabies post-exposure prophylaxis (PEP), responsible pet ownership and how to avoid animal and dog bites, *etc*; rabies video (local language) transmission through local cable network, indoor annual

wall calendar having message on rabies and animal bite prevention was distributed to all the households; folk dance performance; public rallies on rabies and animal bite awareness; rabies and animal bite education through chart on snake and ladder game for school children; school book label having messages on rabies and animal bite prevention, drawing competitions on rabies prevention in schools. Also training and orientation of formal and informal village leaders, women self-help groups, medical and veterinary personnel, school teachers and village level volunteers (rabies volunteers) on rabies and animal bite prevention. Lastly the same households were revisited again on completion of one year and endline survey of animal bite/exposure was done[3].

Post exposure prophylaxis was provided free of cost to all the animal bite victims from study villages *viz.* anti-rabies vaccine (ARV) for category-II exposures and ARV and rabies immunoglobulins for category-III exposures as per WHO recommendation[4]. For the animal bite victims residing in control villages, there was no active interventions. However they did receive treatment from the existing facilities at the villages apart from treatment provided by the project staff when informed. Data collected in the project was analyzed statistically using SPSS version 16.0. The descriptive statistics *viz.* percentages are computed to describe the data. In the inferential statistics, chi square test was applied to know the significant difference between baseline and end line survey. The data was presented in the form of tables and graphs wherever necessary. Geometric mean concentration and geometric standard deviation with 95% confidence intervals were applied to estimate the immunogenicity of pre-exposure intradermal rabies vaccine (IDRV).

3. Results

The total population of study villages was 10220 and in control villages was 6023. The general characters of the population as per the survey conducted in the sample 20% of the population is majority 69% and 67% of the population was in the age group of 15 to 55 years in study villages and control villages. Fifty one percent were males, 75% and 70% were literates, 30.7% and 22.8% were coolies by occupation, 52.8% and 53.1% were currently married, 92.6% and 96.6% were Hindu by religion and 71% and 66% were living in nuclear families in study and control villages respectively. The average family size in study and control villages was 4.3 and 4.5 respectively.

The annual incidence of animal bite/exposure cases in base line survey (History of animal bite /exposure in the last one year) was 2.7% and 2.8% from study and control villages respectively (Table 1). Following the active interventions in study villages with various rabies awareness activities, the incidence of animal bite/exposure cases in study villages decreased to 1.9% at the end of one year when compared to the baseline incidence of 2.7% and was found to be statistically significant ($Z=2.05$, $P=0.039$). This implies that

there was 30% reduction in animal bite/exposure cases reported in the study villages. The incidence of animal bite/exposure cases in control villages also reduced from 2.8% in baseline to 2.5% at the end of one year and the difference was not statistically significant ($Z=0.59$, $P=0.55$). There was 13% reduction in animal bite/exposure case reported in control villages.

Table 1

Incidence of animal bite/exposure at beginning and end of the project.

Incidence in 1 year period	Baseline	End line	Z	P
Study villages (n=1 735)	47 (2.7%)	33 (1.9%)	2.05	0.0398
Control villages (n=1 080)	31 (2.8%)	27 (2.5%)	0.59	0.5501

In the study villages a total of 47 animal bite/exposure cases was reported in baseline (Table 2). Maximum 43 (91.5%) had taken anti-rabies treatment in a hospital and 4 did not take any treatment. A total of 21 (44.7%) had visited local government hospital for treatment. The median age of animal bite/exposure cases was 23 years, minimum age was 2 years and maximum age was 68 years. Majority were males, bitten by dog and stray dog bites. Only 29.8% had followed the correct first aid procedure of washing the wound with soap and water. Majority of the animal bite cases were category II exposures and none of the category III exposures were injected with equine rabies immunoglobulin as per WHO recommendation. The ARV was mostly administered in either arm/anterolateral thigh and less than half of them received the recommended 3 to 5 doses of vaccine.

Table 2

Distribution of post exposure prophylaxis of animal bite/exposure cases.

Particular	Study Village (n=1735)		P
	Baseline (%)	End line (%)	
Age (Years)			
0–4	6 (12.8)	3 (9.1)	0.481
5–14	12 (25.5)	8 (24.2)	
15–44	20 (42.5)	19 (57.6)	
45–64	6 (12.8)	3 (9.1)	
>65	3 (6.4)	–	
Sex			
Male	34 (72.3)	23 (69.7)	0.797
Female	13 (27.7)	10 (30.3)	
Biting animal			
Dog	47 (100.0)	27 (81.8)	
–Pet dog	20 (42.5)	16 (59.2)	0.166
–Stray dog	27 (57.5)	11 (40.8)	
Cow/calf	–	6 (18.2)	
Place of treatment following dog/ animal bite– Hospital	43 (91.5)	33 (100)	0.001
First aid done before visiting hospital: Wash with water and soap	14 (29.8)	30 (90.1)	0.001
Category of exposure			
Category II	30 (63.8)	13 (39.4)	0.031
Category III	17 (36.2)	20 (60.6)	
Anti-rabies Vaccine			
Antirabies vaccines received	41 (87.2)	33 (100.0)	0.001
3 to 5 doses dose of ARV received	22 (53.6)	32 (97.0)*	0.001
Site of vaccination: Deltoid/AL thigh	18 (43.9)	26 (81.2)**	0.001
Fate of biting animal–Observed and informed concerned authorities	6 (12.8)	11 (33.3)	0.001
Rabies Immunoglobulin	–	20 (100.0)	

Note: Chi square/Fisher's exact test, * 1 case took two dose of ARV, ** 6 cases exposed to cow received IDRV.

At the end of one year (Table 2), 33 new cases were reported. All (100%) these bite victims had visited hospital for treatment. The median age of animal bite/exposure cases was 21 years, minimum age was 3 year and maximum age was 60 years. Majority were males, bitten by dog, mostly pet dog bites and 18% had exposures to rabid cow. Majority had followed the correct first aid procedure of washing the wound with soap and water. Majority of the animal bite/exposure cases were category III exposures and all of them were administered equine rabies immunoglobulin and ARV as per WHO recommendation. A majority received 3 to 5 doses of vaccine and only one patient was reported to have taken two doses of vaccine. In most of the cases ARV was administered in either arm/anterolateral thigh. Nineteen percent had received intradermal rabies vaccine as a route of administration.

Three hundred and sixty eight subjects in the study villages had received pre-exposure rabies PCECV as intradermal vaccination thrice on days 0, 7 and 28 d. Majority 323 (87.7%) were school children in the age group of 6 to 15 years and 45 (12.3%) were pet owners/veterinarians. One eighty eight (51%) were females and 180 (49%) males.

Among three hundred and sixty eight subjects who received pre-exposure IDRV, 52 (14.1%) adverse drug reactions were reported. The incidence of adverse drug events in relation to the total number of intradermal doses administered (*i.e.* $368 \times 3 = 1104$) was found to be $52/1104 = 4.7\%$. Twelve (23%) events of itching at the site of vaccine administration was the most common adverse drug reaction; Twenty six (50%) adverse reactions was reported on day zero. Majority of the adverse drug reactions subsided without medication and only 5 (9.6%) subjects received analgesics and antipyretics as symptomatic treatment. There were no serious adverse drug reactions among the vaccinees.

According to WHO, following rabies vaccine administration, a rabies virus neutralizing antibody titer of ≥ 0.5 IU/mL of blood is considered as protective antibody titer indicating protection against rabies. The rabies virus neutralizing antibody titer was estimated using rapid florescent focus inhibition test at the WHO collaborating center for reference and research on rabies, Department of Neurovirology, NIMHANS, Bangalore. The coded serum samples of 61 subjects (15% of total number of vaccinees) who received 0.1 mL of PCECV on day 0, 7, 28 were tested for the rabies virus neutralizing antibodies on day 42. The geometric mean concentration of rabies virus neutralizing antibody titers among school children was 4.77 ± 1.27 (95% CI 4.43–5.11) and among pet owners/veterinarians it was 4.78 ± 1.24 (95% CI 3.97–5.59). Thus all the subjects showed adequate and protective antibody titers of >0.5 IU (Table 3).

Table 3

Distribution of subjects according to rabies virus neutralizing antibody titers present in the blood samples (n=61).

Type	GMC (IU/mL)	GSD (IU/mL)	95% CI
School children	4.77	1.27	4.43–5.11
Pet Owners / Veterinarians	4.78	1.24	3.97–5.59

Note: GMC–Geometric Mean Concentration; GSD–Geometric Standard Deviation; CI–Confidence Interval.

4. Discussion

The age and sex distribution of the population in the study and control villages was similar. This description of the population is similar to the distribution of the population in the other villages of the state^[5]. There was no rabies death reported in the project villages. Though one of the reasons could be better awareness and availability of PEP, however the population of the project villages is too small to actually attribute any reason. The data on animal bites is scanty in India^[6]. At the beginning of the project there was no information available about the incidence of dog / animal bite from the local health and veterinary authorities. During the baseline survey the incidence of animal bite/exposure was found to be 2.7% in the study villages and 2.8% in the control villages. The implementation of the different rabies awareness activities was responsible for a significant decrease in the incidence of animal bite/exposure in study villages when compared to control villages where there was no interventions^[3]. The animal bite incidence rate is 1.7% in India^[2]. The annual incidence of animal bite in Bangladesh was 1.4%^[7]. Most of the animal bite/exposure were classified as possibly exposed *viz.* suspect rabid animal bite and 6 (18.8%) were exposed category *viz.* confirmed rabid animals^[4]. All the bite victims were possibly exposed in the WHO APCRI survey^[2] and no information was available from Bangladesh^[6]. We were also able to measure the incidence of animal bite/exposure after a successful intervention involving the medical, veterinary and animal welfare activity and show a demonstrable decrease in the incidence of animal bite / exposure cases in a rural community^[3].

Majority of the animal bite/exposure cases were males and 15 to 44 years of age. Animal bite incidence was more in children and 68% of the cases were males. The bite victims were poor, males were more affected and animal bite incidence was twice in children than adults^[7].

Seventy two percent of animal bite victims were males, 47.5% were children in the age group 2 to 18 years^[8]. Forty five percent of animal bite cases were in the age group of 15 to 45 years and males accounted for 72%^[9]. Animal bite was more common among males than in females^[10].

The biting animal was only dog in baseline. At the end bites from dog and exposure to cow was observed. Due to the influence of the various rabies awareness activities, there was an increase in the knowledge of people regarding animals other than dogs responsible for transmission of rabies and reporting to health care facility in case of animal bite/exposures^[3].

Most of the bite victims in study villages was from stray dogs in baseline and pet dog during endline. An interesting observation was that most of the bite victims had avoided being bitten by stray dogs during the endline. More animal bite cases due to pets could also be attributed to the treatment seeking behavior of the pet owners due to the various rabies awareness activities. The main biting animal was dog in 91% of bites of which 63% were stray dogs^[2]. Dog bite was the most frequent, reported in 75.3% victims followed by cat bite in 22.7% victims and unidentified in 2.0% victims. Fifty four percent were caused by free-roaming ownerless

animals, 43.0% by free-roaming owned animals and 2.8% by wild animals^[7]. Major biting animal was dog in 92% followed by monkey in 3% and cat in 2%. Of these, 65% bites were inflicted by stray animals and 35% were pets^[8]. Seventy nine patients were bitten by dogs^[9]. Dog was the major biting animal and approximately equal numbers of bites were from pet and street dogs^[10].

All animal bite/exposure victims had resorted to the correct practice of washing wound with soap and water^[3]. Herbal remedies were resorted to by 10.6% of the animal bite cases^[2]. Chillies, salt, turmeric powder, lime, snuff powder, paste of leaves, acid, ash given by Peer Baba (magician) *etc* was applied by 10.8% of bite victims^[8].

Thirty six percent of the bite victims had washed the wound with local applicant in rural area^[7]. Sixty percent of animal bites individuals did not wash the wound with soap and water, 8.6% used traditional first aid, including the application of crushed grass or leaves or treatment by traditional healers^[6].

Maximum of the animal bite/exposure cases in the endline were category III and in the baseline most of the animal bite/exposure cases were category II. The effectiveness of rabies awareness activities could be the probable reason for more category III bites being reported in the end^[3]. Similarly all the category III exposures had received rabies immunoglobulin and maximum had received 3 to 5 doses of antirabies vaccine in the endline whereas none of the cases from baseline received rabies immunoglobulin. This is because of increased awareness and people had access to rabies prophylaxis due to the active interventions of the project team^[3]. The use of tissue culture vaccine was low (30% to 42%) and RIG was very poor (2.1%) and majority 60% preferred government hospitals for PEP^[6]. PEP was not given to 72.8% of the bite victims and only 25.5% had been vaccinated of whom 45.5% had received nerve tissue vaccine and predominantly purchased their vaccines from nearby pharmacies and none of the bite victims were administered rabies immunoglobulin^[7].

All of the vaccine recipients had been bitten by dogs. Among the unvaccinated patients, most people received no treatment at all because of financial constraints, ignorance, or lack of vaccine availability. One of the measures that might improve the management of bites to prevent rabies is the countrywide introduction of cost effective intradermal rabies vaccine^[6].

All the vaccinees who had received PCECV pre-exposure intradermal rabies vaccination showed adequate protective rabies virus neutralizing antibody titres and incidence of adverse drug reaction was very low. Similar observations were made among 206 school children at Thailand, following 3 dose intradermal pre-exposure vaccination (on day 0, day 7 and day 28) with PCECV^[11]. A three years prospective study observed that all the school children who were administered with pre-exposure intra dermal rabies vaccine had developed adequate protective antibody titers with minimal adverse effects^[12].

In conclusion the incidence of animal bite/exposure was measured, all cases had received post exposure rabies prophylaxis and were successful to demonstrated a

decrease in the incidence of animal bite/exposure because of the implementation of one health experiment which is otherwise not happening in the country. There was no case of human rabies reported from project villages. Pre-exposure intradermal rabies vaccination to school children and other risk groups was safe and immunogenic.

Conflict of interest statement

We declare that we have no conflict of interest.

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Comments

Background

The authors have clearly informed about the need and justification for the study which is satisfactory.

Research frontiers

There are no published studies of similar nature from rural area of the country.

Related reports

This is a comparative study done in a rural area with study and control groups. This is also a prospective interventional study with follow up which has never been attempted before.

Innovations & breakthroughs

The study was able to demonstrate decrease in incidence of animal bite following the interventions like behavior change and communication strategies, post exposure prophylaxis was provided to the bite victims and pre-exposure prophylaxis was provided to the at risk population and also from a sample antibody titer estimated.

Applications

The study has shown that people are willing to accept new ideas and follow them.

Peer review

This is a good study in which the authors have come out with a novel idea and demonstrate the success of the one health experiment.

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