

Title: SAFETY AND CLINICAL EFFICACY OF POST EXPOSURE PROPHYLAXIS IN WILD ANIMAL EXPOSURES

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Keywords Wild life exposures, safety, clinical efficacy, anti rabies vaccine, rabies immunoglobulin

Abstract All exposures to wild animals must be considered as high risk in countries enzootic for rabies. Therefore complete post exposure prophylaxis should be initiated as soon as possible; which includes proper wound management and simultaneous administration of rabies immunoglobulin combined with full course of vaccine, which is usually effective in preventing rabies.

Original Article

SAFETY AND CLINICAL EFFICACY OF POST EXPOSURE
PROPHYLAXIS IN WILD ANIMAL EXPOSURESRavish HS¹, Pradeep Kumar DP², Chandana Krishna³, Ashwath Narayana DH⁴,
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ABSTRACT

All exposures to wild animals must be considered as high risk in countries enzootic for rabies. Therefore, complete post exposure prophylaxis should be initiated as soon as possible; which includes proper wound management and simultaneous administration of rabies immunoglobulin combined with full course of vaccine, which is usually effective in preventing rabies. The demand for safe and effective vaccines & immunoglobulin is ever increasing and many new vaccines & immunoglobulins are becoming available in the market. Therefore, there is a need for periodic reinforcement of safety and efficacy using these, especially for high risk exposures. The present study included 65 patients who had received post exposure prophylaxis after wild animal exposures. The mean age of the study subjects was 34.4 ± 12.3 years. The biting wild animals were monkey, bear, horse, fox, pig & camel and all had category III exposure. All the study subjects received post exposure prophylaxis as per WHO recommendations. The incidence of ADRs was found to be 8.0%. All the study subjects were alive and healthy after a period of 1 year following post exposure prophylaxis. In conclusion, post exposure prophylaxis against rabies was found to be safe, efficacious and lifesaving in all wild animal exposures.

Key Words: Wild life exposures, safety, clinical efficacy, anti rabies vaccine, rabies immunoglobulin.

Introduction

Rabies is a neglected zoonotic disease (a disease that is transmitted from animals to humans) caused by the rabies virus of the Lyssa virus genus within the family Rhabdoviridae, that occurs in >100 countries throughout the World and poses a potential threat to > 3.3 billion people Worldwide¹. The virus is transmitted by the saliva of rabid animals and generally enters the body via infiltration of virus-laden saliva from a rabid animal to other animals/ humans through bites, scratches, licks on broken skin and mucous membrane². All carnivores species including wild animals serve as natural reservoirs of the virus.³

A combination of large human and animal interactions has led to more exposures in World Health Organization (WHO)'s South East Asia Region than in any other part of the World. More than 1.4 billion people in this Region are at risk of rabies infection. Therefore, it continues to be a major public health and economic problem

throughout the Region⁴. India is also a rabies endemic country, where animal bites to humans are a major public health problem and an estimated 17.4 million animal bites occur annually which accounts to an incidence of 1.7%⁵.

Rabies is a 100% vaccine-preventable disease. Timely and correct post exposure prophylaxis (PEP) for the exposed victims is necessary to prevent rabies. Every year, more than 15 million people worldwide receive PEP to prevent the disease and this is estimated to prevent hundreds of thousands of rabies deaths annually.¹ Proper wound management and simultaneous administration of rabies immunoglobulin (RIG) combined with anti rabies vaccine (ARV) is almost invariably effective in preventing rabies, even after high-risk exposure. All exposures to wild animals must be considered as high risk in countries enzootic for rabies⁶. Travellers to and residents of these countries should be provided with immediate and complete post exposure prophylaxis whenever there is an exposure¹.

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The demand for safe and effective vaccines & immunoglobulin is ever increasing and many new vaccines & immunoglobulins are manufactured by private pharmaceutical companies and are becoming available in the market. Therefore, there is a need for periodic reinforcement of safety and efficacy using these rabies immune biologicals, especially for high risk exposures. Hence, this study was undertaken to throw more light on the existing information about the safety and clinical efficacy of post exposure prophylaxis following wild animal exposures.

Subjects And Methods

The study was conducted at the anti rabies clinic, of Kempegowda Institute of Medical Sciences (KIMS) Hospital and Research Centre, Bangalore, India. All the case records of wild animal exposures, during the period of 5 years from January 2010 to December 2014, were retrieved. A total of 65 subjects were included in the study, who had come for post exposure prophylaxis after wild animal exposures, during the study period. The case records of all the subjects were studied in detail to know about their socio-demo graphic profile, type of exposure and post exposure prophylaxis provided at the hospital. Assessment of safety was done by studying the case records of all the subjects and any immediate & delayed; local/systemic adverse drug reactions (ADRs) were recorded. Subsequently, all the study subjects were contacted over telephone and wherever required through house visits to confirm that, they were alive and healthy, one year after receiving PEP following confirmed rabies exposure. The local Epidemic Diseases Hospital, which admits human rabies cases, was also visited and its records were verified to rule out any possible rabies death amongst these subjects who received rabies PEP in KIMS Hospital.

All information pertaining to the study subjects were recorded and analysed statistically by computing means & percentages.

Results

The present study included 65 subjects, who had wild animal exposures. The mean age \pm standard

deviation of the study subjects being 34.4 ± 12.3 years and most of them belonged to the age group of 14-65 years (64.6%). Majority of the study subjects were males (51.0%) & from urban area (64.6%) (Table 1). The biting animal was monkey (73.8%) in most of the cases and others wild animals included Bear, Horse, Pig, Fox and Camel (26.2%). All the exposures were category III and most of them were on the limbs (80.0%) with majority being either lacerations or abrasions (95.5%). The immediate washing of wound(s) by water & soap and/or antiseptic by the rabies exposed persons was done only by 64.6% (Table II).

In the hospital, all the bite victims had received complete Post exposure prophylaxis as per the recommendations of WHO, which included thorough wound wash (100%) and all exposures were given total quantity of required rabies immunoglobulin i.e., HRIG (6.2%) & ERIG (93.8%) locally, into and around all the wound/s. Similarly, all the study subjects were given full course of anti rabies vaccination, intramuscularly by Essen regimen using various types of vaccines viz. 39 (60.0%) received PCECV, 22 (33.9%) received PVRV, 3 (4.6%) received PDEV & 1 (1.5%) received HDCV (Table III).

The incidence of adverse drug events (ADEs) was calculated based on number of ADEs reported & recorded, divided by total number of vaccine doses given and it was found to be 8.0% (26/325). All the ADEs were local in nature and there were no systemic reactions. All the ADEs were mild in both the groups and resolved without any complications. The common ADEs were erythema at the site of injection, itching at the site of injection, pain at the site of injection and induration at the site of injection as shown in table 4.

All the 65 study subjects were healthy and alive, after 1 year of completing post exposure prophylaxis.

Discussion

Rabies is a neglected zoonotic disease that is insufficiently addressed by Governments and the

Table : I
Socio demographic characteristics
of the study population

Characteristics	Study Subjects (n=65)
Age (mean±S.D) years	34.4 ± 12.3
<14 years	18 (27.7%)
14- 65 years	42 (64.6%)
> 65 years	05 (07.7%)
Sex:	
Male	33 (51.0%)
Female	32 (49.0%)
Place of residence:	
Urban	42 (64.6%)
Rural	23 (35.4%)

Table : II
Details of exposure in the study population

Details of exposure	Study Subjects (n=65)
Wild animals:	
Monkey	48 (73.8%)
Bear	06 (09.2%)
Horse	04 (06.2%)
Pig	01 (01.5%)
Fox	05 (07.7%)
Camel	01 (01.5%)
Site of bite:	
Lower limb	27 (41.5%)
Upper limb	25 (38.5%)
Trunk	09 (13.8%)
Head & Neck	04 (06.2%)
Type of wound:	
Lacerations	37 (57.0%)
Abrasions	25 (38.5%)
Punctured wound	02 (03.0%)
Licks	01 (01.5%)
Categorization of wound	
Cat III	100%
Immediate wound wash:	
Yes	42 (64.6%)
No	23 (35.4%)

International community, as they are best defined by the people and communities they affect the most i.e., poor people living in remote rural areas and urban slums of the developing World. It is however, the disease most amenable to control, as the tools for prevention i.e., post exposure prophylaxis are available. Therefore, it is the first zoonosis on the list of neglected diseases targeted for regional and eventually global elimination.

India is highly endemic for rabies and has the largest number of animal bites in the World. Therefore, in rabies endemic country like India, where every animal bite is potentially suspected as

Table : III
Details of post exposure prophylaxis
provided at the hospital

Post exposure prophylaxis	Study Subjects (n=65)
Wound wash: Done	65 (100%)
Anti rabies vaccine used:	
PCEC	39 (60.0%)
PVRV	22 (33.9%)
PDEV	3 (04.6%)
HDCV	1 (01.5%)
Rabies immunoglobulin used	Cat III (87)
HRIG	4 (06.2%)
ERIG	61 (93.8%)

Table : IV
Adverse drug events among the study subjects

Adverse drug events	Study subjects (n=65)
Pain	12 (3.7%)
Itching	08 (2.5%)
Erythema	04 (1.2%)
Induration	02 (0.6%)
Total	26/325* (08.0%)

a rabid animal bite, the treatment should be started immediately. Because of long incubation period, which is typical of most cases of human rabies, it is possible to institute post exposure prophylaxis to ensure that the individual will be immunized before the rabies virus reaches the nervous system.

The demand for a safe and effective cell culture vaccines & rabies immunoglobulin for post exposure prophylaxis is ever increasing. In this context, many pharmaceutical companies have started production, and these newer vaccines & immunoglobulins for PEP are always present in the market^{7,8,9,10,11,12}. Therefore, the safety and efficacy of these rabies immune biologicals should be established periodically. Ideally the efficacy of rabies PEP is assessed by rabies virus neutralizing antibodies (RVNA) assay in the bite victims. But, RVNA assays are expensive, scarce, practically not feasible and also not recommended as a matter of routine in all cases. In these circumstances, it is the survival of the exposed persons after rabies PEP and beyond the usual incubation period of the disease, is an indicator of the clinical efficacy of treatment. This is generally considered as six months, as is evident by the WHO- APCRI national multi-centric rabies survey. In this study, it was revealed that all the 65 rabies exposed persons were

successfully given post exposure prophylaxis at the ARC, KIMS Hospital, Bangalore and were alive & healthy even after 1 year.⁵

In conclusion, the study showed that, the presently available rabies immune biologicals i.e., anti rabies vaccines and rabies immunoglobulin were found to be safe and efficacious for post exposure prophylaxis in wild animal exposures.

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ANNOUNCEMENT

The APCRI Newsletter is published every six monthly, in October and in April. APCRI members and the members of the Scientific Community are requested to contribute News Clippings, Photographs and Reports on Scientific activity on Rabies and Related matter for publication in the Newsletter.

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