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Original Research Article

Safety of intradermal rabies vaccine as pre-exposure prophylaxis among veterinary students

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ABSTRACT

Background: Animal bites are a major public health problem in our country. Pre-exposure vaccination using cell culture vaccines is a safe and effective method of preventing rabies and is recommended for anyone who will be at continual, frequent or increased risk of exposure to the rabies virus, as a result of their occupation, such as veterinarians, animal handlers and laboratory workers dealing with any lyssaviruses. The present study was done to assess the safety of purified chick embryo cell rabies vaccine administered as pre-exposure regimen.
Methods: The present study assessed the safety of purified chick embryo cell rabies vaccine administered as a 3 dose intradermal pre-exposure vaccination in healthy volunteered veterinary students of Government Veterinary College, Bangalore.
Results: 122 apparently healthy adults of both sex, between 18 and 30 years of age were enrolled in the study and 105 (86%) completed all three doses. A total of 342 doses of intradermal vaccine were administered, among which 38 adverse reactions were reported from 19 veterinary students. The adverse reactions were pain at the injection site 7 (2.1%), redness 13 (3.8%), itching at the site of injection 11 (3.2%), induration 6 (1.8%) and headache 1 (0.3%). All reactions subsided without any complication and none of them dropped out from the study because of any adverse drug reactions.
Conclusions: Pre-exposure vaccination is a useful tool for protecting high risk groups and purified chick embryo cell rabies vaccine has proved to be safe and well tolerated by intradermal route.

Keywords: Intradermal rabies vaccination, Pre-exposure prophylaxis, Purified chick embryo cell rabies vaccine, Rabies, Safety

INTRODUCTION

Rabies is a vaccine-preventable viral zoonosis which occurs in more than 150 countries of the world.[1] Rabies is transmitted to animals and humans through close contact with saliva from infected animals through bites, scratches, licks on broken skin and mucous membranes and poses a threat to more than 3.3 billion people in the world, primarily in Asia and Africa.[2] In India an estimated 17.4 million animal bites occur annually which accounts to an incidence of 1.7% and hence it is considered to be a public health problem.[3]

Pre-exposure vaccination (PrEP) using cell culture vaccines are a safe and effective method of preventing rabies. PrEP is recommended for anyone who will be at continual/frequent or increased risk of exposure to rabies virus, as a result of their occupation such as veterinarians,

animal handlers and laboratory workers.[4] But a large proportion of at-risk staff members working in veterinary clinics, animal shelters, and wildlife rehabilitation centers are not receiving rabies pre-exposure prophylaxis as per the recommendations.[5]

PrEP can be administered either through intramuscular (IM) or intradermal (ID) routes by 3 doses on days 0, 7 and 21/ 28 using any of the WHO recommended cell culture vaccine.[6] In developing countries where the cost of intramuscular cell culture anti rabies vaccines is the major limiting factor, intradermal rabies vaccination is a safe and immunogenic alternative which reduces the volume and direct cost of vaccine. In this background, the present study was done to assess the safety of purified chick embryo cell rabies vaccine administered intra-dermally as pre-exposure prophylaxis among the veterinary students

METHODS

The study was done among the students of Government Veterinary College, Bangalore as a part of World Rabies day activity. 122 veterinary students of either sex who came voluntarily for pre-exposure prophylaxis and not taken any anti rabies vaccine in the past, not allergic to any of the ingredients of the vaccine and not suffering from any chronic disease were enrolled in the study. The study was done after obtaining institutional ethical clearance in accordance with ICH-GCP guidelines.

The socio demographic profile of all the study participants was recorded. All the subjects were vaccinated free of charge with three doses of 0.1 ml vaccine administered as intradermal pre-exposure vaccination on days 0, 7, and 21. The vaccine administered was purified chick embryo cell rabies vaccine (Rabipur) having a potency of >2.5 IU per single intramuscular dose and procured from the marketed batch bearing the batch number 2649, manufacture date 08/2014 and expiry date 07/2017.

Following vaccination, all the subjects were observed for 30 minutes for possible immediate local/systemic adverse drug reactions (ADR) and recorded if any. This includes pain at the injection site, redness, swelling, fatigue, headache, fever, myalgia, systemic allergic reactions and any other adverse drug reactions. The subjects were provided follow up card for mentioning any delayed local/systemic ADRs and it was collected throughout the study period. PrEP certificate was given to all the study participants indicating the type of vaccine and route of administration.

RESULTS

The present study included 122 apparently healthy volunteered adults. The study subjects were in the age range of 18-30 years with the mean age ± SD of 23.25± 6.76. Among them 79 (67.6%) were males and 43 (32.4%) were females. Majority (94.3%) were Hindus and most (59.8%) of them belonged to upper class according to Modified Prasad BG classification (Table 1).

Table 1: Socio demographic profile of the veterinary students.

Socio demographic profile		Values
Age range (in years)		18-30
Mean age ± SD		23.25±6.76
Sex	Male	79 (67.6)
	Female	43 (32.4)
Religion	Hindu	115 (94.3)
	Muslim	4 (03.3)
	Christian	3 (02.4)
Socio economic status*	I	73 (59.8)
	II	22 (18.0)
	III	17(13.9)
	IV	6 (04.9)
	V	4 (03.4)

Note: Figures in parenthesis indicate percentage; *Modified B. G. Prasad classification.

Table 2: Adverse reactions following vaccination.

Adverse events*	Day 0		Day 14		Day 21		Total
	Immediate	Delayed	Immediate	Delayed	Immediate	Delayed	
Redness	4	5	-	4	-	-	13
Itching	2	4	1	2	-	2	11
Pain	1	2	2	1	-	1	7
Induration	-	4	-	2	-	-	6
Headache	-	1	-	-	-	-	1
Total	**7**	**16**	**3**	**9**	**0**	**3**	**38**

***Multiple response.

Among the study subjects, 105 completed all the 3 doses, thereby, showing the compliance rate of 86.1%. A total of 342 intradermal doses of vaccine was administered to all the study subjects (105X3 doses = 315, 10X2 doses=20, 7X1 dose = 7). A total of 38 ADRs were reported from 19 subjects, among which 10 were

immediate ADRs and 28 were delayed ADRs. The most common adverse drug reaction recorded included redness at the injection site 13(3.8%), followed by itching 11 (3.2%), pain at the injection site 7 (2.1%) and induration 6 (1.7%). All the ADRs were mild and subsided without medication. None of the study subjects dropped out because of ADRs (Table 2).

DISCUSSION

Rabies in humans is considered as 100% fatal but preventable with the help of WHO recommended immunobiologicals either as pre-exposure or post-exposure prophylaxis. Unlike other infectious diseases, where vaccines are typically administered to healthy populations before onset of infection, human rabies vaccine in most cases, is administered post-exposure.[7] But WHO has recommended PrEP for anyone who will be at continual/frequent or increased risk of exposure to rabies virus, as a result of their residence or occupation such as veterinarians, animal handlers, rabies researchers and laboratory workers. PrEP is also being recommended for international travellers and children.[4]

Pre-exposure rabies prophylaxis is considered to be safe and holds several advantages such as, it simplifies management after exposure to rabies by eliminating the need for rabies immunoglobulin (RIG) and decreasing the number of doses of vaccine needed. Also it might offer partial immunity to persons whose post-exposure prophylaxis is delayed. Finally, pre-exposure prophylaxis might provide some protection to persons at risk for unrecognized exposures to rabies.[8]

Modern rabies vaccines i.e., Cell Culture Vaccines (CCVs) are intended for pre-exposure immunization as well as for post-exposure prophylaxis and WHO has recommended the ID route of administration for rabies pre- and post-exposure prophylaxis since 1991.This is because of the high cost of CCVs by the volume required for the standard IM route and equal immunogenicity has been demonstrated by ID route using at least 60% less vaccine than by IM vaccination. Hence making ID route a more economical alternative compared with the IM use of CCVs.[9]

Pre-exposure vaccination with early boosters by intradermal route with purified chick embryo cell Vaccine (PCECV) was found to be safe and immunogenic with production of adequate antibody titers by day 14, which was maintained till the yearly booster doses.[10] Studies done among children who are considered to be high risk group due to their continual, frequent or increased risk of exposure to the animal bites have demonstrated that pre-exposure prophylaxis using PCECV is safe and well tolerated.[11]

Another study conducted among children with PCECV^{PM} administered as PrEP through intradermal route have proved it to be safe and well tolerated with only 25 ADRs for 405 ID doses.[12] The present study also showed that PCECV was well tolerated and safe when administered intra-dermally as PrEP among veterinary students with only 38 ADRs for 342 ID doses. Most of the ADRs were local with only one systemic reaction reported. None of the study subjects dropped out due to adverse reactions and there were no complications reported.

CONCLUSION

Pre-exposure prophylaxis against rabies using PCECV is safe by intradermal route. It is a useful tool to prevent rabies among veterinary students who are at continuous high risk of exposure to rabies, living in highly endemic regions. Therefore, it has to be considered for all the veterinary students in the beginning of their course.

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