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Research Paper

Assessing the Safety of Post-exposure Rabies Immunization in Pregnancy

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ABSTRACT

Fourteen pregnant women who received rabies post-exposure prophylaxis (PEP) at the anti-rabies clinic (ARC) of Kempegowda Institute of Medical Sciences (KIMS) were followed up for assessing the safety of modern rabies vaccines and equine rabies immunoglobulin (ERIG) in pregnancy. The women were in the age range of 18–28 years, mostly from urban area (64%) and exposed to suspect rabid dogs (86%). They had received purified vero cell rabies vaccine (Verorab = 8 & Abhayrab = 4), purified chick embryo cell vaccine (Rabipur = 2) by Essen regimen; and equine rabies immunoglobulin (Equirab = 7 and Pasteur anti-rabies serum = 1). None of the pregnant women reported any adverse events to either vaccine or equine rabies immunoglobulin. All had safe vaginal deliveries and in all cases both the mother and the child were found to be healthy and normal.

INTRODUCTION

Human rabies is endemic in India and annually an estimated 17.4 million animal bites occur and 20,000 persons die of this disease.[1] But these deaths are largely preventable by timely and proper use of modern rabies vaccines and immunoglobulins. Following the discontinuation of sheep brain vaccine in December 2004, all animal bite victims are now receiving either the cell culture vaccines (CCVs) namely purified chick embryo cell (PCEC) vaccine, purified vero cell vaccine (PVRV), human diploid cell vaccine (HDCV) or purified duck embryo vaccine (PDEV). The rabies immunoglobulins (RIG) used in WHO category III exposures includes both equine (ERIG) and human (HRIG).

The pregnant women constitute a special and sizeable group and continue to remain vulnerable to this fatal disease following exposure to rabid animals. However, animal bites in pregnant women are a rare event and the victims mostly consult their family physicians or obstetricians for advice. There is often apprehension and doubt among treating physicians and the obstetricians about the safety of rabies vaccines and immunoglobulins in pregnancy. Some studies have no doubt shown the safety and efficacy of anti-rabies vaccines in pregnancy.[2-8] Still there is a need for its periodic reinforcement, more so as newer anti-rabies vaccines are becoming available in the market. Besides, information on the safety of RIGs in pregnancy is also needed. Hence, this study was undertaken to throw more light on existing information about the safety of rabies immuno biologicals in pregnancy.

SUBJECTS AND METHODS

The anti-rabies clinic at Kempegowda Institute of Medical Sciences (KIMS) has been offering rabies prophylaxis services since 1986. In this present study we retrieved the case record forms of sixteen pregnant women who had received the rabies PEP at our clinic during the preceding five year period from January 2001 to January 2006. Using trained medical investigators and a predesigned proforma, telephone calls and house visits were made to these women to know the outcome of pregnancy with regard to health of the mother and the child born, type of delivery and any adverse events to vaccine and RIGs. Wherever relevant, cross verification of details of delivery at the maternity hospitals was also done. As this was a retrospective study, there was no spontaneous reporting of local or systemic adverse events. The mothers were enquired about any obvious congenital anomalies in their children who were born after rabies PEP. In three instances where the children were available at home during the house visits by the medical investigators the children could be examined for any obvious congenital anomalies.

RESULTS

Of the sixteen pregnant women who had received rabies PEP during this reference five year period, only fourteen could be contacted as the remaining two were not traceable. These women were in the age range of 18–28 yrs at the time of exposure and ten (71%) were in gestational age of twenty or more weeks. Only four (29%) pregnant women were in the period vulnerable to teratogenicity (< 20 weeks) of which three (21%) were in the first trimester at the time of exposure and administration of first dose of vaccine and ERIG. Nine (64%) were from urban areas and 5(36%) from rural areas. Twelve (86%) women were exposed to dog bites and the remaining two (14%) women were bitten by monkeys. All biting animals were only suspect rabid and not confirmed rabid.

Table 1 **Details of post-exposure rabies immunization (N = 14)**

Case No.	Gestational Age at the Time of Exposure to Rabies (Weeks)	Type of Vaccine	No. of Doses	ERIG
1.	16	Verorab	5	Not given
2.	36	Verorab	3	Not given
3.	20	Verorab	5	Pasteur anti rabies serum
4.	24	Abhayrab	5	Not given
5.	32	Verorab	5	Not given
6.	24	Verorab	5	Not given
7.	28	Abhayrab	5	Not given
8.	28	Abhayrab	5	Equirab
9.	12	Rabipur	5	Equirab
10.	28	Verorab	5	Equirab
11.	32	Verorab	5	Equirab
12.	28	Verorab	5	Equirab
13.	12	Abhayrab	5	Equirab
14.	12	Rabipur	5	Equirab

Equirab & Pasteur Antirabies Serum = Equine Rabies Immunoglobulin (ERIG); Verorab and Abhayrab = Purified Verocell Rabies Vaccine (PVRV); Rabipur = Purified Chick Embryocell Rabies Vaccine (PCECV)

A thorough wound wash was done in six (42%) cases and in four (29%) cases it was partial. All had received CCVs namely PVRV (Verorab-8 (57%) women and thirty-eight doses; Abhyrab-4 (29%) women and twenty doses); and PCEC vaccine Rabipur-2 (14%) women and ten doses. The vaccines were administered by Essen regimen, intramuscularly in deltoid, one dose each on days 0, 3, 7, 14 and 28. In one case only three doses were administered as the biting dog was observable and remained healthy and alive after ten days.

Eight (57%) women had received ERIG (Equirab-7 and Pasteur antirabies serum-1) following WHO category III exposure to rabies. The ERIG was administered in dose of 40 IU per kg body weight and all the wounds were infiltrated and any left over volume was administered intramuscularly in the gluteal region (Table 1). None had complained of any systemic or local adverse events to both vaccine and ERIG.

All had safe vaginal delivery, and all the mothers and the babies born were healthy. Incidentally and interestingly all the babies delivered were female which may be coincidental.

DISCUSSION

Human rabies is practically a 100% fatal disease and there are no contraindications to rabies PEP including pregnancy. In clinical practice, live viral vaccines are contraindicated in pregnancy for their possible teratogenic effect. But all modern rabies vaccines are inactivated by beta propiolactone (BPL) and are generally considered safe. Similarly the currently available ERIGs are highly purified (enzyme refined and heat treated) and are known to be safe in pregnancy. Besides, the potential benefit of anti-rabies immunization in pregnancy as a life saving treatment is clearly justified despite certain potential risks perceived by lay people and shared to some extent by treating physicians including some obstetricians. There are rare and occasional instances of medical termination of pregnancies performed following post exposure rabies immunization in pregnant women. This is mostly because of ignorance amongst medical profession and to some extent due to lack of adequate and concrete evidence of safety of rabies biologicals in pregnancy. Hence, many medical professionals including obstetricians are reluctant to administer anti-rabies immunization to pregnant women.

In this study none of the pregnant women reported any adverse events to either the vaccine or ERIG. About one-fourth of them were in the gestational period of less than twenty weeks, vulnerable to potential teratogenic effects at the time of rabies exposure or administration of first dose of vaccine and ERIG. However, all had safe vaginal deliveries and both the mother and child were found to be healthy and normal. The children did not have any obvious congenital anomalies. In conclusion, PVRV & PCECV and ERIG were found to be safe in pregnancy.

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