

Case Report

Post-exposure prophylaxis of rabies during pregnancy: safety and other concerns

Imran Ahmed Khan¹, Mohammad Abu Bashar^{2*}, Hari Shanker Joshi², Shailendra Upadhyay³

¹Department of Community Medicine, ³Department of Anaesthesiology, BRD Medical College, Gorakhpur, U.P., India

²Department of Community Medicine and Family Medicine, All India Institute of Medical Sciences, Gorakhpur, U.P., India

Received: 05 May 2022

Revised: 17 May 2022

Accepted: 18 May 2022

*Correspondence:

Dr. Mohammad Abu Bashar,

E-mail: imback20006@yahoo.in

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ABSTRACT

Rabies is a 100% fatal disease caused mainly due to animal bites but can easily be prevented through timely vaccination in case of its potential exposure. Pregnancy is a special condition in which vaccination against rabies in case of its potential exposure may pose questions on its safety owing to its effect on the growing foetus. Through, this short review, we aim to explain the safety of rabies vaccines during pregnancy and its potential harms. Currently available evidences show that both vaccines and immunoglobulins against rabies are completely safe in pregnancy and adverse effects profile similar to non-pregnant state. Further, both the vaccine and immunoglobulins against rabies have no adverse effect on the growing foetus and therefore may safely be given to pregnant women in case of potential exposure.

Keywords: Rabies, Post-exposure prophylaxis, Vaccine, Immunoglobulin, Safety

INTRODUCTION

Rabies is almost 100% fatal and post-exposure prophylaxis through timely vaccination is the only method for prevention of human rabies. For people exposed to suspected rabies through animal bites, post-exposure prophylaxis (PEP) consists of wound cleansing (under running tap water for at least 15 minutes with soap), passive immunization with rabies immune globulin (RIG) and rabies vaccine as per the schedule for Category III exposures.¹ However, for Category II exposures, only vaccines are given.¹ Pregnancy is not a contraindication to rabies PEP.^{2,3} Despite this consensus, healthcare providers often hesitate treating pregnant women with rabies PEP. This paper is aimed to describe the safety profile of PEP for rabies in pregnant women by reviewing the currently available evidences through a case scenario.

CASE REPORT

A 32-year-old pregnant woman with previous caesarian at 36 weeks gestation reported to obstetrician with history of leaking per vaginum for few hours. She was bitten on her right foot by a pet dog 4 days back. It was a Category-III bite, wound was open and needed some debridement. Attendants confirmed about the complete vaccination status of the dog and also observed no major behavior change in dog. Now they wish for PEP but had some concerns regarding safety of fetus. They were also concerned if other family members may get rabies while caring the pregnant women and the neonate. A caesarean section was conducted under spinal anesthesia, debridement of wound was done and Rabies vaccination started as per schedule. Opinion of a general physician was sought. As 4 days has already been passed with no

remarkable change in the behavior of dog, it was advised to watch the dog and Rabies immunoglobulin was put on hold in view of positive immunization history (for rabies) of dog and a provoked bite (dog bite after tail of dog came under feet of patient). No Tetanus Toxoid-vaccine was advised as two doses of it were already given during the antenatal visits. Patients and attendants were counselled that there is no evidence of person-to-person transmission of rabies and required nursing care can be safely given to this patient.

DISCUSSION

Pregnancy per se is not a contraindication to various immunization. In 1999 Centers for Disease Control and Prevention (CDC) recommended that Anti-HBsAb-negative pregnant women be immunized against hepatitis B virus to minimize the risk of hepatitis B infection.³ Pregnant women beyond the 14th week of gestation are advised to be immunized with pneumococcal vaccine (PPV-23) to provide immune protection to themselves and their newborns.⁴ Currently, COVID-19 Vaccines have also been studied and allowed to be given to the pregnant women. Rabies vaccines usually provide an acceptable antibody response within 7-10 days of starting first dose and passive immunity by immunoglobulin is used for covering the window period of this 7-10 days. Immunoglobulins provide protection for about three weeks.⁵ Several case reports and case series are available in literature indicating safety of rabies immunoglobulins and vaccines in parturients and neonates.^{6,7} In a prospective study of 202 pregnant Thai women who received postexposure treatment for rabies with a tissue culture-derived rabies vaccine and human/equine rabies immune globulin revealed no different adverse reaction to that seen among nonpregnant patients who received similar treatment. Tissue culture-derived rabies vaccines as well as immune globulins were found safe to use for postexposure prophylaxis during pregnancy. Such treatment should never be omitted or delayed if the patient was suspected to be exposed to rabies.⁸ In another study 29 pregnant women exposed to rabies were given rabies vaccine as per the Essen regimen advocated by World Health Organization. None of them experienced any adverse effects to the vaccine. On follow up intrauterine growth and development monitored by ultrasound examination was found to be normal and the outcome of pregnancy was as expected. No congenital anomalies were noticed in any of the infants born and they followed normal course during the one-year follow-up period.

The rabies neutralizing antibody titers between 2 weeks and one year following vaccination in these women was found adequate and well above the minimum protective level of 0.5 IU/ml of serum. Protective levels of antibodies were also detected in some of the babies tested, for up to 3 months. Rabies vaccine was found safe and effective during pregnancy.⁹ Fayaz et al reported six pregnant women aged 22-35 years admitted at treatment and prevention of rabies center in Pasture institute

Teheran in Iran during 2007-2010. Rabies antibody levels was checked in serum of pregnant women who were bitten by rabies suspected animals and cord blood were also examined among those immunized by purified Vero cell rabies vaccine and Human Rabies immunoglobulin (HRIG). Among them two cases were at first trimester, one at second trimester and three at third trimester of conception. The interval between biting and delivery was 5-265 days (mean 121 days). Results of immunoglobulin illustrated that, levels of rabies antibody in maternal sera with the fetus are not equal and uniform but it was proved that babies find efficient immunity as well with minimum protective level of 0.5 IU/ml in all cases except a newborn born after 5 days of mother's immunization and this shorter duration may fail to develop appropriate immune response.¹⁰ Another study aimed to assess the safety of PEP for rabies in pregnant women. Seventy-two pregnant women received the Essen vaccination regimen. Vaccine recipients were monitored for 72 hours for any systemic and local reactions following the immunization and followed until six months after delivery. No noticeable adverse effects occurred in any subject following PEP. During follow-up of 72 subjects, four requested and had voluntary abortions, one had accidental miscarriage, and the remaining 67 subjects delivered healthy babies vaginally or by caesarean section. All babies exhibited normal postnatal course. The rabies vaccine was found safe for the PEP of pregnant women and did not interfere with the development of the fetuses or infants. It was concluded that there is no need of pregnancy terminations due to concerns about rabies and/or vaccination risk.¹¹ During 20 years of use, over 40 million doses of Verorab have been administered in more than 100 countries. No serious adverse event due to Verorab has been reported in clinical trials involving 3937 persons, and Verorab is better tolerated than human diploid cell vaccine (HDCV). Essen, Zagreb, Thai Red Cross Intradermal (TRC-ID) and other post-exposure intramuscular and intradermal regimens are documented. Co-administration of rabies immune globulin (RIG) does not affect neutralizing antibody levels when Essen or TRC-ID regimens are employed. No congenital malformations or spontaneous abortions attributed to PEP has been documented. Safety and efficacy have also been demonstrated in 759 children aged 0-15 years. Intradermal PEP is an effective and inexpensive option for developing countries. Inadvertent subcutaneous administration does not reduce immunogenicity. Extensive clinical experience supports the use of Verorab for intramuscular and intradermal pre- and post-exposure prophylaxis, including in special situations.¹²

CONCLUSION

Available evidence supports that maternal PEP for rabies is a safe and effective means of protecting pregnant women. Whenever such conditions are encountered, we should provide PEP according to existing guidelines. PEP was also found safe for fetuses and newborn. This will also help to implement Global strategic plan to end human deaths from dog-mediated rabies by 2030.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Khan IA, Bashir MA, Joshi HS, Upadhyay S. Post-exposure prophylaxis of rabies during pregnancy: safety and other concerns. *Int J Community Med Public Health* 2022;9:2706-8.