

SPECIAL ARTICLE

Safety of anti rabies vaccination during pregnancy

Dr Snehamay Chaudhuri*

*Associate Professor, Obstetrics and Gynecology; Midnapore Medical College, Midnapore, West Bengal

Rabies has a mortality rate of nearly 100% to pregnant women and an indeterminate risk to the fetus¹. According to WHO-APCRI National Multicentric Rabies Survey, there are an estimated 17.4 million animal bite cases annually in India². Rabies incidence in India has been constant for a decade with 18,000 to 20,000 cases of rabies a year (about 36% of the world's deaths from rabies) and there is no obvious declining trend. The reported incidence is probably an underestimate of true incidence because in India rabies is still not a notifiable disease³. Thus India remains a high-risk environment for rabies.

Symptoms of rabies usually develop 2-8 weeks after contact with a rabid animal. In clinically manifested rabies, nonspecific prodromal symptoms progress to encephalitis marked by confusion, hallucinations, and bizarre thoughts that are interspersed by shortening periods of lucid thought. Dysregulation of the autonomic nervous system and involvement of the brainstem and cranial nerves lead to the classic "foaming at the mouth" appearance⁴. Once symptoms of rabies develop, rabies is fatal. However rabies can be prevented by vaccination. Rabies vaccine is also curative if given post exposure before the manifestation of clinical symptoms.

According to the national guideline the post-exposure prophylaxis is a three-pronged approach⁵. All three carry equal importance and should be done simultaneously as per the category of exposure (i) Management of animal bite wound(s) - Washing of wound(s) should be carried out as soon as possible with soap and water. Since the rabies virus can persist and even multiply at the site of bite for a long time, wound(s) toilet must be performed even if the patient reports late (ii) Passive immunization with Rabies Immunoglobulin (RIG). In category III exposures rabies immunoglobulin should be infiltrated in the depth and around the wound(s) to neutralize the locally present virus. Anti-rabies serum or RIG has the property of binding with the rabies virus, thereby resulting in neutralization and thus loss of infectivity of the virus and hence it is most logical to infiltrate RIG locally at the site of exposure. Two types of RIGs are available: Equine Rabies Immunoglobulin (ERIG): ERIG is of heterologous origin produced by hyper-immunisation of horses. Currently manufactured ERIGs are highly purified Fab 2' fragments and the occurrence of adverse events has been significantly reduced. These are produced in the country in public and private sectors and are known to be safe in pregnancy. Human Rabies Immunoglobulin (HRIG) - HRIG are of homologous origin and are relatively free from the side effects encountered in a serum of heterologous origin. However, it is expensive and is imported from other countries. (iii) Active immunization with Anti-Rabies Vaccines (ARV) Active immunization is achieved by administration of safe and potent cell culture vaccines (CCVs) or purified duck embryo vaccine (PDEV). Currently available CCVs could be administered by IM regimen and CCVs approved for ID use shall be administered by ID regimen⁵.

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 advice⁶. The administration of rabies vaccines and immunoglobulin during pregnancy poses a number of concerns to physicians and patients about the risk of transmission of virus to developing fetus and harmful side effects to the mother and fetus.

For Correspondence: Dr Snehamay Chaudhuri MD(G&O), DNB; Associate Professor, Obstetrics and Gynecology; Midnapore Medical College, Midnapore, West Bengal, Email: snehamay_chaudhuri_dr@yahoo.com

Centre for Disease Control and Prevention (CDC) on general recommendation on immunization mentions that “Benefits of vaccinating pregnant women usually outweigh potential risks when the likelihood of disease exposure is high, when infection would pose a risk to the mother or fetus, and when the vaccine is unlikely to cause harm”⁷. Rabies vaccine is an inactivated whole-cell viral vaccine. In general, there is no evidence exists of risk to the fetus from vaccinating pregnant women with inactivated virus vaccine⁸.

Studies about the safety of rabies post exposure prophylaxis (PEP) in pregnancy had been performed since 1990s. The consensus from all of these studies is that rabies PEP is safe during pregnancy.⁹ There have been no identified associations between rabies vaccination and fetal abnormalities⁴. Sudarshan M.K. reported the safety of pregnant woman in India receiving both the rabies vaccine and RIG for treatment and found safe for the mother and fetus⁶. Following vaccination during pregnancy individual subjects present with mild adverse effects such as pain, erythema, fever, headache and fatigue, which are mild symptoms not requiring medication and do not cause long-term physical or mental effects on the patients. The adverse effects in pregnancy are not more severe than that of general populations⁹.

CDC on its recommendation on anti rabies vaccination concludes that because of the potential consequences of inadequately managed rabies exposure, **pregnancy is not considered a contraindication to postexposure prophylaxis**. Certain studies have indicated no increased incidence of abortion, premature births, or fetal abnormalities associated with rabies vaccination. **If the risk of exposure to rabies is substantial, pre-exposure prophylaxis also might be indicated during pregnancy**. Rabies exposure or the diagnosis of rabies in the mother should not be regarded as reasons to terminate the pregnancy¹⁰.

However, there is concern over the facts that even after receiving PEP the women may sought further information from other physicians, family members and friends. The women may suffer pressure from family and society and as result may refuse to take further PEP or terminate pregnancy^{6,9}. Thus health education of both health care personnel and common people is needed to eliminate the perceived safety concerns over the use of rabies vaccines for pregnant women and to avoid unnecessary consequences like abortions or incomplete PEP. Rabies PEP during pregnancy must be maximized to effectively prevent the occurrence of rabies.

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