



Commentary

Rabies vaccination in pregnancy and lactation

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ABSTRACT

Rabies, associated with the highest fatality rate among all infectious diseases, is endemic throughout the world. Currently, postexposure vaccination is the method of choice for prevention of rabies. Although the rabies vaccine is a live virus vaccine, pregnancy and breastfeeding are not contraindications for vaccination. In high risk patients, pre-exposure vaccination in pregnancy is also possible. In this, review vaccination schemes during pregnancy and lactation were discussed along with the new developments in rabies vaccines and diagnosis of rabies.

Key words: Rabies, vaccination, pregnancy.

Introduction

Rabies is a fatal viral zoonosis characterized by acute progressive encephalitis caused by a RNA virus (Family *Rhabdoviridae*, Genus *Lyssavirus*) [1, 2]. Prevention is the only method for treatment due to almost 100% fatality rate, which is the highest fatality rate of all known viral pathogens. Vaccination is the best method for prevention of rabies in humans. Post-exposure vaccination is recommended for anyone exposed to rabies, especially for animal bites. Similar to general population, the pregnant women in the endemic area may be exposed to rabies.

In this article, we reviewed current information and recommendations about the use of rabies vaccine during pregnancy and lactation.

Exposure

In rabies, exposure is defined as the contact of bite wounds or the contact of damaged skin and mucous membranes with potentially infectious material such as saliva, neural tissue of infected animals [2].

Indirect contact and activities (e.g., petting or handling an animal, contact with blood, urine or feces, and contact of saliva with intact skin) do not constitute exposures and do not require prophylaxis [1].

Sources of infection and exposure

Rabies is prevalent in wildlife and every mammal is susceptible to virus. Therefore, although wildlife oral vaccination is reported to be cost effective [3], currently elimina-

tion of virus is not possible. Transmission of virus to humans is most commonly due to bite of an infected animal (carnivores, bats, etc.).

Throughout the world, the most common mode of transmission is bite by rabid dogs, the most common reservoir and vector species. In developed countries rabies vaccination of pets is obligatory. In vaccination of animals a duration of at least 28 days is required after vaccine in order to be considered immunized [2].

Vaccines

After discontinuation of sheep brain vaccine current vaccines used in humans are either cell culture vaccines or purified duck embryo vaccines. Traditionally, rabies vaccines are produced by serial passage of rabies in cell cultures until attenuated (live virus) or inactivation of the virus (killed virus) [4]. All modern rabies vaccines are inactivated by beta propiolactone and are generally considered safe [5].

Similar to vaccines, the currently available Equine Rabies Immunoglobulins (ERIG) are highly purified (enzyme refined and heat treated) and are known to be safe in pregnancy [5].

Pre- and postexposure vaccination

Pre-exposure vaccination is composed of three intramuscular doses of vaccine that achieve protective immunity that was thought to last 3 to 4 years. Pre-exposure vaccination is indicated in cases with highest risk of exposure (eg. travel to endemic areas). Pre-exposure vaccination does not



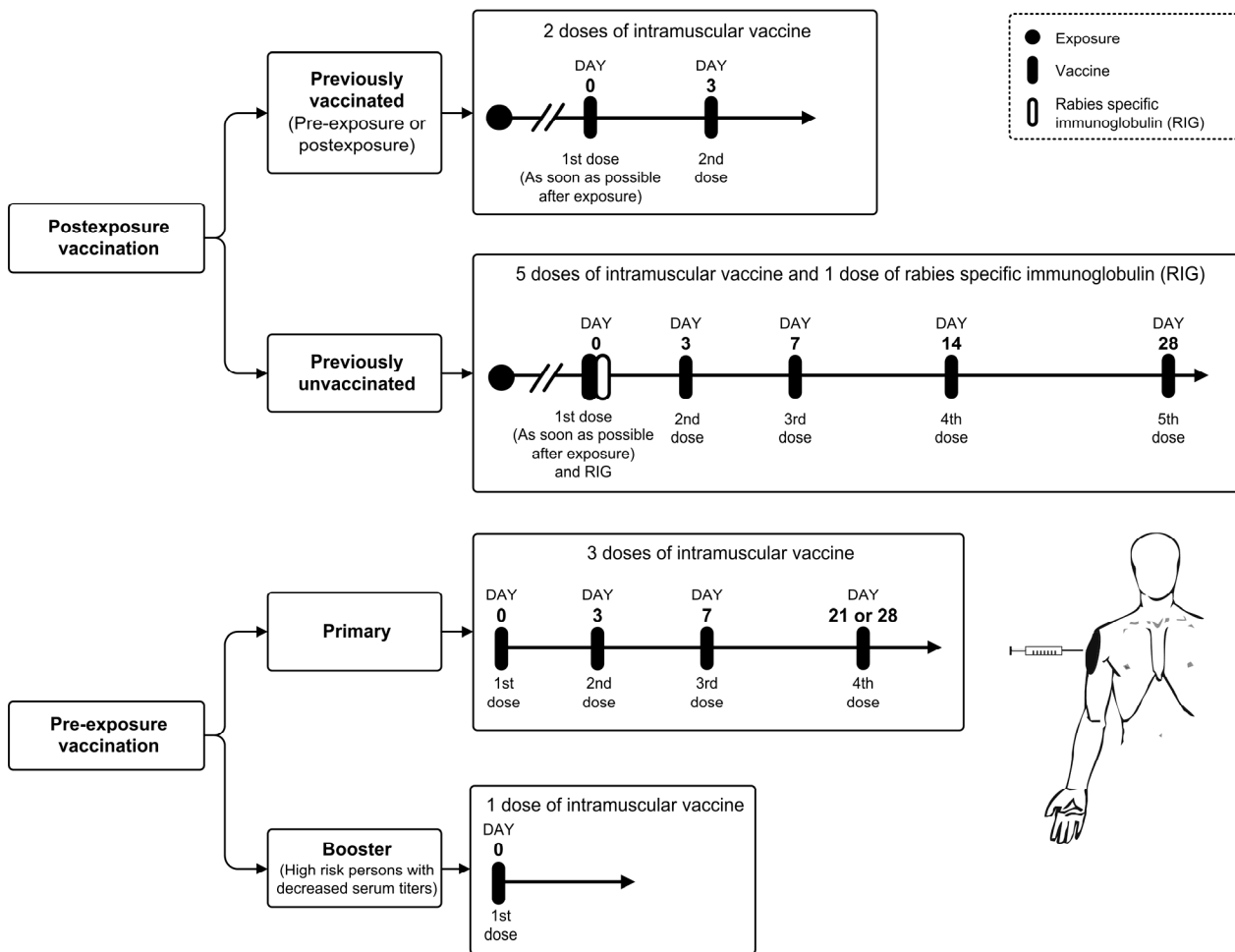


Figure 1. Advisory Committee on Immunization Practices (ACIP) general recommendations for rabies immunization that is also valid for pregnant and lactating women [1]. Prompt and thorough wound cleansing (with soap and water or povidone iodine if available) after exposure is very important for prevention of rabies. Also animal that bite should be kept confined and observed for 10 days. Persons should not begin prophylaxis unless animal develops clinical signs of rabies. Postexposure prophylaxis should be initiated as soon as possible following exposure to wildlife unless the animal available for testing. Vaccine should be administered to deltoid area. For younger children outer aspect of thigh could be used. However, vaccine should never be administered to gluteal area. (Figure © ALKIM BASIN YAYIN Ltd. Şti.)

eliminate the need for additional use of postexposure vaccination and use of specific immunoglobulin (RIG). However, it is still indicated because it helps to reduce the number of doses in postexposure vaccination, eliminate the need for RIG, and might provide some protection especially in cases with unrecognized exposure to virus [1].

Both WHO and ACIP recommend vaccination after exposure to rabies virus [1, 6]. Postexposure vaccination composed 5 intramuscular doses of cell culture vaccines and human rabies immunoglobulin (HRIG) (Figure 1). Current vaccines provide adaptive antibody response within 7-10 days. Immunoglobulin is used to fill this gap by passive immunity (half-life 21 days) [1].

During pregnancy and lactation postexposure vaccination is the preferred method used to prevent rabies [5]. However, in the presence of substantial risk for rabies pre-exposure prophylaxis might also be indicated in pregnancy. With the development of new vaccines including protein

subunit vaccines, DNA vaccines pre-exposure vaccination might be possible in future [4].

All healthy subjects exposed to either pre-exposure or postexposure vaccination demonstrate adequate antibody response [7]. Therefore, there is no need for testing seroconversion except immunocompromised patients [1].

Safety of rabies vaccination in pregnancy

Rabies vaccination in pregnant women is considered as safe for a long time. Any pregnant patients who are bitten by wandering animal are at risk. They need proper postexposure management. The safety of rabies vaccination in pregnant women was widely studied [8, 9]. Arya and Agarwal studied the safety of post-exposure rabies immunization in pregnancy and reported for the high safety of the vaccine [10]. Sudarshan *et al.* also reported for the similar result in their study on post exposure rabies prophylaxis with Purified Vero cell vaccine [11] According to this

work, no adverse effects due to the vaccine have been reported and all mothers and children were healthy. [11]. Toovey *et al.* also reported that vaccine could be safely administered post-exposure to the pregnant women without any problems on congenital malformations or spontaneous abortions [12]. As a result, although a live virus vaccine, rabies vaccine is known to be safe in pregnancy.

Efficacy of rabies vaccination in pregnancy

Sudarshan *et al.* stated that postexposure rabies vaccination had high efficacy [11, 13]. Similar results can be seen in the report of Toovey [12] and Chutivongse *et al.* [14]. Chutivongse *et al.* noted for the importance of post exposure vaccination for any pregnant exposed to rabies with no doubt [14]. Similarly, Fescharek *et al.* [15] and Chutivongse and Wilde [16] also proved for the efficacy of post exposure rabies vaccination in pregnancy.

Thomas concluded that any pregnant travelers to areas where rabies is still endemic should be vaccinated if they were likely to be exposed [17].

Effect of rabies vaccination on fetus

Up to date, there is no report about congenital anomaly attributed to postexposure rabies vaccination in pregnant women [10, 12, 14]. Moreover, modern rabies vaccines containing inactivated virus by beta propiolactone are considered safe [5]. Additionally, rabies exposure during pregnancy should not be considered as an indication for termination of pregnancy [18].

Safety of vaccination during breastfeeding

There is no data about the use of rabies vaccine during breastfeeding. Moreover, there is no data about the excretion of live virus to milk. However, vaccine is widely used throughout the world and up to date no adverse effect on infants was reported. Therefore, lactation is not a contraindication for rabies vaccination [19].

Future prospects about rabies vaccination during pregnancy

Although there are many reports confirming the safety and efficacy of rabies vaccination, there are still many areas to be explored in the future research. Data are limited or absent for pre-exposure vaccination, cost-effectiveness of postexposure vaccination, and efficacy in immunocompromised patients (especially those with human immunodeficiency virus infection) during pregnancy and lactation.

Today, with newer molecular methods that enable both monitoring the serology as well as ante-mortem diagnosis of rabies (so called ‘theragnostics’), it might be possible to avoid unnecessary treatments in rabies [20].

Moreover, new vaccines under development (DNA vaccines, ad vectors, use of new adjuvants) might enable widespread use of preventive vaccination in rabies [4].

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