SciMedCentral

Annals of Vaccines and Immunization

Short Communication

Rabies Vaccines

Sampath Gade*

Formerly, Dy.C.S., IPM, Hyderabad, India

***Corresponding author**

Sampath Gade, Formerly, Dy.C.S., IPM, Hyderabad, India, Tel; +91-9912277002

Submitted: 04 August 2023

Accepted: 08 October 2023

Published: 10 October 2023

ISSN: 2378-9379

Abstract

Rabies is an under reported disease that is present on every continent except Antarctica. It is estimated that 59 000 human deaths occur annually across the world. Most human deaths occur in Africa and Asia .

World Health Organization (WHO) and the World Organisation for Animal Health (OIE), in collaboration with the Food and Agriculture Organization of the United Nations (FAO) and supported by the Global Alliance for Rabies Control (GARC), developed a global framework for the elimination of dog-mediated human rabies by 2030.

Rabies is preventable through timely administration of post-exposure prophylaxis (PEP).

PEP has three components:

(a) local wound treatment

(b) vaccine administration and

(c) administration of rabies immune globulin (RIG) in all category III exposures

The primary objective of PEP is to neutralize and destroy virus that was inoculated into a victim's body at the time of exposure.

Rabies vaccines, especially Cell Culture Vaccines, have proved to be highly effective in preventing human rabies.

Vaccines induce active immunity and have an important role in protecting the individuals, as the host response to the infectious agent in a vaccinated person will be fairly rapid and sufficient to prevent the occurrence of the disease.

HISTORICAL

In the 19th century, the studies of Louis Pasteur led to the development of a vaccine against Rabies.

Louis Pasteur started his studies on Rabies in the 1880s. In those days nothing was known about viruses [1,2].

Louis Pasteur found that rabbits infected by the saliva of a child suffering from Rabies, succumbed to the disease. He discovered that the agent which caused Rabies was concentrated in the central nervous system, particularly in the brain. He thought whether he could weaken this agent and produce an attenuated "toxin" which could give protection against the virulent agent. He started transferring the disease from one rabbit to another rabbit. He observed that

the incubation time which was originally 3 weeks, decreased steadily with the number of transfers till it was only 6 to 7 days.

He found that when the spinal cord of the infected rabbit was exposed to dry air, there was a decrease in virulence over time and finally the virulence completely disappeared. Pasteur first treated animals with the attenuated "virus" and then proceeded to infect the animals with a stronger type of virus and checked if these animals were protected. He was successful in his work.

On 6th July 1885, 9 year old Joseph Meister was brought to the laboratory of Louis Pasteur. The boy was bitten by a rabid dog on 4th July and was advised by his doctor to meet Louis Pasteur. Pasteur had not tried his new method of immunization in human beings and consulted his fiends Dr. Vulpius and Dr. Granchet. The first injection of rabies vaccine, which was a suspension of dried spinal cord of a rabbit infected with rabies, was given by Dr.Granchet in the presence of Louis Pasteur. In the following 10 days, 13 injections prepared from a fresh spinal cord of a rabies infected rabbit, were given to Joseph Meister. This treatment was successful in saving Joseph Meister.

Nerve Tissue based Vaccines (NTVs)

In 1911, Dr.David Semple developed a nerve tissue based rabies vaccine from the brains of sheep infected with fixed virus. The sheep were later killed and the vaccine prepared from the sheep brain was inactivated by phenol. This vaccine was used for almost a century in many countries .

Fuenzalida vaccine prepared from suckling mouse brain and inactivated by phenol or ß propiolactone was being used in Latin America. It is supposed to contain less myelin but it is not free of neurological complications.

Fermi type vaccine, which is incubated at 21°C in the presence of phenol, may contain residual infectious virus.Duck embryo cell vaccine was developed to avoid neuroparalytic reactions, but it carried a risk of allergy.

CELL CULTURE VACCINES

All NTVs are reactogenic and induce a low or moderate immune response. WHO has recommended that they be replaced with Cell Culture Vaccines. Several different cell substrates have been used for the production of rabies vaccines, including Primary Syrian hamster kidney cell , human diploid cells, primary cell lines produced from embryonated chicken and duck eggs, and continuous cell lines produced from Vero cells .

Human Diploid cell vaccine was developed in the 1960s.It is the first cell culture vaccine against Rabies and was the gold standard .It is prepared by growing fixed virus (Wistar's Pitmaan Moore strain) on human diploid cell and inactivated with ß propiolactone.

Rabies Vaccine Adsorbed is prepared from the Kissling strain of rabies virus adapted to a diploid cell line of the fetal rhesus lung. The virus is inactivated with ß propiolactone and concentrated by adsorption to Aluminium phosphate.

Since their development over four decades ago, cell culture-based and embryonated egg-based rabies vaccines (CCEEVs) have proved to be highly effective in preventing human rabies throughout the world. CCEEVs have also allowed a broader use of vaccines for Pre Exposure Prophylaxis [3], thus protecting persons at high risk of exposure. Over the past three decades, sufficient data have been published demonstrating the safety and efficacy of CCEEVs [4,5].

Cell Culture Vaccines (CCVs) were initially administered Intramuscularly only. However, the high cost of CCVs relative to the cost of NTVs, and the large number of patients who required Post Exposure Prophylxis (PEP) in countries endemic for canine rabies became an impediment to the widespread use of CCVs. In an effort to reduce the cost of CCVs without lowering the efficacy of the vaccine, clinical trials were conducted to investigate the efficacy of Intra Dermal (ID) regimens using a fraction of the IM vaccine dose for PEP [6].

Over the past three decades, results from several clinical trials have confirmed the immunogenicity and efficacy of the ID route for rabies PEP . IDRV is now being used in many Asian countries and African countries.

The minimal potency of CCEEVs, recommended by WHO, is 2.5 IU per intramuscular dose.

MECHANISM OF ACTION OF IDRV

The ability of the ID route to induce an immunological response is based on the fact that the skin is an important immune organ and vaccine efficacy is enhanced when antigens are presented into the dermal layer. The administration of antigens into the skin layer facilitates their exposure to the numerous antigen-presenting cells, such as macrophages and dendritic cells that are present in higher numbers in skin than in muscle.

After ID injection, the inactivated rabies vaccine is taken up by antigen-presenting cells (APCs) in the epidermis for ultimate activation of T cells and B cells responsible for Virus Neutralizing Antibody (VNA) production.

Immunization of patients, at the earliest, after exposure plays a major role in protection by the activation of both CD4+ T cell and B cells. This results in the production of VNAs, by plasma cells, that target and destroy the virus.

A Rabies nanoparticle based G protein vaccine, prepared using Virus like Particle technology, has been developed and introduced in India. It is administered intramuscularly in a schedule of three doses on days 0,3 and 7. At present it is approved for use in persons between the ages of 18 to 65 years.

IMMUNE RESPONSE IN DIFFERENT RISK GROUPS

Immunosuppressed patients

Rabies vaccines are highly immunogenic in almost every population, with perhaps the exception of immunosuppressed patients with very low CD4+ cells.

PREGNANT WOMEN

Rabies vaccine is not contraindicated during pregnancy. No risk of abortion or other harm to the fetus has been reported due to administration of

CCV in pregnant women.

PATIENTS TAKING ANTIMALARIAL TREATMENT

The administration of rabies vaccine by the ID route had been reported to produce reduced titres in patients taking chloroquine for antimalarial treatment and, for this reason, vaccine was recommended to be administered to this group of patients through the intramuscular route. However it is now suggested that both ID and IM route of vaccine administration can be used.

INFANTS AND THE ELDERLY

The immune response to rabies vaccine in the elderly and in young children, who are not suffering from any immunosuppressive conditions, is reported to be adequate.

In a study involving 875 patients aged 2-74 years who received either PEP or PrEP, no significant difference in the production of VNA compared to either age or sex was reported. The immune response to rabies PEP was also reported to be highly immunogenic in children with confirmed malnutrition between Grade I and Grade IV.

CONCLUSION

Modern CCVs are among the most immunogenic vaccines in

the world, as is evidenced by the very few reported human rabies deaths in patients who received prompt PEP according to WHO's recommendations.

Many new and shorter vaccine regimens, have been developed, which reduce the cost of PEP and also ensure better compliance of the patients.

REFERENCES

1. WHO Expert Consultation on Rabies, third report. Geneva: World Health Organization; (WHO Technical Report Series, No. 1012). 2018.
2. WHO Weekly epidemiological record No 16, 2018, 93, 201–220 Rabies vaccines: WHO position paper – April 2018
3. Terapong Tantawichien, Charles E Rupprecht. Modern biologics for rabies prophylaxis and the elimination of human cases mediated by dogs. Expert Opin Biol Ther. 2020; 20: 1347-1359.
4. The immunological basis for immunization series: module 17: rabies vaccines. Geneva: World Health Organization; 2017
5. Briggs DJ, Schwenke JR. Longevity of rabies antibody titre in recipients of human diploid cell rabies vaccine. Vaccine. 1992; 10:125-129.
6. Sampath G, Parikh S, Sangram P, Briggs DJ. Rabies post-exposure prophylaxis in malnourished children exposed to suspect rabid animals. Vaccine. 2005; 23: 1102-1115.