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Investigating Effective Methods of Immune Induction as Pre-Exposure Measures for Rabies in Immunocompromised Patients: A Mini-Review

Saman Pazira[a], Sepideh Bourenjan Shirazi[b], Behzad Pourhossein[c], Rouzbeh Bashar[d], Ehsan Zafari[e], Maryam Fazeli[e]*

a. Department of Microbial Biotechnology, School of Biology, College of Science, University of Tehran, Tehran, Iran.
b. Department of Microbiology and Microbial Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran.
c. Pharmaceutical Sciences Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
d. WHO Collaborating Center for Reference and Research on Rabies, Virology Department, Pasteur Institute of Iran, Tehran, Iran.
e. ATMP Department, Breast Cancer Research Center, Motamed Cancer Institute, ACECR, Tehran, Iran.

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*** Corresponding Author:**
Maryam Fazeli

Email: m.fazeli@umsha.ac.ir

Abstract

Neurotropic rabies virus is the cause of fatal encephalitis. Due to the definite mortality of this disease, after symptoms appear, it is of great importance to implement appropriate prevention methods before and after exposure in rabid-bitten people. Knowing that the immune system plays a key role in preventing symptoms after taking efficient measures to control and prevent rabies, this issue becomes imperative in immunocompromised patients. This study has tried to compare all the effective methods of prevention before and after exposure in people with a weak immune system by reviewing various reliable articles and sources**.** In this study, all articles were found online until March 2022 in English through several search engines, including PubMed, EMBASE, and Google Scholar by searching the keywords immunodeficiency, HIV/AIDS, organ transplantation, bone marrow transplantation, and tumors. Malignancy and chemotherapy, hemodialysis, use of systemic corticosteroids, pregnancy alone, and also together with prevention methods before and after exposure to rabies were searched. All the articles related to the measures of controlling and preventing rabies in all healthy individuals and patients with underlying diseases, immunocompromised patients, and pregnant women were considered and analyzed. Methodological integrity was ensured by utilizing the Cochrane risk and bias assessment tool. A total of 60 articles were extracted, but, duplicate records were excluded before the screening. All remaining reports were eligible for review. The most frequent methods found in the articles regarding prevention before and after exposure to rabies in individuals suffering from each of the mentioned diseases were investigated. Overall, the articles reviewed recommended that all immunocompromised, rabies-exposed patients should receive WHO protocol plus a third vaccination**.** Paying attention to immunodeficient patients is highly imperative in the mechanisms of the health system. It can be said that since the rabies vaccine is an inactive one, it is safe to use in most immunocompromised cases.

Keywords: Rabies Virus; Vaccination; Therapeutics; Immunologic deficiency syndromes.

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1. Introduction

Rabies (genus Lyssavirus, family Rhabdovirus) is a neurotropic virus that causes fatal encephalitis and has been a worldwide problem for thousands of years. Rabies is often transmitted to humans or other animals through the bite of a rabid, warm-blooded, carnivorous animal. Widespread in most parts of the world, rabies is considered a serious threat to mammalian health [1, 2]. When symptoms occur, the mortality rate for rabies is extremely high and usually results in death due to respiratory failure and cardiac arrest. Treatment of rabies is therefore a major challenge, especially in developing countries where effective vaccination programs are

lacking. The World Health Organization estimates that rabies kills an average of 60,000 people worldwide each year, 40% of whom are under 15 years of age. With approximately one death every 10 minutes, African and Asian countries have the highest rabies mortality rates in the world [3, 4].

Because rabies can lead to a potential pandemic and an absolute probability of animal deaths, it can not only terrify the population but also cause numerous economic losses, since in Asian countries 96% of the budget spent ($650 million per year) is spent on dealing with this problem.

Since dogs are believed to be one of the main vectors of rabies [5], 14 million people are treated and protected from rabies caused by animal bites, especially dog bites, every year. Studies have shown that the number of animal bites is increasing, and although all age groups are susceptible to animal bites, people under 20 years of age, especially children between 5 and 15 years of age, are most at risk (approximately 65% to 70%) [6].

In general, there are two common types of rabies treatment: Pre-exposure and Post-exposure. Post-exposure treatment can be given by intradermal vaccination and serum four times, depending on the severity and depth of the wound. This should be done at the appropriate time and before the onset of symptoms. Pre-exposure treatment is by three intradermal vaccinations for individuals exposed to the virus (Table 1) [6, 7-11].

In general, vaccination is the only effective measure to prevent, control, and eradicate rabies in humans worldwide. When administered promptly after a bite by a rabid animal, the rabies vaccine can prevent the virus from entering the nerve and causing the disease. Since the development of the nerve tissue-derived rabies vaccine for humans began about 120 years ago, countless lives have been saved. However, the nerve tissue-derived rabies vaccine has caused problems in vaccinated individuals [7]. Currently, cell culture vaccines and vaccines derived from purified chicken embryo cells (PCECV) have replaced nerve tissue-derived vaccines. One of the differences between commercial vaccines is the viral strains used in the development of the vaccine. Different types of these strains are used in the production of inactivated rabies vaccines. All of these strains have in common that they can develop immunity to members of genotype 1 of the rabies virus. However, they may differ in terms of vaccine replication rates [7-12]. Despite the availability of effective vaccines, rabies eradication remains a problem because of the high cost of vaccine production and administration.

Immunocompromised patients are generally unable to fight or eliminate an infectious agent [8, 9]. Long-term conditions such as various cancers, chemotherapy, organ transplantation, chronic diseases treated with cytotoxic drugs or steroids, and HIV infection can cause immunodeficiency [9-13].

Susceptibility to serious infections such as rabies, RSV, parainfluenza, HPV, HBV, and HCV is a common problem in immunocompromised patients. For this reason, choosing the appropriate treatment and prevention method for these patients is important [10-14]. Thus, these patients may require additional doses of the vaccine to achieve adequate immunity. On the other hand, attenuated viruses and bacteria used as vaccines can cause severe reactions in immunocompromised patients, leading to the development of various systemic diseases. However, inactivated rabies vaccines are considered safe for such cases and can be used under certain circumstances. Nevertheless, some precautions or contraindications may need to be considered when vaccinating against rabies in these patients. Vaccination in immunocompromised patients has always been challenging in terms of immunogenicity and vaccine efficacy. Given the high prevalence and lethality of rabies without appropriate treatment, this study investigated the effective methods of inducing immunity through preventive measures before and after exposure to rabies in immunocompromised patients [15, 16].

2. Materials & Methods

In this study, several search engines such as Scopus, PubMed, EMBASE, and Google Scholar were used to find online articles in English up to March 2022. Keywords such as immunodeficiency, HIV/AIDS, organ transplantation, bone marrow transplantation, tumors, malignancy and chemotherapy, haemodialysis, use of systemic corticosteroids, pregnancy alone and also along with prevention methods before and after exposure to rabies were searched. In this survey, articles on rabies control and prevention methods were considered and studied in (1) all healthy persons and those with underlying diseases, (2) immunocompromised persons, and (3) pregnant women (Figure 1).

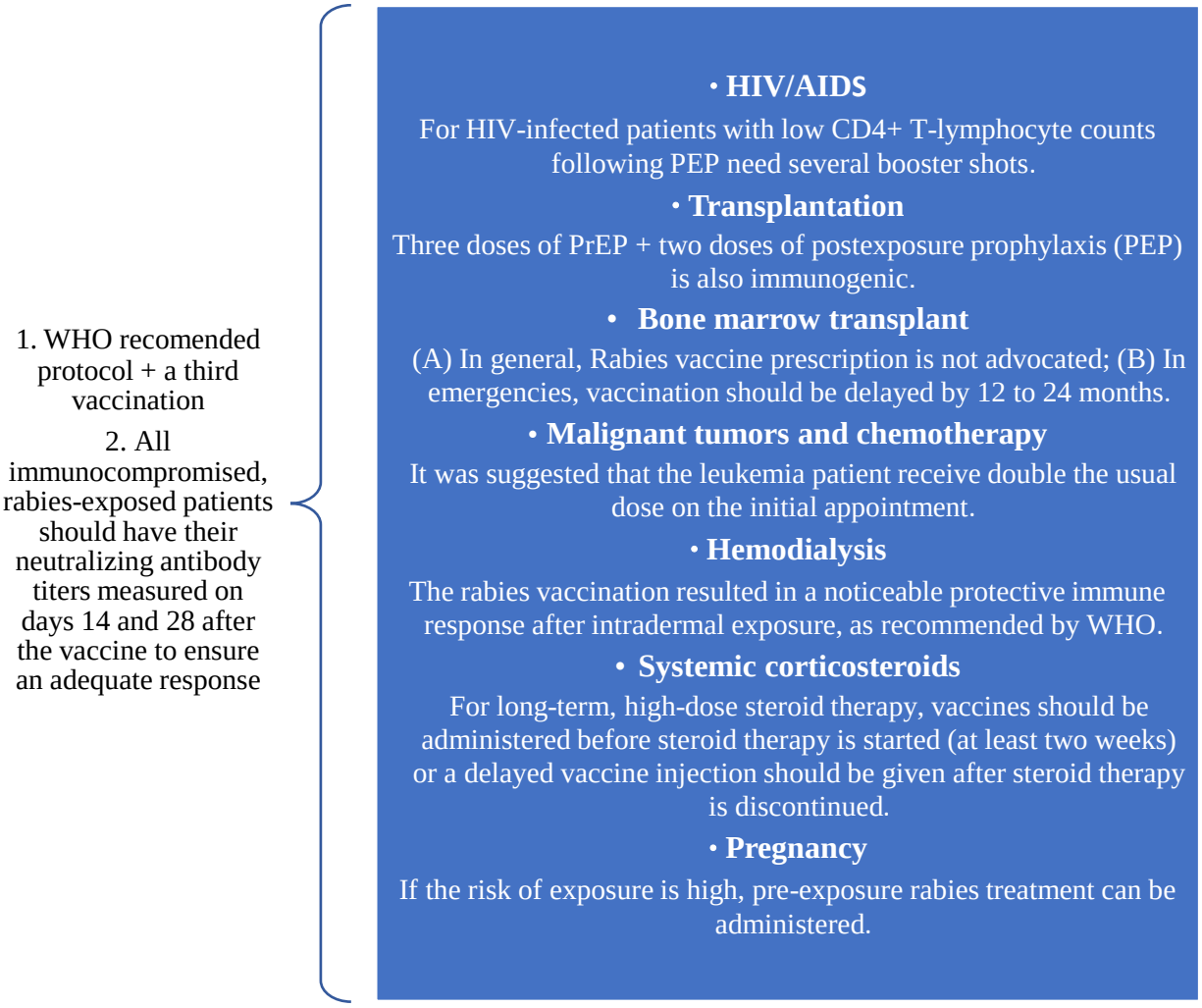

Figure 1: Rabies pre-exposure measurements in immunocompromised patients

* Indicated if the last tetanus vaccine was more than 5 years before exposure

† Completed pre- or post-exposure regimen of human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCEC) after 1985, or received another vaccine with documented serum titer corresponding to complete neutralization at >1:5 serum dilution (or its equivalent, approximately 0.1-0.2 IU/mL) by the rapid fluorescent focus inhibition test (RFFIT).

In the next step, 16 of the 60 extracted articles were excluded before screening because they were duplicated, not citable, or for other reasons. Approximately 44 articles were screened, and all remaining reports were eligible for review. The most common methods used in the pre-and post-rabies prevention articles for rabies exposure in patients with each of the mentioned diseases were presented in the form of a tree diagram.

3. Results & Discussion

3.1 Rabies pathogenesis

Rabies is a virus that can infect a wide range of hosts, including all terrestrial mammals. Although several routes of virus transmission are known, the most common route is the bite of a rabid animal and contact of the rabies virus with mucous membranes. There have

also been reports of unusual circumstances such as the sudden release of rabies virus-infected suspended particles in caves full of bats or laboratories [12, 13].

Rabies in humans has a typical incubation period of 20 to 60 days; although the incubation period can last up to 16 months [14], there are reports of symptoms appearing

Table 1: World Health Organization (WHO) recommendations for human rabies management [6, 7-11].

Categorize of Exposure to Suspected or Confirmed Rabid Animals and Actions Required	
Category I	• Touching or feeding animals • Licks on intact skin • Contact of intact skin with secretions or excretions of a rabid animal or human case ***Action required: not regarded as exposure, no post-exposure prophylaxis is required***
Category II	• Nibbling of uncovered skin • Minor scratches or abrasions without bleeding ***Action required: thorough local wound care and vaccine injection as soon as possible***
Category III	• Single or multiple transdermal bites or scratches • Contamination of mucous membrane with saliva from licks • Licks on broken skin • Exposures to bat bite or scratches ***Action required: thorough local wound care and administration of vaccine and RIG as soon as possible***
Passive Immunization: Rabies Immunoglobulin (IRG)	
Target population	• All people with category III exposure, bite to the head, neck, face, and genitals • Immunodeficient people with category II exposure • Not for previously vaccinated individuals
Type, dose	• Human rabies immunoglobulin: 20 IU/kg body weight • Equine immunoglobulin: 40 IU/kg body weight • $F(ab')_2$ products of equine immunoglobulin: 40 IU/kg body weight
Time and site	• One administration as soon as possible, and within seven days from vaccination • Into or around the wound site or sites. The remaining RIG (if any) should be administrated IM at a site distant from the vaccination site
Active Immunization: Vaccines	
Types	Cell culture vaccine (CCV) and embryonated egg-based vaccine (CCEEVs) • Purified Vero cell rabies vaccine (PVRV) • Purified chick embryo cell vaccine (PCECV) • Human diploid cells vaccine (HDCV) And • Purified duck embryo vaccine (PDEV)
Potency	≥2.5 IU per single IM
	• Intramuscular (IM), 1.0 mL or 0.5 mL (volume depending on the type of vaccine). ○ Vaccine type: any CCEEVs Sites: ○ Adults and children ≥2 years: in the deltoid area of the arm ○ Children ≤2 years: in the anterolateral area of thigh ○ Never in the gluteal area • Intradermal (ID), 0.1 mL per ID site ○ Vaccine type: only PVRV or PCECV Sites:
Route of administration, dose, vaccine type, and injection sites	○ The deltoids ○ Lateral thighs ○ Suprascapular areas

after about five days. Viral replication occurs in striated muscle cells before the virus attacks the axons of motor nerves via the neuromuscular junction [15]. In the next phase, the infection spreads through the nervous system connected by synaptic links; however, the exact underlying mechanism is still unknown. After infection of the brain, the virus escapes from the infection center and spreads to the superficial and automatic nervous system in the superficial organs. In the last phase of the infection cycle, the rabies virus migrates to the salivary glands. After multiplying in the mucosal cells, it passes into the saliva and is ready to be transferred to the next host [16].

In addition to the absence of major pathologic damage to the central nervous system, in most cases of rabies in humans, there is no immune response 7-10 days after the onset of clinical symptoms. These profound differences in the pathogenesis of rabies and most other viral and bacterial infections of the central nervous system are clear evidence that immunosuppression in rabies either has no effect or is harmful [17].

Initial symptoms are generally nonspecific and include general restlessness, fever, and anxiety. Numbness at the bite site may occur and is related to inflammation of the ganglia. After a few days (2 to 10 days), neurologic symptoms appear in two forms: Encephalitis or paralysis. In encephalitis, symptoms range from classic hydrophobia and increased salivation to aerophobia, confusion, and convulsions. Eventually, paralysis and coma occur, leading to the death of the patient [17].

In paralytic rabies, descending weakness of the limbs without loss of consciousness is one of the first symptoms. This weakness of the organs starts from the bite site and spreads to other organs. Eventually, paralysis of the respiratory system occurs and the patient often dies of suffocation [18].

Rabies is a neurophilic virus that causes fatal encephalitis and is transmitted through the saliva of an infected animal by a bite or scratch. During this process, the rabies virus encounters different immune barriers at different stages; initially, the virus particles are transmitted into the skin or muscle by a bite and are quickly recognized by the first line of defense. In other words, the innate immune response, which involves the elimination of local microbes, and the specific immune response by T and B lymphocytes in the environment (i.e., outside the nerves) are activated [4].

After entering the nerves, the virus must overcome the intracellular immune response triggered by the infected neurons to fight the virus. Once the infection has settled in the neurons, the infected neurons are protected from destruction by T cells and infection-limiting mechanisms in the nervous tissue. In addition, the nervous system's assumption of central control of immunologic homeostasis leads to an inappropriate reduction in the immune response in peripheral tissues, which may facilitate viral replication. Maintaining the integrity of the nerve network to the spinal cord provides the virus with the opportunity to reach the salivary glands [4].

3.2 Immunocompromised patients

3.2.1. HIV/AIDS

HIV is a virus of the genus Lentivirus of the family Retroviridae that causes acquired immunodeficiency syndrome (AIDS). A low CD4+ T lymphocyte count (<300-400/mL) in infected individuals results in a weak neutralizing antibody response to rabies vaccination. Some studies have shown that HIV-infected patients with a CD4+ T lymphocyte count of less than 200/ml respond poorly to the intramuscular 4-sided vaccine [19].

The World Health Organization Expert Committee (WHO) on rabies recommends following the protocol in Table 2 for preexposure prophylaxis (PrEP) and receiving a third vaccination between days 21 and 28. According to WHO guidelines, an N-nucleoprotein antibody titer of approximately 0.5 IU/mL is acceptable for protection against rabies [20]. To guarantee a sufficient response, it is recommended that the titers of neutralizing antibodies be determined on days 14 and 28 after the rabies vaccine in all immunocompromised, rabies-exposed individuals [21].

Immunoglobulin administered to neutralize the virus at the inoculation site in HIV-infected patients after post-exposure treatment is significant. In some HIV-infected patients with low CD4+ T-lymphocyte count after PEP, multiple booster injections are necessary if an adequate nucleoprotein response has not been developed (Figure 1) [22].

3.2.2. Transplantation

Effective prevention is essential to maintain the general health of young children after organ transplantation. Prescribing immunosuppressive drugs to such patients increases the risk of dangerous infections [23]. It is possible to prevent the disease and reduce the

multiplication and spread of infectious microorganisms by vaccination. However, the efficacy, safety, and vaccination protocols in organ transplant patients have not been adequately studied.

Rabies transmission through corneal transplantation has been reported [24]. There are no studies yet to demonstrate the efficacy and safety of vaccines in organ transplant recipients. It is recommended that hazardous occupations be avoided in these patients [25].

Three doses of PrEP followed by two doses of postexposure prophylaxis (PEP) is immunogenic in Solid Organ Transplant (SOT) recipients. Because SOT recipients may not have an adequate antibody response to the rabies vaccine (titers > 0.5 IU/ml are considered sufficient), some experts recommend the use of post-exposure human rabies immunoglobulin (HRIG) (HRIG is often prescribed only to unvaccinated individuals) [26].

Because secondary antibody responses in transplant patients are more persistent than primary antibody responses, prevention strategies should be used early in the disease to maximize vaccine-induced immunity [27]. This approach is particularly necessary for organ transplantation and chronic immunosuppressive therapy. Injection of some live attenuated vaccines should be avoided if the patient is severely immunocompromised. Severe adverse events caused by the postexposure injection of inactivated vaccines are more likely to occur in patients suffering from altered immunodeficiency [27, 28].

3.2.3. Bone marrow transplant

Recent developments in vaccine science have led to the improvement of old vaccines and the development of new ones that are essential for vaccines. With prophylactic vaccines, antibody titers decrease after transplantation unless revaccination is given [29-31]. The development of stem cell transplantation means an increase in the number of treatments for cancer [32]. However, infectious complications are considered a major problem in stem cell and organ transplantation. The main risk of infectious complications in stem cell transplantation is during the phase of immune reconstitution in response to donor cells after discontinuation of radio chemotherapy. These patients transform from patients with profound humoral and cellular immunodeficiencies after treatment to patients capable of a functional B- and T-cell response [33, 34]. The maturation of the immune system leads to the ability of transplant recipients to respond to multiple vaccines.

Hematopoietic stem cell transplantation (HSCT) is one of the risk factors for rabies. It is essential to protect these recipients from exposure, which is done by rabies vaccination [35].

In general, rabies vaccine prescription is not advocated.

Although the safety of the rabies vaccine has not been established, CDC believes that vaccinating persons with possible occupational exposure before exposing them to rabies can be useful. However, vaccination should be delayed by 12 to 24 months. Administration of human rabies immune globulin (BayRab, Imogam) and intramuscular (deltoid portion) HDCV vaccine is recommended on days 0, 3, 7, 14, and 28 after exposure (Figure 1) [36].

3.2.4. Malignant tumors and chemotherapy

Although adverse side effects have been observed in patients with cancer who are receiving immunosuppressive treatment after each vaccination, such as an increase in severe infections and a decrease in vaccine efficacy due to a weak immune response to the vaccine, however, the rabies vaccine is used for these individuals [37]. Hence, in some studies, it was suggested that the leukemia patient receive double the usual dose on the initial appointment [38].

Several vaccines have been considered for children facing malignancies and chemotherapy. Studies have not yet measured the efficacy of vaccines in immunocompromised children. While inactivated vaccines are generally considered safe, live attenuated vaccines should be used selectively in these patients. It is recommended that individuals who come into contact with immunocompromised patients, such as family members and healthcare workers, receive all current vaccines. Vaccination should be done cautiously in children with malignancies and chemotherapy because they are at greater risk of exposure to various microbes and life-threatening factors than patients with a normally functioning immune system [37, 39].

In patients with malignancies, immunosuppressive drugs, and chemotherapy often result in a loss of both cellular and humoral immunity. However, the numbers of B cells, plasma cells, natural killer (NK) cells, and immunoglobulins (Ig) return to normal six months after treatment is stopped. However, the return to normal

Table 2: "WHO-recommended and alternative pre-exposure prophylactic regimens" [47, 48].

PrEP regimen	Duration of course	Number of injection sites per clinic visit (days 0, 3, 7, 14, 21–28)
WHO-recommended intradermal regimen		
Two visits	7 days	2-0-2-0-0
WHO-recommended intramuscular regimen		
Two visits	7 days	1-0-1-0-0
PrEP under specific circumstances		
Single visit, intradermal	1 day	2-0-0-0-0
Single visit, intramuscular	1 day	1-0-0-0-0

T-lymphocyte counts is relatively slow, as CD4+ T-lymphocytes remain low for more than 9 to 12 months after treatment in 20 to 50 percent of children with cancer [40].

In immunocompromised patients exposed to vaccine-preventable diseases, the use of antibodies may be offered as passive immunization. There are examples of intramuscular immunoglobulin (Ig) injections for hepatitis A, measles, or rubella prophylaxis. In addition, there are reports of administration of specific Ig products such as hepatitis B Ig, rabies Ig, tetanus Ig, experimental varicella-zoster Ig (VariZ IG), intravenous cytomegalovirus Ig, and intravenous botulism Ig (Figure 1) [39].

3.2.5. Hemodialysis

Diagnosis of chronic kidney disease (CKD) has become an important concern for vaccine providers because the incidence or severity of some vaccine-preventable diseases is more pronounced in immunocompromised individuals. Several vaccines (e.g., inactivated influenza vaccines and pneumococcal vaccines) may therefore be used, particularly in people with chronic kidney disease. In addition, the efficacy of vaccines may change over time, so vaccination may need to be repeated if it loses efficacy [27].

The immune system of most CKD patient's functions adequately to receive all live attenuated vaccines. People with end-stage renal disease (ESRD) have deficiencies in several host defense mechanisms, including complement formation, phagocytosis, and humoral and cellular immune responses. Identifying the mechanism of action of the vaccine, increasing its dosage, and repeating the vaccination in hemodialysis patients (HD) can increase immunity in these patients. Several studies have shown that the standard Thai Red Cross intradermal injection after rabies exposure (TRC-ID) can elicit an adequate immune response in these healthy individuals [41].

Chronically stable hemodialysis patients receiving adequate dialysis have shown an acceptable immune response to the rabies vaccine after subcutaneous exposure [41]. Rabies prophylaxis is considered the basis for preventing rabies infection in chronic hemodialysis patients. However, several basic studies of antibody titers in patients with chronic renal failure and chronic HD patients with adequate dialysis have shown that rabies vaccination resulted in a noticeable protective immune response after intradermal exposure, as recommended by WHO (Figure 1) [28, 42-48].

3.2.6. Systemic corticosteroids

One of the drugs commonly prescribed in systemic treatment is oral corticosteroids. The number of oral corticosteroids is set at a dose of more than 20 mg per day in children weighing 10 kg or more, and from 2 mg/kg per day in children weighing less than 10 kg. Steroid use for a period longer than two weeks impairs immune system function [39]. Topical (skin), inhaled (lung and upper respiratory), and intraarticularly injected corticosteroids are not immunosuppressive.

Inactivated vaccines can be used routinely during corticosteroid therapy. For long-term, high-dose steroid therapy, vaccines should be administered before steroid therapy is started (at least two weeks) or a delayed vaccine injection should be given after steroid therapy is discontinued. The use of live attenuated vaccines should

Table 3: For Healthy, Immunocompetent Individuals, Including Pregnant Women, Post-Exposure Prophylaxis Against Rabies [48].

Vaccination Status	Treatment	Dosage/Administration Guidelines for All Ages	Day of Regimen
Not Previously Vaccinated	• Wound cleansing • Tetanus toxoid booster* • Human rabies immune globulin (HRIG)	• 20 IU/kg body weight • Infiltrate HRIG into and around the wound • Remaining HRIG given IM at a site distant from the vaccination site • Never in the gluteals	Day 0 (HRIG can be given up to day 7)
	• Rabies vaccine	• Four 1.0 mL doses, given IM • Adults/older children: deltoid area • Young children: anterolateral thigh • Never in gluteals	Days 0, 3, 7, 14
Previously Vaccinated†	• Wound cleansing • Tetanus toxoid booster* • Rabies vaccine	• Do not give HRIG • Two 1.0 mL doses, given IM • Adults/older children: deltoid area • Young children: anterolateral thigh • Never in gluteals	Days 0, 3

* Indicated if the last tetanus vaccine was more than 5 years before exposure

† Completed pre- or post-exposure regimen of human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCEC) after 1985, or received another vaccine with documented serum titer corresponding to complete neutralization at >1:5 serum dilution (or its equivalent, approximately 0.1-0.2 IU/mL) by the rapid fluorescent focus inhibition test (RFFIT).

be determined based on the route of administration, dose, and steroid course. Attenuated vaccines are considered safe in persons receiving topical steroids, topical injections, or aerosol inhalations (Figure 1) [28].

3.2.7. Pregnancy

Pregnant women are often at risk of vaccine-related deaths and injuries caused by pregnancy outcomes such as congenital anomalies, spontaneous abortions, preterm births, and low birth weight. Vaccination during pregnancy has direct benefits through passive immunity to the fetus and child (placental transfer of antibodies from maternal vaccination). Post-exposure treatment results in the production of rabies immunoglobulin (Ig) in the body, although this is not required in previously vaccinated individuals [43, 44]. Some limited studies have shown no association between maternal rabies vaccination and spontaneous abortions, teratogenesis, or preterm birth. Therefore, CDC recommends that every pregnant woman be vaccinated and given rabies Ig after moderate or high rabies exposure. If the risk of exposure is high, treatment can be given before exposure (Figure 1 and Table 3) [43, 45, 46].

Rabies is a deadly zoonotic disease of global public health and economic importance. In industrialized countries, human rabies has declined dramatically over the past 50 years due to the routine vaccination of domestic animals. In both developed and developing countries, vaccination is the only acceptable method of rabies prophylaxis, control, and eradication. Since the development of the nerve tissue-derived rabies vaccine for humans about 120 years ago, countless lives have been saved. However, the nerve tissue-derived rabies vaccine also caused problems in vaccinated individuals. Second-generation vaccines include attenuated or recombinant vaccines [49]. In several current vaccines, the virus is genetically attenuated or immunogenically enhanced, and in some, the vaccine is developed based on a viral protein; the latter category refers to subunit vaccines produced based on the G protein or a portion thereof in the case of rabies virus. Inactive vaccines often do not result in high immunogenicity, requiring multiple injections to generate neutralizing antibodies [50, 51].

Vaccination is given to immunize individuals who are at increased risk for rabies. These include physicians, rabies control, treatment, and vaccination center personnel, rabies diagnostic and research laboratory personnel, and persons at higher risk of rabies infection than other community members [6].

Immunocompromised persons are individuals whose immune systems do not function properly against pathogens. Therefore, effective vaccination and appropriate immune response are of utmost importance in these patients. Failure to routinely vaccinate immunocompromised patients may result in an immune system failure to function efficiently. This group should receive all recommended routine vaccinations according to the specific vaccination schedule. In this study, different methods of rabies prevention (PrEP) were investigated based on the World Health Organization's recommended protocols and various articles for these patients.

Because of their non-pathogenicity, the use of inactivated vaccines is generally recommended in these patients [49, 50]. Some studies have shown that HIV/AIDS patients should receive a double dose of cell culture-based rabies vaccine, and in some cases, patients with low CD4+ T lymphocyte counts should receive repeated booster doses [20, 22, 52].

In SOT, it is better to prevent this disease. Some experts suggest using only human rabies immunoglobulin (HRIG) if needed [25, 53]. Several injection protocols have been described for patients undergoing bone marrow transplantation [54]. The use of human rabies immunoglobulin (HRIG) is recommended after exposure (HRIG is often prescribed for unvaccinated individuals) [26]. In severe immunodeficiency, injection of some live attenuated vaccines should be suspended [28]. In stem cell transplantation (SCT), maturation of the immune system results in recipients of SCT being able to respond to multiple vaccines [33, 34]. Rabies vaccination can be used in patients undergoing hematopoietic stem cell transplantation (HSCT), and postexposure prophylaxis with rabies vaccine combined with human rabies Ig can be administered at any time after HSCT [33, 35].

The use of inactivated vaccines in multiple doses is recommended for cancer patients, especially children undergoing chemotherapy who are at risk of malignancy due to an inadequate immune response to vaccination and drugs that block the immune system. Antibodies can be used as passive immunization in immunocompromised individuals exposed to vaccine-preventable infections [39].

Most patients with chronic kidney disease demonstrate a functional immune response and can safely receive live attenuated vaccines. For this reason, the use of a cell culture-based rabies vaccine is safe. Intradermal (ID) injections, dose escalation, and repeated vaccination are recommended for people with end-stage renal disease (ESRD) and hemodialysis patients (HD) to improve their immune function. (TRC-ID) has been recommended in several studies in hemodialysis patients [27, 41].

In patients receiving oral corticosteroids, inactivated vaccines are more appropriate in high-dose, long-term steroid therapy. The vaccine should be administered before steroid therapy is started (at least two weeks) or after steroid therapy is stopped [55]. Some limited studies have shown no association between maternal rabies vaccination and spontaneous abortion, teratogenesis, or preterm delivery. Rabies vaccination is therefore safe during pregnancy [43].

4. Conclusion

Rabies is a common encephalitic disease of humans and animals, which is one of the greatest challenges in developing countries. In different patients, the management of pathogens and diseases varies depending on the area of exposure. In the mechanisms of the health system, it is more important to pay attention to immunocompromised patients. Because the rabies vaccine is inactive, it can be safely used in most immunocompromised patients. However, as mentioned earlier, in some cases, a different vaccination schedule or type of vaccine is required.

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Conflict of interest

There is no conflict of interest.

Ethics

None.

Authors' ORCIDS

Saman Pazira:
https://orcid.org/0000-0002-8787-4557
Sepideh Bourenjan Shirazi:
https://orcid.org/0000-0002-3861-1814
Behzad Pourhossein
https://orcid.org/0000-0002-4263-0612

Rouzbeh Bashar:
https://orcid.org/0000-0001-5469-4472
Ehsan Zafari:
https://orcid.org/0000-0002-1815-0010
Maryam Fazeli:
https://orcid.org/0000-0003-4048-4778

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