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Review on Foot and mouth Disease vaccine immunogenicity and Vaccination Failure

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ABSTRACT

Foot and mouth disease is a contagious virus affecting cloven-hoofed animals and is caused by the FMD virus, which has seven serotypes. The serotype, genotype, and topotype differences of the virus make it a challenge to control the disease. Therefore, vaccination was the most favorable of the other controlling mechanisms. In this review, we analyze different FMD vaccines in terms of their advantages and disadvantages. Among all deoxyribonucleic acid vaccines, vaccines were the most useful and had the fewest disadvantages due to their best efficacy, reduced vaccine dose, and low toxicity. However, vaccine failure factors are the greatest challenges during or after vaccination to control the virus for all vaccine types. Before and during vaccination, vaccine handling, site vaccine administration, and temperature were great challenges. Mainly, temperature affects the protein particles of the virus that cause direct reactions with the immune system. To summarize them, vaccine failures occur due to mismatching of the vaccine strain and the wild one, inhibition activity of maternal antibodies from colostrum, and parasite infestation (shifting the balance of the immune system from a TH1 to a TH2 type, whereas several vaccine-induced immunizations rely on the TH1 responses). Additionally, vaccine efficacy and vaccination coverage are the two fundamental factors in generating the preferred level of herd immunity against FMD in the field, which causes vaccine failure. Furthermore, the concentration of protein particles has a direct correlation with antibody production. In general, this review sums up the vaccine failure and different FMD vaccine immunogenicities in short form.

KEY WORD: *Foot and mouth disease, Vaccine failure and vaccine immunogenicity.*

1. INTRODUCTION

Foot and mouth disease is highly contagious virus which can affect cloven hoof animals. The causative agent of this disease was FMD virus, which have seven serotype. During control of this disease vaccination was the major strategy. Vaccines (derivative protein particle of virus which contain viral nucleic acid and no viral particle drive from culture media) decrease clinical disease, shed and spread and reduce the number of persistent infections in vaccinated ruminants challenged with FMDV (Cox et al., 1999).Due to genetically difference each serotype couldn't induce antibody against each other. There is also period of immune response between vaccination and wild infection. During infection antibody detectable after 7-10 days and level's peak can be detected around 28 days and remain at protective titers, lasted for 40 weeks (Metwally et al., 2016), (OIE, 2004).

Antibody develops against FMD vaccine was start at 3-4 days and come up least at six months, however capacity of neutralizing come dawn after two weeks (Golde et al., 2008). Antibody induced reach maximum titer on 21 days for aqueous vaccines post vaccinations while 28 days for oil vaccine. The shorter duration of immunity in the case of vaccinated animals is due to the vaccine is unstable, inactivated and non-replicative virus particles (Parida, 2009). Killed vaccines are use adjuvant because the antigens alone are not very immunogenic. The adjuvant stimulates an innate immune response to the vaccines through a variety of pathways such as depot/stabilizing effects, inducing cytokine release, attracting and activating macrophages and lymphocytes, and enhancing antigen presentation. This greatly enhances the adaptive immunity and production of antibodies and cell mediate immunity (Awate et al., 2013).

The probability occurrence of selective disease in vaccinated area was named as vaccination failure due to actual vaccine failure or failure to vaccinate appropriately.In general vaccination failure occurs with vaccine strain matching with circulating virus, vaccine quality, the impaired immune response to the vaccine, break in the herd immunity, duration of protective immunity, maternally derived antibody inhibition and FMDV Persistence in recovered animals are the major (Singh et al., 2019). Vaccine potency, the concentration of the immunologically active component had a direct correlation with the amount of humeral antibody-induced (Lyons et al., 2016). The dose of vaccine delivery is estimated by the potency of the vaccine (Doel, 2003).

2. FMD VACCINE IMMUNOGENECITY

The vaccine immune response was determined by the features of the vaccine and the host. The vaccine dose, adjuvant, route and site of administration, timing, and way of vaccine handling can are factors for immunoresponse.

The immune response against FMDV has been related to circulating humoral antibody titer, which is considered to be the most important factor in conferring protection against FMD (Sori et al., 2018). IgM is the first serum-neutralizing antibody that appears at 3–4 days following infection or vaccination, and peaks in a concentration approximately 10–14 days after infection and then declines (Golde at al., 2008). IgG is detected at 4–7 days post-infection or post-vaccination and becomes the major neutralizing antibody by 2 weeks following immunization (Sobrino et al., 2001). In both vaccinated and infected animals, the IgG1 titer has been reported to be higher than IgG2 (Pega et al., 2015).

The major antibody subclasses found in secretions of upper respiratory and GI tracts are initially IgM, followed by IgA and IgG (Salt, 1993). It is well known that parenterally administered inactivated FMD vaccine in cattle elicit very little or no IgA in mucosal secretions (Archetti et al., 1995), but if the vaccinated or naturally infected animal becomes a carrier of FMDV, oropharyngeal replication of virus acts as a constant stimulus to produce a higher amount of IgA in saliva, nasal and oropharyngeal secretions (Parida et al., 2006).

2.1 In activated vaccine immunogenicity

This type of vaccine was developed in the twenty-first century by Frenkel by means of culturing the epithelium tongue of slaughter animals and inoculating them with FMDV, which then flows with formaldehyde in activation (Lombard et al., 2007).After some time, the tongue tissue epithelium was compensated by the cell line, and ethylene imines were used for inactivation (Brown and Newman, 1963; Bahnemann, 1975). Currently, FMD vaccines consist of inactivated, purified antigen (killed virus) devoid of nonstructural viral proteins, usually by chromatographic purification (Iyer et al., 2000).

Inactivated vaccines are commercially formulated in three forms: high-potency vaccines, oil-emulsion conventional vaccines, and aluminum hydroxide vaccines (Rodriguez and Gay, 2011). Emergency vaccines are unstable and should have stored in vaccine back for virus free coutry (Barnett and Carabin, 2002). Immune protect challenge can be induced four to seven days post-vaccination (Salt et al., 1998). The duration of protective immunity after a single vaccination is limited, requiring re-vaccination after 6 months (Cox et al., 2003; Parida, 2009).
The disadvantage of the aluminum hydroxide/saponin adjuvant vaccine was the induction of short-lived antibody responses, which needed relatively frequent revaccinations at intervals of 6 or even 4 months. But, oil-based adjuvant FMD vaccines appear to have many advantages, such as the induction of high titers and long-lived antibody responses, which give more effective protection (Aucouturier et al., 2001; Cloete et al., 2008). Oil-based adjuvant vaccines HAD probability of interfere maternal antibodies in neonates and can consequently be applied earlier in life (Iyer et al., 2000).

2.1.1 DNA vaccine immunogenicity

The deoxyribonucleic acid vaccine is one of the genetically engineered vaccines that is able to induce immunity against any infectious disease (Zhang et al., 2011). This type of vaccine

involves the process of transferring a targeted gene to the animal because they have the ability to absorb DNA molecules. Mainly, it has more advantages relating to efficacy, reducing the vaccine dose, and the toxicity of the vaccine (Wang et al., 2011a). The thing that makes DNA vaccines unique is the use of multicytokines as adjuvants (Shi et al., 2006). The FMD, DNA vaccine, pP12X3C, encodes the viral capsid gene (P1) and the processing proteinase, and pWRMHX encodes a mutation at the cell binding site, preventing the replicated genomes from causing disease Comparisons of both indicate that pP12X3C is strongly immunogenic (Bread et al., 1999). But to increase the immunogenicity of DNA vaccines, formulate them with nanoparticles (Yang et al., 2021).

2.1.2 Peptide vaccine immunogenicity

Peptide vaccines, also named as epitope vaccines, are particle ofvaccines made from peptides. The peptide vaccine was synthesized by chemical mean from different FMDV particle-like antigen epitope and the carboxyl-terminal region of VP1 and corresponded to B cell epitopes (Acharya et al., 1989). The main disadvantage of the vaccine was induce immunity against only specific epitope and single-particle protection (James et al., 1982). Additionally the probability of allergic and reactogenic response occurrence was very law dueto large protein of organism was not incorporated in vaccine (Li *et al.,* 2014)

2.1.3 Novel attenuated vaccine immunogenicity

The novel attenuated vaccine is a biotechnology-based vaccine that removes an oligonucleotide protein that is important for virus receptors and as a virulence factor. For example, FMD binding site deletion from the FMDV attenuated vaccine has been explored to protect cattle from FMD (McKenna et al., 1995). Live-attenuated vaccines lack a leader proteinase, serotype A12 FMDV, which provided effective protection to cattle from the challenge of FMDV (Chinsangaram et al., 1998). This leader proteinase was a virulent gene of FMDV, which acts by blocking the host immune response by inhibiting the production of beta interferon. It has a stable and lower risk of toxicity than the classical attenuated vaccine (Zhang et al., 2011).

3. VACCINATION FAILURE

Vaccination failure and failure to vaccinate were the different terms; lack of seroconversion or seroprotection described the misadministration of vaccines, respectively. The occurrence of an FMD outbreak in previously vaccinated areas indicates vaccination failure, i.e., the immune system can't produce enough antibodies (Heininger et al., 2012). In general, vaccination failure occurs with vaccine strain matching with the circulating virus, vaccine quality, the impaired immune response to the vaccine, a break in herd immunity, the duration of protective immunity, maternally derived antibody inhibition, and FMDV. Persistence in recovered animals is the major problem (Singh et al., 2019). For vaccine potency, the concentration of the immunologically active component had a direct correlation with the amount of humeral antibody-induced (Lyons et al., 2016). The dose of vaccine delivery is estimated by the potency of the vaccine (Doel, 2003). Vaccine quality was the major responsibility of the vaccine manufacturer to check the concentration of protein particles incorporated in the vaccine, which is responsible for inducing antibodies. This process was named the potency test, which focused on vaccine protein particles. Concentration of protein particles has a direct correlation with antibody-induced (Lyons et al., 2016). This was done by comparing vaccinated and non-vaccinated animals; 50% protection was estimated based on the standard (Pattnaik et al., 2012). The temperature was the other factor that affected vaccine potency, putting patients at risk of contracting the diseases even after vaccination (Dairo et al., 2016). Addition improper handling was the major that make challenge with decline in vaccine potency at the time of administration. (Dairo et al., 2016).

3.1 Herd immunity

Herd immunity is resistance to the spread of an infectious disease within a population that is based on the pre-existing immunity of a high proportion of individuals as a result of previous infection or vaccination. Occasionally, FMDV persistence in recovered animals occurs in the epithelia and lymphoid germinal centers of the oro-pharynx and secretes the virus for more than one year, which serves as the carrier (Hayer et al., 2018; Cortey et al., 2019). In general the two factors play vital role in challenge with

expecteted level of hears immunity was Vaccine efficacy and vaccination coverage FMD in the field (McVey and Shi, 2010). The break in herd immunity comfort for the virus silently circulating and spread among heard (Lyons et al., 2016).

3.2 Duration of Protective Immunity

Protection from a primary course of vaccination typically lasts for approximately 4–6 months, depending on the potency of the vaccine (Doel, 3003; Robinson et al., 2011). Depending on the quantification of the antibody titers, the antibody decay is expected (Woolhouse et al., 1996; Sharma et al., 2017).

3.3Vaccine Strain Matching with Circulating Virus

The antigenic variability between and within serotypes can limit the cross-reactivity and, therefore, the in vivo cross-protection of vaccines. The selection of appropriate vaccine strains is crucial to the control of FMD. The determination of indirect relationships (r1-value) between potential vaccine strains and field strains based on antibody responses against both is routinely used for vaccine matching purposes to check for mismatches between the vaccine strains and extant strains (Willems et al., 2020).

Vaccine matching is used to determine whether a given vaccine is likely to provide good protection against a field strain. Vaccine matching and potency testing are used in concert, as more potent vaccines are more likely to be effective against less closely related strains. The selection of potential vaccine strains to match should be based on the serotype of the field virus, its region of origin, and any other information on its characteristics. The protective capacity of the FMD vaccine could be evaluated through vaccine matching based on the calculation of the relatedness between the field isolate and available vaccine strains using in vivo challenge tests. Mismatch virus strain that causes vaccine failures (Goris et al., 2008).

3.4 Maternally Derived Antibody Inhibition

Maternally derived antibodies delay an effective immune stimulation by inactivated vaccines. Anti-FMDV antibodies that exist in the colostrum might be preventing the inducement of antibody for response of the vaccine. In other was interference may occur between maternal antibody and vaccine (Bucafusco et al., 2014; Dekker et al., 2014).

3.5 Parasite infestation

Parasite infestation was the other factor that interferes with vaccine efficacy due to helminth infection, which shifts the balance of the immune system from a TH1 to a TH2 type, whereas several vaccine-induced immunizations rely on TH1 responses (Maizels et al., 1993). To solve this, anti-parasite treatment can avoid immunomodulation caused by parasite antigens, thus improving vaccine efficacy (Malhotra et al., 2015).

4. CONCILUSION

Cloven-hoof animal viral disease FMD was a worldwide-distributed virus, which was a challenge for developing countries. Controlling vaccination bases was the selected opportunity or option, as varying authors suggested. However, using vaccines was not only mandatory, but the selection of vaccine types based on their advantages and disadvantages and immunogenecity was also ordered. Among all deoxyribonucleic acid vaccine was the most useful and less disadvantage due to best efficacy, reduce vaccine dose and toxicity of the vaccine. On the other side, there are many factors that can affect the immunogenicity of a selected vaccine. Therefore, during vaccination and vaccine production, those things should be taken into consideration. Personal vaccine management, like temperature, is the critical point for protein particle degradation. To properly use immunogenic vaccines, additional information such as vaccine manufacturing, herd immunity, maternal antibodies, duration of protective immunity, and parasite infestation are required. To solve this problem, anti-parasite treatments can avoid the immunomodulation caused by parasite antigens, improving vaccine efficacy. Examine parasites and develop a parasite control strategy that is supportive of vaccine immunogenicity.

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