Adjuvant effect of CliptoxTM on the immune response induced by an inactivated vaccine against foot and mouth disease virus in mice

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INTRODUCTION

Foot and Mouth disease (FMD) is an acute, highly contagious viral disease. It is economically important because of the international restrictions it imposes on cattle commercialization. Routine vaccinations in enzoonotic (non-FMD-free) regions can reduce production impact of the disease. Mostly available FMD vaccines are inactivated whole-virus preparations which contain oil emulsions as an adjuvant to improve their efficacy. The effective formulation of FMD inactivated vaccines requires adjuvants and Al(OH)3/saponin and mineral oil-based formulations have been widely employed in experimental studies. However, some currently available FMD vaccines for pigs have been reported to induce weak immune response in vivo. Microparticles have already been shown to be effective delivery systems for vaccine formulation inducing potent cellular and humoral immune responses. Furthermore, they can protect the antigens against the aggressive conditions such as the low pH, the bilirubin, and enzymes. CliptoxTM is a zeolite. The zeolites are microparticles playing an important role in immune system regulation. It was reported that silica, silicates, and aluminosilicates act as non-specific immunomodulators similarly to superantigens with the ability to activate a relatively large fraction (3–25%) of the T cell population, as well as humoral immunity. Earlier results obtained in our lab have demonstrated the adjuvant effect of natural microparticles of clinoptilolite (Cliptox™) using two classic T dependent antigens (ovomucoid and sheep red blood cells). Mice injected in two subcutaneously doses elicited high titers of specific antibodies and irrelevant side effects in the site of inoculation. Adult BalbC mouse is not susceptible of natural infection with FMDV O1, but it can be experimentally infected by ip inoculation. After inoculation, the virus replicates in pancreatic cells and the viremia last for 72 hours without clinical symptoms. When the neutralizing antibodies increase, the viremia ends. The objective of this study was to evaluate the efficacy of Cliptox™ as adjuvant using inactivated FMDV O1C in our murine model. The immune response after inoculation of vaccines formulations were studied in the murine model, in order to know the mechanisms involved in protection.

MATERIALS AND METHODS

Animals: adult mice BALB/c. All the experiments were performed under the international rules of animal welfare. Viral challenge was performed with infectious G1/Campos virus [under biosecurity regulations at Biosafety laboratories INTA 3A of SENASA]. Vaccines: were formulated using 1:8000 of G1/Campos and 1:5 dilutions of Virus. Immunizations and infections: mice were immunized at 0 and 20 days (group x2) or only at 0 day with 0.2 ml of each formulation; control animals were inoculated with saline solution (N group). For mice challenge, mice were infected with 0.5 ml of FMDV (104,5 DICT50/ml) ip. Immunizations and infections: mice were immunized sc at 0 and 10 days (group x2) or only at 0 day with 0.2 ml of each formulation; control animals were inoculated with saline solution (N group). For mice challenge, mice were infected with 0.5 ml of FMDV (104,5 DICT50/ml) ip.

RESULTS

The formulation Cliptox-FMDV is non toxic

The number of Dendritic cells and Macrophages are increased with the use of Cliptox-FMDV vaccine

CONCLUSIONS

In this study we evaluated the capacity of induce specific and protective immune response against FMDV. We demonstrate that Cliptox, a mineral microparticle, is non toxic with adjuvant activity. The formulation Cliptox-FMDV increased the specific antibodies levels and the protection against the virus in the murine model. The different isotype profile elicited by Cliptox-FMDV indicate a Th1/Th2 response. Since it is generally considered that good mucosal immunity will contribute to protection against infection with FMDV, the induction of mucosal immunity (IgA in saliva) by parental immunization is an important result. Since vaccines formulated with Cliptox-iFMDV induce an increase in dendritic cells, macrophages and mononuclear phagocytes in spleen, our hypothesis is that vaccine formulations containing the adjuvant could promote the presentation of the virus so it could increase the immune response and the protection. All these results demonstrate that Cliptox could be a good candidate for the formulation of a vaccine.