Comparing Cytopathic and Noncytopathic Bovine Viral Diarrhea Virus (BVDV) Vaccines: Antigen Trafficking Increased to Mucosal Surfaces with Noncytopathic Vaccines

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Introduction

Bovine viral diarrhea virus (BVDV) is a major pathogen of cattle causing severe respiratory and reproductive disease. Since BVDV infects through the oral-nasal route, increasing mucosal immunity should decrease BVDV infection and disease. This makes parenteral vaccines that can traffic antigens to mucosal lymphoid tissue more advantageous for generating mucosal immunity. This study was aimed at the distribution of bovine viral diarrhea virus (BVDV) in tissues following vaccination with one of three commercial vaccines: two vaccines containing cytopathic (CP) BVDV viruses and one vaccine containing noncytopathic (NCP) BVDV virus.

Materials and Methods

Twenty-four non-suckled newborn calves were procured (three groups of seven vaccinates and one control). A group of animals was randomly assigned to one of three groups of eight (24 calves total, 21 vaccinates and three control animals). At three to four weeks of age, seven animals were vaccinated with one of the three commercial modified live virus vaccines: Group 1, Pyramid 5 with Metastim (CP1): Group 2, Bovishield 4 cytopathic (CP2); Group 3, Jencine 2 (NCP). Clinical signs were taken daily and clinical hematology was taken at days -3, 0, 3, 6, 8, 10, 12, 15 and 18. One animal from each group was euthanized each day on days -3, 6, 8, 10, 12, 15 and 18 post vaccination and the control animal was euthanized at day 0. Animals were necropsied and the 20 tissues sampled (10 lymphoid tissues and 10 other tissues). For each animal tissue, three samples were collected: one tissue sample was snap frozen in liiquid nitrogen for future RNA extraction; one sample was frozen at -80°C for future virus isolation and one sample was formalin fixed for BVDV immunohistochemistry (IHC). IHC was the method of detection of BVDV.

Results

The IHC results for CP1 found antigen present on three days: 8, 10 and 12, and antigen was only visualized in low levels in a single tissue-ileum (Peyer's patches). The IHC results for CP2 vaccinated animals found antigen on a single day, day 8 in the thymus at low levels. For NCP, antigen was present beginning at day 6 in the ileum. By day 8, antigen was present in two mucosal lymphoid tissues and peaked at day 10 when it was present in four different tissues (two mucosal lymphoid tissues [tonsil, Peyer's patches], mesenteric lymph node and the lung). Antigen was present in three tissues at day 12 and decreased to a single tissue on days 15 and 18. The ileum contained virus on all days, and antigen load was high on days 8-18.

Significance

The results indicate that animals vaccinated with a NCP BVDV vaccine had longer antigen retention that trafficked to more mucosal lymphoid tissues than either of the CP vaccines. The mucosal immune system is a common system where antigen stimulation of one mucosal lymphoid tissue in one area will provide T and B antigen-specific cells for other mucosal surfaces, such as the respiratory and reproductive tracts. This ability of NCP vaccines to traffic to these mucosal lymphoid areas could result in better protection against BVDV infection at the portals of entry lined by mucosal surfaces.