

Using single nucleotide polymorphisms (SNPS) to sort out bovine herpesvirus-1 vaccine-induced reproductive disease

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Introduction

Modified live virus (MLV) bovine herpesvirus 1 vaccines have been a major aid to the prevention of reproductive disease in cattle. However, their use (or misuse) can result in major abortion storms. We describe 3 different cases where MLV vaccines resulted in abortion storms and the use of SNP to identify the source.

Materials and Methods

Case 1 occurred in a herd of 106 first-calf beef heifers. The animals were vaccinated twice with Vaccine A, a MLV vaccine containing BHV-1, once at weaning in the fall of 2012 and again in February 2013. The animals were bred in June 2013 and confirmed pregnant by rectal palpation. The animals were vaccinated with an oil adjuvanted scours vaccine and treated with an anthelmintic in January 2014. Five days later the animals began to abort. Case 2 occurred in a herd of ~100 Holstein heifers. The normal vaccination protocol was animals were vaccinated with 2 to 3 doses of MLV vaccine prior to breeding and another dose of MLV was given at pregnancy confirmation. In this group animals had not been pregnancy checked for over 8 months so no vaccine had been administered to these animals in 8 to 12 months. The entire herd was vaccinated with either Vaccine B or Vaccine C; both vaccines were MLV vaccines that contained BHV-1. Two weeks post vaccination 8 abortions were found in the pen. Case 3 occurred in a herd of beef cows with a poor vaccination history. The animals received a single dose of inactivated multivalent viral vaccine containing BHV-1 as heifer calves. Annual revaccination with the same inactivated vaccine was infrequent. In August 2014, calves nursing these cows were given a single dose of MLV multivalent Vaccine C containing BHV-1. Beginning in January 2015, the cows began aborting. Case 4 occurred in a herd of 350 crossbred beef cattle. These cattle were vaccinated following the manufacturer's instructions (i.e., the cows had all been vaccinated a year prior with a similar product from the same company; heifers vaccinated twice with similar product prior to breeding). These animals were between 5 and 6 months gestation and had been vaccinated with Vaccine C about 15 to 20 days

prior to the abortions occurring. Three aborted fetuses from heifers and 1 mummified fetus from a cow were recovered over the course of 2 weeks.

Results

Case 1: Forty-four of the 106 calves were aborted, delivered dead, or were born alive but died within the first 24 hours. BHV-1 was isolated from 4 of the fetuses on 2 separate submissions. The viruses were submitted for genetic analysis to the Animal Disease Research and Diagnostic laboratory at SDSU. Single nucleotide polymorphisms (SNP) analysis indicated that the SNP pattern of the viruses isolated from the fetuses was identical to Vaccine A. Case 2: Two fetuses were submitted and virus isolation and genetic SNP analysis was performed. The SNP pattern indicated that the SNP pattern of the 2 isolates were identical with Vaccine C. Case 3: Two fetuses were submitted and virus isolation and genetic SNP analysis was performed. The SNP pattern of the 2 isolates were identical with Vaccine C. Case 4: All fetuses from the heifers had typical histological lesions of herpesviral abortion (multiple foci of necrosis in multiple organs, some with herpetic inclusions). Three of 3 were FA positive for BHV-1, while virus was isolated from 2 of the 3. The mummified fetus was a typical mummified fetus—tissues were too autolyzed for meaningful histopathology, and all viral assays for BHV-1 were negative (FA and VI negative). One isolate was submitted for genetic SNP analysis. The SNP pattern of the isolate was identical with Vaccine C.

Significance

Use of vaccines containing MLV BHV-1 has inherent risks to reproductive fitness. In Case 1, the MLV vaccine was administered following the label. No vaccine was administered to pregnant heifers. Surprisingly BHV-1 abortions, weak calves and stillborns occurred following the administration of an oil-adjuvanted vaccine in ~40% of the heifers. In the same herd, 350 cows were also vaccinated with oil-adjuvanted vaccine, but no abortions occurred. BHV-1, like all herpesviruses, causes lifelong latent infections. Why this virus was reactivated and caused abortions is unclear. In Case 2 and

Case 3 the animals were inadequately vaccinated. In the small sample size from Case 2, only Vaccine C was detected in the abortions. In this herd, the vaccination interval in some of the animals may have been greater than a year, leading to an increased abortion rate. Case 3 is interesting as no MLV was administered to the cows so the virus spread from the MLV vaccinated calves to the cows. This case reinforces the need

to make sure the cow herd is adequately vaccinated if calves are vaccinated with MLV vaccine while still with the cows. Case 4 is evidence again of the higher susceptibility of heifers to MLV induced abortion even when “properly vaccinated”. In summary, MLV BHV-1 vaccines must be used judiciously following label directions. In spite of the following the label, reproductive issues can still occur.

Impact of passive immunity induced by maternal vaccination on subsequent immunization and disease-sparing in early-weaned beef calves challenged with highly virulent BVDV

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Introduction

Vaccination programs have been developed to limit disease associated with bovine viral diarrhea virus (BVDV) infection. The ultimate goal of BVDV vaccination is to induce immunity that prevents viral replication after infection; however, passively acquired BVDV-specific neutralizing antibodies can impact immunity and vaccine responses in the young calf. The purpose of this study was to examine the impact of passively-derived antibody on vaccine response and mitigation of disease in early weaned beef calves whose passive immune status was documented, and when vaccination and challenge were separated by only 5 days.

Materials and Methods

Sixty-three crossbred beef calves were utilized in this study. All calves were born to heifers raised and bred in biosecure herds, and whose vaccination histories or absence of vaccination were known. Calves were stratified by serotiter to BVDV 2 from serum samples obtained on calves 30 days prior to study. Calves were then randomly assigned to unvaccinated (n=31) or vaccinated (n=32; Inforce3/Bovi-Shield BVD) groups. Calves were weaned (day -7) shipped (day

-6), and vaccinated/unvaccinated (day -5) prior to challenge (day 0) with BVDV 2 strain 1373. Virus isolation from whole blood, serum, and nasal swabs, clinical pathology, clinical illness scores, and virus neutralization assays were performed on calves following challenge.

Results

Vaccinated calves exhibited significantly lower rectal temperature measurements, significantly higher white blood cell and differential cell counts, and significantly better average daily gains than calves that remained unvaccinated. In contrast to 100% of unvaccinated calves becoming viremic, BVDV was not isolated from any clinical sample at any time point from 47% (15/32 calves) of the calves administered modified-live viral vaccine. Viral shedding (nasal swab isolation of BVDV) was significantly reduced in vaccinated calves (1/32) compared to unvaccinated calves (21/31).

Significance

The level of passive immunity induced by maternal vaccination had minimal impact on vaccine response and subsequent protection from clinical disease following challenge.