Priming the Immune System for IBR and BVD with One Dose of Killed Vaccine: Immunization with a Follow up Dose of MLV

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Summary

A field trial was conducted in a cow/calf operation to evaluate the SN titer response to BVD and IBR virus following vaccination with either one or two doses of vaccines. Group 1 received two doses of vaccine. The first dose of vaccine was given 3 weeks prior to weaning and contained killed fractions of IBR and BVD. The second dose was given at weaning and was a four-way modified live vaccine (mlv) (IBR,BVD,BRSV,PI3). Group 2 received only one dose of 4-way mlv vaccine at weaning. Group 3 was not vaccinated and remained with the herd as sentinels. SN titer results were compared to see if the antibody response elicited by a mlv could be primed with one dose of killed vaccine.

The results from this trial indicate that one dose of killed vaccine, administered 3 weeks prior to a dose of mlv vaccine, effectively primed the immune response. The follow up dose of mlv vaccine administered at weaning elicited a rapid and elevated antibody titer response in Group 1 calves compared to Group 2 calves; an indication that priming had taken place.

The findings in this study support a vaccination program tailored for the cow/calf operation where a priming dose of killed vaccine is given before weaning, with a follow up immunizing dose of mlv vaccine given at weaning.

Introduction

In this study, the antibody response to IBR and BVD was determined, following vaccination with various killed and/or modified live vaccines. Importantly, it should be understood that protection against disease is not being measured when SN titers are reported; just an antibody response to antigen. Depending on the virus being studied, there may be a high or low degree of correlation between antibody titer response and protection from disease. A full discussion on protection vs. titer is beyond the scope of this paper, but measurement of antibody titer to vaccines is a good indicator of whether or not the immune system is recognizing and responding to antigens in a vaccine.

Reported lab titer values are a function of lab technique and cell culture line used. Antibody titer values are also dependent on the laboratory strain of virus used in the SN test in relation to the vaccine or field strain virus to which the test animal may have been exposed. For this study, the strains of virus used in the laboratory in assessing antibody titers were not the same strains used in the vaccine. This impact would probably have greater significance for BVD, than IBR, since antigenic variation is great for BVD but minimal for IBR.

The investigator speculates that the immune system can be primed with one dose of killed vaccine, administered pre-weaning. If priming occurs in animals receiving a first dose of killed vaccine, a follow up dose of mlv vaccine administered three weeks later at weaning should elicit a more rapid and greater response compared to animals receiving a single dose of mlv at weaning.

The hypothesis for this study is that killed, properly adjuvanted vaccines, containing a large antigen mass, should effectively expand antigen reactive B cells and/or T cells; in other words, prime the memory cell response. Whether or not true memory cell response, following a single dose of vaccine, is stimulated cannot be measured directly by the SN test.[1] If calves receiving the killed dose first develop a higher titer subsequent to the dose of mlv administered at weaning, it could be established that a possible memory cell response did in fact take place. The effects of the killed vaccine given first, with modified live vaccine given second, would become measurable only following the immunizing dose

of mlv vaccine[1], compared to the response with only one dose of mlv. The current literature supports that the immune system can be primed with mlv vaccine[2], even when given to animals with passive acquired maternal antibody[3].

Materials and Methods

Animals

The 1995 spring calf crop from the MFA research farm beef herd was used in this study. Cows in this herd are routinely boostered in the spring, prior to breeding, with a modified live four-way virus vaccine combined with 5-way lepto. Prior to this study, the calves were vaccinated with Vision 7®[a], 7-way Clostridial vaccine, in July of 1995.

Vaccination

Calves were sorted on paper by birthdate and sex, then randomly assigned to groups 1-3. A random number table was used to assign the calves to groups (Table 1). Groups 1 and 2 had 17 calves each and Group 3 had 14 calves. Calves were vaccinated 3 weeks before weaning (day 0, September 25, 1995) then turned back with the cows. The majority of the calves would have been 5-7 months of age on day 0 of the study. In addition to the assigned viral vaccines administered on day 0, the calves received a clostridial booster, were wormed and castrated. Heifers were vaccinated with strain 19 Brucella vaccine. On day 21 of the study, calves were administered the appropriate dose of viral vaccine and weaned.

Table 1. Vaccine assignment to Groups 1-3.

Vaccine Group	3 Weeks before weaning	Weaning
Group 1 n=17	Horizon® 4	BRSV Vac® 4
Group 2 n=17	Nothing	BRSV Vac® 4
Group 3 n=14	Nothing	Nothing

Note

Horizon® 4 is a combination vaccine containing killed fractions of BVD and IBR and modified live fractions of PI3 and BRSV. Horizon® 4 contains the immuno-potentiating adjuvant PROLONG®. BRSV Vac® 4 contains modified live fractions of BVD, IBR, PI3 and BRSV. The label on BRSV Vac® 4 does not support its use in calves nursing pregnant cows, since it is a 4-way modified live vaccine.

Horizon® 4 and BRSV Vac® 4 both contain the Baker strain of IBR and the Oregon C24V strain of BVD. The serial numbers for vaccine administered were 1487 for BRSV Vac® 4 and 1236-ALQ for Horizon® 4.

Sampling

Calves were blood sampled on days 0, 21, 35, 49 and 70. The serum was harvested, frozen, and later titered for antibodies by SN for IBR and BVD.

Serum Neutralization

Serum samples were processed at the Veterinary Diagnostic Lab, University of Missouri. BVD virus Singer strain, 100 TCI_{50}/.05ml and IBR virus, Colorado strain, 100 TCI_{50}/.05ml were used for the SN test. (Singer strain and Colorado strain were obtained from National Veterinary Services Laboratory, Ames, Iowa). All samples for an individual calf were performed on the same day at the diagnostic laboratory.

Statistical Analysis

Statistical analysis of the data was done using PC SAS[b] and PEPI[c]. P values were generated using the Wilcoxson Rank Sum test. Reported titer values were used to calculate the statistics.

Results

Table 2. IBR Geometric Mean Titer (GMT) Results

Vaccine Combination	Day 0	Day 21	Day 35	Day 49	Day 70
Horizon® 4-BRSV Vac® 4	0	1.4	16[a,b]	10.6[c,d]	6[f,g]
None-BRSV Vac® 4	0	0	2.9[a]	3.5[c,e]	2.4[f]
None-None	1.1	1.1	0[b]	0[d,e]	0[g]

Note: Cells with same superscript are statistically different.

[a] p=.007
[b] p=.0000005
[c] p=.036
[d] p=.00000004
[e] p=.003
[f] p=.029
[g] p=.0000057

Table 3. BVD Geometric Mean Titer (GMT) Results

Vaccine Combination	Day 0	Day 21	Day 35	Day 49	Day 70
Horizon 4-BRSV Vac® 4	1.1	1.3	13.1[a,b]	40.9[c,d]	48.1[f]
None-BRSV Vac® 4	0	0	0[a]	10.2[c,e]	36.2[g]
None-None	0	0	0[b]	0[d,e]	0[f,g]

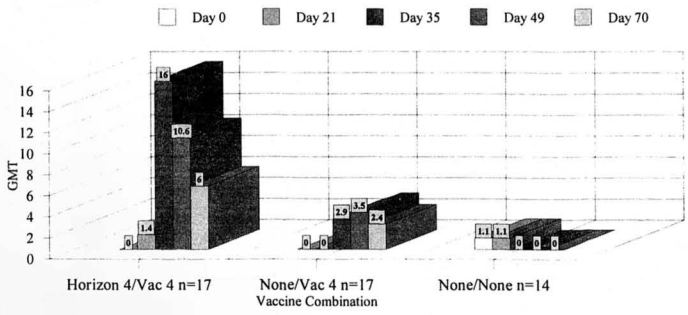
Note: Cells with same superscript are statistically different.

[a] p=.00039
[b] p=.000843
[c] p=.033
[d] p=.000000089
[e] p=.0054
[f] p=.0000098
[g] p=.000036

[a]Bayer Corporation, Shawnee Mission, Kansas
[b]SAS Institute, Inc., Cary, NC 27513
[c]Version 2, USD, Inc., Stone Mountain, GA 30087

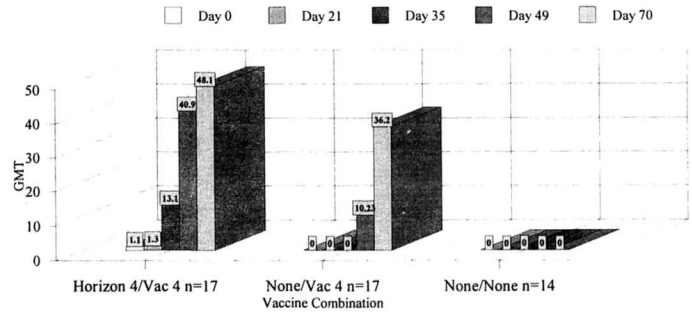
Vaccine Comparison Trial

IBR



Vaccine Comparison Trial

BVD



Discussion

The results in Table 2 show that the IBR titers in the calves primed with the killed vaccine were higher on days 35, 49, and 70 (p=.007, .036, and .029 respectively) than those calves that only received a single dose of mlv at weaning. In studies conducted in the past by the author, a peak response for IBR following a single dose of mlv vaccine occurs around 30-35 days. This held true for the group receiving one dose of mlv at weaning when compared to the non-vaccinated control group (p=.003) on day 49.

The results in Table 3 show that the BVD titers in the calves primed with the killed vaccine were higher on days 35 and 49 (p=.00039 and .033 respectively) than those calves that only received a single dose of mlv at weaning. In studies conducted in the past by the author, peak response for BVD following a single dose of mlv vaccine occurs beyond 50 days. This held true for the group receiving one dose of mlv at weaning when compared to non-vaccinated cattle on days 49 and 70 (p=.0054 and .000036) respectively.

The data supports the hypothesis that the immune response can be primed with a single dose of killed vaccine, and subsequently immunized with a dose of mlv vaccine. It must be emphasized that different adjuvant/antigen combinations will stimulate different immune responses. All killed vaccines may not effectively prime the immune response for immunization with a follow up dose of mlv.

The killed vaccine used in this study was capable of priming the memory cell response.

Age of the calf may dictate whether or not the immune system may respond to a priming dose of killed vaccine. A similar study in veal calves using these vaccines failed to show a priming effect for the mlv or the killed vaccines. It was concluded that this was most likely due to interference by maternally derived antibody and stress related immuno suppression in the calves since they were less than one week old at the time the first dose of vaccine was given.[4]

The information generated by this study will be helpful to cow/calf veterinarians and producers as they plan vaccination programs for calves at weaning. It is reassuring that a killed vaccine, used in the weaning aged calf, can effectively prime the immune response. This information should also be helpful for veterinarians that want to use a killed product on stressed feeder calves as a first dose.

References

1. Brar JS, *et al.* Maternal Immunity to Infectious Bovine Rhinotracheitis and Bovine Viral Diarrhea Viruses: Duration and Effect on vaccination in Young calves. *AM J Vet Res* 1978; 39 No. 2; 241-244. 2. Menanteau-Horta AM, *et al.* Effect of Maternal Antibody Upon Vaccination With Infectious Bovine Rhinotracheitis and Bovine Virus Diarrhea Vaccines. *Can J Comp Med* 1985; 49; 10-14 3. John A. Ellis, et al. Effects of perinatal vaccination on humoral and cellular immune responses in cows and young calves. *JAVMA*, Vol 208, No. 3, February 1, 1996. 4. R.D. Schultz. *Personal communication of unpublished results.*