The Safety of Vaccinating Beef Replacement Heifers at Weaning Against 18 Antigens

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Abstract

Humoral immune responses to vaccination, mean daily gains, morbidity, and mortality were compared in groups of beef replacement heifers from weaning to 4 months after weaning. The only difference in management among groups of heifers was the number and type of vaccines they received. Heifers were vaccinated at weaning (mean age, 205 days) and again 28 days later against 0, 1, 9, 10, 17, or 18 antigens, using commercially available monovalent and multivalent vaccines. Mean daily gain, morbidity, mortality, and serum neutralization antibody titers to bovine respiratory syncytial virus, infectious bovine rhinotracheitis virus, and bovine viral diarrhea virus did not differ among treatment groups. Although the study revealed the safety of vaccinating beef heifers against 18 antigens at weaning, our data emphasized the need for serial vaccination to induce a measurable serum antibody response in animals not exposed previously to the vaccine antigens.

Introduction

Most cow/calf producers wean their calf crop on a single day when the average age is six to seven months. During this process, calves may be weighed, vaccinated, dewormed, treated for external parasites, tagged, and castrated. Producers prefer to perform all these procedures on one day, because it saves time and money, and reduces the number of times calves must be handled and restrained. Arguments for and against this approach to handling calves at weaning are many. Despite any argument, many producers will continue to manage their calves at weaning in the manner described, because of time and labor efficiencies involved.

Vaccination is the only procedure, from those listed previously, that requires a direct and active response from the weaned calf. Consequently, a question arises about the ability of a calf to respond appropriately to a vaccine, or, more likely, several vaccines administered simultaneously, when it experiences stresses associated with the weaning process. All USDA licensed vaccines, monovalent and multivalent, have been tested for safety and efficacy under experimental conditions, and the safety and efficacy of many of these products have been demonstrated in a variety of field conditions. To our knowledge however only one report, previously published by the authors, has examined the safety and efficacy of vaccination programs for beef replacement heifers featuring the concurrent administration of more than one federally licensed multivalent vaccine.[1] In that study heifers were vaccinated at weaning and again 28 days later against 0, 1, 9, 10, 17, or 18 antigens, using commercially available monovalent and multivalent vaccines. Mean daily gain, morbidity, mortality and serum neutralization (SN) antibody titers to bovine respiratory syncytial virus (BRSV) did not differ among treatment groups. Although we were interested in measuring responses of heifers to all immunogens simultaneously administered, serologic testing for each vaccine component was not economically feasible at that time. Eventually, funds were obtained that enabled us to test the previously collected serum for SN antibody titers to bovine viral diarrhea virus (BVD) and infectious bovine rhinotracheitis virus (IBR). The purpose of the study reported here was to supplement the findings of the original study. Specifically, the humoral immune responses of the original study animals to the vaccine strains of BVD and IBR were compared.

Materials and Methods

Cattle

Angus heifers (n = 101), weaned at a mean age of 205 days (range, 140 to 237 days), were housed as a single group and fed once daily during the 140-day study period. The heifers were raised as potential herd replacements. All heifers were treated with a subcutaneous injection of ivermectin[a] four weeks after weaning.

Treatment groups

Heifers were assigned randomly to one of seven treatment groups at weaning. Heifers were not assigned equally to treatments, because mean results of some

[a] Ivomec, MSD Agvet, Rahway, NJ

treatments were to be used more frequently in comparisons than were results of other treatments. The five heifers in group 1 served as unvaccinated controls. The five heifers in group 2 served as controls and received injections of sterile water. The remaining five groups of animals received various vaccines alone or in combination with other vaccines. In group 3, fifteen heifers were vaccinated with a vaccine that contained only attenuated BRSV.[b] BRSV was chosen as the one vaccine component common to all vaccine-treated groups, because of its prevalence and importance as a respiratory pathogen in young calves. In group 4, thirty heifers were vaccinated with a single multivalent vaccine (9-way) containing the following fractions: killed BVD virus, IBR virus, *Leptospira canicola, L grippotyphosa, L hardjo, L icterohaemorrhagica, and L pomona,* and modified live parainfluenza type-3 virus (PI_3) and BRSV,[c] according to the manufacturer's recommendations. In group 5, fifteen heifers were vaccinated with the same vaccine as heifers in group 4, and with a second multivalent vaccine (8-way) that contained killed cultures of seven strains of *Clostridia spp*, and *Hemophilus somnus*.[d] In group 6, fifteen heifers were vaccinated with the same vaccine as heifers in group 4, and with a monovalent vaccine that contained a modified live culture of *Pasturella hemolytica*.[e] In group 7, fifteen heifers were vaccinated with the three vaccines used for groups 5 and 6.[c,d,e] Except for those in group 1, all heifers were given three injections (vaccines and/or sterile water) at weaning and again at four weeks after weaning.

Clinical observations

Heifers were observed regularly by the principal investigator for disease signs such as coughing, nasal and ocular discharge, anorexia, diarrhea and respiratory distress. Rectal body temperature was measured in all heifers on days 0, 7, 14, 28, 35 and 42 of the study. A stationary weight scale was used to record body weights every two weeks from day 0 through 56, and every 28 days after that to day 140.

Serologic testing

Blood was collected from each heifer for determination of SN antibody titers against BRSV, IBR and BVD viruses on day 0 (day of weaning), 7, 14, 28 (day of booster vaccination), 35, 42, 56, 84, 112, and 140. For each SN titer test, all 10 serum samples from a heifer were analyzed at one time. The likelihood of biased results was reduced by keeping the laboratory personnel unaware of treatment and heifer identity. A titer to BRSV > 4, IBR ≥ 4, or BVD > 8 was considered sufficient to consider the heifer as seropositive, based on USDA Animal Plant Health Inspection Service guidelines for testing each of the three vaccine viruses.

Virus isolation

On day 0, the nasal mucosa of each heifer was swabbed with a sterile cotton-tipped applicator. Two tube cultures of bovine turbinate cells were inoculated with 0.3 ml and 0.5 ml of eluate from each nasal swab and were incubated at 37 C. Tubes were examined daily for cytopathic effects (CPE) until cell degeneration was noticed.

Hematologic evaluation

Jugular venous blood samples were collected in vacuum tubes containing potassium EDTA on days 0, 7, 14, 28, 35, and 42, and CBC were determined. Blood films for differential WBC counts were prepared with Wright's stain, and 100 cells were counted. Laboratory personnel were unaware of the identity of heifers and groups.

Statistical analysis

Data were analyzed at each time by one-way analysis of variance with planned comparisons among group means. The contrasts included a comparison of control and BRSV only groups (1 vs. 2, 1 vs. 3, and 2 vs. 3) and when these groups were not different, they were combined to serve as the control in subsequent contrasts. Control groups were then compared with treatment 4. Treatments 4, 5, 6, and 7 formed a 2x2 factorial; contrasts were included to test the interaction and main effects of the 8-way vaccine and *P. hemolytica* vaccine. In addition the following comparisons were made among the four treatments: 4 vs. 5, 4 vs. 6, 4 vs. 7, 5 vs. 7, and 6 vs. 7. Examination of residual plots for titer indicated that within-group variances were linearly associated with group means. Weighted (weight = 1/mean titer) least-squares analysis of variance therefore was used for titer. All other variables were analyzed using ordinary least-squares analysis of variance.

Results

Clinically important differences were not found among the seven treatment groups for any clinical variable measured between days 0 and 42. Mean WBC counts and differential counts for the population of heifers and for group of heifers were consistently within normal laboratory ranges. Virus isolation techniques failed to identify any heifer harboring BRSV, IBR or BVD virus on day 0. All heifers had negative results on serologic testing for BRSV, IBR and BVD antibodies on days 0 and 7. Group 1 and 2 control animals were

[b]BRSV, Norden Laboratories, Lincoln, NE
[c]CattleMaster 4 + L5, Norden Laboratories, Lincoln, NE
[d]Fermicon-7/Somnugen, Boehringer Ingelheim Animal Health, Inc., Bio-Ceutic Division, St. Joseph, MO
[e]Pneumo-Guard H, Norden Laboratories, Lincoln, NE

seronegative to BRSV, IBR and BVD on SN test throughout the course of the study. Group 3 animals were seronegative to IBR and BVD throughout the course of the study. Most vaccinated heifers had a positive BRSV, IBR and BVD titer one week after the booster vaccination (day 35). Length of time that heifers maintained a positive titer for each vaccine component was recorded. Mean heifer body weight for all groups was 213.6 ± 3.0 kg (SEM) on day 0 and 293.1 ± 3.3 kg (SEM) on day 140. Mean daily gain for all heifers was 0.57 ± .007 kg (SEM). Significant differences among groups were not found for body weight, weight gain, morbidity, or mortality.

Conclusions

Vaccinations are integral components of most preventive herd-health programs. Because every farm represents a unique set of biological, physical and financial circumstances, food animal veterinarians spend much time and effort developing personalized vaccination strategies for their clients' herds. Decisions on vaccine selection and use must be based on consideration of many factors such as safety and efficacy of vaccines, the likelihood of exposure to disease agents and the cost effectiveness of vaccines. Vaccination programs for heifers destined for breeding stock are especially difficult to devise. This group is susceptible to a multitude of systemic and localized diseases including those affecting the respiratory, gastrointestinal and reproductive tracts. For example, a vaccination program for beef replacement heifers prior to breeding might involve administration of vaccines against the following common and economically important disease agents: infectious bovine rhinotracheitis virus, bovine viral diarrhea virus, parainfluenza type-3 virus, bovine respiratory syncytial virus, the five major serovars of Leptospira interrogans, *Pasteurella hemolytica* and *P multocida, Hemophilus somnus, Brucella abortus,* and *Clostridia spp* such as *C. perfringens* and *C. chauvoei.*

Abundant availability of safe and efficacious vaccines complicates the decision-making process in selecting vaccines. A minimum of injections can be used to vaccinate cattle against a broad spectrum of disease agents because vaccines are sold in a myriad of combinations. After selecting vaccines for a preventive herd health program, another variable to consider is the timing of vaccine administration. In calves, factors such as the presence of maternal (passive) antibodies and the desire of producers to minimize handling and restraint of calves must be considered.

The purpose of the study reported here was to compare the humoral immune responses, morbidity, mortality and mean daily gain of groups of beef replacement heifers in which various vaccination regimens were used after weaning. The only difference in management among groups of heifers was the number and type of vaccines they received. Heifers were vaccinated at weaning and again 28 days later against 0, 1, 9, 10, 17 or 18 antigens, using commercially available monovalent and multivalent vaccines. Significant differences were not found between the control and treatment groups in morbidity, mortality or mean daily gain from weaning to 140 days after weaning. Measurable BRSV, IBR and BVD specific antibodies did not exist in any study animal at the start of the study. Because control heifers never developed antibodies to BRSV, IBR or BVD, there was no indication that the population was exposed to any of these viruses during the study except through vaccination. The number and type (modified live vs. killed) of antigenic components administered to the heifers at weaning and again four weeks later did not alter their ability to produce humoral antibodies to the BRSV, IBR or BVD components of the vaccines. Among the groups that received one or more multivalent vaccines (groups 4 through 7), biological differences were not detected in the number of days required for development of a seropositive antibody titer or in the duration of maintenance of a positive titer. However, these results demonstrated that, for cattle without previous exposure to a particular disease agent, a booster vaccination is essential to induce a measurable humoral antibody response. Challenge exposure of the study heifers to live nonattenuated BRSV, IBR and BVD viruses to determine and compare more accurately the degree of immune protection was not possible in our circumstances. We concluded that vaccination of these groups of heifers, managed as described, against 9 to 18 modified live and killed disease agents at one time was safe. Heifers in this study produced clinically important amounts of humoral antibodies to BRSV, IBR and BVD despite multiple-vaccine exposure.

References

Carmel DK, Barao SM, Douglass LW, 1992. Effects of vaccination against 18 immunogens in beef replacement heifers at weaning. *JAVMA*, 201 (4):587-590.