ARTICLES

Comparative serological responses in calves to eight commercial vaccines against infectious bovine rhinotracheitis, parainfluenza-3, bovine respiratory syncytial, and bovine viral diarrhea viruses

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Abstract

A field trial was conducted to compare the serological responses in calves to eight commercial vaccines against infectious bovine rhinotracheitis virus (IBRV), parainfluenza-3 virus (PI3V), bovine respiratory syncytial virus (BRSV), and/or bovine viral diarrhea virus (BVDV). Calves given IBRV, PI3V, BRSV, and BVDV vaccines had significantly higher antibodies to these viruses than unvaccinated controls; however, serological responses to killed BVDV vaccines were low. Calves with preexisting antibodies to IBRV, PI3V, BRSV, and the Singer strain of BVDV had lower seroconversion rates following vaccination than calves that were seronegative initially.

Serological responses in calves to IBRV, PI3V, BRSV, and BVDV differed among various commercial vaccines. Antibody titers to IBRV were higher in calves vaccinated with modified-live IBRV vaccines than in those vaccinated with killed IBRV vaccines. Following double vaccination with modified-live IBRV and PI3V vaccines, seroconversion rates and antibody titers to IBRV and PI3V were higher in calves vaccinated intramuscularly than in those vaccinated intranasally. Calves given Cattlemaster 4 had significantly higher titers to BRSV and PI3V, and lower titers to BVDV, than calves given Cattlemaster 3, suggesting that the addition of BRSV to Cattlemaster 4 caused some interaction among antigens.

Résumé

Évaluation de la réponse sérologique de huit vaccins commerciaux contre la rhinotrachéite infectieuse bovine, le parainfluenza type 3, le virus respiratoire syncytial et le virus de la diarrhée bovine chez les veaux

Une étude sur le terrain a été effectuée sur des veaux afin de comparer leur réponse sérologique à huit vaccins commerciaux contre la rhinotrachéite infectieuse bovine (IBR), le parainfluenza type 3 (PL3), le virus respiratoire syncytial (RSV) et/ou le virus de la diarrhée bovine (BVD). Les veaux ayant reçu les vaccins contre IBR, PL3, RSV et BVD ont démontré un taux d'anticorps plus élevé de façon significative, comparativement au groupe témoin; toutefois, les réponses sérologiques au vaccin à virus inactivé contre le BVD ont été faibles. Les veaux qui présentaient des anticorps pré-immunisation contre IBR, PL3, RSV et la souche Singer du BVD ont eu un taux de séroconversion post-immunisation plus bas que les veaux qui étaient initialement séronégatifs.

Chez les veaux, les réponses sérologiques contre IBR, PL3, RSV et BVD ont différé selon les divers vaccins commerciaux. Le vaccin contre IBR à virus vivant atténué a produit des taux d'anticorps plus élevés comparativement à celui à virus inactivé. Une double immunisation contre IBR et PL3 avec un vaccin à virus vivant atténué, administrée par voie intramusculaire, a produit des taux de séroconversions et les titres d'anticorps plus élevés que celui administré par voie intranasale. Les veaux ayant reçu le vaccin Cattlemaster 4 ont démontré de façon significative des titres plus élevés contre RSV et PL3 et des titres plus bas contre BVD comparativement aux veaux immunisés avec le Cattlemaster 3. Ceci suggère que le RSV contenu dans le vaccin Cattlemaster 4 cause une certaine interaction antigénique.

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Introduction

Numerous modified-live and killed virus vaccines to infectious bovine rhinotracheitis virus (IBRV), parainfluenza-3 virus (PI3V), bovine respiratory syncytial virus (BRSV), and bovine viral diarrhea virus (BVDV) are currently available for use as single or combination products (1). The lack of criteria by which vaccine efficacy can be evaluated and the absence of comparative data on different vaccines make it dif-

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Table 1. Properties of eight commercial vaccines given to 260 calves at the Melfort Research Station

Vaccine[a]	Manufacturer	Number of calves vaccinated	Vaccine components			
			IBRV	PI3V	BRSV	BVDV
No vaccine	—[b]	80	—	—	—	—
TSV-2[c]	SmithKline	28	MLV[d]	MLV	—	—
Resbo IBR/PI3	SmithKline	18	MLV	MLV	—	—
Cattlemaster 3	SmithKline	18	MLV	MLV	—	K[e]
Cattlemaster 4	SmithKline	30	MLV	MLV	MLV	K
Triangle 3	Ayerst	19	K	K	—	K
BRSV Vac + Horizon II	Bayvet	11	K	—	MLV	K
Horizon IV	Bayvet	30	K	MLV	MLV	K
Sentry 1 + IBR/PI3/Somnugen	Boehringer	26	MLV	MLV	—	K

[a]For details on vaccine products refer to the Canadian Compendium of Veterinary Pharmaceuticals, Biologicals and Specialties (1)
[b]Not present
[c]Only vaccine given intranasally, all others given intramuscularly
[d]Modified-live virus
[e]Killed virus

ficult for veterinarians and livestock producers to select which vaccines to use. Ideally, the selection of vaccines should be based on efficacy data from controlled field trials (2). However, this information is often not available because studies to compare biological and economic efficacy of different vaccines in controlled field trials are expensive and logistically difficult to conduct. In the absence of such information, veterinarians frequently have to select vaccines based solely on the manufacturers' data from vaccination-challenge studies performed in small groups of animals under experimental conditions (3). Few independent studies have investigated the serological responses to different commercial vaccines in groups of calves under field conditions. Such serological data would provide useful information on the relative potency of different vaccines and thereby assist veterinarians in making judicious vaccine choices depending on the specific management conditions.

The field trial reported herein was undertaken to investigate the comparative serological responses in six-month-old calves to eight commercial vaccines which contain IBRV, PI3V, BRSV, and BVDV.

Materials and methods

Study design

Two-hundred-and-sixty Charolais-cross calves, born in February and March at the Agriculture Canada Research Station, Melfort, Saskatchewan were used in this field trial during the fall of 1988. Calves were kept on one of 12 different pastures during the study because of a preexisting grazing trial that consisted of several pasture groups of unequal numbers of cow-calf pairs.

Calves were randomly assigned within pasture group to one of eight commercial vaccines or left as unvaccinated controls (Table 1). Calves were vaccinated twice, three weeks apart, according to the manufacturers' directions. Thirty unvaccinated calves were kept separately on two pastures. Five vaccine groups were each kept separately on another five pastures. On another three pastures, unvaccinated calves were comingled with a vaccine group. On the remaining two pastures, two different vaccine groups and unvaccinated calves were comingled. Four vaccines were tested in two groups of calves on two different pastures.

Blood samples for measurement of antibody levels to IBRV, PI3V, BRSV, and BVDV were collected from all calves at the time of each vaccination and two weeks after the second vaccination.

Serological methods

Virus neutralizing (VN) titers to IBRV, PI3V, BRSV, and BVDV were determined using heat-inactivated sera. The viruses were propagated in BVDV-free cell cultures that were maintained in MEM supplemented with 5–10% horse serum and antibiotics (Gibco, New York, New York, USA).

Serum VN titers to IBRV were determined in microtiter plates using a plaque reducing assay (4). Two-fold dilutions of sera were incubated with 100 $TCID_{50}$ (100 median tissue culture infectious doses) of the P8-2 strain of IBRV for 60 min at 37°C. The mixtures were transferred to a monolayer of Madin Darby bovine kidney (MDBK) cells in 96-well microtiter plates. The formation of plaques was scored after incubation for two days at 37°C. Titers were expressed as the reciprocal of the highest antibody dilution that caused a 50% reduction of plaques relative to the virus control.

The PI3V used for VN antibody titration of sera was a field isolate obtained from Dr. L. A. Babiuk (VIDO, Saskatoon, Saskatchewan), and propagated in MDBK cells. The VN test was a modification of the method used by Van Wyke Coelingh (5). Serum virus 100$TCID_{50}$ mixtures were incubated and transferred to microtiter plates containing MDBK cells as described above. After an incubation period of five days, the test was read microscopically and the VN titer was defined as the reciprocal of the highest serum dilution that completely inhibited the appearance of virus-related cytopathology of the cells.

Table 2. Effect of preexisting antibodies in calves on subsequent seroconversion rates (%) to IBRV, PI3V, BRSV, and BVDV following vaccination[a]

Virus -vaccine	Seroconversion rate (%)[b] Seronegative	Seropositive[c]	Odds[d] ratio	95%[e] CL
IBR				
— live[f]	100	83	0.00	—[g]
— killed[h]	97	43	0.02	0.00–0.19
PI3				
— live	100	65	0.00	—
— killed	100	50	0.00	—
BRS				
— live	100	51	0.00	—
BVD (killed)				
— New York	22	20	0.89	0.32–2.50
— Oregon	37	23	0.51	0.20–1.28
— Singer	56	19	0.19	0.07–0.52

[a]Only calves vaccinated against IBRV, PI3V, BRSV, and BVDV were included in respective analyses
[b]A fourfold or greater increase in titer following double vaccination
[c]Initial VN titer > 1/2
[d]Odds ratio less than 1 indicates lower seroconversion rate in seropositive calves than in seronegative calves
[e]Cornfield's 95% confidence limits. If CL contains the value 1, the difference in seroconversion rates between seropositive and seronegative calves is not statistically significant
[f]Calves vaccinated with modified-live viral vaccines
[g]Cannot be calculated because of zero values in cell
[h]Calves vaccinated with killed viral vaccines

For BRSV VN titers, two-fold serial dilutions of each serum were added to 100$TCID_{50}$ of BRSV and incubated for 60 min at 37°C. The BRSV strain was obtained from Dr. J. C. Baker (Michigan State University, East Lansing, Michigan, USA), and was propagated in a fetal bovine lung cell culture as described previously (6). The virus-serum mixtures were transferred to a monolayer of fetal bovine lung cells in 96-well microtiter plates and incubated at 37°C. After five days, the test was read microscopically and the VN titer was defined as the reciprocal of the highest serum dilution which completely inhibited the appearance of virus-induced cytopathology.

Similarly, a VN test for BVDV was carried out by adding two-fold dilutions to serum with 100$TCID_{50}$ of BVDV to MDBK cell monolayers (7). The VN test was performed using three different strains of BVDV: the New York 1 strain (noncytopathic), the Oregon C24 strain (cytopathic), and the Singer strain (cytopathic). These strains were selected because they are strains commonly used in BVDV vaccines, and they display antigenic variability (7,8). After incubating for five days at 37°C, the plates were washed, dried, and fixed as described previously (9). The presence of BVDV-infected cells was determined by an indirect immunocytochemical detection method using porcine anti-BVDV serum and a rabbit antiswine IgG peroxidase conjugate, with 3-amino-9-ethylcarbazole (Sigma, St. Louis, Missouri, USA) as chromogen (10). The test was read microscopically and the VN titer was defined as the reciprocal of the highest serum dilution that inhibited the appearance of BVDV-infected cells.

Statistical methods

The serological titers to IBRV, PI3V, BRSV, and BVDV were coded as 0, 1, 2, 3... for endpoint titers of < 1/2, 1/2, 1/4, 1/8, etc. These coded titers corresponded to the reciprocal dilution logarithms to base 2 (11). Seronegative animals were those with a VN titer less than 1/2. The prevalence rate of initial titers at first vaccination was based on the proportion of animals with an antibody titer greater than a coded value of 1, equivalent to a VN titer of 1/2. The seroconversion rate was based on the proportion of animals that had an increase of at least two coded dilutions, equivalent to a four-fold or greater increase in VN titers, between the first vaccination and two weeks after the second vaccination. For IBRV, the seroconversion rate was also calculated following the first vaccination.

It was assumed that vaccine viruses were not shed from vaccinates to in-contact control calves because viral antibody titers in unvaccinated calves decreased over time. Therefore, serological data from the 12 groups of calves were collapsed according to vaccine, and pasture effects were ignored. Statistical tests could not be used to assess pasture effects because of too few observations per vaccine and pasture group. The associations between seroconversion and vaccines, and between prevalence and vaccines, were evaluated using chi-square statistics (12). Differences in the distribution of antibody titers among vaccines were investigated using analysis of variance with multiple comparison of means and repeated measures over time (12). Seronegative animals were included in the calculations of mean titers.

Results

Infectious bovine rhinotracheitis virus

The prevalence of antibodies to IBRV at first vaccination was 42%. There were no significant ($p > 0.05$)

Table 3. Seroconversion rates (%)[a] to IBRV, PI3V, BRSV, and BVDV classified by vaccine

Vaccine	IBRV[b]	PI3V	BRSV	BVDV		
				NY[c]	OR[d]	SI[e]
No vaccine	0,0	2	5	0	0	1
TSV-2	46,59	29	4[na]	0[na]	0[na]	1[na]
Resbo IBR/PI3	83,89	100	6[na]	0[na]	0[na]	0[na]
Cattlemaster 3[f]	39,83	44	0[na]	50	44	61
Cattlemaster 4[f]	43,97	77	73	30	33	30
Triangle 3[f]	37,79	58	0[na]	42	47	53
BRSV Vac +[f] Horizon II	18,82	0[na]	45	0	10	0
Horizon IV[f]	7,73	77	37	0	10	0
Sentry 1 + IBR/PI3/Somnugen	62,96	73	24[na]	4[na]	15[na]	23

[a]A fourfold or greater increase in titer
[b]Seroconversion rate following first vaccination (wk 1-3), seroconversion following second vaccination (wk 1-5)
[c]New York strain
[d]Oregon strain
[e]Singer strain
[f]Strains of BVDV included in vaccine unknown
[na]No antigen in vaccine

Table 4. Serological titers[a] to IBRV classified by vaccine

Vaccine	Titers to IBRV			
	1st[b]	2nd[c]	3rd[d]	Titer change[e]
No vaccine	1.56	0.92	0.64	−0.92
TSV-2	1.64	3.18	3.67	2.03
Resbo IBR/PI3	0.78	4.11	5.11	4.33
Cattlemaster 3	1.33	2.06	5.16	4.28
Cattlemaster 4	1.17	2.40	5.97	4.80
Triangle 3	1.21	1.74	4.16	2.95
BRSV Vac + Horizon II	0.64	1.00	4.18	3.54
Horizon IV	1.03	0.83	3.67	2.64
Sentry 1 + IBR/PI3/Somnugen	0.69	3.19	4.81	4.12

[a]Arithmetic mean of coded titers
[b]No difference ($p > 0.10$) in IBRV titers among vaccines at first vaccination
[c]Significant ($p < 0.0001$) difference in IBRV titers among vaccines at second vaccination (wk 3)
[d]Significant ($p < 0.0001$) difference in IBRV titers among vaccines 2 wk after second vaccination (wk 5)
[e]Significant ($p < 0.0001$) titer changes to IBRV, and titer changes varied among vaccines ($p < 0.0001$)

differences in the prevalence of titers to IBRV among vaccine groups; however, calves with preexisting antibodies to IBRV had significantly ($p < 0.05$) lower seroconversion rates following vaccination with either modified-live or killed IBRV vaccines than seronegative calves (Table 2). All calves vaccinated intranasally with modified-live IBRV vaccines were seronegative at first vaccination; therefore, the association between prevalence and seroconversion by route of administration could not be assessed.

Vaccination significantly ($p < 0.05$) increased antibody levels to IBRV. The seroconversion rates (Table 3) and the distribution of titers to IBRV (Table 4) varied significantly ($p < 0.0001$) among vaccines. We did not assess which particular vaccines varied from each other in serological responses to IBRV, PI3V, BRSV, or BVDV because of the large number of multiple 2 × 2 comparisons.

Following a single vaccination, seroconversion rates, titers, and titer changes to IBRV were significantly ($p < 0.05$) higher in calves given modified-live IBRV vaccines in comparison to those given killed IBRV vaccines (Table 5). After two vaccinations, there was no difference ($p > 0.05$) in the seroconversion rates between modified-live and killed IBRV vaccines; however, titers to IBRV remained higher ($p < 0.05$) in calves given the modified-live IBRV vaccines (Table 5). There were significant ($p < 0.05$) differences among various modified-live IBRV vaccines in their ability to induce antibodies to IBRV at weeks 3 and 5. There were also significant ($p < 0.05$) differences among various killed IBRV vaccines in their ability to induce antibodies to IBRV at week 3, but by week 5 they all induced similar antibody levels.

There were no differences ($p > 0.05$) in seroconversion rates and titers to IBRV between intranasally and intramuscularly administered modified-live IBRV vaccines following a single vaccination (Table 6). However, after double vaccination with modified-live IBRV vaccines, both seroconversion rates and changes in titer to IBRV were significantly ($p < 0.05$) higher in calves vaccinated intramuscularly than in those vaccinated intranasally. There were significant ($p < 0.05$) differences in antibody levels to IBRV at weeks 3 and 5 among various intramuscularly administered modified-live IBRV vaccines (Table 4).

Parainfluenza-3 virus

The prevalence of antibody titers to PI3V at first vaccination was high at 82%, and it varied among vaccine groups. Calves with preexisting antibodies to PI3V had significantly ($p < 0.05$) lower seroconversion rates following vaccination with either killed or modified-live (intranasal and intramuscular route) PI3V vaccines than seronegative calves (Table 2).

Table 5. Serological titers[1] and seroconversions (%) to IBRV, PI3V, and BRSV classified by type of vaccine

Virus	Type of vaccine		
	None	Live	Killed
IBR			
Average titers			
— first sample[2]	1.56[a]	1.14[a]	1.02[a]
— second sample[3]	0.93[a]	2.96[b]	1.15[a]
— third sample[4]	0.64[a]	5.01[b]	3.92[c]
— titer change[5]	−0.91	3.87	2.90
Seroconversion[6]			
— wk 1-3	0[a]	53[b]	18[c]
— wk 1-5	0[a]	85[b]	77[b]
PI3			
Average titers			
— first sample	2.96[a]	3.39[a]	3.74[a]
— third sample	1.56[a]	6.00[b]	5.79[b]
— titer change[4]	−1.50	2.61	2.05
Seroconversion			
— wk 1-5	2[a]	66[b]	58[b]
BRS			
Average titers			
— first sample	2.99[a]	3.20[a]	—[7]
— third sample	2.12[a]	4.87[b]	—
— titer change	−0.85[a]	1.68[b]	—
Seroconversion			
— wk 1-5	6[a]	54[b]	—

[1]Arithmetic mean of coded titers
[2]Titer at first vaccination
[3]Titer at second vaccination (wk 3)
[4]Titer 2 wk after second vaccination (wk 5)
[5]Significant differences ($p < 0.05$) in titer changes among types of vaccines
[6]A fourfold or greater increase in titer
[7]Not studied
[abc]Superscripts with a different letter within a row indicate significant ($p < 0.05$) differences among types of vaccines

Table 6. Serological titers[1] and seroconversions (%) to IBRV and PI3V classified by route of administration of modified-live IBRV and PI3V vaccines

Virus	Route	
	Intranasal	Intramuscular
IBR		
Average titers		
— first sample[2]	1.67[a]	0.99[b]
— second sample[3]	3.15[a]	2.89[a]
— third sample[4]	3.67[a]	5.40[b]
— titer change	2.03[a]	4.41[b]
Seroconversion[5]		
— wk 1-3	46[a]	55[a]
— wk 1-5	59[a]	92[b]
PI3		
Average titers		
— first sample	3.00[a]	3.46[a]
— third sample	3.68[a]	6.44[b]
— titer change	0.68[a]	2.98[b]
Seroconversion		
— wk 1-5	29[a]	74[b]

[1]Arithmetic means of coded titers
[2]Titer at first vaccination
[3]Titer at second vaccination (wk 3)
[4]Titer 2 wk after second vaccination (wk 5)
[5]A fourfold or greater increase in titer
[ab]Superscripts with a different letter within a row indicate significant ($p < 0.05$) differences between routes of administration

Seroconversion rates (Table 3) and the distribution of titers to PI3V (data not shown) varied significantly ($p < 0.05$) among vaccines. Vaccination significantly ($p < 0.05$) increased antibodies to PI3V, and there were no differences ($p > 0.05$) in serological responses to PI3V between modified-live and killed PI3V vaccines (Table 5). However, there were significant ($p < 0.05$) differences in serological responses to PI3V among various modified-live PI3V vaccines (Table 3).

Seroconversion rates and changes in titer to PI3V were significantly ($p < 0.05$) higher in calves given modified-live PI3V vaccines intramuscularly than in those given modified-live PI3V vaccines intranasally (Table 6). The serological responses to PI3V varied ($p < 0.05$) among different intramuscularly administered modified-live PI3V vaccines (Table 3).

Bovine respiratory syncytial virus

Eighty-nine percent of the calves had serum antibodies to BRSV at first vaccination. Initial levels of antibodies to BRSV were moderately high (Table 5). Calves with preexisting antibodies to BRSV had lower ($p < 0.05$) seroconversion rates following vaccination than calves that were seronegative initially (Table 2).

Vaccination with modified-live BRSV vaccines significantly ($p < 0.05$) increased antibody titers and seroconversion rates to BRSV (Table 5). The serological responses to BRSV differed ($p < 0.05$) among various modified-live BRSV vaccines (Table 3).

Bovine viral diarrhea virus

The initial antibody titers and prevalence to BVDV varied among BVDV strains (Table 7). The prevalence was 67% for the New York strain, 67% for the Oregon strain, and 81% for the Singer strain. Calves with preexisting antibodies to the Singer strain of BVDV had significantly ($p < 0.05$) lower seroconversion rates following vaccination than calves that were seronegative initially (Table 2). This association between seroconversion and prevalence was not observed in calves with preexisting antibodies to the New York and Oregon strains of BVDV.

Although vaccination with killed BVDV vaccines significantly ($p < 0.05$) increased antibody titers to BVDV (Table 7), these serological responses were weak and they varied among different BVDV strains (Table 7) and BVDV vaccines (Table 3).

Results from this trial indicated that there were marked differences in serological responses to IBRV, PI3V, BRSV, and BVDV among various multivalent vaccines. Because of these findings, we decided to compare two combination vaccines from the same manufacturer to see if the addition of another antigen to a product would affect the serological responses to common antigens within both vaccines. Cattlemaster 3 (SmithKline Beecham Animal Health, Mississauga, Ontario) and Cattlemaster 4 (SmithKline Beecham Animal Health) are identical products except that Cattlemaster 4 contains BRSV. The serological responses to IBRV, PI3V, BRSV, and BVDV following double vaccination of calves with these vaccines

Table 7. Serological titers[1] and seroconversions (%) to BVDV in calves vaccinated with killed BVDV vaccines

BVDV	Unvaccinated	Vaccinated[2]
New York strain		
Average titers		
— first sample[3]	2.20[a]	2.88[b]
— third sample[4]	1.24[a]	2.69[b]
— titer change	−0.97[a]	−0.21[b]
Seroconversion[5]		
wk 1-5	0[a]	20[b]
Oregon strain		
Average titers		
— first sample	2.44[a]	3.08[a]
— third sample	1.48[a]	3.21[b]
— titer change	−1.03[a]	0.11[b]
Seroconversion		
— wk 1-5	0[a]	27[b]
Singer strain		
Average titers		
— first sample	3.48[a]	3.25[a]
— third sample	2.15[a]	3.56[b]
— titer change	−1.36[a]	0.29[b]
Seroconversion		
— wk 1-5	1[a]	27[b]

[1]Arithmetic mean of coded titers
[2]Vaccinated twice, three weeks apart, with a killed BVDV vaccine
[3]Titer at first vaccination
[4]Titer 2 wk after second vaccination (wk 5)
[5]A fourfold or greater increase in titer following double vaccination
[ab]Superscripts with different letters within a row indicate significant ($p < 0.05$) differences between unvaccinated and vaccinated calves

Table 8. Serological titers[1] and seroconversions (%) to IBRV, PI3V, BRSV, and BVDV following vaccination with Cattlemaster 3 or Cattlemaster 4

Virus	Cattlemaster 3	Cattlemaster 4
IBR		
— titer wk 1[2]	1.3[a]	1.2[a]
— titer wk 5[3]	5.6[a]	6.0[a]
— seroconversion[4]	83[a]	97[a]
PI3		
— titer wk 1	3.4[a]	4.3[a]
— titer wk 5	4.7[a]	6.6[b]
— seroconversion	44[a]	77[b]
BRS[5]		
— titer wk 1	2.9[a]	3.1[a]
— titer wk 5	1.9[a]	5.6[b]
— seroconversion	0[a]	73[b]
BVD — New York strain		
— titer wk 1	3.4[a]	3.4[a]
— titer wk 5	5.1[a]	3.4[b]
— seroconversion	50[a]	30[a]
BVD — Oregon strain		
— titer wk 1	4.1[a]	3.6[a]
— titer wk 5	5.1[a]	3.8[a]
— seroconversion	44[a]	33[a]
BVD — Singer strain		
— titer wk 1	3.9[a]	3.9[a]
— titer wk 5	6.3[a]	4.2[b]
— seroconversion	61[a]	30[b]

[1]Arithmetic mean of coded titers
[2]Titer at first vaccination
[3]Titer 2 wk after second vaccination (wk 5)
[4]A fourfold or greater increase in titer following double vaccination
[5]Cattlemaster 4 contains BRSV; Cattlemaster 3 does not contain BRSV
[ab]Superscripts with a different letter within a row indicate significant ($p < 0.05$) differences between Cattlemaster 3 and Cattlemaster 4

are shown in Table 8. As expected, antibody levels to BRSV were significantly ($p < 0.05$) higher in calves vaccinated with Cattlemaster 4. However, there were also significant ($p < 0.05$) differences between Cattlemaster 3 and Cattlemaster 4 in serological responses to PI3V and to the New York and Singer strains of BVDV. Calves vaccinated with Cattlemaster 4 had significantly ($p < 0.05$) higher titers to PI3V and lower titers to the New York and Singer strains of BVDV than calves vaccinated with Cattlemaster 3.

Discussion

The results of this trial indicated that serological responses to IBRV, PI3V, BRSV, and BVDV in calves varied among different commercial vaccines, between and within modified-live and killed vaccines, and routes of administration. Although levels of antibody are not a direct measure of vaccine efficacy in the field, they do give some indication of the relative potency of different vaccines and the risk of disease (13-20). For example, calves with antibodies to IBRV, PI3V, BRSV, and BVDV on arrival at a feedlot are at lower risk of respiratory disease (13-15). In this study we could not assess any association of antibody levels with disease because none of these calves were treated for illness.

Vaccination with any of the eight commercial IBRV, PI3V, BRSV, and BVDV vaccines used in this study significantly increased respective viral antibody titers in calves, even in the presence of preexisting antibodies. The response to vaccination with killed BVDV vaccines, however, was poor, similar to that reported previously (16). Calves with preexisting antibody titers to IBRV, PI3V, BRSV, and the Singer strain of BVDV had significantly lower seroconversion rates following vaccination than calves that were seronegative initially (15). Preexisting antibodies may have reduced measurable serological responses because: 1) they were passive antibodies and there was no anamnestic response (17), or 2) they were at levels sufficient to inhibit further antibody production. Preexisting antibodies to the New York and Oregon strains of BVDV did not reduce the magnitude of subsequent serological responses to BVDV vaccination, probably because calves were not challenged by vaccination with these two strains of BVDV, or their initial titers to BVDV were too low to inhibit further antibody production.

Serological responses varied between modified-live and killed virus vaccines, and also within each type (modified-live, killed) of vaccine, indicating differences in potency among the various vaccines. Serological responses were higher in calves given one dose of modified-live IBRV vaccines than in those given one dose of killed IBRV vaccines, as has been reported previously (18,19). Following the second vaccination, seroconversion rates to IBRV were similar in calves given either modified-live or killed IBRV vaccines, yet

antibody titers to IBRV remained higher in calves given the modified-live IBRV vaccines. This observation suggested a stronger serological response to modified-live IBRV vaccines than to killed IBRV vaccines. Differences in serological responses to modified-live and killed IBRV vaccines have been associated with differences in the level of protection from clinical IBR (19). There were no differences in titers to PI3V between calves given modified-live and killed PI3V vaccines, probably because calves had moderately high pre-existing titers to PI3V and vaccination with either type of PI3V vaccine caused an anamnestic response.

There were no differences in seroconversion rates and titers to IBRV between intranasally and intramuscularly administered modified-live IBRV vaccines following single immunization, in agreement with previous reports (20,21). Following double vaccination, however, seroconversion rates and antibody levels to IBRV and PI3V were significantly higher in calves vaccinated intramuscularly than in those vaccinated intranasally with modified-live IBRV and PI3V vaccines. Whether or not these serological differences are associated with differences in levels of protection from disease would undoubtedly depend on the level of challenge. Single immunization of calves with modified-live IBRV vaccines by either route has provided protection against experimental challenge of IBRV (20,21).

Calves are frequently vaccinated with numerous monovalent vaccines or a multivalent vaccine in an attempt to protect them from infection by a plethora of infectious organisms. It is often assumed that none of the antigens are immunosuppressive, and that they do not interact with each other. However, in this study we showed that serological responses in calves to PI3V and BVDV varied between two identical combination vaccines when an additional antigen (BRSV) was added to one of these multivalent vaccines. It is not known if these differences in potency between individual components of Cattlemaster 3 and Cattlemaster 4 affect the safety and efficacy of the vaccines.

In conclusion, the results of this trial show that there are significant differences in serological responses in calves to various commercial IBRV, PI3V, BRSV, and BVDV vaccines. Whether or not these differences in antibody titers reflect differences in vaccine efficacy in the field requires further study. The results of this trial have also raised the concern that vaccinating calves simultaneously with multiple antigens may affect the serological responses to individual antigens. Further study is warranted to investigate whether or not this interaction affects the safety and efficacy of vaccines in the field.

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