A New Approach to Vaccination for Infectious Bovine Rhinotracheitis (IBR) and Bovine Viral Diarrhea (BVD) Using a Ballistic Implantation System

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Introduction

Two of the most common production limiting diseases of cattle are Infectious Bovine Rhinotracheitis (IBR) (1, 2) and Bovine Viral Diarrhea (BVD) (3). These diseases cause serious losses to the cattle industry through fetal wastage, reduced milk production, reduced weight gain and feed efficiency, increased medication costs, increased labor cost for treatment of sick animals and, in some cases, death loss (4). Actual financial loss may be greatest from the less dramatic losses associated with animal productivity rather than from the more dramatic loss due to death of animals. Both diseases are viral in nature and affect the respiratory tract and are associated with the development of the bovine respiratory disease complex, or "shipping fever."

Effective vaccines have been developed to control both diseases. Both modified live virus and killed vaccines are available for both diseases (5, 6). However, usage of these vaccines is still less than optimal, because livestock owners frequently do not appreciate the cost benefit from vaccination. Decisions not to vaccinate are often based on the inconvenience of having to confine and handle the animals in order to administer the vaccine. There are definite disadvantages in the current syringe administration procedure. These include: 1) labor cost to confine animals for administration of the vaccine; 2) possible injury and/or stress to animals during the confinement process; 3) transmission of diseases, e.g., anaplasmosis, by use of the same needle to vaccinate several animals; and 4) abscess formation at the injection site resulting in carcass condemnation.

The purpose of this paper is to describe a method of delivering IBR and BVD vaccines using an innovative ballistic implantation system. This paper will present the experimental data demonstrating the efficacy of vaccinating animals by this system compared to those vaccinated by the conventional syringe method.

Materials and Methods

Animals, Vaccine Preparation and Delivery

Two separate studies were conducted: one for IBR and the other for BVD. The experimental design for the BVD study was as follows—

Group A—Ballistic Implantation Group

The Ballistic Implantation group consisted of 20 animals. Each animal received a ballistic implant in the neck area. Each implant contained a single dose of BVD vaccine. The procedure for loading the vaccine containing bullets was to reconstitute a commercial lot of BVD vaccine with sterile 5% Klucel[1]. The Klucel bullets were sterilized with ethylene oxide and, after sterilization, each received 0.5 ml of the vaccine Klucel solution which was equivalent to a normal dose of vaccine. After filling, the bullets were immediately frozen at -78°C and lyophylized.

Group B—Conventional Vaccination

This group consisted of five animals. Each animal received an intramuscular injection consisting of 2.0 ml of

1) Hydroxyprophyl cellulose from the Hercules Powder Co.

commercial BVD vaccine, reconstituted according to the manufacturer's directions. A single 50 dose container was reconstituted and used for vaccination. The unused portion of the container was maintained in ice and assayed for BVD virus.

Group C—Control

The control group contained five animals and received no vaccination for BVD.

The experimental design for the IBR study was as follows:

The experimental population consisted of 79 calves which had been divided into four groups by a randomization procedure.

I. Control Group (White Group)—23 animals; no vaccination.

II. Ballistic Vaccinate Group (Blue Group)—23 animals; each received a ballistic implant in the neck. The implant contained a freeze-dried IBR vaccine equivalent to the dose received by the Conventional Vaccinate Group.

III. Conventional Vaccinate Group (Red Group)—23 animals; each received 2.0 ml of commercial IBR vaccine via deep intramuscular injection into the neck.

IV. Klucel Vaccinate Group (Yellow Group)—10 animals; each received 2.0 ml of IBR vaccine reconstituted in 5% Klucel solution. Klucel was used as a binder in the vaccine loaded ballistic implants.

Serum Neutralization Titers

The serum neutralization titers were conducted according to the recommended standard laboratory procedures for diagnosing IBR and BVD described by Carbrey, et al. (7).

Challenge Procedure

The procedure of Sinclair and Tamoglia was used to administer the challenge virus (8). The challenge virus for both the IBR and BVD studies was supplied by the National Animal Disease Center, Ames, Iowa.

Clinical Observation for the BVD Study

After vaccination the animals were observed for clinical signs and blood samples taken for white count and antibody titer. Four weeks after vaccination all animals in the four groups were challenged with virulent BVD virus. The response of the calves to challenge was recorded for two weeks following challenge. The clinical observations made included: temperature, observation of general attitude and appearance of each animal.

Clinical Observation for the IBR Study

After vaccination the animals were observed and samples taken for antibody titer. Four weeks after vaccination all animals in the four groups were challenged with virulent IBR virus. The response of the calves to challenge was recorded for two weeks following challenge. The animals were observed daily. The rectal temperature of each animal and the results of the clinical examination by the attending veterinarian were tape-recorded and transcribed. In addition, the clinical signs and temperatures were scored on a numeric basis by assigning values to the various observations. The assignment of values is somewhat arbitrary but, nevertheless, represents an attempt to numerically summarize the clinical data for each animal over the challenge period. The basis for scoring is as follows:

Clinical Sign Scores.

0 point = normal
1 point = pustule or papule on nasal mucus membranes or pustular nasal discharge.
2 points = congestion and inflammation of mucus membranes.
3 points = fibrous-necrotic lesions on nasal mucus membranes.
4 points = respiratory distress (audible nasal and tracheal respiratory sounds).

Temperature Scores.

0 point = temperature of 103.5°–104.5°.
1 point = temperature of 104.5°–105.5°
2 points = temperature of 105.5°–106.5°.
3 points = temperature of 106.5°–107.5°.
4 points = temperature of 107.5° or greater.

The daily score for each animal was totaled over the challenge period to arrive at the clinical score for each animal.

Results

BVD Vaccination Study

The animals in this study were observed daily for evidence of clinical disease following vaccination. No clinical disease was evident prior to challenge with BVD virus 4 weeks later. Following challenge with BVD virus the temperature of all animals in the ballistic and conventional vaccinated groups remained normal during the 2 week observation period. It varied between 101.0° F and 102.8° F. The temperature curve of the unvaccinated controls was quite different during this period. These animals had a typical bi-phasic BVD infection response. There was a temperature spike of 104.5° F on days 3 and 8 post challenge.

The other clinical signs in the control group during the observation period were minimal. Animals were observed to have a sero nasal discharge. Some coughing was observed but diarrhea was not present.

Animals in the vaccination group remained normal and no signs of disease were observed.

The total leucocyte count of the ballistically and conventially vaccinated groups remained between 6500-8000 mm3 during the 2 week observation period. While that of the unvaccinated controls dropped to 4500 per mm 3 between days 3-7 post challenge.

Table I presents the sero-conversion data. The percentage

of animals (85%) seroconverting in the ballistically vaccinated group was significantly better than the (40%) which sero-converted in the conventionally vaccinated group.

TABLE 1. 1. Sero-Conversion of Animals in the BVD Vaccination Study.

Group	No. Positive	No. Negative
A—Ballistic	17	3
B—Conventional	2	3
C—Control	0	5

IBR Vaccination Study

The animals in this study were observed for evidence of clinical disease following vaccination. No clinical disease was evident prior to challenge with IBR virus 4 weeks later. The data on the sero-conversion of animals following vaccination is presented in Table 2. The clinical scores of all groups of animals following challenge with virulent IBR are summarized in Table 2.

Some animals in the vaccinated groups exhibited mild clinical signs but none showed signs as severe as those observed in the unvaccinated control animals. The clinical difference between the vaccinated calves and non-vaccinated control calves was striking. There was a high degree of clinical protection provided by vaccination.

All animals in the test were sero-negative. The herd of animals from which the calves were obtained was a closed herd with no history of IBR infection or vaccination. The control animals remained sero-negative during the 28 days post-vaccination. Therefore it can be assumed that the development of a positive SN titer was a direct result of a successful vaccination and not due to a chance infection with virulent virus.

TABLE 2. Test Results and Scores by Group for IBR Vaccinated Animals.

	(1)	(2)	(3)	(4)
Group	% Sero-conversion	Maximum SN titer	Day of Max. titer	Clinical score
I Control	0.0 (0/23)	0	—	34.39 (±8.23)
II Ballistic Implant	73.9 (17/23)	7.29 (±3.29)	18.12 (±1.30)	6.91 (±1.84)
III Convention	60.8 (14/23)	6.71 (±4.65)	16.78 (±1.43)	12.13 (±2.21)
IV Conventional + Klucel	80.8 (8/10)	4.87 (±3.93)	17.00 (±1.90)	10.90 (±2.66)

± = 95% confidence limits on the mean.
(1) % of animals with SN titer of 1:2 or greater.
(2) Average value for the maximum SN titer recorded during first 28 days following vaccination. Only animals with a positive sero-conversion are included in the data for columns 2 and 3.
(3) Average value of the day on which the maximum titer was recorded.
(4) Average value of the total clinical scores of all animals in the group.

The experimental animals were sufficiently susceptible to infection for a valid test. Twenty-one of the twenty-three control animals (91.3%) showed a temperature exceeding 105.0°F within 7 days post challenge with virulent IBR virus. The temperature rise and the clinical signs of the control animals indicated that the experimental population, in the absence of protection by vaccination, were susceptible to infection by IBR virus.

Discussion

The results of this study demonstrated that modified live virus vaccines could be delivered by the dry state by a ballistic implantation procedure and give satisfactory immunity. The protection provided in this study proved to be satisfactory for protection from challenge exposure and from the stand-point of development of a serologic titer in a standard period of time. The test results demonstrated that in all cases both BVD and IBR vaccine delivered by ballistic implantation gave immunity equal to or better than that produced with the standard syringe technique.

The ballistic implantation procedure offers several advantages over the syringe technique. These are: 1) Reduced labor costs to administer the vaccine, 2) Reduced need for extensive restraining facilities, 3) Reduced stress on the animals during administration of the vaccine.

Addendum

The challenge dose of BVD virus was one ml titered at $10^{52}TCID_{50}$ and suspended to 4 ml in a balanced salt solution and administered as indicated. The challenge dose of IBR virus was one ml titered at 10^{6} $^{4}TCID_{50}$ diluted to 4 ml of a balanced salt solution and administered as indicated.

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