Evaluation of Inactivated Infectious Bovine Rhinotracheitis Vaccines

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ABSTRACT

Sixty-five calves of approximately three months of age and of mixed sex were vaccinated twice at four week intervals with either attenuated or inactivated infectious bovine rhinotracheitis vaccines.

Following initial vaccination there was no demonstrable serum infectious bovine rhinotracheitis titer in any of the calves receiving the inactivated vaccine with 20.7% of the calves receiving the attenuated vaccines having demonstrable titers. Following a second administration of vaccine at eight weeks post-initial vaccination 63.9% of the calves receiving the inactivated vaccine had no demonstrable titer with 72.4% of the calves receiving the attenuated vaccine exhibiting a blood titer of four or greater.

RÉSUMÉ

Cette expérience visait à vacciner contre la rhino-trachéite infectieus bovine 65 veaux des deux sexes et âgés d'environ trois mois, à deux reprises et à quatre semaines d'intervalle. On en vaccina 36 avec un vaccin inactivé et 29, avec quatre vaccins atténués.

Après la première vaccination, il s'avéra impossible de déceler des anticorps dans le sérum des veaux qui avaient reçu le vaccin inactivé; par ailleurs, 20.7% des sujets auxquels on avait donné un vaccin atténué possédaient des anticorps sériques. Ultérieurement à la deuxième vaccination, c'est-à-dire huit semaines après la première, 63.9% des veaux ayant reçu le vaccin inactivé ne possédaient pas d'anticorps sériques décelables. Toutefois, 72.4% de ceux à qui on avait donné un vaccin atténué possédaient un taux d'anticorps sériques égal ou supérieur à 1:4.

INTRODUCTION

The most frequently employed infectious bovine rhinotracheitis (IBR) vaccines have been in the attenuated form. It has been demonstrated that cattle vaccinated with the attenuated preparations will shed the virus from the nasal secretions, urine, semen and milk and that these secretions can serve as a source of infection to susceptible animals (15, 20, 23, 24, 25). Shedding of IBR virus has been stimulated by stressing the animal with corticosteroids or naturally by undetermined stimuli. Shedding of IBR virus will occur in the presence of a humoral titer. However, the presence of the viral agent will not always stimulate development of a humoral titer (1, 4, 5, 10, 11, 13, 22, 24, 26).

Cattle breeders selecting replacement animals are becoming cognizant of the IBR virus shedding problem (recrudescence) and are reluctant to purchase cattle exhibiting titers to the IBR virus (17).

It has been recognized that the attenuated form of IBR vaccine more frequently provides a greater humoral titer than the inactivated preparation unless an adjuvant is included in the inactivated form (2, 7, 8,

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9, 12). However, the attenuated vaccines have provided problems such as postvaccination reactions (16, 19, 20, 21). Abortion is another recognized postvaccination problem of the attenuated IBR vaccines (3, 6, 14, 18, 21, 27).

Utilizing inactivated IBR vaccine is one approach to avoiding the problems of the attenuated vaccine administration. This investigation was initiated to evaluate the immunological response in calves following the administration of inactivated IBR virus vaccine.

MATERIALS AND METHODS

Experimental Animals

Sixty-five Holstein male and female calves approximately three months of age were employed in this investigation. The calves were raised on whole milk, milk replacer and pelleted calf ration and alfalfa hay. All calves were purchased when one day old and raised in individual pens in a conventional barn. Collection of blood by jugular vein puncture was made when the calves were purchased prior to vaccination (control serum) and at four and eight weeks after the first vaccination. Sera were separated from the blood clots by centrifugation after refrigeration overnight at 4°C.

Experimental Procedure

Thirty-six calves were initially vaccinated subcutaneously with 10 ml of a commercially available inactivated IBR vaccine. Repeat vaccination was made four weeks later using 10 ml of the vaccine. Twenty-nine calves were vaccinated with four commercially available attenuated IBR vaccines. Each calf received 2 ml of the attenuated vaccine initially with a repeat vaccination of 2 ml four weeks following the initial administration. Vaccines were administered with 16 gauge one inch needles using care to prevent drainback.

The test virus used in the serum neutralization test was 15th passage IBR virus Cooper isolate (Colorado) grown on bovine endocardial cells (BEC). The virus titer was $10^{6.5}$ $TCID_{50}$/ml. The tissue cultures were of BEC origin and were between fifth and 20th passage. The tissue cultures were maintained in a minimum essential medium (MEM) consisting of Earle's salt with 1% lactalbumin hydrolysate, 10% sodium pyruvate and 10% heat-inactivated calf serum.

Serum antibody levels were titered using twofold dilutions by conventional neutralization procedures. The test virus preparation (1 ml) and serum dilution (1 ml) were mixed and allowed to remain at room temperature for 45 minutes. Two-tenths ml of the virus serum mixture was placed in each of three tubes of BEC tissue culture. The inoculated tubes were again incubated at room temperature for 45 minutes. Then 0.8 ml of MEM was added to each tube and incubation was continued at 37°C for 48 hours. Titers were reported as the reciprocal of the highest serum dilution exhibiting complete neutralization of the cytopathic effect of the test virus.

RESULTS

The results of these investigations are tabulated in Table I.

None of the calves vaccinated with inactivated IBR vaccine exhibited a response as based on blood titer four weeks following the initial vaccination. Eight weeks later and four weeks following a second vaccination 63.9% of the calves still exhibited no blood serum titer for IBR. The highest titer observed was eight in 8.3% of the calves.

The administration of the attenuated vaccines provided no demonstrable titer at four weeks postvaccination in 20.7% of the calves with a high titer of 32 in one calf (3.4%). At eight weeks postvaccination and four weeks following a second administration all calves had a titer of two or more with one calf having a titer of 64. At eight weeks 27.6% of the calves receiving the attenuated vaccine had titers greater than the highest titer recorded for the calves receiving the inactivated vaccine.

No adverse effects were observed following the administration of the inactivated

TABLE I. Blood Serum Titers of Vaccinated Calves Four and Eight Weeks Postvaccination

Titer	0	2	4	8	16	32	64
Inactivated vaccine[a]							
Eight weeks							
Number of calves	23	7	3	3	0	0	0
Percent of calves	63.9	19.4	8.3	8.3	0	0	0
Attenuated vaccine[b] — control calves							
Four weeks							
Number of calves	6	6	9	6	1	1	0
Percent of calves	20.8	20.8	31.1	20.8	3.4	3.4	0
Eight weeks							
Number of calves	0	8	8	5	4	3	1
Percent of calves	0	27.6	27.6	17.2	13.7	10.3	3.4

Titers are recorded as the reciprocal of the highest serum dilution exhibiting complete neutralization of the cytopathic effect of the test virus

[a]Bovine Rhinotracheitis-Parainfluenza-3 Vaccine (Bar-4™), Elanco Products Company, Division of Eli Lilly Company, Indianapolis, Indiana 46206

[b]Four commercially available brands of attenuated bovine rhinotracheitis vaccines

vaccines. Mild reactions including depression, increased nasal secretions, increased lacrimation and some anorexia was observed for several days following the administration of the attenuated vaccines in some of the calves.

DISCUSSION

Because of the postvaccination adverse reactions reported for the attenuated IBR vaccine a definite need exists for an efficacious inactivated IBR vaccine. Recent reports indicate that a preparation of this nature can be prepared by addition of an adjuvant (12). A vaccine of this nature would be advantageous in that the problem of abortions, latent or permanent infections and spread of disease by vaccination would be eliminated and high humoral antibody titers could still be established.

The inactivated vaccine utilized in this investigation did not produce demonstrable humoral titers in calves following initial vaccination and either low or no titer following a second administration.

REFERENCES

1. **BITSCH, V.** Infectious bovine rhinotracheitis virus infection in bulls, with special reference to preputial infection. Appl. Microbiol. **26**: 337-343. 1973.
2. **BOUTERS, R., M. VANDEPLASSCHE and G. WELLEMANS.** Vaccination of bull against balanoposthitis associated with infectious bovine rhinotracheitis — infectious pustular vulvovaginitis (IBR-IPV virus infection). Band 1, pp. 753-756. Internationaler Kongress fur Tierische Fortpflanzung, Munchen 1972.
3. **CRANE, C. S., G. N. LUKAS and W. W. WATKINS.** Infectious bovine rhinotracheitis abortion in California beef cattle. J. Am. vet. med. Ass. **144**: 13-18. 1964.
4. **DAVIES, D. H. and J. R. DUNCAN.** The pathogenesis of recurrent infections with infectious bovine rhinotracheitis virus induced in calves by treatment wth corticosteroids. Cornell Vet. **64**: 340-366. 1974.
5. **HUCK, R. A., P. G. MILLAR and D. G. WOODS.** Experimental infection of maiden heifers by the vagina with infectious bovine rhinotracheitis/infectious pustular vulvo-vaginis virus: An epidemiological study. J. comp. Path. **83**: 271-279. 1973.
6. **KELLING, C. L., I. A. SCHIPPER and G. E. STRUM.** Infectious bovine rhinotracheitis (IBR) abortion observations on incidence in vaccinated and non-vaccinated and exposed cattle. Cornell Vet. **63**: 383-390. 1973.
7. **KELLING, C. L., I. A. SCHIPPER and C. N. HAUGSE.** Vaccination of calves with modified live infectious bovine rhinotracheitis IBR virus vaccines. North Dakota Farm Research **30**: 17-19. 1974.
8. **KELLING, C. L., I. A. SCHIPPER and C. N. HAUGSE.** Antibody response in calves following administrations of attenuated infectious bovine rhinotracheitis (IBR) vaccines. Can. J. comp. Med. **37**: 309-312. 1973.
9. **KENDRICK, J. W. and B. I. OSBURN.** Immunologic response of the bovine fetus to inactivated infectious bovine rhinotracheitis-infectious pustular vulvovaginitis virus. Am. J. vet. Res. **34**: 1567-1571. 1973.
10. **KOHLER, Von H. and G. KUBIN.** Virology, serology and pathomorphology of the male genital tract after natural and experimental infection with IBR/IPV virus. Dt. tierärztl. Wschr. **79**: 121-144. 1972.
11. **KOHLER, H. and KUBIN, G.** Zur virologie, Serologie und Pathomorphologie des Mannlichen Nach Naturlicher und Experimenteller Infektion mit dem IBR/IPV Virus. Dt. tierärztl. Wschr. **79**: 209-214. 1972.
12. **KOLAR, J. R., I. L. SCHECHMEISTER and W. G. KAMMLADE.** Use in cattle of formalin-killed polyvalent vaccine with adjuvant against infectious bovine rhinotracheitis, bovine viral diarrhea and parainfluenza-3 viruses. Am. J. vet. Res. **33**: 1415-1420. 1972.
13. **KUBIN, G.** Intermittierender Nachweis des Blasche-nausschlag Virus (IPV) bei einen Naturlich Infirzierten Stier. Wien. tierärztl. Mschr. **56**: 336-337. 1969.

14. **McFEELEY, R. A., A. M. MERRITT and E. L. STEARLY.** Abortion in a dairy herd vaccinated for IBR. J. Am. vet. med. Ass. **153**: 657-661. 1968.

15. **McKERCHER, D. G. and G. L. CRENSHAW.** Comparative efficacy of intranasally and parenterally administered infectious bovine rhinotracheitis vaccines. J. Am. vet. med. Ass. **159**: 1362-1369. 1971.

16. **MACKEY, D. R.** IBR vaccination safe, necessary. Feedlot, p. 98, November 1971.

17. **MAGWOOD, S. E.** Vaccination against infectious bovine rhinotracheitis may hamper export trade in breeding cattle. Can. vet. J. **15**: 260. 1974.

18. **MITCHELL, D.** An outbreak of abortion in a dairy herd following inoculation with an intramuscular infections bovine rhinotracheitis virus vaccine. Can. vet. J. **15**: 148-151. 1974.

19. **REED, D. E., E. J. BICKNELL and R. J. BURY.** Systemic form of infectious bovine rhinotracheitis in young calves. J. Am. vet. med. Ass. **163**: 753-755. 1973.

20. **ROBERTS, A. W. and G. R. CARTER.** Infectious bovine rhinotracheitis virus recovered from the milk of a cow with mastitis. J. Am. vet. med. Ass. **164**: 413. 1974.

21. **ROBINSON, V. B., J. W. NEWBERNE and F. E. MITCHELL.** Vaccination of pregnant cattle with infectious bovine rhinotracheitis vaccine. Vet. Med. **56**: 437-440. 1961.

22. **SAXEGAARD, F.** Serological investigations of bulls subclinically infected with infectious pustular vulvovaginitis virus (IPV virus). Nord. VetMed. **20**: 28-32. 1968.

23. **SCHIPPER, I. A. and C. L. KELLING.** Infectious keratitis in feeder cattle. North Dakota Farm Research **27**: 19-20. 1970.

24. **SHEFFY, B. E. and SUSAN RODMAN.** Activation of latent infectious bovine rhinotracheitis infection. J. Am. vet. med. Ass. **163**: 850-851. 1973.

25. **SNOWDON, W. A.** The IBR-IPV virus: Reaction to infection and intermittent recovery of virus from experimentally infected cattle. Aust. vet. J. **41**: 135-141. 1965.

26. **WHITE, M. B. and W. A. SNOWDEN.** The breeding record of cows inseminated with a batch of semen contaminated with infectious bovine rhinotracheitis virus. Aust. vet. J. **49**: 501-506. 1963.

27. **WILSON, T. E.** Observations and comments on two outbreaks of abortion associated with IBR virus. Can. vet. J. **15**: 227-229. 1974.