PEER REVIEWED

A Comparison of Serological Responses when Modified-Live Infectious Bovine Rhinotracheitis Virus Vaccine and *Mannheimia haemolytica* Bacterin-Toxoid are Administered with Needle-free versus Conventional Needle-based Injection in Yearling Feedlot Steers

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Abstract

A total of 111 yearling feedlot steers were vaccinated with 5-way modified-live virus vaccine and *Mannheimia haemolytica* (MH) bacterin-toxoid, utilizing either needle-free or conventional needle-and-syringe injection techniques. Blood samples were collected from all steers at the time of vaccination and 21 days later, and serum was analyzed for antibody titers to infectious bovine rhinotracheitis (IBR) virus and *M. haemolytica* (MH) leukotoxin. Serological response to the IBR viral fraction of the 5-way viral vaccine was significantly higher (P=0.001) on day 21 following administration with needle-free injection, compared to conventional needle injection. Serological responses to the MH supernatant and cell-associated antigens were not statistically different (P=0.06) on day 21 following administration with needle-free injection, compared to conventional needle injection.

Résumé

Un total de 111 bouvillons de parcs d'engraissement ont été vaccinés avec un vaccin à virus modifiés vivants pentavalent et une bactérine-toxoïde de *Mannheimia haemolytica* (MH) administré avec la technique sans aiguille ou avec la technique d'injection conventionnelle avec aiguille et seringue. Des échantillons de sang ont été recueillis chez tous les bouvillons au moment de la vaccination et 21 jours plus tard. Le sérum a été analysé pour les titres d'anticorps contre le virus de la rhinotrachéite infectieuse bovine (IBR) et la leucotoxine de *M. haemolytica* (MH). La réponse sérologique à la fraction virale IBR du vaccin pentavalent était significativement plus élevée (P = 0.001) au jour 21 suite à la vaccination sans aiguille qu'à la vaccination conventionnelle. La réponse sérologique contre le surnageant de MH et les antigènes cellulaires associés n'était pas significativement différente (P = 0.06) au jour 21 suite à la vaccination sans aiguille ou à la vaccination conventionnelle.

Introduction

Beef quality assurance (BQA) guidelines recognize that inadequate animal restraint or use of small diameter needles may result in needle breakage, which poses a hazard to those who handle or eat the meat. They also recognize that blood-borne infectious diseases, such as bovine leukosis or anaplasmosis, may be transmitted animal-to-animal when a single needle is utilized to inject multiple animals.[6] One technology that potentially minimizes these problems is a pneumatically-powered, needle-free injection device that utilizes air pressure to drive the vaccine through the skin and into the underlying subcutis or muscle.[11]

Needle-free technology traces its roots to industrial accidents in the 19th century when French workmen using pressurized grease guns in factories inadvertently injected themselves. This concept was developed into "jet injectors" which were adopted for use by the United States military to vaccinate draftees/recruits following World War II, and to administer smallpox vaccine in the early 1960s.[9] Needle-free injection

devices have been used extensively since that time in human and veterinary medicine to deliver vaccines and drugs.[2,4,7,8,10] Immunogenicity studies in humans and animals have shown no significant decrease, and an occasional increase, in vaccine efficacy when vaccines were delivered with needle-free delivery systems versus conventional needle systems.[1,3,5] The purpose of this study was to compare the serological response when a modified-live virus vaccine containing infectious bovine rhinotracheitis (IBR) virus antigen and a *Mannheimia haemolytica* (MH) bacterin-toxoid were injected into yearling feedlot steers utilizing either needle-free injection[a] or conventional needle injection methods.

Materials and Methods

Animal Background

A total of 111, 806 lb (366 kg) yearling steers originating from a single Kansas ranch were utilized. Approximately five months prior to initiation of the current study, while at the ranch of origin, these steers were vaccinated with two doses of 4-way modified-live virus vaccine, one dose of *Mannheimia haemolytica-Pasteurella multocida* bacterin-toxoid and one dose of 7-way clostridial bacterin-toxoid as part of a preconditioning program. Brand names of vaccines and bacterin-toxoids used at the ranch were not available. Steers were then moved to wheat pasture in central Oklahoma and managed as a single group through the winter grazing season (J. Bohn, personal communication, 2004). In early March they were transported to a commercial feedlot in south-central Kansas to begin the study.

Randomization

On day 0, individual sequentially-numbered ear tags were applied to the left ear of each steer and the modified-live virus vaccine and bacterin-toxoid treatments were administered. A random number generator was utilized to randomize the treatments to individuals of each successive pair of steers through the chute.

Treatments

Treatment 1 consisted of a needle-free intramuscular (IM) injection of 2 mL of 5-way modified-live virus vaccine[b] in the left side of the neck (Figures 1 and 2), and a conventional subcutaneous (SC) injection of 2 mL of MH bacterin-toxoid[c] in the right side of the neck. The needle-free injector pressure was set to 85 pounds per square inch (psi) to ensure IM injection of the modified-live virus vaccine (DL Cook, personal communication, 2004). The conventional subcutaneous injection utilized a standard automatic-refill syringe and disposable 16-gauge, 3/4-inch needle. Proper one-handed SC injection technique was utilized. Needles were changed between each animal.

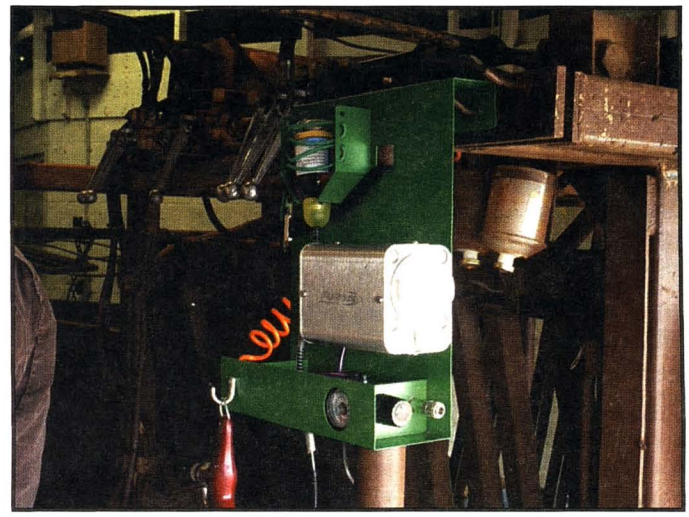

Figure 1. Felton pneumatic system with variable dose and pressure settings.

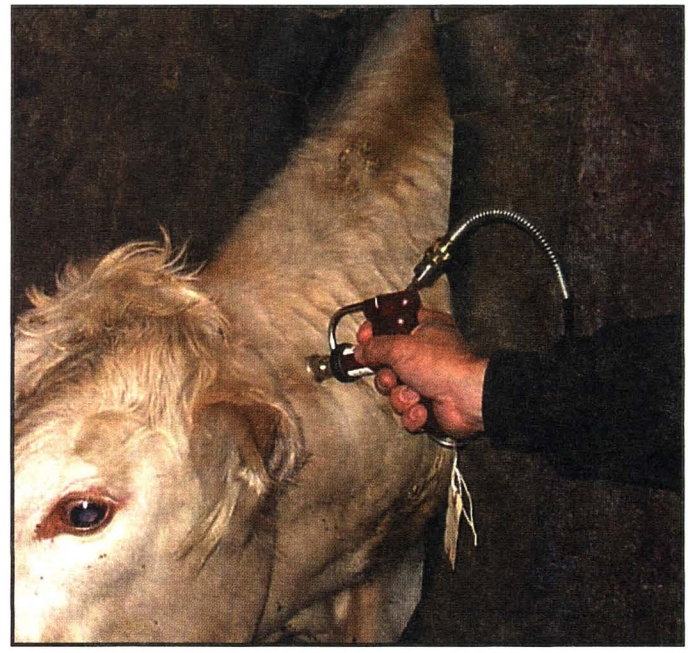

Figure 2. Felton needle-free injector.

Treatment 2 consisted of a needle-free SC injection of 2 mL of MH bacterin-toxoid in the right side of the neck, and a conventional IM injection of 2 mL of 5-way modified-live virus vaccine in the left side of the neck. The needle-free injector pressure was set to 75 psi to ensure SC injection of the bacterin-toxoid (DL Cook, personal communication, 2004). The conventional IM injection utilized a standard automatic-refill syringe and disposable 16-gauge, 1-inch needle, with the needles changed between each animal.

Additionally, all animals were administered a footrot bacterin, 7-way clostridial bacterin-toxoid, inject-

able dewormer and growth-promotant implant, according to feedlot protocol. Each product was given in a consistent injection site. A four-inch (10.2 cm) spacing was maintained between adjacent injection sites to help ensure that additional injections did not interfere with study treatments.

Animal Management

Steers were housed in a single feedlot pen and managed as a single unit. Water and feed were available *ad libitum* according to feedlot protocol. Animals were observed daily by feedlot pen riders for signs of disease. No adverse reactions were observed. No animals required treatment during the 21-day study.

Sample Collection and Evaluation

Blood samples were collected from each animal on day 0 and day 21. All blood samples were chilled and forwarded to the Kansas State University Veterinary Diagnostic Laboratory where serum was harvested, frozen and held for serological evaluation. Routine $\log^{-2}$ serum neutralization evaluation for the presence of antibody to IBR virus was performed as an indicator of the serological response to the modified-live virus vaccine. Enzyme-linked, immunosorbent assays (ELISA) using whole-cell and supernatant antigens of *M. haemolytica* were used to estimate serum antibody response to the MH bacterin-toxoid.

Data Management and Analysis

Statistical analyses for titer levels were performed with the Mixed Procedure of SAS (SAS, 2000; SAS Institute Inc, Cary, NC). A split-plot analysis was conducted to account for repeated measurements that included the fixed effects of treatment and day of bleeding as the repeated measure. Satterthwaite adjustment was used for the degrees of freedom. All treatment means were separated ($P < .05$) using the Least Significance Difference procedure when the respective F-tests were significant ($P < .05$), unless otherwise stated.

Results and Discussion

Treatment Least-Squares Means of IBR virus and *M. haemolytica* serological responses on day 0 and day 21 are shown in Table 1. There was no pre-existing statistical difference in IBR titer means on day 0. There was a highly significant difference in IBR treatment means on day 21 ($P=0.001$) following administration with the needle-free injection system. There was no pre-existing statistical difference in MH leukotoxin means on day 0. The MH response means approached being statistically different on day 21 ($P=0.06$) following administration with the needle-free injection system. This study did not measure the immunological determinants that led to the differences observed.

The findings of this study indicate that use of a needle-free injection system to vaccinate yearling feedlot steers can produce IBR and MH serological responses at least equivalent to those obtained with conventional needle-and-syringe injection systems. Use of the Felton Pulse™ 250 system offers a viable option for vaccinating beef cattle when it is desirable to reduce potential for needle injury to animal handlers, prevent losing broken needles in tissue, or possibly prevent transfer of blood-borne disease.

Further research is needed to define the cell mediated immune response to vaccination, and to determine if differences in tissue reaction exist when vaccinating cattle with a needle-free injection system as compared to traditional needle-based injections.

Conclusion

Serological response to the IBR fraction of the 5-way virus vaccine was significantly higher on day 21 following IM administration with the needle-free injection system when compared to the conventional needle-and-syringe route of administration. Serological response to the *M. haemolytica* bacterin-toxoid was numerically higher, but not significantly different, on day

Table 1. Treatment Least-Squares Means of IBR and *Mannheimia haemolytica* serological responses.

Administration method/antigen	Day 0 titer	SE	Day 21 titer	SE
Needle-free / IBR	2.50	0.47	70.14	10.80
Needle / IBR	1.96	0.67	41.75	5.91
[a] P value	0.95		0.001	
Needle / *M. haemolytica*	0.240	0.009	0.299	0.011
Needle-free / *M. haemolytica*	0.259	0.011	0.326	0.011
[a] P value	0.20		0.06	

[a] P value for comparisons within antigen and day.

21 following SC administration with the needle-free injection system.

Footnotes

[a] Felton Pulse™ 250 Needle-Free Injector System, Felton International, Lenexa, KS

[b] Bovi-Shield® Gold 5 (modified-live bovine rhinotracheitis-virus diarrhea-parainfluenza 3-respiratory syncytial virus vaccine), Pfizer Animal Health, New York, NY

[c] One Shot® (*Pasteurella [Mannheimia] haemolytica* bacterin-toxoid), Pfizer Animal Health, New York, NY

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References

1. Aguiar JC, Hedstrom RC, Rogers WO, Charoenvit Y, Sacci JB Jr, Lanar DE, Majam VF, Stout RR, Hoffman SL: Enhancement of the immune response in rabbits to a malaria DNA vaccine by immunization with a needle-free jet device. *Vaccine* 20(102):275-280, 2001.

2. Bennett J, Nichols F, Rosenblum M, Condry J: Subcutaneous administration of midazolam: a comparison of the Bioject jet injector with the conventional syringe and needle. *J Oral Maxillofac Surg* 56(11):1249-1254, 1998.

3. Cook DL, Kruse F, Phillips R, Sick F, Okkinga K, Polson D, Demontis G: Pulse 200 effective application method for PRRS vaccine in gilts. *Proc Int Symp on Emer and Re-emer Pig Dis* 134, 2004.

4. Grosenbaugh DA, Leard T, Pardo MC, Motes-Kreimeyer L, Royston M: Comparison of the safety and efficacy of a recombinant feline leukemia virus (FeLV) vaccine delivered transdermally and an inactivated FeLV vaccine delivered subcutaneously. *Vet Therapeut* 5(4):258-262, 2004.

5. Houser TA, Sebranek JG, Thacker BJ, Baas TJ, Nilubol D, Thacker EL, Kruse F: Effectiveness of transdermal, needle-free injections for reducing pork carcass defects. *Meat Sci* 68:329-332, 2004.

6. Kansas Beef Quality Assurance Guidelines, 2001.

7. Sarno MJ, Blase E, Galindo N, Ramirez R, Schirmer CL, Trujillo-Juarez DF: Clinical immunogenicity of measles, mumps and rubella vaccine delivered by the Injex jet injector: comparison with standard syringe injection. *Pediatric Infect Dis J* 19(9):839-842, 2000.

8. Senn MK, Bradford JR, Cook DL, Luskotov A: Comparison of pharmacokinetic parameters for Excenel® RTU when injected by needle or Felton Pulse™ 250 needle-free injector. *Proc Am Assoc Swine Pract* 263-265, 2004.

9. Snowbeck, C: Reviving an old technology for large-scale vaccination. Post-gazette.com/ healthscience/20011120hjet2.asp. 2001.

10. Whitford HW, McConnell S: The application of jet injection to veterinary medicine. *SW Vet* 27(1):69-75, 1974.

11. www.Feltonint.com/Animal.html