PEER REVIEWED

Comparison of milk production changes in adult Holstein cows vaccinated with a 5-way modified-live virus vaccine containing a *Mannheimia haemolytica* toxoid versus a 5-way modified-live virus vaccine containing a 5-way *Leptospira* bacterin

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Abstract

A total of 105 Holstein cows 21 to 31 days-in-milk were vaccinated with a 5-way modified-live virus (MLV) vaccine containing bovine herpesvirus-1, bovine viral diarrhea virus (types 1 and 2), parainfluenza-3 virus, and bovine respiratory syncytial virus combined with either a *Mannheimia haemolytica* toxoid or a 5-way *Leptospira* bacterin. Milk production was monitored for 3 days pre- and 3 days post-vaccination. There was a 0.52 lb (0.24 kg) increase in mean milk production for the group vaccinated with the 5-way MLV vaccine plus 5-way *Leptospira* bacterin. There was a 0.32 lb (0.15 kg) decrease in mean milk production in the group vaccinated with the 5-way MLV vaccine plus *M. haemolytica* toxoid. The difference in mean milk production between the 2 groups was 0.85 lb (0.38 kg) ($P = 0.4076$). There was no statistical difference in mean daily milk production changes between treatment groups when parity was taken into account. Vaccination during lactation using a *M. haemolytica* toxoid in combination with a 5-way MLV vaccine resulted in a small, but insignificant, decrease in milk production.

Key words: vaccine, leptospira, mannheimia, milk production

Résumé

Un total de 105 vaches Holstein, entre 21 et 31 jours en lactation, ont été vaccinées avec un vaccin pentavalent à virus vivants modifiés contenant l'herpèsvirus bovin 1, le virus de la diarrhée virale bovine (types 1 et 2), le virus parainfluenza 3 bovin et le virus respiratoire syncytial bovin en combinaison avec un toxoïde de *Mannheimia haemolytica* ou une bactérine contre cinq souches de *Leptospira*. La production de lait a été suivie sur une période de 3 jours avant et après la vaccination. La production de lait moyenne a augmenté de 0.52 lb (0.24kg) chez les vaches vaccinées avec le vaccin pentavalent à virus vivants modifiés en combinaison avec la bactérine contre cinq souches de *Leptospira*. La production moyenne de lait a quant à elle diminuée de 0.32 lb (0.15 kg) chez les vaches vaccinées avec le vaccin pentavalent à virus vivants modifiés en combinaison avec le toxoïde de *Mannheimia haemolytica*. La différence entre les deux groupes pour la production moyenne de lait était de 0.85 lb (0.38 kg) ($P = 0.4076$). Il n'y avait pas de différence statistiquement significative dans la production moyenne de lait entre les deux groupes tenant en compte la parité. La vaccination durant la lactation avec un vaccin pentavalent à virus vivants modifiés en combinaison avec un toxoïde de *Mannheimia haemolytica* a entrainé une légère diminution non significative de la production de lait.

Introduction

Vaccination of dairy cattle is practiced by approximately 75% of dairy farms in the United States.[6] Protection against viral pathogens that cause reproductive losses and respiratory diseases are used most frequently. The most common modified-live virus (MLV) vaccine used contains bovine herpesvirus-1 (BHV-1), bovine viral diarrhea virus (types 1 and 2) (BVDV), parainfluenza-3 virus (PI-3), and bovine respiratory syncytial virus

(BRSV) antigens. In addition, 70% of farms vaccinate against leptospirosis.[6]

According to the National Animal Health Monitoring System Dairy 2007 report, pneumonia affects only 3.3% of adult dairy cattle, but accounts for 11.3% of adult dairy cattle deaths.[6] *Mannheimia haemolytica* is considered one of the most important and commonly isolated pneumonia pathogens in adult dairy cattle.[7] This pathogen is known to be a commensal organism that causes disease with stress or immune suppression. Housing, stage of lactation, and nutritional imbalances are factors that can contribute to stress and/or immune suppression.[3] There is a paucity of referenced literature on respiratory disease in adult dairy cattle, which makes it difficult to define disease outbreaks, and forces extrapolation from other production classes of cattle where literature is more robust.

In the authors' experience, a combination pentavalent MLV-5-way *Leptospira* bacterin product is commonly used to vaccinate postpartum dairy cows. The objective of this study was to compare milk production between cows vaccinated with a pentavalent MLV vaccine containing a 5-way *Leptospira* bacterin to a MLV pentavalent vaccine containing a *M. haemolytica* toxoid.

Materials and Methods

Animals

Holstein primiparous and multiparous cows from the Iowa State University Dairy Farm that were between 21 and 31 days-in-milk (DIM) were used for the trial. Prior to enrollment, 1 member of the research group evaluated the cows to ensure they were free of disease for at least 2 weeks prior to enrollment, and that daily milk production was increasing. To prevent bias, no attempt was made to evaluate level of milk production at enrollment and balance production levels within the groups. The Animal Care and Use Committee at Iowa State University approved the study, which was conducted between July 2013 and October 2013.

Cows were housed and managed in freestalls with other lactating cows. Barn construction consisted of 2 rows of freestalls per pen. Cows were fed once per day, and milked 3X daily. Study cows did not undergo pen moves during the period that started 1 week prior to vaccination through trial completion (day -7 to day 3), nor were any medications or vaccines administered during the same period. A vaginal progesterone insert[a] was placed in each study cow on day -3 to prevent estrus during the study. The vaginal insert remained in place until 72 hours post-vaccination (day 3).

Vaccine Administration

At time 0, cows were randomly assigned to 1 of 2 treatment groups by flipping a coin for each cow; this was done by a separate member of the study team. Group 1 cows were administered a combination MLV vaccine containing BHV-1, BVDV (types 1 and 2), PI_3V, BRSV plus a *M. haemolytica* toxoid[b]. Group 2 cows were administered a combination MLV vaccine containing BHV-1, BVDV (types 1 and 2), PI_3V, BRSV, and a 5-way *Leptospira* bacterin[c]. Vaccines were administered subcutaneously in the neck by study personnel according to label directions after the first milking of the day while cows were restrained in headlocks for daily management tasks. A second study member verified vaccine assignment prior to administration. Daily milk weights were obtained from the on-farm milk meter system for 3 days prior to and for 3 days following vaccination.

Statistical Analysis

Descriptive statistics and differences in mean milk weight changes were analyzed using a 2-tailed t-test in JMP[d]. No cows were excluded from the statistical analysis. Significance was set at $P < 0.05$.

Results

A total of 105 cows were enrolled in the study, 54 in Group 1 (5-way MLV virus vaccine + *M. haemolytica* toxoid) and 51 in Group 2 (5-way MLV vaccine + 5-way *Leptospira* bacterin). All cows were between 21 and 31 days-in-milk at enrollment; the mean DIM for Group 1 cows was 24.6 ± 0.29 (± SEM), and 26.9 ± 0.29 for cows in Group 2 ($P < 0.0001$). The pre-vaccination average daily milk production was 97.3 lb (44.2 kg) for Group 1 cows, and 86.3 lb (39.2 kg) for Group 2 (Table 1). There was a 0.52 lb (0.24 kg) increase in mean daily milk production for Group 2 cows during the 3-day post-vaccination period, while there was a 0.32 lb (0.15 kg) decrease in Group 1 (Table 2). This equates to a 0.60% increase in mean daily milk production in Group 2, and a 0.34% decrease in mean daily milk production for cows in Group 1 over the 3-day post-vaccination period; the overall difference in the mean daily milk production between the 2 groups was 0.85 lb (0.39 kg) ($P = 0.4076$). When examined by parity, the difference in change in mean daily milk production between lactation 1, 2, and 3+ for the 2 vaccine groups was 0.80 lb (0.36 kg), 2.10 lb (0.95 kg), and 0.82 lb (0.37 kg), respectively. There was no statistical difference ($P \geq 0.4076$) found when vaccine groups were analyzed by parity.

Discussion

The present body of knowledge for *M. haemolytica* toxoids is focused on beef cattle and dairy calves. A 2012 meta-analysis by Larson and Step suggests vaccination against *M. haemolytica* is beneficial in feedlot cattle and dairy calves.[4] There is a paucity of published

Table 1. Number of animals and milk production, prior to vaccination, in each treatment group by lactation.

	Group 1*		Group 2†			
	No. cows	**Mean milk production (lb)**	**No. cows**	**Mean milk production (lb)**	**Milk production difference (lb)**	***P*-value**
All lactations	54	97.3	51	86.3	11.0	0.0017
Lactation = 1	24	101.1	20	75.1	26.2	<0.0001
Lactation = 2	17	106.8	15	89.4	17.4	0.0001
Lactation = 3+	13	95.9	16	82.9	13.3	0.017

*Cows vaccinated with combination MLV BHV-1, BVDV (types 1 and 2), PI_3V, BRSV vaccine + *Mannheimia haemolytica* toxoid; Pyramid® 5 + Presponse® SQ, Boehringer-Ingelheim Vetmedica Inc., St. Joseph, MO
†Cows vaccinated with combination MLV BHV-1, BVDV (types 1 and 2), PI_3V, BRSV vaccine + 5-way *Leptospira* bacterin; Pyramid® 10, Boehringer-Ingelheim Vetmedica Inc., St. Joseph, MO

Table 2. Change in mean daily milk production in the 3 days post-vaccination compared to the 3 days prior to vaccination with 1 of 2 vaccine combinations.

	Group 1*	**Group 2†**	**Difference**	***P*-value**
All lactations (lb)	-0.3222	0.5235	0.8458	0.4076
Lact=1 (lb)	-0.2417	0.5550	0.7967	0.9959
Lact=2 (lb)	-1.9471	0.1533	2.1004	0.8650
Lact = 3+ (lb)	1.6538	0.8313	0.8226	0.9982

*Cows vaccinated with combination MLV BHV-1, BVDV (types 1 and 2), PI_3V, BRSV vaccine + *Mannheimia haemolytica* toxoid; Pyramid® 5 + Presponse® SQ, Boehringer-Ingelheim Vetmedica Inc., St. Joseph, MO
†Cows vaccinated with combination MLV BHV-1, BVDV (types 1 and 2), PI_3V, BRSV vaccine + 5-way *Leptospira* bacterin; Pyramid® 10, Boehringer-Ingelheim Vetmedica Inc., St. Joseph, MO

information exploring the effect of vaccination on milk production, and to our knowledge this is the first study comparing identical virus vaccines that use either a *M. haemolytica* toxoid or a 5-way *Leptospira* bacterin as the diluent. Most reports focus on differences between 2 different commercial vaccine products with similar antigen combinations. One major difference amongst the literature and the current study was the inclusion of a negative control, which was saline in other trials. A negative control was not utilized in the current study, as this data has been published previously by others.

Two studies evaluated the effect of killed viral vaccines on milk production, whereas the current study evaluated vaccines containing MLV viral antigens combined with *M. haemolytica* or 5-way *Leptospira* bacterin.[1,5] Milk production losses in cows vaccinated with killed virus vaccine vs control cows range from 0.04 lb (0.018 kg) to 3.10 lb (1.41 kg)/cow/day the first 2 days post-vaccination.[1] Scott et al reported cumulative milk production losses totaling up to 11.80 lb (5.36 kg) for 7 days post-vaccination.[5] That same study found a total increase of 9.0 lb (4.1 kg) in the control (saline) group.[5] Garrett compared MLV vaccines and reported milk production losses from 3.15 lb (1.43 kg)/day to 2.28 lb (1.03 kg)/day when compared to saline-injected controls.[2]

In the current study, there was a small, non-significant change in milk production. The greatest change in milk production was in the second lactation cows in Group 1, which had a mean milk production decrease of 1.95 lb (0.88 kg)/day. In contrast, the lactation 3 and greater cows in Group 1 had an increase of 1.65 lb (0.74 kg) of milk/day, while cows in Group 2 had an increase of 0.52 lb (0.24 kg) of milk/day (Table 2).

Despite randomization of cows in the study, there was a significant difference (11.0 lb (5.0 kg); $P = 0.0017$) in the mean daily production for the 3 days prior to vaccination (Table 1). This was not expected as all cows enrolled were in the same stage of lactation, the distribution by lactation group was similar, cows were healthy prior to enrollment, and they were randomly assigned to treatment group. Even though the average DIM at enrollment was different, Group 1 cows, which started with a higher average milk production, had a lower average DIM at enrollment. Therefore, the milk difference cannot be explained by DIM differences.

The viral components contained in both vaccines used in the current study were the same viral strains and contained the same adjuvant, and both were MLV vaccines containing BHV-1, BVDV (types 1 and 2), PI3V, and BRSV. They only differed in that 1 vaccine contained a 5-way *Leptospira* bacterin and the other a *M. haemolytica* toxoid as the diluent. Farms experiencing elevated pneumonia rates in adult dairy cows may consider the use of a vaccine containing *M. haemolytica* as part of an overall respiratory disease management program.

Conclusions

Vaccinating cows with a product containing *M. haemolytica* toxoid may cause a small, non-significant decrease in milk production compared to pre-vaccination levels. This data provides additional information to veterinarians and producers to help make informed decisions regarding vaccine selection. When making the decision to vaccinate, producers and their advisors must consider the potential costs vs risks of vaccination including vaccine price, labor, and milk production changes in relation to the potential benefit of reducing the impact of respiratory disease in dairy cows caused by *M. haemolytica*.

Endnotes

[a]Eazi-Breed™ CIDR®, Zoetis Animal Health, Florham Park, NJ
[b]Pyramid® 5 + Presponse® SQ, Boehringer-Ingelheim Vetmedica Inc., St. Joseph, MO
[c]Pyramid® 10, Boehringer-Ingelheim Vetmedica Inc., St. Joseph, MO
[d]JMP Pro 10.0.2, SAS Institute

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