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Influence of vaccination with a combined chemically altered/inactivated BHV-1/BVD vaccine or a modified-live BHV-1/BVD vaccine on reproductive performance in beef cows and heifers

George A. Perry, PhD[1]; **Thomas W. Geary**, PhD[2]; **Julie A. Walker**, PhD[1]; **Jerica J.J. Rich**, MS[1]; **Emmalee J. Northrop**, MS[1]; **Stephanie D. Perkins**, MS[1]; **Christina L. Mogck**[1]; **Megan L. Van Emon**, PhD[3]; **Abby L. Zezeski**, MS[2]; **Russell F. Daly**, DVM, MS, DACVPM[4]

[1]Department of Animal Science, South Dakota State University, Brookings, SD 57007
[2]USDA-ARS, Fort Keogh Livestock Range and Research Station, Miles City, MT 59301
[3]Department of Animal and Range Sciences, Montana State University, Bozeman, MT 59717
[4]Department of Veterinary and Biomedical Sciences, South Dakota State University, Brookings, SD 57007
Corresponding author: Dr. George A. Perry; 605-688-5456; George.Perry@sdstate.edu

Abstract

A field trial was conducted on 10 herds of previously-vaccinated cows and heifers (n=1,567) to evaluate the reproductive effects of prebreeding vaccination with either a modified-live virus (MLV) or a chemically altered/inactivated (CA/IV) BHV-1/BVDV vaccine. Animals received a single (cows) or 2 injections (heifers) of either vaccine, with the final injection between 27 and 89 days before breeding, which consisted of timed AI following a 7-d CO-Synch + CIDR synchronization. Conception rates to AI were greater in the CA/IV vaccine group compared to the MLV vaccine group (P=0.05; 60% vs 52%). Interval from vaccination with either vaccine until AI also influenced conception rates (P=0.02), with animals vaccinated 27 to 29 (52%) days or 30 to 37 (52%) days prebreeding exhibiting decreased conception rates compared to animals vaccinated 46 to 89 days prebreeding (P<0.03; 64%). There was no treatment by interval interaction (P=0.79), effect of treatment (P=0.18), or treatment by interval interaction (P=0.17) on breeding season pregnancy rates. In summary, vaccination of previously vaccinated beef cows and heifers with a MLV vaccine pre-breeding (27 to 89 d) was associated with decreased AI conception rates compared to a CA/IV vaccine.

Key words: modified-live, inactivated, vaccine, reproduction, conception rates

Résumé

Un essai sur le terrain a été mené avec 10 troupeaux de vaches et de génisses préalablement vaccinées (n=1567) pour évaluer les effets sur la reproduction de la vaccination avant l'insémination avec soit un vaccin à virus vivants modifiés (VVM) ou soit un vaccin avec HB-1/VDVB altérés chimiquement/inactivés (VAC/I). Les animaux ont reçu une simple injection (vaches) ou deux injections (génisses) de l'un ou l'autre des vaccins avec injection finale entre les jours 27 et 89 avant l'insémination. La reproduction comprenait une insémination artificielle sur rendez-vous suivant une synchronisation de 7 jours avec CO-Synch et CIDR. Le risque de conception suivant l'insémination artificielle était plus élevé dans le groupe VAC/I que dans le groupe VVM (P=0.05; 60% vs 52%). L'intervalle de temps entre la vaccination avec l'un ou l'autre des vaccins et l'insémination artificielle a aussi modifié le risque de conception (P=0.02). Ainsi, les animaux vaccinés entre 27 et 29 jours ou entre 30 et 37 jours avant l'insémination avaient un risque de conception moins élevé que les animaux vaccinés entre 46 et 89 jours avant l'insémination (P<0.03; 64%). Il n'y avait pas d'interaction entre le traitement et l'intervalle (P=0.79) ni d'effet du traitement (P=0.18) ni d'interaction entre le traitement et l'intervalle (P=0.17) sur le taux de gestation dans la saison de reproduction. En résumé, chez des vaches et des taures de boucherie préalablement vaccinés, la vaccination avec un vaccin VVM avant la reproduction (27 à 89 jours) a diminué le risque de conception à l'insémination artificielle par rapport à la vaccination avec un vaccin VAC/I.

Introduction

Reproductive performance is of critical importance to the profitability of cow-calf operations. Numerous factors, such as heifer development, nutrition, cow body condition at calving, bull fertility, and environment, affect herd reproductive efficiency;[9,10] however, in reproductive management,

managing 1 or more of these factors extremely well does not compensate for management mistakes. Instead, these mistakes tend to cancel out the factors that are well-managed. Mismanagement of infectious reproductive disease is 1 of those details that can potentially create significant losses in reproductive performance. Therefore, veterinarians regularly recommend that beef producers vaccinate female beef cattle with either a modified-live virus (MLV) or inactivated virus vaccine (IVV) in order to reduce the risk of reproductive failure due to infectious agents such as bovine viral diarrhea virus (BVDV) and bovine herpesvirus (BHV-1).

It has been established through several studies that vaccination of naïve heifers with a MLV vaccine around the onset of standing estrus results in negative effects on corpus luteum (CL) function[14,17] and pregnancy success.[3] These negative effects have included reduced first-service conception rates, as well as second-service conception rates.[3,12] In addition, when some heifers were infected with BHV-1 at or near estrus, normal estrous cycles were delayed for up to 2 months,[8] and BVDV antigen has been detected in the ovary up to 30 days post-vaccination.[4] The adverse effects of vaccination on pregnancy success among previously vaccinated animals, however, has been more variable. Animals vaccinated 3 times with the same MLV prior to breeding (the second dose was administered 90 days prior to peak breeding day and the third dose either 40 days or 3 days prior to peak breeding) exhibited no difference in conception rates between treatments.[1] In another study, heifers were vaccinated with a MLV vaccine either 30 days or 9 days prior to the start of the AI breeding program with no differences in estrus response or pregnancy success between treatments.[16] However, both of these studies focused on differences in the interval between vaccination and breeding. More recent studies have compared MLV to IVV vaccination and have reported large but non-significant differences in pregnancy success between treatments. In the first study,[18] heifers vaccinated with the IVV had a 15% to 20% greater pregnancy success compared to those vaccinated with the MLV. In a subsequent study, non-vaccinated heifers had a 20% greater pregnancy success compared to heifers vaccinated with a MLV.[19] However, both of these studies used limited numbers of animals in their evaluation of reproductive efficiency. Another recent study evaluated reproductive performance on 1,436 previously vaccinated cows and heifers that were vaccinated with either a MLV, IVV, or saline. In this study, the group receiving IVV exhibited increased AI conception rates compared to the group receiving MLV, with the saline control group intermediate between the other 2.[11]

Comparisons between IVV and MLV center not only around safety, but also efficacy. Some evidence exists to suggest that MLV exhibit a broader and more efficacious immune response against viral pathogens than do IVV.[13,21] However, heifers vaccinated with a MLV prior to their first breeding season and then vaccinated with a chemically altered/inactivated vaccine (CA/IV) before their second breeding season had similar levels of abortions following both a BVD and BHV-1 challenge as animals vaccinated with a MLV before their second breeding season.[19] Therefore, the objective of this study was to further build upon these findings and to determine if vaccination with either a MLV or CA/IV impacted reproductive performance in previously vaccinated beef cows and heifers.

Materials and Methods

Animals

Protocols were reviewed and approved by the South Dakota State University institutional animal care and use committee and the Fort Keogh Livestock Range and Research Station institutional animal care and use committee. All animals were managed according to herd standard operating procedures utilizing routine animal husbandry procedures.

Ten spring-calving commercial cow-calf herds in South Dakota and Montana (Table 1), comprised of previously vaccinated (all animals had received 2 vaccinations with a MLV around weaning and a yearly booster with a MLV prior to the start of the study) mature post-partum beef cows and/or beef heifers (n=1,567) were utilized for the study. The prior vaccination protocol included an annual MLV BHV-1/BVDV/PI-3/BRSV/5-way leptospirosis vaccine[a] before the start of each herd's breeding season, and all heifers had received a MLV BHV-1/BVDV/PI-3/BRSV vaccine[b] around the time of weaning.

Vaccination

Cows and heifers were blocked within herd by age and days post-partum and randomly assigned to 1 of 2 vaccine groups: 1) MLV or 2) CA/IV vaccine. Mature cows were vaccinated 27 to 89 days prior to fixed-time AI, with vaccine timing dependent upon each herd's management schedule. Cows in the MLV treatment group received a single dose of a commercially available MLV vaccine.[a] Cows in the CA/IV treatment received a single dose of a commercially available CA/IV vaccine.[c] Virgin heifers received 2 doses of the same vaccine (either MLV or CA/IV) with the second dose occurring 27 to 89 days prior to fixed-time AI. All vaccinations were administered by research personnel that had been properly trained in handling and administering of vaccines. All animals were individually identified (ear tag or freeze brand) to be able to track them throughout the study.

Synchronization and breeding

All animals were synchronized with the 7-day CO-Synch + CIDR protocol. Ten days prior to the start of the breeding season, animals were administered progesterone as a vaginal implant[d] and gonadorelin hydrochloride (GnRH).[f] Vaginal implants were removed and animals were administered dinoprost tromethamine[f] on day -3. Artificial insemination (AI) occurred at the appropriate time after vaginal implant removal (cows 60 to 66 hours; heifers 52 to 56 hours) and an injection of GnRH was given concurrent with insemination.

Table 1. Selected characteristics of each herd vaccinated with either modified-live virus (MLV) or chemically altered/inactivated (CA/IV) vaccine.

Herd	Treatment	No. of animals	Age (range), yrs	DPP* (range)	Interval from vaccination (range), d†	AI‡ (%)	Season§ (%)
1	MLV	43	Heifers	N/A	27	58%	91%
1	CA/IV	44	Heifers	N/A	27	59%	86%
2	MLV	145	Heifers	N/A	33	53%	83%
2	CA/IV	142	Heifers	N/A	33	49%	81%
3	MLV	35	2	51 to 117	27 to 33	37%	89%
3	CA/IV	37	2	19 to 117	27 to 33	43%	78%
4	MLV	129	3 to 13	76 to 101	54 to 89	66%	93%
4	CA/IV	135	3 to 13	64 to 90	54 to 89	66%	89%
5	MLV	36	2	43 to 90	30	53%	97%
5	CA/IV	35	2	49 to 89	30	63%	97%
6	MLV	15	Heifers	N/A	57	67%	93%
6	CA/IV	14	Heifers	N/A	57	57%	71%
7	MLV	136	3 to 13	37 to 93	30	43%	99%
7	CA/IV	134	3 to 13	36 to 92	30	49%	96%
8	MLV	99	Heifers	N/A	30	53%	85%
8	CA/IV	112	Heifers	N/A	30	43%	87%
9	MLV	31	Heifers	N/A	30	26%	74%
9	CA/IV	29	Heifers	N/A	30	28%	72%
10a	MLV	85	3 to 13	47 to 92	27 to 89	45%	91%
10a	CA/IV	85	3 to 13	39 to 97	27 to 89	48%	88%
10b	MLV	22	3 to 13	34 to 72	27 to 89	23%	77%
10b	CA/IV	24	3 to 13	39 to 73	27 to 89	46%	88%

*Days post-partum (interval from calving to fixed-time AI)
†Interval from vaccination to AI
‡Percentage of animals that conceived to AI
§Percentage of animals pregnant at the end of the breeding season

Within each herd, sires were used equally between treatments. All females within each herd were comingled and maintained as a single group throughout the study. Following AI, females remained separated from fertile bulls (bulls that passed a breeding soundness exam) for at least 10 days after AI, and then were exposed to fertile bulls for a 30 to 60-day breeding season. Artificial insemination pregnancy success was determined by transrectal ultrasonography between day 28 and 86 after AI, and breeding season pregnancy success was determined > 30 days after the end of the breeding season. All pregnancy examinations were performed by 1 of 2 trained ultrasound technicians. Presence of a fetal heartbeat was used to determine fetal viability and crown-rump length was used to determine fetal age. Within each herd, animals were pregnancy diagnosed at random and technician was blinded to treatment.

Statistical analysis

Animal was used as the experimental unit in this study as the treatment was applied to each individual animal. The binominal outcomes of AI pregnancy success and breeding season pregnancy success were analyzed using the GLIMMIX procedure in SAS[g] (METHOD = LAPLACE; ILINK = LOGIT DIST = BINOMIAL SOLUTION ODDSRATIO). The statistical model included treatment, vaccination interval, day post-partum, treatment by vaccination interval, and treatment by days post-partum in the model. Herd was included as a random variable, thus the treatment within herd interaction was used as the error term in order to enable valid data interpretation across all herds. Animals were grouped into 3 vaccination intervals: 1 based on animals vaccinated at a shorter interval than label recommendation (27 to 29 days), 1 for animals vaccinated in general accordance with label recommendations (30 to 37 days), and 1 for animals vaccinated at a greater interval than label recommendations (46 to 89 days). No animals were vaccinated between 37 and 46 days prebreeding. All data are reported as LSmeans ± standard error of the mean. Differences were considered to be significant when $P \leq 0.05$.

Results

Days post-partum tended ($P=0.065$) to influence conception rates (Table 2). Cows with shorter post-partum intervals (≤ 60 d) had a decreased AI conception rate compared to cows that were 61 to 100 days post-partum. Fur-

Table 2. Impact of days post-partum on pregnancy success among previously vaccinated animals.

	n =	AI conception (%)	Breeding season pregnancy success (%)
Heifers	673	58 ± 3 [ab]	84 ± 2 [a]
< 60 days	129	49 ± 5 [b]	97 ± 2 [b]
61 to 80 days	308	60 ± 4 [a]	96 ± 1 [b]
81 to 100 days	406	64 ± 4 [a]	94 ± 1 [b]
101 to 120 days	51	50 ± 7 [b]	84 ± 6 [a]

LSMeans within a column having different superscripts are different [ab]$P<0.05$

thermore, breeding season pregnancy success was decreased in cows that were < 60 days post-partum at the beginning of the breeding season compared to cows that had longer post-partum intervals. There was no treatment by days post-partum interaction (P=0.26). There was a main effect of treatment on AI conception rates (P=0.047). Conceptions to AI were greater in the CA/IV vaccine group compared to the MLV vaccine group (60% vs 52%, respectively; Table 3) irrespective of vaccination interval. Interval from vaccination with either vaccine until AI also influenced AI conception rates (P=0.022). Animals vaccinated 27 to 29 days prebreeding and animals vaccinated 30 to 37 days prebreeding had similar (P=0.975; 52% and 52%) conception rates; however, both were decreased compared to animals vaccinated 46 to 89 days prebreeding (P<0.030; 64%). There was no treatment by vaccination interval interaction (P=0.794) on AI conception rates (Figure 1). Treatment (MLV vs CA/IV) did not impact breeding season pregnancy success (P=0.24; 94% and 92%, respectively), and there was no effect of treatment by vaccination interval (P=0.58). However, vaccination interval did influence breeding season pregnancy success. Animals vaccinated fewer than 30 days prior to the breeding season had decreased (P=0.03) breeding season pregnancy rates compared to animals vaccinated 30 to 37 days prior to the breeding season (Table 3).

Discussion

In the present study, there was a significant decrease in AI conception rates among beef cows and heifers vaccinated with MLV compared to CA/IV BHV-1 and BVD vaccine prior to breeding. This is similar to an earlier study in which previously vaccinated beef females vaccinated with a MLV vaccine had decreased AI conception rates compared to animals vaccinated with an IVV vaccine 30 days prior to a fixed-time AI,[11] and 2 other studies that reported large but non-significant differences between MLV and IVV[18] vaccines and between MLV and saline.[19]

A recent review article[2] discussed the influence of BHV-1 on cattle reproductive performance. This review indicated that latency is characteristic of all herpesviruses, but no studies have investigated the effects of management stress on reactivation of the viruses. In addition, it pointed

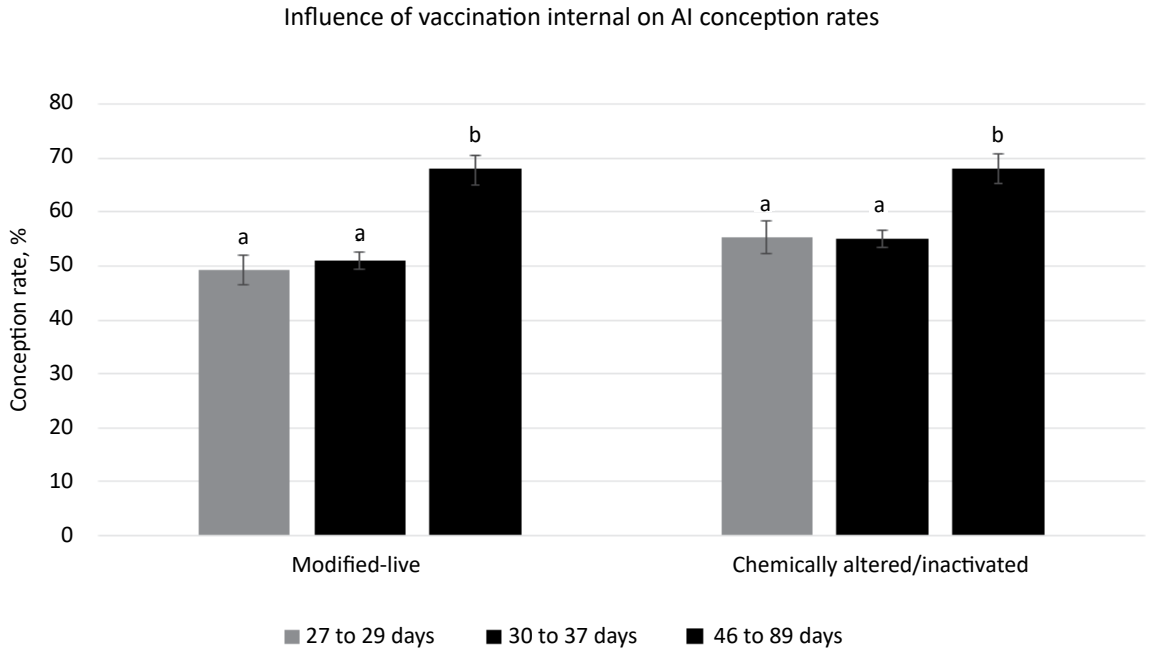

Figure 1. Conception rates to AI for modified-live and chemically altered/inactivated vaccines based on interval from vaccination to AI (days). Overall, there was no treatment by vaccination interval interaction (P=0.794), but within each vaccination type AI conception rates were increased among animals vaccinated 46 to 89 days before AI compared to animals vaccinated 37 days or fewer before breeding. Bars within vaccine type having different superscripts are different (P<0.04).

Table 3. Impact of vaccine and timing of vaccine before start of breeding (AI) on pregnancy success among previously vaccinated animals.

	n =	AI conception (%)	Breeding season pregnancy success (%)
Modified-live	775	52 ± 4 [a]	94 ± 1
Chemically altered/inactivated	792	60 ± 4 [b]	92 ± 2
27 to 29 days	217	52 ± 5 [a]	92 ± 2 [a]
30 to 37 days	1053	52 ± 3 [a]	95 ± 2 [b]
46 to 89 days	299	64 ± 4 [b]	91 ± 2 [ab]

LSMeans within a column having different superscripts are different [ab]$P<0.05$

out that increased estradiol at estrus was correlated to decreased T cells specific to herpes simplex virus in mice and women, and that this decrease in immunity could increase the possibility of reactivation. Thus, variation in how animals perceive the stress of the multiple handlings required for a fixed-time synchronization protocol, combined with the elevated concentrations of estradiol that occur at the onset of estrus, could account for some variation reported between herds and studies.

Contrary to the results of the current study, 2 studies reported no impact of vaccination with a MLV vaccine prior to breeding on pregnancy success in previously vaccinated animals.[1,16] However, both of these studies drew this conclusion by comparing different intervals between vaccination and the start of the breeding season: 40 or 3 days prior to peak breeding,[1] and 30 days or 9 days prior to the start of the AI breeding program.[16] In the present study there was no difference in AI conception rates between animals vaccinated 27 to 29 days prior to breeding and those vaccinated 30 to 37 days prior to breeding. Thus, the same conclusion could be drawn from the current study; however, animals vaccinated 46 to 89 days prior to the start of the breeding season had increased AI conception rates and breeding season pregnancy rates compared to either of the other 2 groups, and this increase was irrespective of the vaccine used. Thus, the specific mechanisms involved in these vaccination effects on reproductive efficiency continue to be inadequately characterized.

Overall, there was no treatment by vaccination interval interaction (P=0.794), but within each vaccination type AI conception rates were increased (P<0.04) among animals vaccinated 46 to 89 days before AI compared to animals vaccinated 37 days or fewer before breeding (Figure 1). A recent study in dairy cattle reported no difference in conception rates between vaccinating primiparous dairy cows that had been previously vaccinated (3 MLV vaccinations as calves and 1 prebreeding as a heifer) with either a MLV or inactivated vaccine 45 days prior to fixed-time AI.[20] If vaccination impacts follicular development and/or oocyte quality, it is realistic to expect that pre-breeding vaccination intervals greater than 42 days would have little or no impact on fertility. Bovine follicles require 27 days to grow from 0.13 mm to 0.67 mm (pre-antral to early antral), 6.8 days to grow from 0.68 mm to 3.67 mm, and 7.8 days to grow from 3.68 mm to 8.56 mm.[7] Thus, it takes approximately 2 estrous cycles for follicles to grow from 0.13 mm to follicular deviation. At any time during follicular growth, anti-viral vaccination could affect the growing follicle and impact oocyte quality and future luteal function. However, inflammation itself resulting from vaccination could also decrease fertility through effects on either the ovary or uterus.

A recent review reported possible links between mastitis and decreased conception rates in dairy cows.[5] The review discussed studies indicating that early embryonic loss in mastitic cattle is due to activation of immune responses at sites outside the reproductive tract. Impacts on the reproductive tract may be mediated through increased concentrations of cytokines in these animals.

In the present study, days post-partum also influenced conception rates, with cows less than 60 days post-partum having decreased AI conception rates compared to cows that were greater post-partum at fixed-time AI. This was expected as others have reported conception rates were improved among animals with longer post-partum intervals compared to animals with shorter post-partum intervals.[6,15]

Conclusion

In conclusion, vaccination with a MLV vaccine prior to the start of a breeding season was associated with decreased conception rates to fixed-time AI, regardless of when vaccination occurred. In addition, vaccination at 37 or fewer days prior to the start of the breeding season, regardless of vaccine type (MLV or CA/IV), resulted in decreased AI conception rates and decreased breeding season success compared to vaccination at 46 or more days before the start of the breeding season. The exact mechanism for these decreases in conception rates is not known at this time, but they may be mediated through stress and/or an inflammatory response in the body.

Endnotes

[a]Bovi-Shield GOLD FP L5®, Zoetis Animal Health, Florham Park, NJ

[b]Bovi-Shield GOLD® 5, Zoetis Animal Health, Florham Park, NJ

[c]CattleMaster GOLD FP5®, Zoetis Animal Health, Florham Park, NJ

[d]Eazi-Breed CIDR® implants, Zoetis Animal Health, Florham Park, NJ
[e]Factrel®, Zoetis Animal Health, Florham Park, NJ
[f]Lutalyse®, Zoetis Animal Health, Florham Park, NJ
[g]SAS® Version 9.4, Cary NC

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