Field trial of the effect of vaccination against Bovine herpesvirus 1 on milk yield and rumination time: comparison between two live marker vaccines

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SUMMARY

In a dairy farm using a voluntary milking system (VMS), two homogeneous groups of dairy cows were formed. For each group the VMS automatically determined daily data related to individual milk yield (MY) and rumination time (RT). Data were analyzed from 3 days before vaccination to 6 days after vaccination, which was performed with 2 live attenuated IBR marker vaccines regularly marketed in Italy (group A: BioBos IBR marker live and group B: Bovilis IBR marker live). Data from groups A and B were statistically compared to determine differences within the group before and after vaccination, as well as differences between the groups. The between group analysis failed to find a difference in MY, but A had higher RT than B the first day after vaccination ($P<0.05$). In group A, vaccination had no effect on both MY and RT, conversely, in group B, MY did not change after vaccination and RT decreased on the day after vaccination, but returned to pre-vaccination values on day there. Rumination time is known to be one of the indicators of animal welfare, i.e., absence of stressors. This study showed that vaccination against IBR with the selected products had no effect on milk yield and had a very little effect on RT limited to the first day after vaccination. The latter is mainly due to reduction of RT in group B and indicated a slightly altered physiological homeostasis, whereas group A maintained the same rumination behavior as before vaccination.

KEY WORDS

Dairy cow; BHV-1 vaccination; Milk yield; Rumination time.

INTRODUCTION

Bovine herpesvirus 1 (BHV-1) is a cattle pathogen that causes infectious bovine rhinotracheitis (IBR) and infectious pustulous vulvovaginitis/balanoposthitis (IPV/IPB) in adult cow. After recovery from acute BHV-1 infection, animals retain a lifelong latency of the virus, which can be reactivated under unfavourable conditions (1,2). Italy is characterized by a fragmented epidemiological situation, with few regions officially free of BHV-1 and most others where the virus still circulates, justifying systematic prophylactic vaccination with an attenuated marker live vaccine. Veterinarians have frequently pointed out that one of the obstacles to proper planning of vaccination prophylaxis is the fear of farmers that vaccination may be «stressful» for animals and associated with a reduction in milk yield and heath status of vaccinated animals. This fear is particularly pronounced for vaccinations that affect the entire herd at the same time, such as vaccinations to prevent respiratory disease or for diseases that have not been diagnosed on the farm for some time, such as prophylaxis against IBR. Such behaviour can become a serious obstacle to the correct implementation of the vaccination programme proposed by the veterinarian and can significantly compromise the effectiveness of the established programme and, most importantly, the immune protection of the herd (3).

The evaluation of stress intensity in animals can be done by different methods, many of which are expensive and complicated. One of the behavioural changes observed in the cow during malaise or in the course of overt disease is the slowing or cessation of rumination. Thus, the idea of using this behaviour to indirectly measure animal well-being is not new, although it initially clashed with data collection difficulties. Direct observation, video recording, or the use of halters equipped with pressure sensors were the first systems used, but their complexity limited their use to research purposes. The advent of automatic measurement systems, mainly based on microphones (4) or three-dimensional accelerometers (5), has allowed the recording of data in real time and for indefinite periods, making the recording of rumination time available in herd management software. Using this approach, Soriani (6) has shown how measuring the duration of rumination negatively correlates with heat stress, which not only reduces the total time spent ruminating but also alters the daily distribution by reducing the frequency during the day and increasing it at night. Researchers from

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the Catholic University of Piacenza also later found (7) that rumination time increases when data from a few weeks before calving are compared with those from the first weeks of lactation; they also found that animals with metabolic and clinical problems are also characterised by shorter rumination times, and concluded that rumination times may be early indicators of incipient discomfort in cows in the first weeks after calving. Malasauskeie and coworkers (8) also pointed out that in the first month of lactation, decreases in rumination times are associated with increases in blood cortisol levels. A recent bibliographic review (9) reported that there is solid scientific basis for considering the measurement of rumination time as a reliable and objective parameter that allows the identification of stressed animals that are about to become ill or are already affected by clinically manifest diseases. The automatic monitoring systems that record rumination time, when connected to a milking system that also records milk yield and other characteristics, such as the voluntary milking system (VMS - milking robot), make it possible to obtain these data in a simple, precise and continuous way.

Based on these scientific observations, in addition to measuring daily milk yield, we chose to measure rumination time as an indicator of the level of discomfort/stress caused by vaccination for our study. The experiment involves the comparison of live IBR virus vaccines produced by two different companies. Infectious rhinotracheitis vaccination was chosen because it meets two of the main characteristics that increase farmers' reluctance to vaccinate: it is a vaccination that is usually performed simultaneously on the whole herd, and it is often a disease that has not been diagnosed on the farm for a long time, so the breeder has a different perception of the risk-benefit ratio of vaccination.

The first objective of this work was to verify, with objective data, if prophylaxis with live IBR vaccines has negative effects on milk production and if it is a stress factor for the animals. The second objective was to determine any differences between two different commercially available vaccines.

MATERIALS AND METHODS

The experiment was conducted in a dairy farm with about 200 dairy cows in the Po Valley, Reggio Emilia province. All animals are milked with 4 Lely Astronaut voluntary milking systems (VMS; Lely, Maassluis, The Netherlands). The farm routinely performs prophylaxis against infectious rhinotracheitis with a marker live vaccine.

Daily milk yield (MY, kg/day) and rumination time (RT, min/day) were recorded directly from the VMS management software. Data collection began 3 days before vaccination and continued 6 days after (DpV).

The vaccines used for the experiment were two products regularly licensed and marketed in Italy, whose characteristics are described in the respective summaries of product characteristics available online (10):

Group A: BioBos IBR Marker live® (Bio98 s.r.l., Italy).

Group B: Bovilis IBR Marker live® (Intervet International B.V., The Netherlands).

The vaccines were administered intramuscularly at the same volume (2 ml) according to the manufacturer's instructions; all animals received booster vaccination as part of a vaccination program that required administration at 6-month intervals. For the experiment, 197 dairy cows were selected, divided into two groups that were paired according to parity, milk production, and days in milk. At the beginning of the trial, 40% and 45% of the cows in groups A and B were primiparous and, in general, there was no significant association between vaccine group and parity ($P>0.05$). Days in milk were also similar between the vaccine group (mean ± se; 157.1 ± 10.47, 160.5 ± 9.93 for A and B, respectively; $P>0.05$).

On the day of vaccination (day 0, DpV0), the cows were vaccinated by two experienced veterinarians who performed the vaccinations and recorded the animals' identification data. The two groups of animals were housed in the same place, fed the same ration, and milked by the same VMS.

STATISTICAL ANALYSIS

Data were analysed using R software, vers. 4.0.4 (R Core Team, 2021) and SPSS vers. 17 software (SPSS Inc., Illinois). Normality of the data distribution and the residuals of the statistical model adopted was tested using Shapiro-Wilk test. At the beginning of the trial, the difference between vaccine group (A vs. B) in days in milk was tested using Mann-Whitney U test, while the association between vaccine group (A, B) and parity (primiparous, multiparous) was tested using Chi-Square Test. In order to assess differences between vaccines, milk yield and rumination time were analysed using generalized estimating equations applied on a covariance model with vaccine group as fixed and day after vaccination (DpV1, DpV2, DpV3, DpV4, DpV5, DpV6) as repeated factor. The interaction vaccine group × day after vaccination was also considered. The mean performance (MY, RT) of three days preliminary period was used as covariate factor. Sequential Bonferroni was used as post-hoc test. In order to assess the effect of the vaccine over time on milk yield and rumination time, the two vaccines were analysis separately using generalized estimating equations. These equations were applied on a model with the day (the mean performance of the of three days preliminary period, DpV, and six days after vaccination, DpV1, DpV2, DpV3, DpV4, DpV5, DpV6) treated as repeated factor. Sequential Bonferroni was used as post-hoc test.

RESULTS

The effects of vaccine group and day after vaccination on MY and RT are shown in Table 1. MY was similar between vaccine groups ($P>0.05$), and changed during post vaccination period ($P<0.05$). In particular, MY increased from DpV1 to DpV2 ($P<0.05$), remained constant from DpV2 to DpV3 ($P>0.05$) and decreased from DpV3 to DpV6 ($P<0.05$). RT was affected by both vaccine group ($P<0.05$) and DpV ($P<0.05$). However, as the interaction vaccine group × DpV was statistically significant ($P<0.05$), the main effects can not be discussed separately. Considering the results of interaction from the perspective of the vaccine factor. A had higher RT than B at DpV1 (estimated marginal means adjusted to initial values ± se; 445 ± 3.6 vs. 404 ± 5.1 min/d for B and R, respectively; $P<0.05$; data not reported in Tables), but not in all the other days post vaccination (DpV2: 449 ± 3.9 vs. 442 ± 4.4 min/d; $P>0.05$; DpV3: 447 ± 4.4 vs. 442± 4.7 min/d; $P>0.05$; DpV4: 435 ± 4.2 vs. 440± 4.5 min/d; $P>0.05$; DpV5: 466 ± 4.3 vs. 466± 4.7 min/d; $P>0.05$; DpV6: 457 ± 4.5 vs. 454± 5.1 min/d; $P>0.05$; data not report-

Table 1 - Estimated marginal means adjusted to initial values (average of three days before vaccination) of milk yield (MY) and rumination time (RT) in the six days after vaccination.

	Vaccine (V)		Day post vaccination (DpV)						SEM	*P*-value		
	A	B	1	2	3	4	5	6		V	DpV	V×DpV
MY, kg	39.0	38.8	38.1^{a}	39.4^{bc}	39.6^{c}	38.8^{abc}	38.9^{abc}	38.6^{ab}	0.23	0.63	<0.01	0.313
RT, min/d	450	441	425^{a}	445^{bc}	444^{b}	437^{b}	466^{d}	455^{c}	2.1	0.04	<0.01	<0.01

A: BioBos IBR Marker live® (Bio98 s.r.l., Italy); B: Bovilis IBR Marker live® (Intervet International B.V., The Netherland); ^{a,b,c,d}: Within the same row with unlike letters differ significantly at *P*<0.05.

Table 2 - Estimated marginal means of milk yield (MY) and rumination time (RT) before vaccination (DbV) and in the six days after vaccination (DpV1, DpV2, DpV3, DpV4, DpV5, DpV6) in animals treated with A vaccine.

	Days of experimental period							SEM	*P*-value
	DbV	DpV1	DpV2	DpV3	DpV4	DpV5	DpV6		
MY, kg	39.0^{ab}	38.5^{a}	39.6^{bc}	39.8^{c}	39.3^{abc}	39.3^{abc}	38.7^{ab}	0.98	<0.01
RT, min/d	439^{a}	449^{ab}	452^{bd}	450^{ab}	439^{ad}	470^{c}	461^{bc}	4.5	<0.01

^{a,b,c,d}: Within the same row with unlike letters differ significantly at *P*<0.05.

Table 3 - Estimated marginal means of milk yield (MY) and rumination time (RT) before vaccination (DbV) and in the six days after vaccination (DpV1, DpV2, DpV3, DpV4, DpV5, DpV6) in animals treated with B vaccine.

	Days of experimental period							SEM	*P*-value
	DbV	DpV1	DpV2	DpV3	DpV4	DpV5	DpV6		
MY, kg	38.5^{ab}	37.6^{a}	39.2^{b}	39.4^{b}	38.4^{ab}	38.6^{ab}	38.4^{ab}	0.94	<0.01
RT, min/d	429^{b}	400^{a}	438^{bc}	438^{bc}	436^{b}	462^{d}	450^{cd}	4.9	<0.01

^{a,b,c,d}: Within the same row with unlike letters differ significantly at *P*<0.05.

ed in Tables).

The effects of the vaccine A over time are shown in Table 2. MY before vaccination (DbV) was similar to the values observed during the six days after vaccination (P>0.05) with the only exception of day 3 (DpV3), which showed a higher value (P<0.05). RT values were similar before (DbV) and after 1 (DpV1), 3 (DpV3), 4 (DpV4) days after vaccination (P>0.05); higher values were observed at 2 (DpV2), 5 (DpV5) and 6 (DpV6) days after vaccination (P<0.05). The effects of the vaccine B over time are shown in Table 3. MY did not change after vaccination (P>0.05), on the contrary, RT decreased the day post vaccination (DpV1; P<0.05), then increases from DpV1 to DpV2 (P<0.05), remained constant from DpV2 to DpV4 (P>0.05) and reached the highest values at DpV5 and DpV6 as observed for vaccine A.

DISCUSSION

The economic impact of BHV-1 infection in dairy cows is well established and justifies vaccine prophylaxis. The objective of this experiment was to demonstrate that vaccination against BHV-1 virus does not cause significant economic or animal welfare problems in dairy cows. The beneficial effects of vaccination in seropositive herds have been documented (11); however, the effects of vaccination on herds where the virus is not circulating are less clear.

The results reported here show that milk yield does not decrease significantly in the days after vaccine administration. Bosch et al (12), in a field trial in the Netherlands with a BHV-1 gene-deleted vaccine administered to naive dairy cows, reported a slight but significant decrease in milk production in the six days after vaccination, especially after the second dose. They concluded that vaccination had a significant but negligible negative effect on average milk production over six days. However, unlike our protocol, that of Bosch and colleagues (12) used a control group of animals receiving PBS injection to compare the effect of vaccination, and this control group produced 1 litre more than the treated group before treatment, although the animals were paired for calving date. In addition, data for the second injection, which had a significant effect on milk production (0.6-0.7 kg less milk in the vaccinated animals), were collected four weeks after the first vaccination. The animals were from five different farms with different health status (BHV positivity) and different milk recording systems. The vaccine used was also different. Overall, these differences could explain the discrepancies between our results and those of Bosch et al (12). Recently, Dubovi et al. (13), who used a multivalent virus vaccine that included IBR viruses in dairy cows, found no change in milk production, which is consistent with our results.

Rumination time was not changed in group A, whereas a slight but significant decrease was observed in group B the day after vaccine administration ($P < 0.05$). However, also the mean value recorded on the first day after vaccination in group B was within the range reported by Beauchemin (14) for lactating dairy cows. The effects of vaccination on rumination time have not been studied in dairy cows, so comparison with literature data is not possible. However, in a recent article, Munoz

et al (15) reported that there was no difference in rumination time in newly housed beef cattle subjected to pentavalent vaccination with modified live viruses that also contained live BHV-1 virus. Our observation confirmed the negligible effect of vaccination against BHV-1 on animal welfare. The significant difference observed between the two vaccine types on the day after vaccination could be due to differences in formulation (e.g., adjuvant used) or antigen type.

CONCLUSION

This study showed that vaccination against IBR with the selected products had no statistically detectable effect on animal production under the experimental conditions.

With respect to the stress-inducing effect of vaccination, which was assessed by measuring rumination time, the two vaccines were found to be slightly different under the experimental conditions only the first day after vaccination. Thus, in group A, there was no statistically significant difference in rumination time after vaccination, while in group B, rumination time decreased significantly the day after vaccination, indicating a moderately effect of the vaccine on the animals physiological homeostasis. However, further experiments are recommended to confirm the result in a larger group of animals before final conclusions are drawn.

Thanks to the information provided by the milking robots, this test is repeatable in different livestock situations, so that objective data on tolerance for a given farm can be obtained relatively quickly and the risk-benefit ratio of a given treatment or procedure can be evaluated.

Conflict of Interest: Dr. A. Soriolo declares that he has a conflict of interest because he is an employee of the company that manufactures one of the vaccines tested. However, he confirms that he was not involved in the selection of animals between the two groups, nor in the collection and statistical processing of the data. The other authors declare that they have no conflicts of interest.

References

1. Kaashoek M.J., Straver P.H., Van Rooij E.M., Quak J., Van Oirschot J.T. (1996). Virulence, immunogenicity and reactivation of seven bovine herpesvirus 1.1 strains: clinical and virological aspects. Vet. Rec., 139: 416-421. doi.org/10.1136/vr.139.17.416
2. Jones C., Chowdhury S. (2007). A review of the biology of bovine herpesvirus type 1 (BHV-1), its role as a cofactor in the bovine respiratory disease complex and development of improved vaccines. Anim. Health Res. Rev., 8: 187-205. doi.org/10.1017/S146625230700134X
3. Cresswell E., Brennan M.L., Barkema H.W., Wapenaar W. (2014). A questionnaire-based survey on the uptake and use of cattle vaccines in the UK. Vet Rec Open, 1:e000042. doi.org/10.1136/vropen-2014-000042
4. Schirmann K., von Keyserlingk M.A.G., Weary D.M., Veira D.M., Heuwieser W. (2009). Technical note: Validation of a system for monitoring rumination in dairy cows. J Dairy Sci, 92: 6052-6055. doi.org/10.3168/jds.2009-2361
5. Borchers M.R., Chang Y.M., Tsai I.C., Wadsworth B.A., Bewley J.M. (2016). A validation of technologies monitoring dairy cow feeding, ruminating, and lying behaviors. J Dairy Sci, 99: 7458-7466. doi.org/10.3168/jds.2015-10843
6. Soriani N., Panella G., Calamari L. (2013). Rumination time during the summer season and its relationships with metabolic conditions and milk production. J Dairy Sci, 96: 5082-5094. doi.org/10.3168/jds.2013-6620
7. Calamari L., Soriani N., Panella G., Petrera F., Minuti A., Trevisi E. (2014). Rumination time around calving: An early signal to detect cows at greater risk of disease. J Dairy Sci, 97: 3635-3647. doi.org/10.3168/jds.2013-7709
8. Malašauskienė D., Televičius M., Juozaitienė V., Antanaitis R. (2019). Rumination time as an indicator of stress in the first thirty days after calving. Pol J Vet Sci, 22: 363-368.
9. Paudyal S. (2021). Using rumination time to manage health and reproduction in dairy cattle: a review. Vet Q, 41: 292-300. doi.org/10.1080/01652176.2021.1987581
10. VETINFO, https://www.vetinfo.it/j6_prontuario/public/
11. Raaperi K., Orro T., Viltrop A. (2015). Effect of vaccination against bovine herpesvirus 1 with inactivated gE-negative marker vaccines on the health of dairy cattle herds. Prev Vet Med, 118: 467-76. doi: 10.1016/j.prevetmed.2015.01.014
12. Bosch J.C., Frankena K., van Oirschot J.T. (1997). Effect on milk production of vaccination with a bovine herpesvirus 1 gene-deleted vaccine. Vet Rec, 140: 196-199
13. Dubovi E.J., Gröhn Y.T., Brunner M.A., Hertl J.A. (2000). Response to modified live and killed multivalent viral vaccine in regularly vaccinated, fresh dairy cows. Vet Ther, 1: 49-58.
14. Beauchemin K.A. (2018). Current perspectives on eating and rumination activity in dairy cows. J Dairy Sci, 101: 4762-4784. doi: 10.3168/jds.2017-13706.
15. Munoz V.I., Samuelson K.L., Tomczak D.J., Seiver H.A., Smock T.M., Richeson J.T. (2020). Comparative efficacy of metaphylaxis with tulathromycin and pentavalent modified-live virus vaccination in high-risk, newly received feedlot cattle. Applied Animal Science, 36:799-807. doi.org/10.15232/aas.2020-02054