Comparison of Postvaccinal Milk Drop in Dairy Cattle Vaccinated with One of Two Different Commercial Vaccines*

R. Bergeron, DVM a
J. Elsener, DVM, MSc b,†

a Clinique Vétérinaire Bon Conseil
132 rue Notre-Dame C.P. 175
Notre-Dame-Du-Bon-Conseil, Quebec J0C 1A0
Canada

b Wyeth Animal Health
400 Michener Road
Guelph, Ontario N1K 1E4
Canada

CLINICAL RELEVANCE

Several veterinarians and dairy producers elect to vaccinate dairy herds with killed combination products in the fall or spring. Postvaccinal milk drop has been reported following the use of some killed vaccines, making it important to identify vaccines that can cause milk drop and evaluate the magnitude of postvaccinal milk drop. This study compared the pre- and postvaccinal milk production levels of dairy cows vaccinated with two commercial vaccines or injected with a saline placebo. Dairy cows receiving vaccine C (Cattlemaster Gold FP5; Pfizer Animal Health, Montreal, Canada) experienced a statistically significant difference in mean postvaccinal milk drop (−1.83 kg/cow/day) compared with cows receiving vaccine T (Triangle 4 + Type 2 BVD, Wyeth Animal Health, Guelph, Canada; −0.63 kg/cow/day) or saline (−0.02 kg/cow/day).

INTRODUCTION

Several North American dairy herds are routinely vaccinated against bovine viral diarrhea virus (BVDV), bovine herpesvirus type 1 (BHV-1; the causative agent of infectious bovine rhinotracheitis [IBR]), bovine respiratory syncytial virus (BRSV), and parainfluenza-virus-3 (PI-3) to prevent respiratory or reproductive diseases caused by these viruses.

Because of the risk incurred by vaccinating pregnant cattle with modified-live IBR and BVDV vaccines and the convenience of whole-herd vaccination, many veterinarians or producers elect to vaccinate the entire herd with killed vaccines in the fall or spring. With a whole-herd vaccination strategy, vaccinated cows are at different stages of production, with a sizeable proportion being in lactation.

Although some studies did not report any adverse effects of vaccination on milk production,1,2 other studies reported occurrences of transient fever and/or postvaccinal milk drop in dairy cattle.3-5 Milk drop of up to 21.5% per

*This research was financially supported by Wyeth Animal Health, Guelph, Ontario, Canada.
†Correspondence should be sent to Dr. Elsener: phone, 418-651-0505; fax, 418-651-3575; email, jelsener@wyeth.com.
lactating cow for up to 7 days after vaccination was reported in one study. However, the cows in that study also experienced dermatologic allergic reactions, which were not reported in the other studies. In studies with no reports of allergic adverse reactions, a significant milk drop of a smaller magnitude, ranging from 1.4 to 5.3 L of milk/cow for a period of up to 4 days after vaccination, was observed.

All reported postvaccinal milk drops occurred after the administration of a killed vaccine. It has been postulated that the inclusion of an adjuvant system or of an endotoxin-producing gram-negative bacteria fraction was responsible for the milk drop. However, whereas some adjuvanted viral vaccines produce a significant milk drop, other vaccines with similar viral fractions do not induce significant milk drop; therefore, a difference in reactivity between adjuvant systems might exist.

Scientific comparisons of postvaccinal milk drop with commonly used commercial vaccines are scarce despite the obvious interest for such data among practitioners and producers. The objective of this study was to compare the milk production in cows vaccinated with two different commercial adjuvanted BVDV–BRSV–IBR–PI-3 vaccines, one of them being a product recently introduced in the North American market.

MATERIALS AND METHODS

Herd Description

A commercial dairy herd with 650 lactating Holstein cows was selected for the trial. The herd is located in Quebec, Canada. At the time of the trial, June 2007, the average milk production of the herd was 27 kg/cow/day and the herd was milked three times daily at 0400, 1200, and 2000. In the past years, the herd had been vaccinated annually in the spring with Triangle 4 + Type 2 BVD (Wyeth Animal Health, Guelph, Canada), and the herd was due for its annual revaccination at the time of the trial. Owner consent was sought and obtained for this trial. The procedures performed during the trial were not different from the procedures routinely used in this herd at the time of annual revaccination.

Treatment Groups

Four hundred fifty-six Holstein dairy cows were selected by alimentary group (group 1, 2, or 3), parity (1 and 2, 3 and 4, or >4), and daily milk yield (0 to 20 kg, 20.1 to 30 kg, 30.1 to 40 kg, 40.1+ kg). The alimentary groups correspond to different nutrition level and nutrient content of the ration fed according to the physiologic requirements and milk production level of the cows. Alimentary group 1 represented first-parity cows; alimentary group 2 consisted of cows with a parity of ≥2, milk production of >25 kg/day, and <225 days in milk. During their lactation, cows from alimentary group 2 were transferred by the owner to alimentary group 3 when their daily milk production fell below 25 kg/day and they reached 225 days in lactation. For blocking by daily milk yield, daily milk yield was calculated as the mean milk production over the 7-day period before treatment allocation. Cows were randomly allocated to one of the following treatment groups:

• Group T: Vaccinated SC with 2 ml of Triangle 4 + Type 2 BVD
• Group C: Vaccinated SC with 2 ml of Cattlemaster Gold FP5 (a recently introduced vaccine from Pfizer Animal Health, Montreal, Canada)
• Group S: Injected SC with 2 ml of physiologic 0.9% saline (Solution Saline Physiologique, Vetoquinol Canada, Lavaltrie, Quebec, Canada)

All cows were injected SC in the caudal flap on the right side of the tail using a 1-inch, 20-
gaugeneedle. All vaccines were purchased from a provincial drug distributor (CDMV, St-Hyacinthe, Quebec, Canada), and were stored between 2°C and 7°C until use.

The Triangle 4 + Type 2 BVD vaccine has a proprietary adjuvant system containing saponin,7 and the adjuvant system in CattleMaster Gold is comprised of Quil A (a refined form of saponin), cholesterol, and Amphigen (an oil-based component).8,9 These two commercial vaccines contain the same antigen combination: PI-3, BRSV, BHV-1, and BVDV types 1 and 2. All the viral fractions in Triangle 4 + Type 2 BVD are killed, whereas only the BVDV fraction (both types 1 and 2) in Cattlemaster Gold is killed. All cows were vaccinated at the same time on day 0. The average prevaccination daily milk production of the 456 cows included in the trial was 24.8 kg/cow/day.

Inclusion/Exclusion Criteria
A cow was entered in the trial if it had been successfully grouped into one of the vaccination groups based on production data provided before the trial and was successfully vaccinated on day 0 of the trial. A cow was excluded from the trial if it was not lactating; less than two-thirds of the milk production data was available before or after vaccination (i.e., from 3 days before to 3 days after treatment); any anomaly relating to milk production or management data (cow number, parity, feed group) was identified during manual validation of records; or it experienced clinical disease during the trial period. A cow experiencing clinical disease was defined as one that received any therapeutic treatment (with the exclusion of hormones to control the reproductive cycle) or that spent time in the hospital section during the trial period. All individual clinical signs and treatments were recorded by employees daily and entered into computerized individual cow files.

Outcome
Individual milk yield was recorded for each milking from 7 days before vaccination (day –7) through 7 days after vaccination (day 7). Milk production data were captured using an on-farm computerized application that recorded milk production and herd management information (BouMatic Agricomp 2050 Provan
tage Network Controller, BouMatic, Madison, WI). Milk production data for the whole herd was downloaded daily to an ASCII file for the 15 days of the trial.

Statistical Analysis
Data formatting, validation, and statistical analyses were performed using Stata/SE 8.2 for Windows (STATA, version 8.2, StataCorp, College Station, TX). Statistical significance of the mean difference in daily milk production between the 3-day postvaccination period and the 3-day prevaccination period was evaluated using an analysis of variance procedure at a significance level of 5% (P < .05).

Cows in Group C experienced a mean postvaccinal milk drop of 1.83 kg/cow/day while the mean postvaccinal milk drop was 0.63 kg/cow/day for Group T and 0.02 kg/cow/day for Group S.
RESULTS

After applying the inclusion–exclusion criteria, a total of 137 cows were included in Group T, 146 cows in Group C, and 136 cows in Group S for statistical analysis (N = 419). The comparison of the milk production for the 3-day postvaccination period with that of the 3-day prevaccination period revealed that the cows in Group C experienced a mean postvaccinal milk drop of 1.83 kg/cow/day while the mean postvaccinal milk drop was 0.63 kg/cow/day for Group T and 0.02 kg/cow/day for Group S (Table 1). The difference between the 3-day postvaccinal daily mean milk production between Group S and Group C was statistically significant (P < .001), while the difference between Group S and Group T was not (P = .501). The difference between the 3-day postvaccinal daily mean milk production between Group C and Group T was statistically significant (P = .027).

For Group C, in which milk drop was highest, the peak milk drop occurred 1 day after vaccination. For this group, the cows in the daily milk yield category of 30.1 to 40 kg experienced the highest milk drop, with an average decrease of 2.60 kg/cow/day. Cows of parity 3 or 4, with an average milk decrease of 2.39 kg/cow/day, were more affected than were cows of parity 1 or 2 or >4. For Group C, the cows of parity 3 or 4 in the daily milk yield category of 30.1 to 40 kg experienced the highest milk drop, with an average decrease of 4.4 kg/cow/day.

DISCUSSION

In this study, we targeted a priori a trial period of 3 days before vaccination to 3 days after vaccination based on the timing of the postvaccinal milk drop occurrence reported in the literature.3–5 As Bosch and colleagues clearly stated,4 if a longer period after vaccination is selected, even large short-term effects would not be detected by using the mean milk production during that period.4 However, we elected to record the daily milk production for a longer period (spanning 7 days before to 7 days after vaccination) to verify the stability of the milk production before vaccination and to avoid any confusion regarding the starting and ending dates of the trial on the part of the farm employees who recorded the milk production.

As demonstrated by the results of this study, killed or partly killed adjuvanted vaccines with the same viral fractions can differ in their reactivity level in lactating dairy cows. This finding was reported previously in a study comparing two commercial vaccines containing the same four viral fractions as in the current study and five Leptospira serovars.3 Possible explanations for the safety discrepancy between the two vaccines may include the antigen concentration, the level of attenuation of the live fractions, the level of vaccine purification, and the adjuvant system. Because the antigen concentration, attenuation level, and purification level of the two vaccines are unknown, it is difficult to ar-

| TABLE 1. Comparison of Milk Production for the 3-Day Postvaccination Period with the 3-Day Prevaccination Period by Treatment Group |
|---------------------------------|-----------------|-----------------|-----------------|
| **Treatment Group**             | **No. of Cows** | **Mean Difference (± SE) in Milk Production (kg of milk/cow/day)** | **95% CI** |
| Group T: Triangle 4 + Type 2 BVD | 137             | −0.63b (±0.38)  | +0.12, −1.37    |
| Group C: Cattlemaster Gold FP5  | 146             | −1.83a (±0.30)  | −1.24, −2.42    |
| Group S: Saline control         | 136             | +0.02b (±0.30)  | +0.61, −0.57    |

*Values with different superscripts within the column differ significantly (P < .05).
rive at a conclusion about the causal relationship for the difference in reactivity observed in this study.

It has been reported in the scientific literature that some adjuvant systems are more reactive than others. Freund complete adjuvant, for example, has been described as a very reactive adjuvant and thus is very seldom used in veterinary vaccines.\(^\text{10}\) Moreover, different commercial preparations of the same adjuvant can differ in their reactivity. In a study conducted by Strobbe et al.,\(^\text{11}\) six commercial saponins were found to have different irritant activity when injected in cattle. To our knowledge, no peer-reviewed paper has evaluated the impact of different adjuvant systems on milk production in dairy cattle; therefore, it is impossible to conclude that the difference in the adjuvant formulation between the two vaccines used in this study was responsible for the difference in reactivity.

A transient fever resulting in reduced milk production in some cows has been proposed as the possible mechanism behind postvaccinal milk drop.\(^\text{3}\) In this study, the body temperature of individual cows was not measured for welfare reasons; therefore, such a correlation cannot be made. However, a postvaccinal increase in body temperature has been reported elsewhere: Scott and associates reported a significant mean temperature increase of 0.41°C one day after vaccination for the group of lactating dairy cows that experienced the most pronounced postvaccinal milk drop.\(^\text{3}\) These authors also reported that the high-production cows (>35 kg/cow/day) are most susceptible to postvaccinal drops in milk production.\(^\text{3}\) In this study, we found that for Group C, the highest milk drop was not observed in the highest production subgroup but rather in the second highest production subgroup (30.1 to 40.0 kg/day). This discrepancy between the two studies could be related to the very low number of cows in the 40.1+ kg/day subgroup of Group C (\(n = 4\); data not shown).

The design of this study precludes making inferential statements about the relation between milk drop and milk production level or parity number.

\section*{CONCLUSION}

Milk drop may occur after administering commercial bovine vaccines. The magnitude of the milk drop may differ among products, even if they contain the same antigen combination. This type of information is of importance for dairy producers who have to meet production levels in countries with milk quotas or for producers who have to plan their weekly revenues in countries without milk quotas.

\section*{ACKNOWLEDGMENTS}

We thank Dr. Pascal Michel, DVM, PhD, Department of Microbiology and Pathology, Faculty of Veterinary Medicine, University of Montreal, for his input and support for the statistical analysis.

\section*{REFERENCES}


