J. Dairy Sci. 101:1–10
https://doi.org/10.3168/jds.2017-14271


# Field trial to evaluate the effect of an intranasal respiratory vaccine protocol on calf health, ultrasonographic lung consolidation, and growth in Holstein dairy calves

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## ABSTRACT

The objective of this field trial was to evaluate the effect of a vaccine protocol using a commercially available trivalent vaccine designed for intranasal use. Experimental challenge studies have demonstrated varying efficacies of vaccines administered via the intranasal route. A total of 468 calves from 3 herds were enrolled and randomized into 3 treatment groups (positive control, PC, n = 211; intranasal vaccine, IN, n = 215; negative control, NC, n = 42) and followed for 8 to 12 wk. The PC consisted of one dose of commercially available multivalent injectable vaccine against bovine respiratory syncytial virus, infectious bovine rhinotracheitis, parainfluenza 3, and bovine viral diarrhea administered subcutaneously at 6 wk of age. The IN was administered at enrollment and 6 wk of age, and contained antigen against bovine respiratory syncytial virus, infectious bovine rhinotracheitis, and parainfluenza 3. The NC was sterile saline administered intranasally and subcutaneously at enrollment and 6 wk of age. Clinical illness was assessed using systematic respiratory scoring, and thoracic ultrasonography was used to identify the lung consolidation associated with pneumonia. Rib fractures were identified in 6% of calves, and an association was observed between rib fractures and calving ease. Overall, 54% of the calves had at least one episode of an abnormal respiratory score (ILL). Vaccination protocol did not affect the occurrence of ILL. Similarly, 54% of the calves had at least one episode of lung consolidation ≥3 cm (CON). Vaccine protocol affected the odds of CON. The odds of CON in PC were 1.63 (95% confidence interval: 1.04–2.56) times the odds of CON in IN, and 0.38 (95% confidence interval: 0.16–0.93) times the odds of CON in NC. The odds of CON in IN were 0.23 (95% confidence interval: 0.09–0.59) times the odds of CON in NC. The outcomes ILL and CON were associated; however, the measure of agreement was only fair (kappa = 0.38). Multivariable linear regression revealed an interaction between vaccine protocol and herd on average daily gain (ADG); therefore, these data were stratified. In herd 1, IN (0.53 ± 0.03 kg/d) decreased ADG compared with PC (0.63 ± 0.03 kg/d). In herd 2, IN increased ADG (0.41 ± 0.03 kg/d) compared with PC (0.38 ± 0.03 kg/d). In contrast, none of the protocols affected ADG at herd 3. In conclusion, this commercially available trivalent IN vaccine protocol did not alter the incidence of ILL, reduced the risk of lung lesions associated with pneumonia, and improved the ADG of the calves in one of the commercial study herds.

**Key words:** bovine respiratory disease, intranasal vaccine, thoracic ultrasound

## INTRODUCTION

Calves are born agammaglobulinemic and must ingest maternal colostrum for immune support. Although maternal transfer of antibody to the newborn calf provides many great benefits (Faber et al., 2005), high levels of maternal antibodies are associated with delayed antibody production by the neonate, as well as selective inhibition of lymphocyte responses (Tizard, 2013). The potential for maternal blockade has caused concern regarding the practice of early life vaccination to prevent bovine respiratory disease (**BRD**), as maternal antibodies can be present for up to 6 mo of age (Menanteau-Horta et al., 1985). Vaccination to reduce the incidence of BRD would be beneficial, as BRD is a

Received December 11, 2017.
Accepted May 1, 2018.
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leading cause of morbidity and mortality in preweaned dairy calves (Windeyer et al., 2014).

It has been established that 3- to 8-d-old Holstein calves are capable of mounting a mucosal immune response, even when maternal antibodies are present (Hill et al., 2012). Over the last 10 yr, reports have been inconsistent regarding the potential for intranasal vaccination to protect young dairy calves, regardless of maternal antibody status, from infection with bovine respiratory syncytial virus (**BRSV**) and parainfluenza 3 (**$PI_3$**). In one study, calves between 3 and 8 d of age were vaccinated intranasally with a product intended for subcutaneous administration, and challenged with BRSV 21 d later, or at 4.5 mo of age (Ellis et al., 2010). After the delayed challenge at 4.5 mo, seropositive calves had wider temperature fluctuations compared with seronegative calves; however, no differences were detected in other health parameters. Seronegative calves that were vaccinated intranasally with a low dose of BRSV antigen, and challenged with BRSV 21 d later, had less extensive lung lesions at postmortem examination, even though no differences in clinical scores or mortality were noted (Ellis et al., 2010). Intranasal vaccination in 3- to 8-d-old calves resulted in improved partial pressure of oxygen, fewer lung lesions, and lower mortality rate than in unvaccinated calves, when they were challenged with BRSV at 9 wk, but not 14 wk, indicating that the duration of immunity is short (Ellis et al., 2013). Additionally, 2 doses of monovalent injectable BRSV product used intranasally resulted in complete protection from clinical disease, one dose resulted in minimal clinical signs, whereas unvaccinated calves experienced severe clinical signs (Ellis et al., 2007).

The previously mentioned challenge studies often found that IN calves had less extensive lesions associated with lung consolidation than control calves despite the lack of observable clinical changes. In the beef industry, several reports suggest that evaluation of lung lesions at harvest may be a more accurate means of documenting BRD than clinical observations (Wittum et al., 1996; Thompson et al., 2006; White and Renter, 2009). Unfortunately, documenting lung lesions directly requires euthanasia, which often limits the size of study populations. As an alternative, thoracic ultrasonography (**TUS**) can be performed quickly and provides an accurate ante-mortem assessment of lung health (Rabeling et al., 1998; Ollivett et al., 2013, 2015). When lung consolidation identified by TUS was confirmed by the gold standard postmortem examination, TUS manifested a sensitivity of 85 and 94% in chronic clinical (Rabeling et al., 1998) and acute subclinical (Ollivett et al., 2015) cases, respectively; and specificity was 98 and 100%, in chronic clinical and acute subclinical cases, respectively. Additionally, Buczinski et al. (2015) using Bayesian latent class analysis determined the sensitivity and specificity to be 79.4 and 93.9%, respectively.

The primary objective of this randomized controlled field trial was to evaluate the effect of an intranasal vaccine protocol on the health of young Holstein dairy calves. The secondary objectives were to evaluate the effect of this vaccine on ultrasonographic lung consolidation and growth.

## MATERIALS AND METHODS

### *Animals and Facilities*

This study was carried out on 3 dairies in southwestern Ontario, Canada, between January and December 2012. Two of these herds were the Elora (herd 1) and Ponsonby (herd 3) Dairy Research Centres associated with the University of Guelph. The third dairy was a privately owned commercial herd (herd 2). Each herd was visited twice a week (all herds) or 3 times a week during periods of high enrollment (herd 2 only) to enroll calves twice a week. Male and female Holstein calves were enrolled between 3 to 6 d of age into 3 groups according to vaccine protocol (positive control, **PC**; intranasal vaccine, **IN**; and negative control, **NC**) and followed for 8 to 12 wk. A birth record was filled out by the dairy producer after the birth of each calf. The PC (Bovi-Shield Gold 5, Zoetis, New York, NY) consisted of one dose of commercially available multivalent injectable vaccine against BRSV, infectious bovine rhinotracheitis, $PI_3$, and bovine viral diarrhea administered by subcutaneous injection at 6 wk of age. The IN (Inforce 3, Zoetis) was administered twice (first dose: 3 to 6 d of age; second dose: 6 wk of age) and contained BRSV, infectious bovine rhinotracheitis, and $PI_3$ antigens. The NC, sterile saline, was administered both intranasally and subcutaneously twice (first dose: 3 to 6 d of age; second dose: 6 wk of age). All doses of IN were administered via a single-use plastic nasal cannula (Zoetis) into one nostril. All injections were administered subcutaneously in the neck. Treatments were administered by members of the research team not involved in respiratory scoring or TUS. Different randomization methods were used to assign calves to the 3 treatment groups at each herd because of differences in barn design. Treatment groups were housed in separate areas to prevent contamination of PC and NC calves from the potential nasal virus shedding by IN calves following vaccination. Weight, respiratory score (**RS**), and TUS observations were performed by the principal investigator (TLO) who was blinded to treatment throughout all data collection. This study was conducted with the approval of the University of Guelph's Animal Care Committee (AUP #11R110).