Evaluation of a novel vaccine based on siderophore receptor proteins and porins (SRP Technology) for controlling *Klebsiella* mastitis in a dairy herd

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Introduction

Siderophore receptor proteins (SRP) are iron-regulated proteins shown to be highly conserved between members of the family Enterobacteriaceae, making them novel vaccine targets. Siderophore receptor proteins of *Salmonella* Newport have been successfully exploited to control *Salmonella* Newport in the dairy industry for over a decade. This same technology has now been developed to combat *Klebsiella* mastitis. The objective of this study was to evaluate efficacy of a *Klebsiella* vaccine based on SRP technology to reduce *Klebsiella* mastitis in a dairy herd with ongoing disease that was not controlled with J5 vaccination. The study was conducted at the Iowa State University (ISU) Dairy in Ames, Iowa.

Materials and Methods

The ISU Dairy consists of approximately 400 milking cows plus heifers and dry cows, and was chosen for this study due to an ongoing *Klebsiella* mastitis problem in the dairy. In all, 569 cows and heifers were enrolled in the study. Cows were randomized to receive the *Klebsiella* pneumoniae bacterial extract (KPBE) vaccine or a placebo vaccine containing adjuvant only. The study was double-blinded and animals were blocked so groups were approximately equally distributed based on their lactation (1st, 2nd, and 3+), somatic cell count (SCC), and days-in-milk (DIM). A whole-herd enrollment was conducted at study onset by vaccinating cows subcutaneously with their assigned treatment. Cows within 5 weeks of parturition were not vaccinated at initial enrollment, but instead vaccinated 2 weeks after parturition. Vaccinations were repeated in 3 weeks. Each week throughout the study, lactating cows and new heifers achieving ~217 days carrying calf (DCC) were vaccinated and followed with a repeat dose 3 weeks later. For each cow, the eligible observation period began 2 weeks after the second vaccination and were continued for the first 90 days-in-milk. Cows were monitored for clinical mastitis, and if confirmed positive, a milk sample was taken and submitted to the ISU Veterinary Diagnostic Laboratory to determine the causative agent for clinical mastitis. Samples were plated onto culture agar and bacterial identification was confirmed by MALDI. Cows were treated according to standard protocols for the dairy. Data on milk production was recorded daily, and SCC were determined by DHIA at approximately 5-week intervals. The study was approximately 10 months in duration.

Results

The prevalence and incidence of *Klebsiella* mastitis was significantly reduced in KPBE-vaccinated cows compared to placebo-vaccinated controls. For prevalence, there were 18 cows clinically diagnosed with *Klebsiella* mastitis during their first 90 days-in-milk. Fourteen of these cows were in the placebo group, and 4 cows were in the KPBE-vaccinated group ($P = 0.02$). These results showed a Prevented Fraction of 0.71 (95% CI=0.15 to 0.90). There were 20 incidents of *Klebsiella* mastitis from cows 1 to 90 days-in-milk. Sixteen of these incidents were from cows in the placebo group, and 4 were from cows in the KPBE-vaccinated group ($P = 0.006$). These results showed a Prevented Fraction of 0.76 (95% CI=0.28 to 0.92).

Milk production increased in KPBE-vaccinated cows by 2.0 lb (0.91 kg)/cow/day compared to placebo cows ($P < 0.001$). The most significant differences in milk production occurred during the summer months. Overall, KPBE vaccinated cows had a 42% reduction in SCC compared to placebo controls ($P < 0.001$).

Significance

Vaccination with a *Klebsiella pneumoniae* vaccine based on SRP Technology provided statistically significant protection from *Klebsiella* mastitis. The significant increase in milk production and decrease in SCC among KPBE-vaccinated cows compared to controls requires further evaluation, since it cannot be explained solely by the control of clinical mastitis.