EVALUATION OF ANTIBODY TITRES IN RESPONSE TO VACCINATION WITH KOLIBIN NEO GIVEN INTRAMUSCULARLY OR SUBCUTANEOUSLY

Background

Kolibin Neo is a vaccine registered for use in pregnant dairy cattle to provide passive immunity by colostral transfer to newborn calves. Kolibin Neo contains antigens for bovine rotavirus (BRV), bovine coronavirus (BCV) and *Escherichia coli.* The vaccine has been marketed in New Zealand since early 2016.

Study objective

To evaluate and compare serological response to subcutaneous and intramuscular administation of the Kolibin Neo vaccine in naive cows.

Study design

The study was undertaken in a single herd, in the Waikato region of New Zealand. Study animals were pregnant, rising 2-year old dairy heifers, that had not been previously vaccinated with any vaccine containing bovine rotavirus, bovine coronavirus or *E. coli* antigens.

Sixty heifers were randomly selected and had blood samples collected for pre-enrolment testing, measuring serum antibodies of rotavirus, coronavirus and *E. coli.* Two animals returned a positive result for *E. coli* antibodies, and all animals returned unexpectedly high results for bovine rotavirus and coronavirus antibodies. The later result was attributed to these heifers having experienced an outbreak of viral scours as young calves (18 months prior). The youngest calves were clinically affected with rotavirus and coronavirus isolated from a small sample of faecal samples analysed at the time of the outbreak. The 10 heifers that returned the highest results for bovine coronavirus and rotavirus combined were excluded from the study group, and the remaining 50 animals were enrolled.

Two groups of 10 heifers were then randomly assigned to the treatment groups for this study, as shown in Table 1.

All Kolibin Neo treatments were administered by a Veterinarian. Two vaccine doses each of 2mL were administered 3 weeks apart with the only difference between groups being the route of administration. The vaccine was administered within 2 - 12 weeks of planned start of calving. All vaccine doses were administered in the neck.

Blood samples were collected from the coccygeal vein prior to each administration of vaccine (on days 0 and 21) as well as at 14 (day 35), 35 (day 56) and 56 (day 77) days after the booster vaccination. Vaccination sites were observed at the second vaccination, and the vaccination site observed again at blood sampling 14 days after booster vaccination, for any swelling or abnormality.

Group Number	Treatment	Number
1	Kolibin Neo, 2 doses given 3 weeks apart, administered by intramuscular injection	10 animals
2	Kolibin Neo, 2 doses given 3 weeks apart, administered by subcutaneous injection	10 animals

Table 1: Study groups for comparison of vaccine administration

Blood samples were processed by a laboratory that was blind to treatment group. Bovine rotavirus antibody titre was measured using virus neutralisation method. Bovine coronavirus and *E. coli* antibody titres were measured using haemagglutination inhibition methods. Titre results were converted to a linear scale of log base$_2$ for comparison and analysis.

For each time point and each of the three antigens within the vaccine, the log$_2$ of the last dilution that gave a positive result for the presence of antibody was analysed by covariance in Genstat with the corresponding Day 0 log$_2$ value as covariate for each animal.

Results

There were no abnormal findings observed in any of the enrolled cows, or any lesions at the injection sites in any animals during the study period.

The pre-vaccination mean log$_2$ values were not significantly different for the 2 treatment groups, for any of the antigens.

Means of log$_2$ values for each day are shown in Figures 1, 2 and 3 for bovine rotavirus (BRV), bovine coronavirus (BCV) and *E. coli* respectively. The standard error of difference (sed) for comparing the vaccine given intramuscularly with the vaccine given subcutaneously is also shown.

The only significant difference observed for any time point for any antigen was a higher mean antibody titre for bovine

MEAN ANTIBODY TITRE FOR BOVINE ROTAVIRUS OVER TIME IN ANIMALS VACCINATED BY IM OR SQ ADMINISTRATION

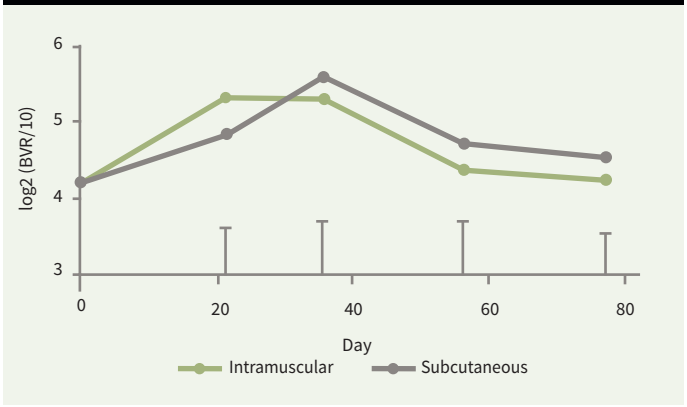

Figure 1: Antibody titre (mean log_2) for BRV

MEAN ANTIBODY TITRE FOR BOVINE CORONAVIRUS OVER TIME IN ANIMALS VACCINATED BY IM OR SQ ADMINISTRATION

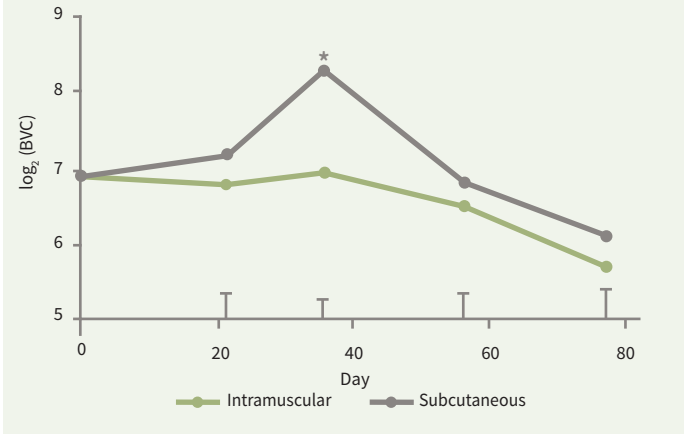

*Figure 2: Antibody titre (mean log_2) for BCV. *represents significant difference p<0.001*

MEAN ANTIBODY TITRE FOR *E. coli* OVER TIME IN ANIMALS VACCINATED BY IM OR SQ ADMINISTRATION

Figure 3: Antibody titre (mean log_2) for E. coli

coronavirus in the subcutaneous group compared with the intramuscular group at day 35 (8.21 vs 6.89 respectively, p <0.001). This result was consistent across all of the animals in the group, and not caused by an outlier result. All other antibody titres at all time points for all 3 antigens were not statistically different between the treatment groups.

Discussion

There was only a single time point (14 days after the booster vaccination) for a single antigen (bovine coronavirus) where there was a statistically significant difference between treatment groups, in favour of subcutaneous administration. For the rest of the timepoints, for all antigens there were no statistically significant differences seen in antibody titres when comparing Kolibin Neo administered via intramuscular or subcutaneous injection.

There were no local or systemic reactions observed in any animal when administering the vaccine intramuscularly or subcutaneously, demonstrating the vaccine was safe to administer via either route.

Administering the vaccine subcutaneously was as effective as administering intramuscularly in this study, measured by serological response to bovine rotavirus, coronavirus and *E. coli.*

Conclusion

Kolibin Neo is as safe and effective when administered by the subcutaneous route, compared to the intramuscular route.

This study supports the registration and use of Kolibin Neo administered either subcutaneously or intramuscularly.