

Efficacy of a vaccine against *Neospora caninum* related abortions in New Zealand dairy herds

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Summary

A clinical trial was carried out to evaluate the efficacy of a new vaccine against abortion caused by *Neospora caninum* (NEO) in cattle. Five dairy herds were selected including 2,240 cows at 25-45 days of pregnancy. Cows were randomly allocated to vaccination with Neoguard[®] or placebo, both followed by a 4-week booster. Vaccination was associated with a minimal site reaction and marked increase of antibodies. Matched analysis resulted in a significant vaccine effect in two of five farms ($p < 0.01$; efficacy 30% and 54%). It was concluded that efficacy depended on specific farm conditions.

Introduction

The protozoan parasite *Neospora caninum* is one of the most important infectious agents causing abortion in cattle worldwide including New Zealand (1,2). A vaccine is available but has not yet been proved to effectively prevent abortion of infected pregnant cows. The current trial has been carried out to test the efficacy of Neoguard[®], Intervet Ltd. in New Zealand dairy herds infected with *Neospora caninum*.

Material and Methods

Five seasonally calving, commercial New Zealand dairy farms with a documented history of high abortion rates (>8%) and confirmed presence of *Neospora caninum* infection were enrolled in the trial. All pregnant animals within each herd were selected by systematic random allocation within herd and injected twice 5ml subcutaneously at intervals of 3-4 weeks with *Neospora caninum* vaccine or 0.9% NaCl. The booster injection was applied <90d into gestation. The immune-fluorescent antibody (IFAT) response of a random subset ($n = 414$) was measured before and after vaccination. Reactions at the injection site were monitored in a sample of both vaccinated and control animals 72 hours after vaccination ($n = 354$). The response of interest was the gross abortion rate. The sample size (n) aimed to achieve a power of 90% to test the hypothesis that vaccination reduced the rate of abortion from around 8% to 4% with 95% confidence. The sample was doubled ($2n$) due to expected differences in vaccine efficacy between farms. The data were analysed by logistic regression with abortion (yes/no) as binomial outcome. Matching (i.e. blocking) within herd was considered by stratification on herd using a GEE marginal model with a uniform correlation pattern within herd (proc genmod in SAS). The model included interaction terms for vaccination by herd, vaccination by age (cow/heifer) and vaccination by pre-vaccination NEO-sero-status (positive/negative). The analysis of a vaccination effect was based on the difference between least square means of

cumulative abortion incidences of the interaction strata. Efficacy was calculated as $1 - RR$ where RR was the ratio of abortion incidence in vaccinated divided by that in placebo cows. Efficacy was interpreted as the proportion of abortions that were prevented by the vaccine.

Results

In total, 2240 cows were enrolled and allocated randomly to vaccinated ($n = 1125$) and placebo ($n = 1115$). In both trial groups, 11% of all animals were sero-positive to *Neospora caninum* antibodies (IFAT ≥ 200). The distribution of farm, age and pre-vaccination IFAT titre was similar in vaccinated and placebo cows, hence random allocation was successful. A mild reaction at the injection site was observed in 14% after the first and in 13% after the second vaccination in vaccinated animals; 4 cows (3.4%) had a strong local reaction after the booster. Only 1 of 168 placebo cows showed a mild reaction. The sero-prevalence in vaccinated cows increased from 11.6% to 88.0% and in placebo cows from 10.5% to 22.7% ($p < 0.001$).

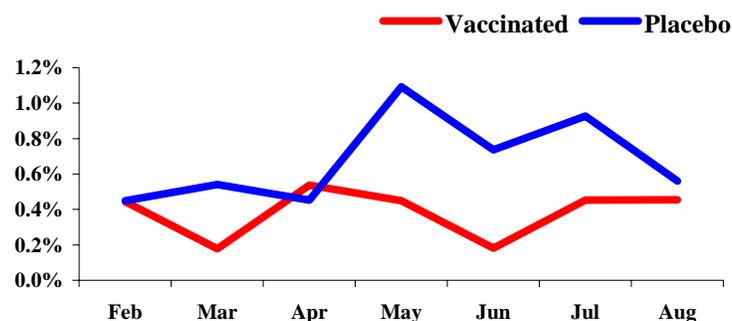


Figure 1: Monthly incidences of abortion in vaccinated and placebo animals

Among the 1115 non-vaccinated animals, 63 (5.65%) aborted, and 48 aborted among 1125 vaccinated animals (4.27%); the crude rate of 5.7% in the placebo group was considerably lower than the expected rate of approximately 8-10%. The overall abortion rate of 4.3% in vaccinated versus 5.7% in non-vaccinated animals resulted in a vaccine efficacy of 24.6%. The vaccine effect was particularly evident and significant in mid-gestation (Figure 1). In addition, 11 placebo and 17 vaccinates were found non-pregnant at the expected calving date in September. These cows presumably lost the foetus during the first trimester of gestation when the vaccine may not yet have been fully protective.

Figure 2 shows that only two herds (farm 6 and farm 8) had abortion rates as high as expected. The vaccine had a significant efficacy of 54% in one of these herds (Farm 6; $p < 0.001$); this herd also had the highest pre-vaccination antibody prevalence (22% IFAT, Table 2). The other herd showed no vaccine effect and had 14% pre-vaccination antibody prevalence. Farm 4 resulted in a non-significant vaccine efficacy of 27% (pre-vacc. IFAT 7.4%) and farm 7 a significant efficacy of 30% ($p = 0.0097$; pre-vacc. IFAT 5.2%). The latter two farms had low overall rates of abortion. A vaccine efficacy could neither be found on farm 8 despite a high pre-vaccination prevalence and abortion frequency, nor on farm 3.

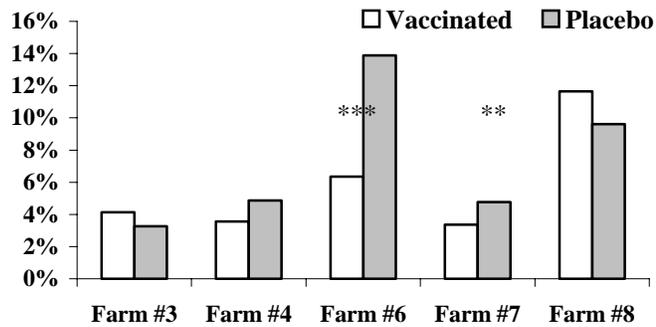


Figure 2: Least square means of abortion incidences of vaccinated and placebo animals in the five trial herds

Discussion

The dynamics of transmission of *Neospora caninum* between cows and the consequence of infection are still poorly understood. While horizontal (postnatal) transmission due to infected and shedding dogs appears to occur in many infected dairy herds with consistently high abortion rates (3), vertical (transplacental) transmission is apparently much more frequent than postnatal transmission (4). Both routes may be present and this was presumably the case in the trial herds. Vertical transmission was indicated by a history of chronic infection in all herds. The increase in prevalence of serologically positive cows in the placebo group suggested that horizontal transmission or recrudescence in early lactation had occurred as well.

References

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