Cross-neutralization between Bovine Viral Diarrhea Virus (BVDV) types 1 and 2 after vaccination with a BVDv-1a modified-live-vaccine

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Objectives

BVDV-1 and BVDV-2 are responsible for major reproductive problems in cattle such as abortions, pregnancy losses and, most importantly, the birth of Persistent Infected (PI) animals that are responsible for maintaining the disease in the herd. This results in large economic losses.

Since there are many genotypes within BVDV-1 and BVDV-2 species, it is important to know whether the use of a monovalent vaccine could protect cattle against other genotypes. This study provides evidence that serum from animals immunized with Mucosiffa®, a modified-live-vaccine containing a BVDV-1a strain can neutralize other BVD-1 and BVDV-2 strains in-vitro.

Material and methods

A study to obtain the "12-month fetal protection" indication for Mucosiffa® was conducted. Fetal protection was demonstrated in an experimental challenge with the BVD-1f-Hanover strain inoculated 363 days after vaccination (Achard *et al.,* 2018). Seronegative heifers were vaccinated (D0) and blood samples were taken at D28, D203 and D363 before challenge.

For the present study, these sera were used to test their ability to neutralize several strains of BVDV: 1a-NADL, 1f-Hanover, 1e, 1b and two BVD-2a strains. All these strains are non-cytopathic except the BVDV-1a-NADL.

Seroneutralization (SN) assays were performed for the 6 BVDV strains and each selected day in a 96-well cell microplate (4 duplicates per sample) with a constant amount of virus (200 TCID50 per well) as already described (Hamers *et al.,* 2002; Meyer *et al.*, 2021). The reading was taken after staining and the titers were calculated as the inverse of the serum dilution protecting 50% of the cell culture wells. They were expressed as Log2ED50/mL using the Spearman-Kärber method.

A two-way ANOVA with repeated measures (three-factor split-plot ANOVA) was used to analyze SN titers. When the effects of the “day” and “treatment” factors were significant among interactions, a Bonferroni test between contrasts was used to compare the treatments on each day post challenge.

Results

We identified three different patterns of virus neutralizing titers (VNT), depending on the strains.

- BVDV-1a and BVDV-1b: rapid increase until D28 followed by a lower increase until D203 and then stability in time (until D363)
- BVDV-1e and BVDV-1f-Hanover: rapid increase until D28, stability until D203 and then slightly decrease until D363
- BVDV-2a: increase until D203 and then stability until D363. At D28, VNT were statistically lower than for the BVDV-1 strains.

Interestingly, statistical analysis showed no significant difference ($p>0.05$) in VNT between BVDV-1f-Hanover, BVDV-1e and the two BVD-2 strains at D203 and D363. As the vaccine has been shown to be effective to prevent a fetal contamination with the BVDV-1f-Hanover strain, 363 days after vaccination, this suggests that Mucosiffa® vaccination provides humoral cross immunity, which may also protect against fetal infection by BVDV genotype 2 (Grange *et al.,* 2023).

Conclusions

Our study showed that sera from cattle vaccinated with Mucosiffa® were able to neutralize strains of BVDV-2a. Interestingly, neutralizing antibody titers against these BVDV-2a strains and the BVDV-1f-Hanover strain were similar from D203. Although confirmation by experimental challenge with a BVDV-2a strain could be useful, we can hypothesize that the vaccine is clinically effective against infection with a BVDV-2a strain.

References

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