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Compatibility of a live infectious bovine rhinotraheitis (IBR) marker vaccine and an inactivated bovine viral diarrhoea virus (BVDV) vaccine

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Abstract

The target animals and vaccination regimes for vaccines against the bovine rhinotracheitis (IBR) and the bovine viral diarrhoea virus (BVDV) are very similar. Therefore, we have compared different schedules for the combined use of a live IBR marker vaccine and an inactivated BVD vaccine.

The neutralizing antibody response against BVDV did not reveal any differences between the group vaccinated only with the BVD vaccine and the groups that were vaccinated simultaneously (together in the same syringe) or concurrently (two separate injections) with the IBR marker vaccine at the first or second dose and the third dose of the BVD vaccine. Likewise, the bovine herpesvirus 1 (BHV-1) neutralizing antibody titres did not exhibit any negative effect by the simultaneous or concurrent use of the two products as compared to the single IBR marker vaccination.

These results indicate that the two vaccines can be applied at the same day for the first or second dose of the BVD basic vaccination and then at the booster vaccinations (third dose onwards).

Keywords: Pestivirus; Herpesvirus; Cattle; Marker vaccine; Compatibility

1. Introduction

The bovine herpesvirus type 1 (BHV-1) and the bovine viral diarrhoea virus (BVDV) are both target of eradication programs in a number of countries of the European Union [1,2]. Vaccination is therefore widely applied to control these viruses. The target animals and vaccination regimes for BHV-1 and BVD vaccines are very similar. In general, multivalent cattle vaccines are the preferred choice of farmers and veterinarian because they simplify animal handling and therefore, also reduce costs of vaccination and animal stress. However, in compliance with the BHV-1 eradication programs, it is essential that vaccines allow differentiation between vaccinated and infected animals (so-called IBR marker vaccines) [3]. Till today, no IBR marker/BVD combination vaccines are available. Moreover, the multivalent BVD vaccines currently used in Europe have not proven fetal protection although it is a key requirement for vaccines used to combat BVDV.

In order to respond to the market requirements to reduce animal handling to a minimum, we have examined whether two commercially available vaccines, one live IBR marker vaccine and one inactivated BVD vaccine with a proven foetal protection claim can be applied on the same day. The possibility to combine the immunisation protocols for the two vaccines may prove very beneficial to the farmers and veterinarians due to the dual advantages of reducing labour and costs.

In a previous study, the safety of the simultaneous (inactivated vaccine serves as solvent for the live vaccine) and the concurrent (vaccines injected at two different sites) use of the two vaccines had been tested under field conditions. No local

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and/or general reactions were noticed in that study (G. Valla, unpublished data). In the study reported here, the immune responses against BHV-1 and BVDV for different combined vaccination schedules have been compared.

2. Materials and methods

2.1. Experimental design

The study was carried out on three commercial dairy farms, as randomised, partially blinded and controlled field study. In total 57 heifers at the age of 6–8 months and seronegative for BHV-1 and BVDV were included in the study. The animals were assigned at random to one of the vaccination or control groups (see Table 1).

2.2. Vaccinations

Commercial batches of the live IBR marker vaccine Bovilis® IBR marker live (Intervet International, The Netherlands) and the inactivated BVD vaccine Bovilis® BVD (Intervet International) were used. The animals were vaccinated three times, with an interval of 4 weeks between the first and second vaccination and an interval of 6 months between the second and third vaccination (see Table 1).

For simultaneous application of the two vaccines, the inactivated BVD vaccine was used to reconstitute the freeze-dried live vaccine. Two millilitre of this combined vaccine contained one dose IBR marker vaccine and one dose BVD vaccine. The single or combined vaccines were administered as one injection of 2 ml at one site of the neck. For concurrent application, the two vaccines were applied at the same time but as two injections of 2 ml at separate injection sites.

2.3. Antibody testing

Blood samples were taken just prior to each vaccination and 3 weeks after the second and third vaccination (trial days 0, 28, 49, 208 and 229).

2.3.1. BHV-1 gE specific antibodies

Antibodies specific for BHV-1 gE were determined to monitor for interfering infection with BHV-1 field virus. Two commercially available ELISA tests were conducted according to the manufacturer's instructions:

ELISA_A: Chekit BHV1-gE ELISA (IDEXX Laboratories, The Netherlands).
ELISA_B: HerdCheck Anti-IBR gE test (IDEXX Laboratories).

Blood samples taken at trial day 28 were tested in ELISA_A and samples collected on trial date 229 were tested with ELISA_B.

2.3.2. BVDV NS 3 (p80) specific antibodies

Antibodies specific for the non-structural NS 3 (p80) protein of BVDV were determined to monitor for intercurrent infection with BVDV field virus. All samples were tested in two commercially available ELISAs:

ELISA_C: Pourquier® BVD/MD-BD P80 Ab Blocking ELISA Kit (Pourquier, Montpellier, France).
ELISA_D: INGEZIM BVD COMPAC (INGENASA, Madrid, Spain) ELISA.

The instructions of the manufacturer were followed.

2.3.3. BHV-1 and BVDV neutralising antibodies

The titres of BHV-1 and BVDV neutralising antibodies were determined according to the end-point dilution method. Two-fold dilution series of the heat-inactivated sera were prepared. Each serum was tested in quadruplicate. The serum dilutions were mixed with an equal volume of a viral inoculum containing 100 tissue culture infection doses 50 ($TCID_{50}$)/25 μl of the cytopathic BHV-1 Colorado strain (BHV-1 test) or the cytopathic BVDV 1 strain Oregon C24V (BVDV test). After 1 h of incubation, the serum-virus mixtures were transferred into 96-well plates and a suspension of Georgia bovine kidney (GBK) cells (BHV-1 test) or bovine trachea (EBTr) cells (BVDV test) was added. The plates were incubated for 5 (BHV-1 test) or 7 (BVDV test) days and then scored for cytopathic effect. The titres were calculated as the reciprocal of the highest serum dilution corresponding to a 50% endpoint of neutralisation according to the formula devised by Spearman–Kärber [4].

Table 1
Grouping and vaccination schedule

Group	Number of animals	Day 0	Day 28	Day 208
IBR	8	IBR	IBR	IBR
BVD	5	BVD	BVD	BVD
IBR in BVD 1 2 3	9	IBR in BVD[a]	IBR in BVD	IBR in BVD
IBR in BVD 1 3	8	IBR in BVD	BVD	IBR in BVD
IBR in BVD 2 3	9	BVD	IBR in BVD	IBR in BVD
IBR in BVD 3	8	BVD	BVD	IBR in BVD
IBR and BVD 1 2 3	10	IBR + BVD[b]	IBR + BVD	IBR + BVD

[a] IBR in BVD—simultaneous application: inactivated BVD vaccine used as solvent for live IBR marker.
[b] IBR + BVD—concurrent application: inactivated BVD vaccine and live IBR marker vaccine applied at the same time but at separate injection sites.