Quantification Of Experimental Transmission Of Bovine Herpes-Virus 1 In Cattle Vaccinated With Marker Vaccines

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Abstract

An attenuated and an inactivated bovine herpesvirus 1 (BHV1) gE-negative vaccine and an experimental BHV1 gD-subunit vaccine were evaluated for their ability to reduce BHV1 transmission. For that purpose, experiments to quantify transmission among vaccinated and unvaccinated cattle were carried out. Three separate experiments, including 90 cattle, were performed. Each group was housed separately. Two groups were vaccinated, each with a different marker vaccine, and the third served as an unvaccinated control group. At 4 weeks after the second vaccination, from each group five animals were taken out, and the remaining five were challenged intranasally with 10^5 $TCID_{50}$ of the Dutch Lam strain of BHV1. After 24 hours, the animals were placed back into their original stables. The transmission of the virus to and among the five non-challenged, in-contact animals was then monitored. An animal was defined as being infected when it shed virus from its nasal fluids or developed antibodies to glycoprotein gE of BHV1. Based on the findings, the R, i.e. the average number of secondary cases per infectious individual, was calculated. Only the attenuated gE-negative vaccine was able to significantly reduce the transmission of BHV1.

Introduction

The efficacy of a vaccine is primarily tested in a vaccination-challenge experiment in the laboratory under standardized conditions. Basically, such an experiment is composed of animals that are randomly assigned to two groups: one vaccinated group and one unvaccinated control group. The difference in clinical signs and in virus excretion measured in both groups is then considered a measure for efficacy of the vaccine. Apart from the individual immunity evaluated in such a vaccination-challenge experiment, the induction of herd immunity is also an important criterion for vaccine. The use of marker vaccines and their companion diagnostic tests enables us to identify infected animals among vaccinated populations, and consequently to measure transmission of virus in such populations. De Jong and Kimman (1994) have evaluated the induction of herd immunity by marker vaccines against suid herpesvirus 1 infections in small populations under laboratory conditions.

Recently, marker vaccines against bovine herpesvirus 1 (BHV1) have been developed and assessed for efficacy (Kaashoek *et al.*, 1994, 1995, Van Drunen Little-van den Hurk *et al.*, 1994). This study deals with the effect of vaccination with these BHVJV1 gE negative marker vaccines on transmission of field virus in small populations of cattle in the laboratory.

Materials and Methods

Experimental design

Three separate transmission experiments were performed along the lines designed by De Jong and Kimman (1994). In each trial, 30 BHV1-seronegative yearling cows were randomly allocated to three groups of 10; each group was housed separately. The cattle were moving freely in their pen. Two groups were vaccinated twice, according to the directions of the manufacturer, the third group served as an untreated control. Four weeks after the second vaccination, from each group five randomly chosen animals were placed in another isolation pen. The five remaining cattle in each group were challenged intranasally with $10^{5.3}$ $TCID_{50}$ of the Dutch Lam strain. After 24 hours, the non-challenged cattle were returned to their original isolation pen.

In total, three vaccines were tested twice: in the first trial the inactivated (Kaashoek *et al*, 1995) (Bayovac^R IBR-Marker inactivatum) and the attenuated gE-negative vaccine (Kaashoek *et al*, 1994) (Bayovac^R IBR-Marker vivum), in the second trial the inactivated gE-negative vaccine and an experimental gD-subunit vaccine (Pfizer Animal Health, Lincoln, Nebraska, USA), and in the third trial the attenuated gE-negative and the experimental gD-subunit vaccine.

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Virus isolation and determining antibodies to gE of BHVI

Nasal swabs were collected one day before challenge and for 16 days after challenge. Virus isolations were performed as previously described (Kaashoek et al, 1994). Blood samples were collected weekly during the entire experiment. Sera were stored at —20 C until all tested the same time in gE-ELISA test (Van Oirschot *et al*, 1995).

Estimation of reproduction ratio®

Contact cattle were considered infected if they had virus in their nasal swabs or developed antibodies to gE. The reproduction ratio R, which is the average number of secondary cases per infectious individual, was calculated per vaccine group as a measure for virus transmission. The R was calculated and statistical analysis was essentially done as described previously De Jong and Kimman, 1994).

Results

In the control groups and in the groups vaccinated with the inactivated gE-negative vaccine or the gD-subunit vaccine all contact cattle became infected. In the groups vaccinated with the attenuated gE-negative vaccine four out of 10 animals became infected. The reproduction ratio R was lower than unity only in the group given the attenuated gE-negative vaccine (Table 1).

Table 1. Reproduction ratio in vaccinated and unvaccinated control groups.

Vaccine groups	R
Inactivated gE-negative	2.28
Attenuated gE-negative	0.92*
Experimental gD-Subunit	2.28
Control	2.28

•is significantly (p-0.012) different from that of the control group.

Discussion

The transmission of the wild-type strain Lam was significantly reduced in the groups of yearling cows vaccinated with the live vaccine as compared to that in the control groups. No difference in transmission was found between the groups vaccinated with the inactivated gE-negative vaccine or the gD-subunit vaccine on the one hand and the control groups on the other hand.

The results of these transmission experiments demonstrate that only the live BHVI gE-negative vaccine was able to induce a herd immunity resulting in a reduced transmission of wild-type virus under laboratory conditions. These findings suggest that the live BHVI marker vaccine is the best candidate to be involved in combined vaccination-eradication programmes for BHVI. Such programmes will start with a period of several years of intensive vaccination in herds with a high prevalence of BHVI, and may eventually lead to eradication of BHVI.

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