ARTICLE IN PRESS

The Veterinary Journal xxx (2009) xxx–xxx

Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

Short Communication

Different infection parameters between dairy cows and calves after an infection with foot-and-mouth disease virus

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A R T I C L E   I N F O

Article history:
Accepted 3 June 2009
Available online xxxx

Keywords:
Foot-and-mouth disease
Cattle
Transmission
Virus excretion

A B S T R A C T

Clinical observations of a foot-and-mouth disease (FMD) virus infection in dairy cows and calves were different. This raised the question whether they would also differ with respect to virus excretion and transmission. Data were available from transmission experiments carried out with groups of dairy cows and calves. Half of each group was inoculated with FMDV O/NED/2001; the other half contact-exposed to inoculated animals. Virus excretion, clinical signs and antibody response were measured and virus transmission was quantified. Infected calves showed mild clinical signs which did not affect general health or appetite, and not all contact calves became infected. Dairy cows, on the other hand, showed severe FMD lesions resulting in clinical mastitis, severe lameness and decreased feed intake. Also fever was observed for three consecutive days. All contact cows became infected and showed the same severity of clinical signs. The total and mean daily virus excretion differed significantly between cows and calves ($P < 0.05$). Possibly, virus replication and clinical manifestation are associated, but the underlying mechanism of these differences needs to be elucidated. We did not observe a significant difference in virus transmission between calves and cows.

Foot-and-mouth disease virus (FMDV) is known to induce severe clinical disease in cattle. However, during the FMD epidemic in 2001 in the Netherlands, hardly any signs were observed in infected calves. On the veal calf farm where FMDV was introduced from France, the farmer had not noticed any clinical signs in the calves, although later when goats on the same farm did show clinical signs, 4/74 calves were tested positive for antibodies. On the other hand, infected dairy cows showed clear and sever signs of FMD (Bouma et al., 2003). These field observations were supported by experimental studies (Bouma et al., 2004; Orsel et al., 2005, 2007). These findings may have implications for surveillance programmes, which are based on clinical detection. Animals with more severe clinical signs might contribute more to the spread of the infection as they may excrete more virus. On the other hand, they may spread less, as their infectious period might be shorter due to rapid detection and culling, or due to reduced contact frequency. As it is of utmost importance to limit between-herd virus transmission, we analysed the data by quantifying several clinical, virological and immunological parameters, and subsequent transmission of FMDV in groups of dairy cattle and calves.

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Data were obtained from two transmission experiments that had been published previously (Orsel et al., 2005, 2007). All experiments were approved by the Animal Care Committee of Central Veterinary Institute in Lelystad. Only non-vaccinated animals serologically negative at the start were included in the analysis. Animals were housed in groups of 2×10 multiparous dairy cows, or 4×4 calves of 8–10 weeks of age. In each trial, half of the cattle in each group was inoculated intra-nasally with FMDV O/NET/2001 field strain; the other half of each group of cattle was exposed to virus by direct contact with the inoculated group mates. Clinical signs were registered and blood and oro-pharyngeal fluid (OPF) samples were collected daily during the first 14 days post inoculation.

Several aspects of virus excretion were analysed: (1) the total amount of virus excreted quantified as area under the curve (AUC), that is the sum of the ^{10}log plaque forming units per millilitre OPF sample measured during the observational period of 14 days, (2) the mean daily virus excretion (MDVE) per animal, that is the average virus titer of ^{10}log plaque forming units per millilitre per day of virus that was detected in oro-pharyngeal fluid samples, and the duration of virus excretion in days.

To analyse the total amount of virus excreted, a linear mixed effect model was used with 'age-category' (calf or cow) and 'status' (inoculated or contact-exposed) as fixed variables and 'group'

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doi:10.1016/j.tvjl.2009.06.031

(experimental unit) as a random effect. This resulted in the model: AUC ∼ age-category + status + age-category ∗ status. Differences in MDVE were tested using a Mann Whitney *U* test (SPSS 12.0.1). To compare duration of virus excretion between the two age-groups survival analysis with a Cox proportional hazard model was performed (S-Plus 7.0). Finally, a stochastic S–I–R (susceptible–infectious–recovered) model was used, to quantify virus transmission (De Jong and Kimman, 1994). The contact-exposed animals were all categorised in the S-category, whereas inoculated cattle that either showed clinical signs and/or tested positive in one of the laboratory tests, were allocated to the I-category. After recovery from infection, the animals were classified as R. The total number of recovered animals at the end of the experiment is the final size. The final size of infection was used to estimate the reproduction ratio R by means of a maximum likelihood estimator (MLE) (Bouma et al., 1996; Kroese and de Jong, 2001). The epidemiological model is described in more detail by Orsel et al. (2005).

In the groups of calves, mild clinical signs, without disturbance to the health of the calves, were observed and not all contact-exposed calves became infected or shed virus or became positive for FMDV antibodies. Dairy cows, however, developed severe clinical signs (salivation, loss of appetite, lameness, mastitis) and all contact-exposed cows became FMDV infected.

Both 'age-category', 'status' as well as the interaction-term had a significant effect on the total amount of virus shed; cows had a significantly higher total virus excretion compared to calves, and being contact-exposed lowered the AUC significantly (age-category: $P = 0.03$, status: $P = 0.0005$, interaction: $P = 0.0002$).

Also the MDVE differed significantly between cows and calves of the same 'status' ($P = 0.049$ and $P = 0.004$) as illustrated in Fig. 1. However, no significant difference in MDVE was observed between inoculated and contact-infected animals in the same age group.

Both 'status' and the interaction between 'status' and 'age-category' contributed significantly to the duration of virus excretion in our model ($P = 0.002$, $P = 0.0006$, respectively). The fixed variable 'age-category' did not have a significant effect ($P = 0.11$). The number of days animals excreted virus is listed in Table 1. With the data available to us we were not able to show differences in the reproduction ratio between cows and calves: both estimates were above 1 ($R_{calves} = 2.52$ [1.13;52.1], $R_{cows} = \infty$ [1.3; ∞]) and did not differ significantly. It should be noted that the point estimate of R_{cows} is infinity due to the experimental setting in which all individuals became positive. Therefore the confidence limits are given.

Our studies illustrate that not only the clinical manifestation of an FMDV infection differed between adult and young cattle, but that cows and calves also differed in the amount of excreted virus. These differences did not however result in a significant difference in virus transmission, which could be due to limited power of the experiments. Nevertheless, the point estimates of R for cows and calves allows us to speculate that for FMDV field isolate O/NET/2001 it is more likely that small outbreaks would occur among calves than among adult cattle. This is supported by the study of Bouma et al. (2004) that showed no transmission amongst calves individually housed. It could also be hypothesised that the risk of

Table 1
Duration (days) of virus excretion in all inoculated and contact-exposed calves and cows; sorted on increasing duration.

Animal ID	Four categories of cattle included in the study (duration (days) of virus excretion)			
	Calves inoculated	Calves contact-exposed	Cows inoculated	Cows contact-exposed
1	0	0	5	5
2	3	0	5	5
3	4	0	6	5
4	4	0	7	6
5	4	0	7	7
6	5	0	7	7
7	5	0	7	7
8	8	1	7	7
9	8	1	7	8
10	9	4	7	9
11	13	6		
12	13	7		

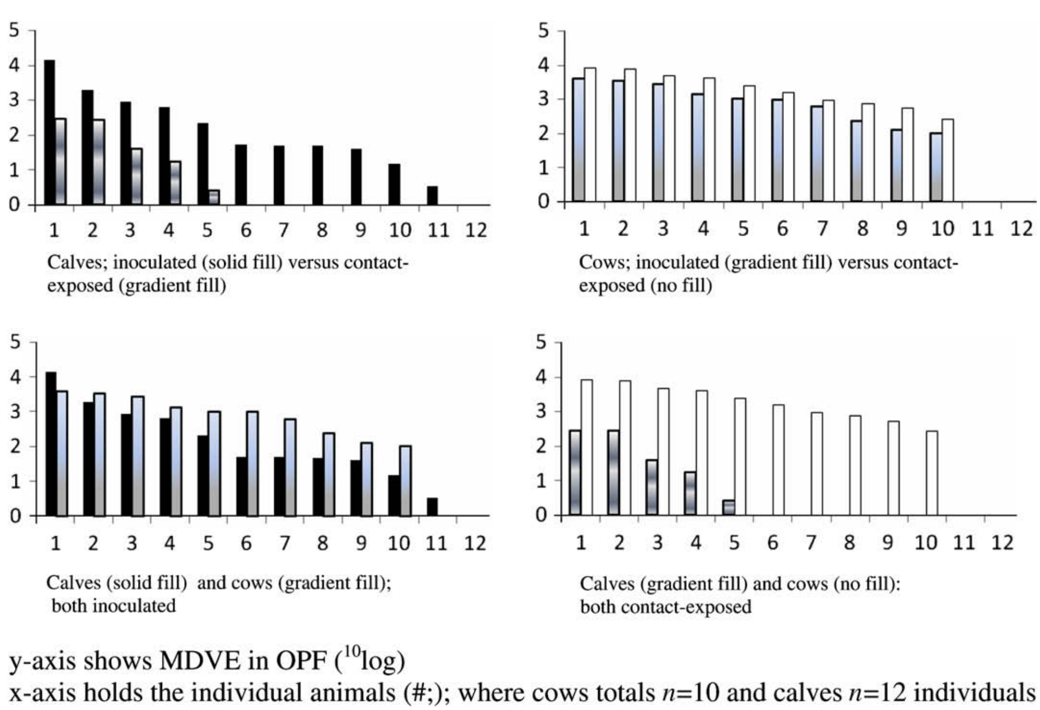

Fig. 1. Mean daily virus excretion for several groups of cattle, all sorted by decreasing mean daily virus excretion.

Please cite this article in press as: Orsel, K., et al. Different infection parameters between dairy cows and calves after an infection with foot-and-mouth disease virus. The Veterinary Journal (2009), doi:10.1016/j.tvjl.2009.06.031

spread of the infection from calves is more likely to go unnoticed compared to dairy cows.

The observation that clinical signs were more severe in dairy cows is remarkable, as for many infectious diseases the opposite has been seen (Radostits et al., 2008). It would be interesting to see the underlying mechanisms of this phenomena being clarified.

Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

Acknowledgements

This work was supported by the Ministry of Agriculture in the Netherlands (BOP 7-428) and the European Union (EU SSPE-CT-2003-503603). We thank animal and laboratory technicians from the FMD-facilities in Lelystad for their assistance.

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