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Reduction in daily milk yield associated with sub-clinical Bovine Herpes Virus 1 infection

Jonathan M. E. Statham [a,*], Laura V. Randall [a,b], Simon C. Archer [b]

[a] RAFT Solutions Ltd, Bishopton Veterinary Group, Mill Farm, Studley Road, Ripon, North Yorkshire, HG4 2QR, UK

[b] University of Nottingham, School of Veterinary Medicine and Science, Sutton Bonington Campus, Sutton Bonington, Leicestershire, LE12 5RD, UK

* Corresponding author. Tel +44 (0)1765 645893

Email address: jonathan@raftsolutions.co.uk (J.M.E. Statham).

Abstract

The aim of this observational cohort study was to investigate the potential economic effect of sub-clinical Bovine Herpes Virus 1 (BoHV-1) infection in a commercial UK dairy herd in terms of milk yield depression. Infection status of cows (infected or not infected) was assigned from serology on a single occasion. A multi-level linear model was used to evaluate the effect of infection status on milk production, using milk records that were routinely collected over two years. BoHV-1 seropositive cows produced 2.6 kg/day less milk over the study period compared with cows that were seronegative. This result highlights the importance of appropriate management of risks associated with BoHV-1 as part of proactive herd health and production management.

Keywords: Bovine Herpes Virus 1; Infectious Bovine Rhinotracheitis; Bio-security; Milk yield

Introduction

Losses from infectious diseases of livestock are most easily comprehended if associated with clinical signs. For example, incursion of Bovine Herpesvirus 1 (BoHV-1) into a naïve population of adult dairy cows typically leads to a variety of clinical syndromes described as Infectious Bovine Rhinotracheitis (IBR). These may include respiratory, ocular and nervous signs, accompanied by pyrexia, infertility and abortions and associated sudden decrease in milk yield (Nettleton 2007). However, both in previously exposed groups with recrudescence of virus from latently infected cattle, or in new infections of naïve animals, BoHV-1 may instead lead to sub-clinical disease and insidious production losses, rather than overt clinical signs (van Schaik and others 1999). Despite an effective systemic immune response, BoHV-1 can persist in sensory nervous ganglia of infected cattle contributing to endemic herd infection (Ackermann and Engels 2006). The intractable nature of BoHV-1 contributes to potentially serious economic consequences and an adverse impact on animal welfare. Trade restrictions are a significant driver of decisions to implement co-ordinated control at a national level. This has encouraged the Governments of six European countries to make IBR a notifiable disease, legislate to cull infected cattle from herds, and become 'IBR-free' (Ackermann and Engels 2006). Elsewhere, the management of BoHV-1 infection has been generally less regulated, although compulsory regional eradication schemes are in place, for example in the Italian province of Trento, with European Commission approval and voluntary health schemes are available to support and certify eradication at herd level (Statham 2011).

In England and Wales, the prevalence of dairy herds endemically infected with BoHV-1 has seemingly increased in recent decades based on the presence of specific antibody in bulk milk (Paton and others 1998; Williams and Winden 2014) and completely naïve UK dairy herds are probably uncommon in cattle dense regions (Woodbine and others 2009).

Estimates of the direct costs of IBR to the UK farming industry have been put at up to £4 million per annum (Bennett 2003). Data on milk production impacts of BoHV-1 are described by van Schaik and others (1999) in herds that experienced clinical IBR outbreaks. However, milk production losses from sub-clinical disease in commercial dairy cows have not been demonstrated. Bosch and others (1996, 1997) described the dynamics of BoHV-1 infection in experimental challenge studies on 30 yearling animals, but a major challenge remains in assessing the relative economic importance of sub-clinical versus clinical impacts associated with BoHV-1 infection in commercial dairy herds. Understanding whether the losses are due to incursion of a new infection with BoHV-1 compared with reactivation of existing latent infection is also important in understanding the relative importance of biosecurity in control of IBR. Hage and others (1998) estimated a reduced milk yield of 9.5 litres per animal at the time of seroconversion in the Netherlands. However, Hage (1998) measured production effects over only five weeks and van Schaik and others (1999) over nine weeks. The effects of sub-clinical BoHV-1 infection on milk production over a longer period have not been studied.

The aim of this study was therefore to investigate the potential effect of subclinical BoHV-1 infection on milk production over a two year period in a commercial UK dairy herd.

Materials and methods

Study herd background

The data refer to an autumn-calving dairy herd of 129 pedigree Holstein cows with approximate annual milk yield of 9,000 kg per cow. The main farm was in a low cattle density region of Northern England, with land double fenced or bordered by open moorland.

No cattle had been moved onto the farm from another holding since before 2000 and replacements were homebred by artificial insemination with no use of stock bulls. Heifers were sometimes grazed away from the main farm at the periphery of the holding. Protective clothing was provided for essential visitors. Based on annual or biannual bulk milk serology and intermittent blood samples from young stock, the herd was assumed uninfected with BoHV-1. In 2009, the conventional milking parlour was replaced with two robotic milking machines. At the same time, the diet was adjusted to include higher proportions of concentrate feed and milk yields increased. Serological testing of bulk milk was deemed ‘negative’ up to and including February 2010 but was seropositive by May 2010 (Table 1).

Apparent incursion of BoHV-1

Three adult cows aborted in May 2010; one developed respiratory signs and died. Investigation using serology for BoHV-1 antibody via blocking glycoprotein ‘B’ (gB) Enzyme- Linked Immunosorbent Assay (ELISA) (de Wit and others 1998) was performed and these cows were found to be seropositive. Antibodies to BoHV-1 were also identified in bulk milk in May 2010 and the herd was classified seropositive. No other clinical signs associated with BoHV-1 were detected throughout the herd; the remaining cows appeared healthy, and were individually blood sampled for BoHV-1 antibody via blocking glycoprotein ‘B’ (gB) Enzyme- Linked Immunosorbent Assay (ELISA) (de Wit and others 1998). Cows were classified as ‘BoHV-1 seropositive’ and ‘BoHV-1 seronegative’ using a threshold optical density > 0.25 as seropositive (Pritchard and others 2003). Seventy two per cent of cows were seropositive to BoHV-1 on individual sampling in May 2010 based on a commercial competitive ELISA (IDEXX IBR gB ELISA, Animal and Plant Health Agency (APHA); Table 2).

Ten animals from the seronegative group blood sampled in May 2010 were selected on convenience and resampled using the IDEXX IBR gE blocking ELISA (APHA) in August 2010 for the presence of antibodies against BoHV-1 glycoprotein ‘E’ (gE)).

Data analysis

Data from monthly cow level test day milk records (National Milk Records, Chippenham, UK) between January 2009 and December 2010 were collected. Records of milk, fat and protein production along with somatic cell count (SCC) for each test day were collated alongside BoHV-1 antibody status for each cow. A multi-level linear model was used for analysis, and this took the form;

$$y_{ij} = \alpha + X_{ij}\beta 1 + X_j \beta 2 + u_j + e_{ij}$$

$$u_j \sim \text{Normal}(0, \sigma^2_u)$$

$$e_{ij} \sim \text{Normal}(0, \sigma^2_e)$$

where y_{ij} = milk yield at test day i, for cow j, α = intercept value, X_{ij} = matrix of exposure variables for each test day, $\beta 1$ = vector of coefficients for X_{ij}, X_j = matrix of exposure variables for each cow, $\beta 2$ = vector of coefficients for X_j, u_j = a random effect to account for residual variation between cows (assumed to be normally distributed with mean = 0 and variance = σ^2_u), and e_{ij} = residual level 1 error (assumed to be normally distributed with mean = 0 and variance = σ^2_e). Model parameters were estimated by the iterative generalized least squares procedure (Goldstein 2003), using MLwiN 2.22 (Rasbash and others 2009). Categorical variables were constructed for calendar month (1 = January, 2 = February, 3 = March, 4 = April, 5 = May, 6 = June, 7 = July, 8 = August, 9 = September, 10 = October, 11 = November, 12 = December), and parity (1, 2, 3, $\geq$ 4). The category with the smallest impact on test day milk yield was used as the baseline. Lactation curve shape was included as number of days in milk (DIM) + $e^{(-0.065 \times DIM)}$ (Silvestre and others 2006; Archer and others 2013), and these variables were centred on 5 DIM. To adjust test day milk yield according to its composition, percentage of fat and protein were included, centred on their means. SCC was investigated on linear and log linear scales (Green and others 2006), centred on mean values. Biologically plausible interactions were assessed. Variables were retained from the saturated model where $P \leq 0.05$ and their inclusion resulted in a decrease in the deviance. Model fit was assessed by graphical inspection of residuals.

Results

Seventy two per cent of cows were seropositive to BoHV-1 on individual blood samples taken in May 2010. Risk of seroconversion varied with parity (Table 2 and 3). The 129 cows had 2,121 test day records over the two year study period. Means (standard deviation) of test day milk yield, DIM, and parity were 34 (10) kg, 174 (105) days, and 2.7 (1.7), respectively. Importantly, cows that were seropositive to BoHV-1 in May 2010 produced 2.6 (95% CI 2.0 to 3.2; p =< 0.05) kg/day less milk throughout lactation compared to those that were seronegative (Table 3; Figure 1). Confounding factors influencing test day milk yield were calendar month, parity, stage of lactation, test day fat and protein percentage, and SCC (Table 3). Residuals from the model were distributed normally indicating a good fit to the data. Ten animals that were seronegative for the presence of gE antigen to BoHV-1 in May 2010 remained seronegative three months later in August 2010.

Discussion

This study has identified a large decrease in the potential daily milk yield of cows associated with subclinical infection with BoHV-1. Compared to seronegative cows, those cows with antibodies to BoHV-1 on average failed to produce almost 1,000 kg of milk per year. In the herd studied this could relate to lost income of £200/ cow[1] having accounted for the reduction in feed costs assuming feed conversion efficiency is unchanged (margin = £0.2 / kg) (Kingshay Farming, personal communication). The mean estimate of potential milk loss in this study is larger and predicted to last longer than previous estimates which have varied from nil (Pritchard and others 2003) in an English herd in East Anglia, to 10 kg per cow over 2 weeks (Hage and others 1998), or around 1 kg per cow per day over 9 weeks (van Schaik and others 1999) in Dutch dairy herds. This variation could relate to differences in disease dynamics between cows in different herds, between studies, BoHV-1 strain or in the analytical methods used.

Infection status of cows is assumed based on a single individual sampling for serology in this herd. We therefore infer nothing about the temporal dynamics of virus circulation in the herd, other than the observed change in herd classification based on bulk milk serology. This approach to identifying a change in herd infection status based on bulk milk sampling has been previously described (van Schaik and others 1999). Once cows are infected with BoHV-1 the infection is long standing, and they remain antibody positive indefinitely (Nettleton 2007). Therefore, the most likely error in our classifications is that some negative cows seroconverted following sampling. If this occurred we may have underestimated the mean association of BoHV-1 infection with daily milk yield. Repeat sampling of cows from the seronegative cohort failed to show evidence of seroconversion between May and August 2010. No published test characteristics are available for the ELISA test assay used. However, Kramps and others (1994) estimated the sensitivity of an analogous non-commercial test to be 0.99.

The outbreak may have occurred through a new incursion of BoHV-1 virus or reactivation of unidentified latent infection. It is not possible to definitively identify the

[1] £1 = approx. US$1.64, €1.21 at 17 January 2014: http://uk.reuters.com/business/currencies

source of infection in this case but on balance a new incursion seems more likely, as there was no evidence of infection before 2010. We believe BoHV-1 may have been introduced to the herd through introduction of heifers. These were sometimes managed on separate more peripheral grazing at the boundary of the farm holding prior to calving. A biosecurity breach in this group would be consistent with the observed high prevalence of seropositive cows in parity 1 (Table 1). Parity ≥4 cows have been in the herd longer and are therefore more likely to have been exposed to BHV-1 and developed immunity; they may be infected but not infectious. These are two potentially vulnerable groups in this herd, with social stress factors for parity 1 animals entering the herd but higher yield and energy deficit for parity ≥4 cows; both potentially compromising immune function (Wathes and others 2007; Friggens and others 2013).

BoHV-1 is an increasingly important cattle pathogen (Woodbine and others 2009). The challenge in commercial dairy herds is often to develop strategies to manage higher yielding cows to optimise health and productivity and selecting for robust cows with characteristics that are suited to the particular system (Friggens and others 2013). As milk yields increase, even 'closed' dairy herds typically require more inputs through deliveries and visitors which could compromise bio-security and increase infectious disease risks. Herd health and production management (HHPM) includes prioritisation of management interventions (Green 2012). Sub-clinical disease may be inapparent without an effective monitoring strategy. The large potential loss in milk production in this study associated with sub-clinical disease highlights the importance of effective risk management such as through biosecurity and vaccination in infectious disease control.

Conflict of interest statement

None of the authors has any financial or personal relationships that could inappropriately influence or bias the content of the paper.

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Table 1. Summary of bulk milk Bovine Herpes Virus 1 (BoHV-1) serology results.

BoHV-1 status			
Bulk milk antibodies to BoHV-1 sampling date (Laboratory)	Cow management group	Bulk milk Optical Density (OD) result	Reference range
04.08.2005 (APHA[1])	Pooled milking herd	0.071 negative	(Negative <0.10)
16.02.2010 (SAC[2])	Pooled milking herd	1% seropositive	(negative <3%; positive>5%)
10.5.2010 (SAC[2])	Pooled milking herd	45% positive	(negative <3%; positive>5%)
17.5.2010 (APHA[1])	Parlour group	0.94 High positive	(High positive>0.7;

			>60% seropositive)
17.5.2010 (APHA[1])	Robot group	0.22 Low positive	(Low positive 0.10-0.40; <20% seropositive)

[1]Animal and Plant Health Agency (IDEXX IBR Pool Milk ELISA; negative <0.10; low positive 0.10-0.40; high positive>0.7)

[2]Scottish Agricultural College (Svanovir® IBR Ab ELISA, indirect; negative <3%; positive>5%)

Table 2. Counts and proportions of cows identified with Bovine Herpes Virus 1 infection[1] by parity in May 2010.

	BoHV-1 status		
Parity	Negative	Positive	Proportion positive
1	5	24	0.83
2	16	20	0.56
3	11	14	0.56
≥4	5	34	0.87

[1]Based on identification of antibodies in serum (optical density > 0.25).

Table 3. Final multi-level linear model for test day milk yield (kg/day) within cow

Fixed effects (baseline)		Mean effect	95% Confidence interval[1]	
Intercept		25.8	18.8	32.8
BoHV[2] (BoHV = 0)		-2.6	-3.2	-2.0
Parity (1)	2	6.4	0.8	12.0
	3	6.2	0.0	12.4
	≥4	8.9	3.7	14.1
DIM[3] (5)		-0.02	-0.02	-0.02
$e^{(-0.065 \text{ x DIM})}$ (DIM = 5)		-9.5	-20.7	1.7
DIM & Parity	2	-0.03	-0.03	-0.03
	3	-0.05	-0.05	-0.05
	≥4	-0.05	-0.05	-0.05
$e^{(-0.065 \text{ x DIM})}$ & Parity	2	-11.8	-20.4	-3.2
	3	-22.0	-31.6	-12.4
	≥4	-18.8	-26.8	-10.8
Calendar Month				
(December)	January	4.8	-2.4	12.0
	February	8.2	1.4	15.0
	March	8.6	-1.0	18.2
	April	-5.7	-15.5	4.1
	May	3.8	-4.4	12.0
	June	10.5	-2.3	23.3
	July	2.8	-11.8	17.4

	August	6.6	-4.4	12
	September	3.1	-6.3	12.5
	October	2.3	-6.1	10.7
	November	5.7	-6.9	18.3
DIM & Calendar month	January	0.02	0.02	0.02
	February	0.02	0.02	0.02
	March	0.00	0.00	0.00
	April	-0.00	-0.00	-0.00
	May	0.01	0.01	0.01
	June	-0.00	-0.00	-0.00
	July	-0.02	-0.02	-0.02
	August	-0.00	-0.00	-0.00
	September	-0.01	-0.01	-0.01
	October	0.00	0.00	0.00
	November	0.00	0.00	0.00
$e^{(-0.065 \times DIM)}$ & Calendar month	January	17.0	5.2	28.8
	February	20.0	8.8	31.2
	March	16.3	1.1	31.5
	April	-5.8	-21	9.4
	May	10.2	-3.2	23.6
	June	15.9	-3.7	35.5
	July	0.10	-0.1	0.3
	August	8.5	-8.5	25.5
	September	0.5	-14.7	15.7

	October	4.3	-9.7	18.3
	November	10.0	-10	30
SCC (‘000/mL) (mean)		-0.00	0.00	0.00
Fat % (mean)		-2.1	-2.5	-1.7
Protein % (mean)		-6.4	-7.6	-5.2
Random effects		Variance		
Cow level		22.8	18.8	26.8
Recording level		17.9	14.5	21.3

[1] The 95% confidence interval includes values where $P \leq 0.05$. This is significant if the interval excludes 0

[2] Seroconversion to Bovine Herpes Virus 1 (binary exposure)

[3] Days in milk

Figure 1. Mean predicted lactation curve shape by BoHV-1antibody status. Refers to parity 1 cows in December with mean milk fat, protein and somatic cell count.