Preventive Veterinary Medicine 120 (2015) 169–176

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

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

# Prediction of respiratory disease and diarrhea in veal calves based on immunoglobulin levels and the serostatus for respiratory pathogens measured at arrival

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ARTICLE INFO

*Article history:*
Received 10 June 2014
Received in revised form 15 April 2015
Accepted 16 April 2015

*Keywords:*
Bovine respiratory disease
Failure of passive transfer
Immunoglobulin
Neonatal diarrhea
Average daily gain
Veal calves

ABSTRACT

Failure of passive transfer is a common problem in calves destined for veal production. At present it is unknown whether the risk for respiratory disease (BRD) or neonatal calf diarrhea (NCD) in the veal herd is associated with total immunoglobulin (Ig) and/or on the serostatus for respiratory pathogens measured at arrival. Therefore, the first objective of this prospective longitudinal cohort study was to determine associations between serum protein fractions as determined by routine electrophoresis (total protein, albumin, alpha-1 and -2 globulins, beta-globulins and Ig's) at arrival and BRD and NCD in the first 3 weeks of the production cycle. The second objective was to determine whether the serostatus (seropositive/seronegative) of seven respiratory pathogens (bovine respiratory syncytial virus (BRSV), parainfluenzavirus-3, bovine coronavirus (BCV), bovine herpesvirus-1, bovine viral diarrhea virus, *Mannheimia haemolytica* and *Mycoplasma bovis*) of these arrival serum samples could be associated with the risk of having BRD. The third objective was to determine which of the electrophoresis proteins and respiratory serostatuses were associated with average daily gain (ADG) in the study period. The study population consisted of 150 rosé veal calves housed in a single air–space. The study period ended at day 18 post arrival, when BRD incidence was judged to be too high to further postpone a group treatment. A Cox regression model was used to determine the effect of the studied protein fractions and antibodies on the time to BRD and NCD occurrence. The effect of the studied predictors on ADG was determined by linear regression. Calves with Ig levels under 7.5 g/L had an increased BRD hazard (hazard ratio (HR) = 1.9 (95% confidence interval (CI) = 1.2–3.0)). NCD was only positively associated with the alpha-2 globulin concentration. Calves with a negative serostatus for BCV (HR = 1.7 (95% CI = 1.0–2.8)) or BRSV (HR = 2.0 (95% CI = 1.0–3.9)) had an increased BRD hazard. Average daily gain (ADG) was 0.242 kg/day (SD = 0.142) and was not related to the occurrence of BRD or NCD. Calves with Ig's below 7.5 g/L and with increased levels of alpha-2 globulins showed a decrease in ADG. This study showed the importance of providing sufficient colostrum to veal calves and the potential benefit of the presence of BCV and BRSV antibodies at arrival to reduce the BRD hazard in the first 3 weeks.



## 1. Introduction

In recent years, high levels of antimicrobial (multi)resistance have been detected in pathogenic, commensal indicator and zoonotic bacteria in both the European and North American veal sector (Catry et al., 2005; Di Labio et al., 2007; Cook et al., 2011; MARAN, 2012). The emergence of livestock associated methicillin resistant *Staphylococcus aureus* and extended beta-lactamases (ESBL's) in enterobacteriaceae from food animals has initiated a public discussion in Western Europe, which severely increased pressure on veterinary antimicrobial use (Graveland et al., 2010; Vandendriessche et al., 2013). Antimicrobial resistance selection is predominantly driven by antimicrobial use (Bosman et al., 2013). Therefore, the intensive antimicrobial use in the veal sector

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http://dx.doi.org/10.1016/j.prevetmed.2015.04.009
0167-5877/

urgently needs to be reduced, both for public health and political and economic reasons (MARAN, 2009, 2011; Pardon et al., 2012a).

Selection of calves based on disease risk and subsequently targetting metaphylactic antimicrobial treatment toward the high risk batches, is one potential strategy to rationally reduce antimicrobial consumption. Calf selection parameters include age at arrival, body weight, infection status for bovine viral diarrhea virus (BVDV), presence of disease (umbilical infection, bovine respiratory disease (BRD) or neonatal calf diarrhea (NCD)) (Wilson et al., 2000) and sufficient uptake of colostrum (Gulliksen et al., 2009; Brscic et al., 2012; Pardon et al., 2013). Failure of passive transfer (FPT) shows a prevalence ranging between 20 and 80% in the United States (McDonough et al., 1994; Wilson et al., 2000; Stilwell and Carvalho, 2011). Also in Belgium on average 40% of veal calves had FPT, assuming that immunoglobulin G (IgG) levels lower than 10 g/L upon arrival indicate colostral deficiency (Pardon, 2012). The crucial role of sufficient IgG uptake in protecting calves from BRD, NCD and mortality has been evidenced on multiple occasions (Postema and Mol, 1984; Furman-Fratczak et al., 2011; Stilwell and Carvalho, 2011). These effects have been shown to last up to 3 months for BRD (Virtala et al., 1996). To evaluate colostrum uptake, several tests have been validated for healthy animals in the age category of 2–7 days (Weaver et al., 2000). Although that cheap indirect screening tests, such as determination of total protein (TP) with a refractometer, perform reasonably well, direct determination of immunoglobulins (Ig) or IgG is generally more specific (Weaver et al., 2000). In calves sampled within a week after birth a cut off value for IgG of 10 g/L is generally accepted to determine FPT, and has been linked with disease occurrence, although some studies reported higher cut-offs in particular situations (Waldner and Rosengren, 2009; Furman-Fratczak et al., 2011; Stilwell and Carvalho, 2011). In contrast, it is currently unknown whether Ig levels measured at the age of arrival in veal calves (2–4 weeks old) can be used as predictors of BRD or NCD. For the veal sector it would be interesting to identify, through testing of calves upon arrival, individual calves requiring an adapted treatment and herds of origin with an insufficient colostrum management.

Therefore, the first objective of the present study was to determine whether Ig's or any other protein determined by routine electrophoresis measured at arrival, are associated with occurrence of BRD or NCD in veal calves in the first weeks after arrival, and are therefore potentially useful for risk classification of calves at arrival. The hypothesis was that calves with low TP or Ig would have a substantial higher risk acquiring BRD or NCD.

To gain further insight in which antibodies might play a protective role for BRD, the second objective was to determine the association between the serostatus for 7 respiratory pathogens, measured at arrival, and BRD occurrence.

Since earlier studies demonstrated a direct effect of FPT on average daily gain (ADG) in the first 3 months of life (Robison et al., 1988; Virtala et al., 1996), the third objective was to determine which of the studied serum parameters (electrophoresis protein fractions and respiratory antibodies) and diseases were associated with ADG in the study period.

## 2. Materials and methods

The study design was a prospective longitudinal cohort study. The study protocol was reviewed and approved by the ethical committee of the Faculty of veterinary medicine (Ghent University) under license EC 2013/184.

### 2.1. Study population and study period

The study was carried out in a typical rosé starter veal farm located in the South of the Netherlands, in January 2014. This type of operation is specialized in raising calves for 8 weeks, after which they are transported to a finisher herd. The sole criterion for farm selection was willingness to cooperate. Study calves were housed on slatted floors in the same air–space. During the first 6 weeks calves were housed individually in metal framed pens, with 1.4 $m^2$ floor surface and an air volume of 9.0 $m^3$ per calf. After this period the metal framework was removed and the animals were kept in groups of 6 animals for the remaining of the raising period. The study compartment was physically isolated from the other calf units present at the farm by full walls and a separate ventilation system. The stable was mechanically ventilated at a 20% refreshing rate and temperature was maintained at 17 °C. Calves were fed a 21.2% crude protein (CP), 17.7% crude fat (CF) milk replacer (MR) diet at dry mater base. The amount of MR was gradually increased from 1.5 L (90 g powder/L) morning and evening at day 1 to twice daily 3 L at 110 g/L at the end of the study (day 18). Milk was individually provided in drinking buckets. In addition to MR calves received chopped straw (from 20 to 50 g/day over the 18 day study period) and starter concentrates (from 10 to 350 g/day; CP = 16%; CF = 2.8%). The study group was not vaccinated and did not receive any antimicrobial group treatment at arrival.

### 2.2. Sample size calculations

Sample size was calculated to detect a 25% difference in BRD incidence between calves with more or less than 10 g Ig/L (25% vs. 50%), with 95% confidence and 80% power (Winepiscope 2.0., Thrusfield et al., 2001). For a two-tailed test 56 animals within each group were needed. For practical reasons and to account for mortality, the study group consisted of all animals present in the same airspace, being 150 animals.

### 2.3. Measurements

For ethical and economic reasons it was agreed beforehand that the study would finish when the responsible veterinarian deemed it necessary to initiate a group treatment. Although no objective criteria were set, this usually is done when 10% of the animals is ill on the same day, which occurs with high predictability between week 2 and 3 (Pardon et al., 2011, 2012a). In casu, the study period lasted from arrival to day 18.

#### 2.3.1. Health monitoring, case definitions and antimicrobial treatment

At arrival, all calves were clinically examined. Health status was monitored twice daily (morning and evening) for the duration of the study by the same veterinarian. The case definition for NCD was presence of diarrhea (partial) anorexia and depression. For BRD the case definition was based on a scoring system using the following symptoms: depression, cough, rectal temperature and nasal discharge (Table 1). Animals with a score of $\geq$5 were considered a case. Omphalitis was defined as the presence of a painful umbilical swelling at arrival.

Animals diagnosed with omphalitis were treated with 10,000 IU of benzylpenicillin (Procpen30®, Dopharma, Raamsdonksveer, The Netherlands) IM daily, for 5 days. NCD was treated with sulphadoxin–trimethoprim (Dofatrim-ject, Dopharma, Raamdonksveer, the Netherlands) (16 mg/kg IM, sid, 5 days) and meloxicam (Novem, Boehringer Ingelheim Vetmedica GmbH, Ingelheim/Rhein, Germany) (0.5 mg/kg IM, sid, 1 day). In case there was no response to treatment, NCD cases were treated with 2 mg/kg gentamicin IM (Genta-ject® 10%, Dopharma, Raamsdonksveer, Nederland). BRD cases were treated with a single injection of tildipirosin (4 mg/kg subcutaneously) (Zuprevo 18%, Merck, USA) and meloxicam. The drug use during the study period was quantified by standard daily dose methodology as described previously