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Research paper

Design and evaluation of multi-indicator profiles for targeted-selective treatment against gastrointestinal nematodes at housing in adult dairy cows

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ABSTRACT

Targeted-selective treatments against gastrointestinal nematode (GIN) in adult dairy cows require the identification of “cows to treat”, i.e. cows whose milk production (MP) would increase after treatment. This study aimed at quantifying the ability of multi-indicator profiles to identify such cows.

A randomized controlled clinical trial was conducted at housing in 25 French pasturing dairy herds. In each herd, treated cows received fenbendazole orally, control cows remained untreated. Daily MP was recorded and the MP variation between the pre- and post-visit periods was calculated (ΔMP) for each cow.

ΔMP was modelled with control cows data (n = 412) (piecewise linear mixed model). Estimated parameters were applied to treated cows data (n = 414) to predict the expected ΔMP in treated cows if they had not been treated. Treated cows with an observed ΔMP (with treatment) higher than the expected ΔMP (without treatment) were labelled as “cows to treat”. Herds where at least 50% of the young cows were “cows to treat” were qualified as “herds to target”.

To characterize such cows and herds, the available candidate indicators were (i) at the cow-level: parity, stage of lactation and production level, faecal egg count (FEC), serum pepsinogen level and anti-*Ostertagia* antibody level (expressed as ODR); (ii) at the herd-level: bulk tank milk (BTM) *Ostertagia* ODR, Time of Effective Contact (TEC, in months) with GIN infective larvae before the first calving, and percentage of positive FEC. These indicators were tested one-by-one or in combination to assess their ability to characterize “herds to target” and “cows to treat” (Chi-square tests).

115 out of 414 treated cows (27.8%) were considered as “cows to treat”, and 9 out of 22 herds were qualified as “herds to target”. The indicators retained to profile such cows and herds were the parity, the production level, the BTM *Ostertagia* ODR and the TEC. Multi-indicator profiles were much more specific than single indicator profiles, induced lower treatment rates, thereby minimizing the selection pressure on parasite populations. Particularly, to target a herd, the specificity was better with the profile “high BTM *Ostertagia* ODR and low-TEC” than with the BTM ODR value taken into account alone. The targeted-selective treatment of “young cows, belonging to herds with a high BTM ODR at housing and a low TEC” appeared as a pertinent solution, enabling a global approach for the control of GIN infection in which GIN control in heifers is connected to GIN control in adult cows.

1. Introduction

Gastrointestinal nematode (GIN) infections are highly prevalent in adult grazing dairy cows, *Ostertagia ostertagi* being the most frequently recovered species in the abomasum of dairy cows (Agneessens et al., 2000; Borgsteede et al., 2000; Chartier et al., 2013). Even though the infection remains subclinical most of the time, it can induce milk production losses: in the past 30–40 years a large number of studies showed that milk yield could be increased after anthelmintic treatment (Gross et al., 1999; Sanchez et al., 2004; Charlier et al., 2009). However, substantial variations of this effect of treatment on milk production have been observed

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between trials (Gross et al., 1999; Sanchez et al., 2004; Charlier et al., 2009), between herds (O'Farrell et al., 1986; Bisset et al., 1987; Ploeger et al., 1989, 1990; Kloosterman et al., 1996; Charlier et al., 2007; Mason et al., 2012; Ravinet et al., 2014) and between cows (Vanderstichel et al., 2013; Ravinet et al., 2014; Verschave et al., 2014). Accordingly, in a population of treated dairy cows, there would be cows with a positive post-treatment milk production response, and cows whose milk yield is not improved by the treatment. Therefore, at the herd level, the cumulative milk production response would depend on both the proportion of cows with a positive response as well as on the mean production response of these cows. Thus, systematic whole-herd blanket treatments for GIN are not appropriate (Reinemeyer, 1995; Ravinet et al., 2014), especially if we keep in mind the need to reduce the selection pressure exerted on parasites populations to prevent the emergence of anthelmintic resistance (van Wyk, 2001; Charlier et al., 2014). To establish more rational anthelmintic control programs in adult dairy cows, several authors have emphasized the need to have reliable and easy-to-use indicators enabling (i) to better target herds subjected to potential production losses due to GIN infection, and (ii) to better select cows for which an increase in milk production may be expected after anthelmintic treatment (Ploeger et al., 1989; Vercruysse and Claerebout, 2001; Sanchez et al., 2004).

The identification of such herds and cows can be based on herd and individual cow-level indicators statistically associated with the milk production response after anthelmintic treatment. At the herd-level, the anti-*Ostertagia* antibody level (mean of individual serum levels, or bulk tank milk level, measured by ELISA), considered as a marker of the mean exposure to GIN of the lactating herd, has been extensively examined (Ploeger et al., 1989, 1990; Kloosterman et al., 1996; Sithole et al., 2005; Charlier et al., 2007; Ravinet et al., 2014). Moreover, the Time of Effective Contact with GIN infective larvae before the first calving (TEC) was tested as a new indicator expected to reflect indirectly the development of immunity against GIN, and was found to be associated with the post-treatment milk production response (Ravinet et al., 2014). At the individual cow-level, three parasitological indicators were studied: (i) anti-*Ostertagia* antibody levels (measured in serum or in individual milk samples) (Sanchez et al., 2002b, 2005; Charlier et al., 2010; Vanderstichel et al., 2013; Ravinet et al., 2014; Verschave et al., 2014), (ii) faecal egg counts (Ravinet et al., 2014; Verschave et al., 2014) and (iii) serum pepsinogen levels (Ravinet et al., 2014). Production-based indicators, more easily available and less costly and time-consuming, were also considered: (i) parity (Ploeger et al., 1990; McPherson et al., 2001; Nødtvedt et al., 2002; Charlier et al., 2010; Mason et al., 2012; Ravinet et al., 2014; Verschave et al., 2014), (ii) days in milk at the time of treatment (Charlier et al., 2010; Mason et al., 2012; Ravinet et al., 2014), (iii) level of production (Bisset et al., 1987; Ploeger et al., 1989, 1990; Mason et al., 2012; Ravinet et al., 2014) and (iv) body condition score (Bisset et al., 1987; Verschave et al., 2014). In all these studies, the indicators significantly associated with the milk production response after anthelmintic treatment were considered as promising predictive factors of the effect of treatment, and therefore as criteria potentially enabling the implementation of targeted-selective treatment. However, these herd or individual-level indicators were always taken into account one-by-one. Moreover, their relationships with the effect of treatment could lack statistical significance (Kloosterman et al., 1996; Nødtvedt et al., 2002; Ravinet et al., 2014), or were varying or not confirmed from one study to another (Ploeger et al., 1989, 1990; Sanchez et al., 2005; Ravinet et al., 2014; Verschave et al., 2014), or could be inconclusive or equivocal (Charlier et al., 2007, 2010), or reported in only one study (Ravinet et al., 2014). As a result, evidence-based guidelines for anthelmintic treatment in adult dairy cows cannot yet be provided on the basis of these indicators taken into account one-by-one, and several authors suggested that a combination of several indicators (a multi-indicator profile) could be more efficient to identify herds and cows to treat (Ploeger et al., 1989; Chartier, 1995; Ravinet et al., 2014). The added value of such combinations has never been studied.

Furthermore, once an indicator significantly and positively associated with the post-treatment milk production response has been identified, herds or animals characterized by such an indicator are expected to provide a better response to treatment. However, there is no certainty that all herds and cows meeting the indicator's criterion will show an increase in milk production. Therefore, in practice the pragmatic question "which cows have to be treated?" runs up against this uncertainty linked to the variability of the treatment response. To answer this question, the approach developed here consisted in (i) firstly defining what a "cow to treat" is (on the basis of its treatment response higher than the mean milk production response) and what a "herd to target" is (according to its proportion of "cows to treat" as formerly defined), and (ii) then quantifying the uncertainty (risk of error) if we target and select such herds and cows for anthelmintic treatment according to indicators as described above. A special emphasis has been given to the design and the assessment of multi-indicator profiles, based on the combination of single indicators.

2. Materials and methods

This study comprised three key stages: (1) the identification of "cows to treat" and "herds to target", (2) the design of multi-indicator profiles, and (3) the evaluation of indicators taken into account one-by-one or in combination within the profiles.

2.1. Identification of "cows to treat"

Cows to treat selectively are cows whose milk production (MP) is increased after anthelmintic treatment. In other words, "cows to treat" are those which produce more than they would have produced if they had not been treated. Thus, to identify these cows, it would be necessary to predict what they would have produced without treatment and to compare this prediction with the observed MP after anthelmintic treatment.

2.1.1. Data used

This study was based on the data collected in a previous randomized controlled clinical trial conducted in the North-West of France, firstly in 10 commercial dairy herds visited in autumn 2010, and secondly in 15 commercial dairy herds visited in autumn 2011 (Ravinet et al., 2014). In these herds, all cows were of the same breed (Holstein). Briefly, in each herd, lactating cows present at housing on the day of the visit were randomly assigned to the treatment group (Fenbendazole, Panacur® 10%, with a zero withdrawal time for milk in France at the time of the trial), or the control group (untreated). Daily individual cow MP data were recorded from 14 days before treatment until 60–100 days after treatment and were averaged by week (Ravinet et al., 2014).

2.1.2. Principle

In this previous study, Ravinet et al. (2014) described the evolution of the treated cows' MP gain over time (in comparison with control cows) and reported the pattern/kinetics of the global treatment response which was maximal in weeks 5, 6 and 7 after treatment (+0.54, +0.85, and +0,57 kg/cow/day, respectively), the first day of week 0 being the day of visit and treatment. The approach proposed here relied on the hypothesis that the difference in MP gains between cows with a positive MP response and cows without MP response was maximal at the time of peak effect, i.e. in weeks 5, 6 and 7 after treatment. Therefore, as a way to