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Research paper

A multi-country study to assess the effect of a treatment with moxidectin pour-on during the dry period on milk production in dairy cows

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ABSTRACT

A randomized clinical study was conducted in a total of 45 commercial dairy farms in France (14 farms), Germany (28 farms) and the UK (3 farms) to evaluate the effect of an anthelmintic treatment on milk yield in the subsequent lactation. A total of 1287 animals with suspected exposure to *Ostertagia ostertagi* were included in the study. Animals were treated during the dry period (7–77 days before parturition) with moxidectin pour-on (Cydectin® 0.5% Pour-On, Zoetis; 638 animals) or left untreated (649 animals) according to a randomized block design. Animals were either heifers (n = 296) or multiparous cows (n = 991). The milk production was monitored at regular intervals after treatment up to 335 days after lactation, and analysed using a general linear mixed model with the milk production as outcome variable and several random effects. The effect on milk yield after anthelmintic treatment over the whole subsequent lactation varied from no effect (−0.43 kg/day; $P = 0.35$) to an increase of milk yield with 2.35 kg/day ($P = 0.01$), depending on the study region and parity of the cows. Lactation curve analysis suggested that the treatment effect was mainly caused by a slower decay of the milk production in the treated animals compared to untreated animals. The present study highlights the beneficial effect of a topical treatment with moxidectin before parturition on milk yield in the subsequent lactation, as well as the importance of a careful evaluation of nematode exposure risk based on local grazing management practices to guide and target production-based anthelmintic treatment decisions.

1. Introduction

Over the last decade, it became increasingly clear that gastrointestinal nematodes may have a negative impact on the milk production in dairy cattle. Studies into the effect of gastrointestinal nematodes on milk yield were greatly enhanced by the advent of macrocyclic lactones with a short withdrawal time for milk (Shoop et al., 1996) and an *Ostertagia ostertagi* ELISA allowing to assess the exposure to gastrointestinal nematodes in bulk tank milk samples (Charlier et al., 2009). Important variations have been reported in the milk yield response after treatment between different studies (Gross et al., 1999; Sanchez et al., 2004) and between different herds within the same study (Verschave et al., 2014). In a meta-analysis, the overall milk-production response after anthelmintic treatment in studies published until 2002 was estimated at 0.35 kg milk/cow per day (Sanchez et al., 2004), and treatment responses were higher when endectocides were used. Charlier et al. (2009) summarized anthelmintic treatment studies from 2000 onwards and reported a potential milk yield increase under western European conditions in the magnitude of 1 kg/cow per day.

All of these latter studies as well as more recently published ones focused on the effect of a treatment with either eprinomectin

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(Mason et al., 2012; Vanderstichel et al., 2013) or fenbendazole (Ravinet et al., 2014). So far, only few studies are available that have evaluated the effect of moxidectin treatment on milk yield and none were conducted under western European conditions or published in the peer-reviewed scientific literature (Murphy, 1998; Rock and Clymer, 2002). Moxidectin is an anthelmintic belonging to the milbemycin group of macrolides and is a broad spectrum endectocide with activity against a wide range of gastro-intestinal nematodes and lungworm (Morin et al., 1996).

Previously, it has been shown that the economic benefit of integrating internal parasite control in the periparturient cow management can be highly significant (Charlier et al., 2012a). The purpose of the present study was therefore to evaluate the benefit of a single moxidectin pour-on treatment during the dry period on milk yield in the subsequent lactation period. The study was a randomized clinical study conducted in France, Germany and the UK on farms with a suspected exposure to *O. ostertagi*.

2. Materials and methods

2.1. Study locations and farm recruitment

The study was conducted on a total of 45 commercial dairy farms located in 4 different regions in 3 countries (Fig. 1): Niedersachsen (Germany, 28 farms), Normandie (France, 3 farms), Loire and Rhône (France, 11 farms) and Northumberland (UK, 3 farms). The study sites were selected from the clientele of cooperating veterinary practices in each country. The farms were selected based on a history of grazing for nutritional requirements and a medium to high bulk tank milk antibody level (>0.6 optical density ratio (ODR)) for *O. ostertagi* (Svanovir® *O. ostertagi* AB ELISA, Sweden) recorded during the 12-month period prior to the study start. All herds were composed of Holstein-Friesian, Montbéliarde dairy cattle or crossbreds (with Holstein-Friesian).

2.2. Study design

Animals were allocated to a treatment with moxidectin (Cydectin® 0.5% Pour-On, Zoetis) or no treatment. In Germany, a third group was implemented which received treatment with eprinomectin (Eprinex® Pour-On, Merial), but as for reasons mentioned below were not further included in the analysis. Within each farm, the design was a split-plot design: within each parity class (primiparous vs. multiparous), animals were blocked based on the expected calving date and the treatments were randomly assigned within the block. This was practically organised by a predefined random treatment allocation plan (RTAP) for primiparous cows and one for multiparous cows.

2.3. Treatment administration

Before treatment, a clinical examination of the animal was performed to decide whether the animal was suitable for inclusion in the study. All included animals had to be healthy. The animals were treated within the routine health management procedures by the herd veterinarian during monthly herd visits. All animals were treated during the dry period, 77–7 days before parturition. The weight of each animal was estimated using a calibrated weight scale or girth tape and the appropriate dosage (Cydectin® Pour-On, 0.5 mg/kg) was poured on the back of the animal from girth to tail, according the manufacturer's instructions. Animals were enrolled in the study between July 2011 and August 2012 in Germany and between June 2012 and November 2013 in France and the UK.

Table 1
Number of farms and animals enrolled in the study, and *Ostertagia ostertagi* ODR per region.

Region	Number of farms	Number of animals	Average ODR (min–max)
Niedersachsen (Germany)	28	435	0.74 (0.36–1.07)
Normandy (France)	3	171	0.83 (0.80–0.90)
Northumberland (UK)	3	247	0.75 (0.66–0.85)
Loire and Rhône (France)	11	434	0.88 (0.64–1.06)
Overall	45	1287	0.78 (0.36–1.07)

2.4. Animal and production data

Animal and milk production information was collected from the dairy company Rücker (Aurich, Niedersachsen) in Germany, or directly from farm management records in the other regions. Following variables were obtained on an individual cow basis: test day milk production over the whole lactation following treatment (kg), lactation stage (days in milk (DIM)) and parity (primiparous vs. multiparous). In Normandy, monthly records of the total milk yield per animal were obtained and these were back-transformed to daily milk yield by dividing the total milk yield by the number of days in the test-day interval. No transformation was needed in the other regions.

2.5. Data analysis

The effect of moxidectin treatment on milk production was analysed using a general linear mixed model with the test day milk production (kg milk) as outcome variable and following random effects: (i) herd within region, (ii) herd within region by treatment interaction, (iii) block within herd, parity, and farm and (iv) cow nested in herd. The fixed effects included region, treatment (yes/no), parity (primiparous vs. multiparous), season in which treatment occurred, the two-way interactions of treatment with parity, season, and region, the two-way interaction of parity with season and region, and the three-way interaction of treatment and parity with season and region, and finally the days in milk (DIM) and Wilmink's function ($DIM^{-0.05}$) as continuous factors. Because an eprinomectin group was only used in farms in Niedersachsen, the means and contrasts with other treatments were non-estimable and only the data from moxidectin and the control group were used in the reporting and the final analysis. The analysis was conducted using the Mixed Procedure in SAS v9.4 (SAS Institute Inc., Cary, NC).

The effect of treatment on the shape of the lactation curve was investigated according to the MilkBot® lactation model (DairySight LLC, Argyle, New York) as described by Ehrlich (2011, 2013). This model describes the shape and magnitude of the lactation curve according to 4 parameters (scale, ramp, decay and offset). The offset parameter describes the offset in time between parturition and the start of lactation. Because test day records were only available at a monthly and not a daily interval, the offset was fixed to zero (Ehrlich, 2013). The data were fitted using a Levenberg-Marquardt nonlinear least-squares algorithm.

3. Results

3.1. Data description

The number of recruited farms together with the *O. ostertagi* ODR and number of participating animals are summarized in Table 1. In total, there were 1287 animals enrolled in the study, of which 638 were allocated to the moxidectin group and 649 to the control group. Table 2 provides the distribution of the animals over the treatment groups as well as region, parity and year quarter.