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Acaricide treatment prevents adrenocortical hyperplasia as a long-term stress reaction to psoroptic mange in cattle

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ABSTRACT

In cattle, infestation with *Psoroptes ovis* mites may cause severe dermatitis (psoroptic mange) which compromises the health and welfare of the animals and may lead to significant economic losses. To investigate yet undocumented effects of psoroptic mange mite infestations and how successful therapy promotes animal health, the present study examined alterations of the skin, lymph nodes and adrenal glands of *P. ovis* infested Fleckvieh (Simmental) bulls treated with either ivermectin long-acting injection (IVM LAI; IVOMEC[®] GOLD, Merial; 3.15% ivermectin w/v) or saline (*n* = 16 each). Approximately 8 weeks subsequent to experimental infestation with *P. ovis*, the bulls had developed mange and were administered either IVM LAI or saline once at 1 mL/50 kg body weight by subcutaneous injection. Mite counts were conducted in weekly intervals for determination of efficacy of treatment, and following humane euthanasia of the animals 8 weeks after treatment, skin samples from affected (mangy or previously mangy) and unaffected areas, prescapular lymph nodes and adrenal glands were collected for gross and pathohistological examination. In addition, four age-matching, uninfested Simmental bulls were sampled as controls for comparison.

No *P. ovis* mites were detected on any IVM LAI-treated bull after 28 days following treatment whereas saline-treated bulls maintained infestation throughout the study. At sampling (approximately 16 weeks after experimental infestation and 8 weeks following saline or IVM LAI treatment), saline-treated bulls displayed a severe, exsudative dermatitis with significantly increased skin thickness and inflammatory cell infiltration, significantly enlarged, hyperplastic prescapular lymph nodes, as well as significantly increased adrenal gland weights and volumes as compared to *P. ovis*-infested, IVM LAI-treated bulls and uninfested controls. Quantitative stereological analysis revealed that the adrenal gland enlargement in *P. ovis*-infested, saline-treated bulls was due to a selective increase of the volume of the zona fasciculata in the adrenal cortex. Compared to uninfested controls and *P. ovis*-infested, IVM LAI-treated bulls, the number of epithelial cells in the zona fasciculata cell volumes did not differ between the three groups of cattle. While the single

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point determination of serum cortisol concentrations did not reveal significant differences between the three groups of cattle at tissue sampling, the hyperplastic growth of the adrenal cortex in the *P. ovis*-infested, saline-treated bulls provides morphologic evidence that a chronic stress reaction is one consequence of mange mite infestations that can be prevented by efficacious acaricidal treatment.

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1. Introduction

Psoroptic mange of cattle is caused by infestation with the mange mite Psoroptes ovis. The infestation is highly contagious and usually spread by close contact between animals (Mullen and O'Connor, 2009). P. ovis has a onehost life cycle confined to the skin surface, where the non-burrowing mites abrade the stratum corneum of the skin and cause intense pruritus, severe exsudative inflammation, excoriation and formation of characteristic sticky vellowish crusts (Mullen and O'Connor, 2009: Stromberg and Guillot, 1989). The lesions are usually located at the shoulders (withers) and rump, but may spread all over the body. Bovine mange can result in considerable losses due to poor weight gain, reduced feed conversion efficiency, decreased milk production, decreased carcass traits, increased susceptibility to other diseases, and substantial devaluation of the leather obtained from infested animals (Cole and Guillot, 1987; Lonneux et al., 1998; Mullen and O'Connor, 2009; Rehbein et al., 2003b). Aside from losses of production and consequent economic loss, instances of psoroptic mange require rapid intervention because of its impact on the health and welfare of the affected animals (Wall, 2007).

The macrocyclic lactone ivermectin is known worldwide as highly effective and safe antiparasitic agent, displaying activity against a wide range of internal and external parasites including mange mites of diverse livestock species (Benz et al., 1989; Vercruysse and Rew, 2002). Recently, the efficacy of ivermectin long-acting injection (IVM LAI; IVOMEC® GOLD, Merial; 3.15% ivermectin w/v) for the treatment and control of bovine psoroptic mange was evaluated and re-confirmed in two studies conducted in Germany (Hamel et al., inpress). To allow for an advanced, quantitative assessment of histopathological skin lesions resulting from psoroptic mange and to investigate previously uncharacterized effects of P. ovis mange mite infestations, the present study examined skin, lymph nodes and adrenal glands of P. ovis infested bulls treated with either saline or IVM LAI, compared with uninfested control animals by gross- and histopathological evaluation including morphometrical and quantitative stereological analyses.

2. Materials and methods

2.1. Experimental animals, mite infestation, treatment of psoroptic mange

The investigations reported here were performed on tissue specimens derived from cattle which were enrolled in two controlled studies that were conducted to evaluate the efficacy of ivermectin long-acting injection (IVM LAI, IVOMEC[®] GOLD, Merial; 3.15% ivermectin w/v) against experimentally induced *P. ovis* infestation (psoroptic mange) as detailed by Hamel et al. (inpress). These studies were designed and conducted under one protocol in compliance with relevant guidelines for *Good Clinical Practices* for evaluating the efficacy of acaricides against mange mites on ruminants (Vercruysse et al., 2006). Animals were handled and treated with due regard for their welfare and in compliance with Merial Institutional Animal Care and Use Committee approvals, as well as according to applicable local regulations.

Briefly, 16 healthy, 6–8 months old Fleckvieh (Simmental) bulls were included in each infestation study (n=32in total). The cattle were held indoors under conventional conditions and individually stanchioned so as to prevent self-grooming and physical contact between animals. They were maintained on a forage-based diet and water was supplied by automatic drinkers.

In each study, animals were infested experimentally with 1000 P. ovis mites. A second infestation with 1000 P. ovis mites was repeated 2 weeks later. Approximately 8 weeks after infestation, when the bulls presented active mange lesions spreading from the withers over the shoulder and the back, animals per study were weighed, ranked according to body weight and formed into replicates of two animals each, and were allocated within each replicate at random to one of two groups to be treated either with saline (*P. ovis* infested, saline-treated, n=8per study) or IVM LAI (P. ovis infested, IVM LAI-treated, n=8 per study). The treatments were administered once by subcutaneous injection at 1 mL/50 kg body weight. Animals were weighed prior to treatment for allocation and dose calculation and at the termination of study 8 weeks after treatment administration (Supplemental Fig. 1). The efficacy of the IVM LAI treatment was assessed by counting of live mites in scrapings collected from the edges of active lesions or, if lesions regressed during the study, from the area where active lesions had been present at study commencement, and scoring of the character and extent of mange lesions in weekly intervals for 8 weeks following treatment (Hamel et al., inpress).

2.2. Serum cortisol concentration, necropsy, tissue collection

Before humane euthanasia and necropsy at the day after completion of the studies, blood samples were taken from all bulls for preparation of serum. Serum cortisol concentrations were determined by an external laboratory (VetMed Download English Version:

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