Corticosteroid treatment prevents the reduction in food intake and growth in lambs infected with the abomasal parasite *Teladorsagia circumcincta*

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ABSTRACT

Recent studies with *Trichostrongylus colubriformis* have provided some direct evidence to support the view that the major contributor to reduced production in gastrointestinal nematode infections is the host immune response, rather than damage from the parasite *per se*. However, it is unknown if this is also true for abomasal infections. Parasite naïve lambs were either trickle infected with *Teladorsagia circumcincta* L3 larvae; similarly infected and concurrently immuno-suppressed with the corticosteroid methylprednisolone acetate; immuno-suppressed only; or remained as controls. Immuno-suppression abrogated the reduction in intake and subsequent production losses and reduction in feed conversion efficiency associated with infection suggesting the damage caused by this abomasal parasite *per se* may have little detrimental effect on lamb productivity. These findings add weight to the view that components of the developing immune response are generally the cause of reduced productivity in infected lambs. They may have ramifications for the genetic selection of animals that are predisposed to mount a strong immune response.

Keywords: immuno-suppression; nematodes; intake; feed conversion efficiency; sheep.

INTRODUCTION

The inevitable infection of grazing lambs with gastrointestinal nematode parasites results in a suppression of feeding motivation and loss of performance observed as decreased live-weight gain and reduced feed conversion efficiency (FCE). These losses have been attributed to partitioning of nutrients toward their immune response (Coop & Kyriazakis, 1999), and have raised concerns about the benefit of selecting animals that invoke a strong immune reaction (Colditz, 2002). When immune function was suppressed during infection with the intestinal parasite *Trichostrongylus colubriformis*, anorexia and reductions in the gross efficiency of energy utilisation were prevented, suggesting that components of the developing immune response may limit productivity (Greer *et al*., 2005). The small intestine is only one of the organs commonly infected, and it is not known if this is a general effect with nematode parasites inhabiting other areas of the gastro-intestinal tract. This study used immuno-suppression to quantify the effect of the immune response to the abomasal parasite *Teladorsagia circumcincta* on lamb productivity.

MATERIALS AND METHODS

Animals and treatments

Forty, six-week-old Coopworth ewe lambs were weaned and removed from pasture until the start of the trial at six months of age to minimise exposure to nematode larvae. Upon housing, all animals were drenched with 1 ml 5 kg^{-1} live weight (LW) of a combination drench (37.5 g l^{-1} levamisole and 23.8 g l^{-1} albendazole, Arrest, Ancare New Zealand Ltd, Auckland, New Zealand). Animals were allocated hierarchically by LW (mean 26.0 kg ± 1.7 SE) into one of four treatment groups (n = 10). One group was infected with the abomasal parasite *T. circumcincta* (group IF); a second group received the same infection while concurrently treated weekly with an intramuscular injection of 1 ml per 30 kg LW of the corticosteroid (40 mg methylprednisolone acetate ml^{-1}, Depredone, Jurox Pty Ltd, Rutherford, New South Wales, Australia) in order to suppress immune function (group ISIF); the third group received the corticosteroid treatment only (group IS) while a fourth group remained as a control (group C), creating a 2 x 2 factorial design. This experiment was carried out with approval from, and in accordance with, the Lincoln University Animal Ethics Committee.

Management and measurements

All animals had access to fresh water and were offered, *ad libitum*, a complete ruminant diet containing 12.1 MJME $kgDM^{-1}$ and 130 gCP $kgDM^{-1}$ supplying 68 g metabolisable protein $kgDM^{-1}$ (AFRC, 1993). Feed refusals were collected and weighed at weekly intervals with sub-samples taken for determination of dry matter (DM) percentage after 72 hours at 90ºC. Live weight was recorded weekly, with fasted LW measured on days 0 and 63. At the conclusion of the trial, four IS and four C animals were housed in metabolism crates for the determination of *in vivo* DM digestibility. Animals were offered the diet *ad libitum* with daily intake and faecal production measured for 11 days. Feed refusals and a subsample of both feed offered and faeces produced were bulked and stored at 4ºC until determination of DM.

Parasitology

Animals were trickle infected with the equivalent of 4000 L3 infective *T. circumcincta* larvae day^{-1} (130 L3 larvae per kg initial LW, Lincoln Kumeroa strain

PB252/14) in a three-times-weekly dosing regime from day 2 onwards. The larvae were pipetted from an aqueous suspension of a known concentration onto filter paper, which was then rolled and orally administered using a balling gun. Faecal samples for the determination of faecal nematode egg counts (FEC) were collected directly from the rectum at weekly intervals commencing from day 0. Nematode eggs in faeces were determined using a modification of the McMaster method (Ministry of Agriculture, Fisheries and Food, 1979) and expressed as eggs per gram of fresh faeces (epg).

Statistical analysis

Data were analysed using GENSTAT 4.2 statistical package (Lawes Agricultural Trust, 2001, Rothamstead Experimental Station, VSN International Ltd). Feed conversion efficiency was analysed using a general analysis of variance (ANOVA). Food intake, LW and FEC underwent sequential comparison of ante-dependence structures for repeated measures before being analysed using restricted maximum likelihood (REML). FEC were log transformed ($\log_{10}$ (count + 1)) before analysis, with back-transformed means presented. One animal from group C was found to be an outlier, with a consistently low intake and liveweight, and was accounted for by blocking during analysis.

RESULTS

Data are presented as group means unless otherwise stated. Digestibility of the feed offered was not affected by cortico-steroid treatment, being 63.6 ± 2.1 (SE) and 62.1 ± 3.9 (SE) for treated and non-treated animals, respectively (P = 0.51).

Faecal egg counts

Eggs were detected in the faeces of IF animals from day 21 and peaked at 715 epg on day 28, thereafter declining to less than 50 epg from day 35. FEC of ISIF animals were similar to IF animals at day 28 and greater than IF from day 35 ($P < 0.001$), reaching a plateau of around 1600 epg at day 42, which they maintained with the exception of a decline to 1200 epg at day 63. No eggs were found in the faeces of non-infected sheep at any stage.

Intake

Mean DM intakes are shown in Table 1. Overall, infection alone (group IF) caused a non-significant (11%) reduction in average daily intake compared to control animals (group C) ($P > 0.05$). However, significant reductions of 20% were observed between days 15 and 28 ($P < 0.05$). Thereafter, weekly intakes tended to remain 7 to 15% lower than C sheep ($P > 0.05$). Immuno-suppression alone (group IS) caused a non significant overall increase in food intake of 11% compared with group C. Differences between groups were greater on days 14 (22%) and 42 (27%) at which time differences were significant ($P < 0.05$ in both cases). Infection combined with immuno-suppression caused no reduction in intake, with ISIF animals at all times consuming food at rates similar to IS animals ($P > 0.05$), while maintaining rates of food intake 22-43% greater than IF animals between days 15 and 56 of infection ($P < 0.05$).

Live weight

Mean live-weight gain (LWG) during the course of infection is shown in Table 1. The LWG of IF animals was impaired from day 15, resulting in IF animals having an 8% lower live weight than C animals at day 28 ($P < 0.05$), a difference that increased until day 63 when IF animals had 11% lower fasted liveweight ($P < 0.025$). Live weights of lambs simply immuno-suppressed (group IS) or infected while immuno-suppressed (group ISIF) were not different from C animals throughout ($P > 0.05$).

Feed conversion efficiency

Feed conversion efficiency (FCE; g LWG per kg DM consumed) was calculated for individual sheep by dividing LWG (kg) by total feed consumption (kg DM). Mean FCE for each group is shown in Table 1. Infection resulted in a 37% reduction in FCE in IF relative to C animals ($P < 0.05$). Immuno-suppression alone (IS animals) resulted in a non significant 20% reduction in FCE. However, infection in immuno-suppressed sheep caused no reduction in FCE, with ISIF sheep displaying a non significant 6% greater FCE than IS animals.

TABLE 1: Average daily intake, live-weight gain (LWG) and feed conversion efficiency for lambs infected for 63 days with 4000 *T. circumcincta* L3 larvae day^{-1} (IF), similarly infected while concurrently immuno-suppressed (ISIF), immuno-suppressed only (IS) or remained as untreated controls (C)

	IF	ISIF	IS	C	SEM
Average intake (kg DM day^{-1})	1.33^{a}	1.67^{b}	1.65^{b}	1.49^{ab}	0.084
LWG (kg)	6.5^{a}	10.1^{b}	9.7^{b}	10.6^{b}	1.14
Feed conversion efficiency (g LWG per kg DM)	71^{a}	95^{b}	90^{ab}	112^{b}	9.3

Within rows, values with different subscripts are significantly different ($P < 0.05$)

DISCUSSION

These results demonstrate that suppression of immunological responses of young lambs with corticosteroids alleviates the production losses associated with infection of the abomasal parasite *T. circumcincta*. These findings are consistent with those obtained with the intestinal parasite *T. colubriformis* by Greer *et al*. (2005) and are the first reported involving abomasal parasitism.

The ubiquitous reduction in appetite is a significant contributor to reduced production in parasite-infected lambs. The extent and timing of the reduction in intake of the present IF animals were comparable to observations in other studies with *T. circumcincta* (Symons *et al*., 1981; Coop *et al*., 1982), therefore making the absence of anorexia in ISIF animals, also observed by Greer *et al*. (2005) in infections with the intestinal parasite *T. colubriformis,* of particular interest. The cause of anorexia in infected animals has been the subject of much speculation. Recent attention has been drawn to pro-inflammatory cytokines involved in the signalling of the non-specific acute phase response invoked during the development of immunity that are believed to have anorectic effects (Johnson, 1997). This may explain the lack of a depression in appetite in ISIF animals, as the immuno-suppression treatment would be expected to modify cytokine signalling.

Given the expected relationship between intake and productivity, it is not surprising that IF animals suffered a 39% reduction in LWG and consequent 37% reduction in FCE. Despite maintaining higher intakes, the non significant 20% reduction of FCE experienced by IS animals suggest the treatment with corticosteroids alone affected FCE. This may be attributable to changes in nutrient partitioning as both IS and ISIF animals appeared to have greater amounts of subcutaneous adipose tissue, and Greer *et al*. (2005) observed increased adipose tissue deposition in animals treated with the same immuno-suppressive agent used here. Given that adipose deposition requires 3.7 times more energy than the equivalent weight in lean tissue, it is plausible that greater amounts of metabolisable energy were deposited as energy dense adipose tissue, thus reducing the calculated FCE (g LWG per kg DM consumed).

Increases in the endogenous nitrogen losses through the leakage of plasma proteins as a consequence of mucosal pathology can be expected to restrict the availability of amino acids for productive functions in infected animals (Sykes & Coop, 1977; Poppi *et al.,* 1986). Interestingly, the absence of an infection-induced decrease in LWG or FCE in animals receiving the immuno-suppressive treatment suggests a lessening of nutrients available for growth did not occur in these animals. However, it is not known if the greater FCE in ISIF animals was due to an improved nutrient supply as a consequence of reduced physical damage and therefore reduced plasma protein leakage or increased reabsorption of nutrients from the gastrointestinal tract. Additionally, immuno-suppressed animals may have had an increase in nutrient availability for growth from a decrease in the amount of nutrients invested into repair of the gastro-intestinal tract, as observed by Turini *et al*. (2003) in dexamethasone treated rats, presumably as a consequence of the net catabolic actions of corticosteroid compounds. Reductions in FCE in IF animals may also have been a consequence of increased cell proliferation during the development of the immune response that is considered to increase demand for potentially rate limiting amino acids (MacRae, 1993). The absence of a reduction in FCE in ISIF compared with IS animals may, therefore, also be a result of reduced energy and/or protein expenditure through the suppression of immunological cell proliferation, supporting suggestions that the immune response does impose a significant nutritional cost to the animal (Colditz, 2002). It is apparent that further research is needed to both determine the effect that immuno-suppression has on gut pathology and to identify the component of the immune response that is responsible for reduced performance during nematode parasitism.

In conclusion, immuno-suppression prevented the anticipated reduction in feed intake and losses in both LWG and FCE in young lambs infected with the abomasal parasite *T. circumcincta*. It adds further weight to view that production losses associated with gastrointestinal nematode parasitism may largely be a consequence of the host's immune response and cautions against imposing heavy weightings in genetic selection indices on the ability of animals to mount a strong immune response to gastro-intestinal nematodes.

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