

## ORIGINAL PAPER

# Effect of homeopathic medicines on helminth parasitism and resistance of *Haemonchus contortus* infected sheep<sup>☆</sup>

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**This study evaluated the effects of homeopathic treatment on control of *Haemonchus contortus* infection in sheep. Twenty lambs were randomized to three treatments: treated with the homeopathic medicines, *Ferrum phosphoricum*, *Arsenicum album* and *Calcarea carbonica*; treated with a conventional antihelminthic, doramectin, and an untreated control group. Fecal and blood samples were taken from each animal on days 18, 38 and 68 after start of treatment.**

**A significant reduction in number of *H. contortus* larvae ( $p < 0.01$ ) was observed for animals in the homeopathic treatment group compared to the control group. Fecal egg counts showed negative correlation between haematocrit and haemoglobin concentrations in the homeopathic treatment group ( $p < 0.01$ ); however, the biochemical and immunological parameters showed better correlation, indicating that the homeopathic medicine improved vital functions. Daily weight gain in the homeopathic treatment group was superior to the control and to the antihelminthic groups, 31 and 6.5%, respectively. The cost benefit analysis confirmed that homeopathy group increases economic trend when compared with the other groups. *Homeopathy* (2008) 97, 145–151.**

**Keywords:** Sheep; Immune response; Homeopathy; *Haemonchus contortus*; Nematodes

## Introduction

Infection with *Haemonchus contortus* represents the main cause of economic loss in ovine breeding in tropical and subtropical areas of the world. Although sheep breeds with better productive indexes are imported from developed countries, they do not express their genetic potential in

environments where there are great chances of having parasitic infections.<sup>1</sup> Control of gastrointestinal (GI) nematodes in sheep relies heavily on antihelminthic treatments of flocks. The first sign that it has failed is the appearance of drug-resistant nematode populations.<sup>2</sup> This situation is especially serious in the small ruminant industry of South America, where resistance to all broad-spectrum antihelminthic drugs has been detected.<sup>3</sup> Several studies have revealed antihelminthic resistant nematodes in sheep flocks from four Mercosur countries (Argentina, Brazil, Paraguay, Uruguay), and most of the studies have found resistance to ivermectin.<sup>4</sup>

Besides grazing management, other non-chemotherapeutic strategies for controlling GI nematodes in sheep and goats include the following: vaccines, genetic selection for resistance and grazing rotation, alternate grazing with adult cattle on the control of nematode parasites in sheep.<sup>5</sup> In addition, biological control of parasitic livestock

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nematodes is currently under development and represents another tool that may be integrated into helminth parasite control strategies.<sup>6</sup> Besides all the alternatives available, homeopathy may have a role in reducing the pathology in the host.<sup>7,8</sup> In Brazil its acceptance has been increasing due to characteristics of low cost, absence of residues in meat and milk and its low environmental impact.

The objective of this study was to evaluate the effectiveness of homeopathic medicine on the control of *H. contortus* in sheep, through the following parameters: fecal parasitological examinations, immunoglobulin concentrations, haematological and serum biochemical analyses, weight gain and cost benefit.

## Materials and methods

### Animals and study location

Twenty male and female lambs (Morada Nova, Rabo Largo and Santa Inês native breeds crossbred with Dorper breed) belonging to the Agricultural Development Company of Bahia (EBDA) were evaluated from birth until  $218 \pm 8$  days. Rain-fall during the study period was 381 mm, distributed monthly as follows: 103 mm, 33 mm, 25 mm, 70 mm, 102 mm, 55.50 mm and 92.50 mm. Ambient temperature was between 22.7 and 17.1°C. Animals were maintained on naturally infected ryegrass in an EBDA experimental pasture station; located in the municipal district of Jaguaquara, southwest Bahia State, Brazil.

### Study design

The animals were raised in a semi-intensive production regime. After weaning, they were fed with a supplemented ration containing 18% protein until they were 260 days old. All lambs were vaccinated against enterotoxaemia at 30 and 60 days of age (Clostridovac<sup>®</sup> – IRFA Laboratory, RS Brazil). Between 30 and 75 days of age, the animals are naturally infected by protozoa of the genus *Eimeria*. This type of infection is common in intensive and semi-intensive breeding systems. The animals were treated with 50 mg/kg sulphamonomoxaline sodium (Coccifin<sup>®</sup> – Laboratory Ouro Fino) according to standard recommendations. All normal sanitary procedures were followed, such as the cutting and disinfecting of umbilical cords and control of ectoparasites and other infections.

### Treatment protocol

When animals reached  $135 \pm 8$  days of age and an average fecal egg counts (FECs)  $> 700$ , they were randomly allocated to the following three treatment groups, each of six or seven animals. The sample size was based upon several similar researches described in current literature.<sup>9</sup>

Group 1 ( $n = 7$ ): Conventional antihelminthic; doramectin (1 mL/50 kg, Dectomax<sup>®</sup>, Pfizer). Positive control.

Group 2 ( $n = 7$ ): Homeopathy (oral) initially, they received *Ferrum phosphoricum* 6D and *Arsenicum album* 6D alternate days for 10 days, then *Calcarea carbonica* 12D twice a day for 10 days.

Group 3 ( $n = 6$ ): Untreated control.

The animals were identified with plastic earrings and nylon collars, with a specific colour for each group. Fecal and blood samples were collected weekly from birth until 90 days of age, and every 2 weeks during the rest of the experimental period ( $218 \pm 8$  days). The animal body weight was also recorded before the first daily meal on the same days. Fecal and blood samples were taken from each animal on days 18, 38 and 68 after finishing treatment.

### Homeopathic medications

The homeopathic medicines *Ferrum phosphoricum* and *Arsenicum album* were selected on the basis of *Materia Medica*<sup>10</sup>: *Arsenicum album* produces rapid prostration, with dark bloody dysentery of putrid odour. *Ferrum phosphoricum* produces marked prostration together with inflammatory conditions and local congestions and haemorrhagic tendency too<sup>11</sup>. The choice of the homeopathic medicines was also based on clinical experience and its success for the control of *H. contortus* in goats.<sup>12</sup> The use of *C. carbonica* was based on its activity on general nutrition and leucocytes count and the fact that it produces emaciation and anaemia.<sup>13</sup> The homeopathic medications were prepared from Irmãos Soares da Cunha & CIA laboratories (Salvador, Bahia, Brazil) according to Brazilian Pharmacopoeia.<sup>14</sup>

### Parasitological techniques

The fecal samples were examined for eggs (FEC) and larval (larvae per gram of feces (LPGFs)) counts of GI nematodes. Microscopic egg counts (eggs per gram) were carried out using the Mac Master method (Ueno and Gonçalves<sup>15</sup>). Distinction between genera of the Strongylida-order was made by larval culture according to the method of Robert and O' Sullivan, as modified by Ueno and Gonçalves.<sup>15</sup> The larval culture was performed mixed 2 g of feces with 2 g of the sawdust substrates and 2 mL of distilled water. The material was processed and incubated in a chamber at 27°C, relative humidity  $> 70\%$ , for 7 days. The third stage larvae were recovered after 4 h of sedimentation for counting and identification.

### Biochemical and haematological values

Haematological parameters were tested on whole blood obtained with anticoagulant ethylenediamine tetra-acetic acid (EDTA). Humoural immune response and biochemical parameters were tested with serum samples obtained from blood collected without anticoagulant.

The determination of total serum protein was accomplished by biuret spectrophotometry (Bioclin<sup>®</sup>); albumin was evaluated through the bromocresol green technique and globulin concentration was calculated from the arithmetic difference between the total protein and albumin concentrations. Packed cell volume (PCV), haemoglobin (Hb) concentration, red blood cell (RBC) and white blood cell (WBC) counts were determined using the standard methods described by Birgel et al.<sup>16</sup> Haematocrit was obtained by the microhaematocrit centrifugation technique. Total

circulating leukocyte (WBC) count was determined using a Neubauer chamber and the differential leukocyte count was obtained with blood smears stained by the Rosenfeld method according to Birgel.<sup>16</sup>

### Quantification of immunoglobulins

Total serum immunoglobulin G (IgG) was measured by radial immune diffusion (RID) using kits from Bethyl<sup>®</sup> (Bethyl, Inc., Montgomery, TX, USA) in samples collected on days 0, 18 and 38 after the use of medicine. All samples and standard sera were tested in duplicate.

Serum specific antibody levels were determined by enzyme linked immunosorbent assay (ELISA). Worms for preparing antigenic extracts were obtained from slaughtered lamb's abomasum at a local abattoir; they were removed immediately after slaughter, opened and washed with 0.9% saline solution up to a volume of 2 L. Water-soluble extracts from adult worms were obtained by homogenization in a Potter manual tissue grinder, and the protein recovered was determined. Microtiter plates were coated with an antigenic extract at 200 µg/mL in pH 9.6 carbonate buffer (18 h, 4–8°C). Optimal dilutions of both sheep sera and the second antibody were determined in a checkerboard manner.

Briefly, 100 µL of serum samples diluted 1/10 in (phosphate buffer saline) PBS containing 0.05% Tween 20, and 0.25% defatted milk were added to the plates and then incubated for 1 h at 37°C in a humidified chamber. Serum from a mature ewe with a high infection level was used as a positive control, while serum from colostrum-deprived lambs was the negative control. All serum samples (test, negative and positive controls) were done in triplicate. After washes, 100 µL of peroxidase labelled donkey antiserum IgG (Sigma Chem. Co., USA) was used at 1:1000 in the same solution used to dilute the sera. Reactions were developed by addition of 100 µL of chromogenic solution, 15 mL citrate phosphate buffer (0.1 M, pH 5.1) containing 6 mg of ortho-phenyldiamine (OPD) (Sigma Chem. Co., USA) and 10 µL of hydrogen peroxide. The plates were then incubated in the dark for 20 min and the colour reaction was halted with 50 µL of solution 1 N sulphuric acid. Reactions were measured spectrophotometrically at 450 nm in an ELISA reader (Stat Fax<sup>®</sup>).

### Cost benefit analysis

Cost benefit analysis was based on medicine costs, the live weight volume of the animals (US\$ 1.65).

### Statistical analysis

FEC and LPGF were  $\log_{10}(x+1)$  transformed to normalize variance. The means from the treatment groups were compared by analysis of variance using the SAS general linear models (GLM) procedure,<sup>17</sup> applying Software Statistical Package for the Social Science (SPSS) (version 12). Follow-up comparisons were performed by the Tukey test. Correlation between values from different parameters was calculated for each group using Pearson's correlation coefficient.

## Results

### Parasite counts

Haemonchus spp. was the predominant genus in fecal samples. *Eimeria* sp., *Trichostrongylus* sp., *Oesophagostomum* sp., *Trichuris* sp., *Skrjabinema* sp. and *Moniezia expansa* infections also occurred. Infection with *H. contortus* was different in the three study groups. The mean of FEC observed in the homeopathy group was 933 (eggs per gram) at 68 days after completion of treatment, while the group treated with antihelminthic and the control group showed FEC of 1.483 and 1.229 (eggs per gram), respectively (NS) (Fig. 1A). The homeopathy and antihelminthic treated groups did not show a significant differences in terms of FEC ( $p > 0.05$ ), but reduction of LPGF in the group of animals treated with homeopathy was highly significant compared to the control group ( $p < 0.01$ ) (Fig. 1B).

### Haematological, parasitological and biochemical results

No statistical significant differences in haematological parameters were observed among the three study groups. However, there was significant correlation between parasitological and haematological results in homeopathy group ( $p < 0.01$ ) and control group ( $p < 0.05$ ), but not significant ( $p > 0.05$ ) in the antihelminthic group (Table 1). There were no significant differences among groups in relation to total serum protein concentration during the phases of experiment.

The average haematocrit values obtained from animal groups at the end of the experiment were 31.50, 30.43 and 30.67% for the control, antihelminthic and homeopathy groups, respectively, with no significant differences between the groups.

The average eosinophil (EOS) counts were higher in the group treated with homeopathy compared to the other groups, but this was not statistically significant.

### Total and specific immunoglobulins

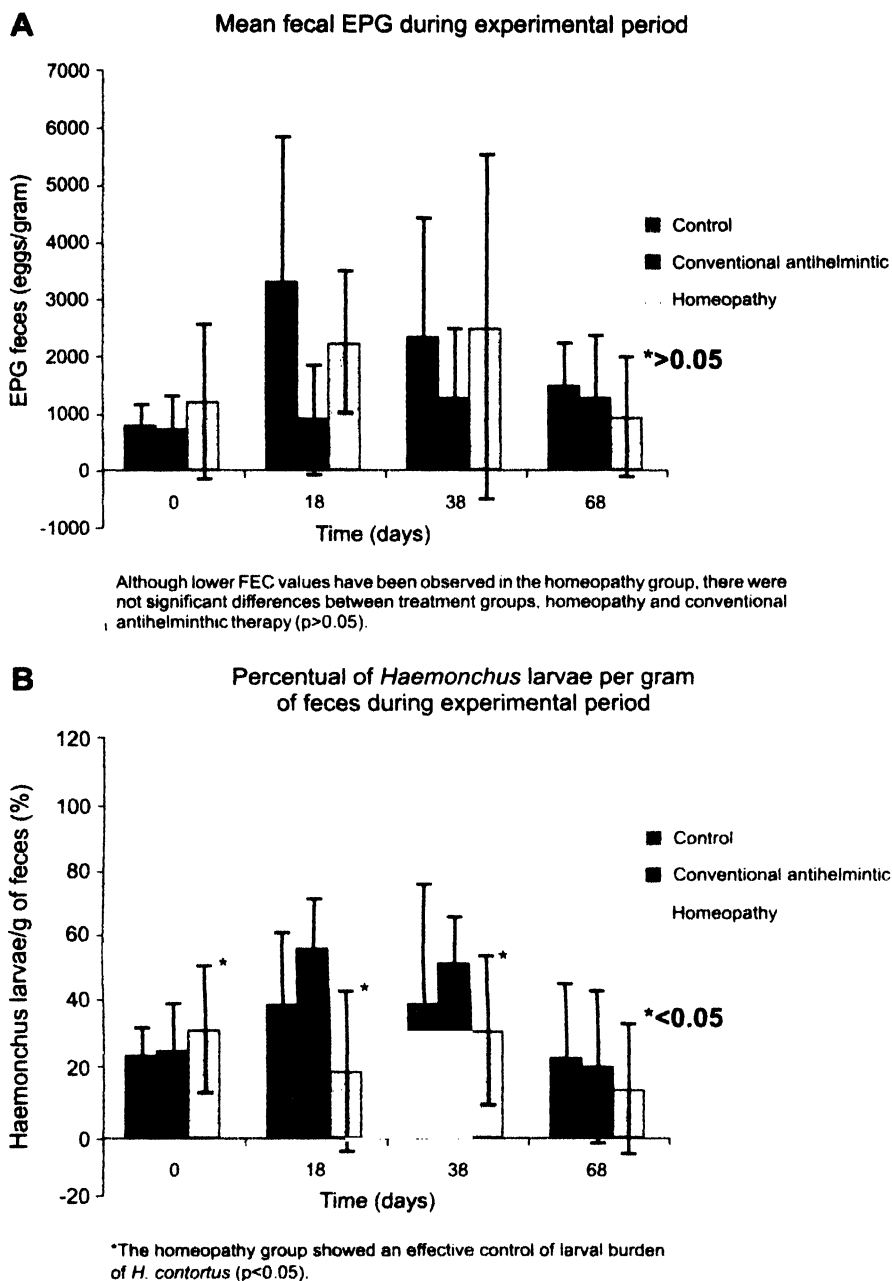
The IgG concentrations were higher in the homeopathy than the other two groups (Table 2). After standardizing the ELISA the mean for negative control sera was 0.05 O.D. The homeopathy group showed the greatest rise of specific immunoglobulins (Table 2).

### Weight gain

The weight gain in the groups is shown in Fig. 2. The animals in the homeopathy group on average gained weight of 8.45 kg while the antihelminthic and control groups gained an average of 7.90 and 5.83 kg, respectively (Table 2). These differences are not statistically significant.

### Cost and benefit analysis

The value per kg of live weight was estimated at US\$ 1.20, at the experimental period. The cost of total medicine costs per homeopathy was US\$ 2.47 and US\$ 3.03 for the conventional treatment. The overall cost benefit was in



**Fig. 1** (A) Mean FEC during experimental period. Homeopathy group (*Arsenicum album* and *Ferrum phosphoricum* alternately for a period 10 days, then they received *Calcareo carbonica* twice a day for 10 days). Conventional anthelmintic group received doramectin (1 mL/50 kg, Dectomax<sup>®</sup>, Pfizer). Control group was not treated. FEC results were  $\log_{10}(x + 1)$  transformed to normalize variance. The means from different groups were compared by analysis of variance using SAS GLM. (B) Mean *Haemonchus* LPGF during experimental period.

US\$ 7.68 for the homeopathy group. US\$ 6.42 for the conventional group and US\$ 6.00 for control group.

## Discussion

It is well known that the climatic factors have a large influence in the development of the parasites in tropical areas.<sup>18</sup> During this work the temperature was within the limits required for development of parasite infection. The same observation was true for rain-fall (monthly mean above 50 mm). *H. contortus* was the main nematode species present in the sheep flock. The peak of parasitism by *H. contortus* occurred between  $135 \pm 8$

and  $159 \pm 8$  days revealing that the period immediately after the weaning favours infection. This fact leads some authors to recommend the use of anthelmintics in to control parasitism in flock sheep after the weaning period even though there are no signs of parasitism.<sup>19</sup> Another important factor to consider is that the native Northeast Brazilian sheep breeds used in this work (Morada Nova, Santa Inês, Rabo Largo) were crossed with Dorper sheep of South African origin. Several authors have demonstrated the importance of native breeds for the control of nematodes and their superiority in comparison with exotic breeds.<sup>20,21</sup> Evidently, genetic aspects influence the incidence of the parasitism.

**Table 1** Correlation coefficients between parasitological, haematological, biochemical and cellular parameters observed during the phases of experimentation

	Larvae	EPG	Hct	Hb	Protein	Alb	EOS	Leu	IgG/IDR <sup>1</sup>
<b>Homeopathy group</b>									
Eggs per gram of feces (EPG)	0.422***								
Haematocrit (Hct)	-0.379***	-0.656**							
Hb	-0.535*	0.834**	0.893**						
Whole proteins	-0.490*	-0.475***	0.587*	0.640**					
Albumin (Alb)	-0.688**	-0.315***	0.541*	0.524*	0.603*				
EOS	-0.085***	0.344***	0.309***	0.400***	-0.02***	-0.231***			
Leukocytes (Leu)	-0.020***	-0.233***	0.312***	0.402***	-0.019***	-0.258***	0.83**		
Globulin	0.056***	-0.280***	0.202***	0.282***	0.648**	-0.217***	0.02***	0.223***	0.61*
<b>Control group</b>									
Eggs per gram of feces (EPG)	0.751**								
Haematocrit (Hct)	-0.583**	-0.425*							
Hb	-0.768**	-0.624**	0.740**						
Whole proteins	-0.309***	-0.323***	0.221***	0.272***					
Albumin (Alb)	-0.269***	0.371***	0.161***	0.009***	0.134***				
Eosinophils EOS	-0.280***	-0.132***	0.393***	0.606**	-0.03***	-0.427*			
Leukocytes (Leu)	-0.368***	0.063***	0.485*	0.636**	-0.196***	-0.39***	0.739**		
Globulin	0.105***	-0.053***	0.094***	0.244***	0.788**	-0.505*	0.242***	0.413*	0.239***
<b>Anthelmintic group</b>									
Eggs per gram of feces (EPG)	0.241***								
Haematocrit (Hct)	0.273***	0.412***							
Hb	-0.110***	-0.399***	0.904**						
Whole proteins	-0.147***	0.133***	0.346***	0.457*					
Albumin (Alb)	0.521*	-0.248***	0.616**	0.609**	0.582**				
EOS	-0.551*	0.142***	0.221***	0.404***	-0.146***	-0.015***			
Leukocytes (Leu)	-0.241***	-0.145***	0.543**	0.605**	0.185***	-0.063***	0.725**		
Globulin	0.296***	0.385***	0.143***	0.003***	0.675**	-0.208***	0.188***	0.165***	0.255***

\*\* $p < 0.01$ , \* $p < 0.05$ , \*\*\*ns,  $p > 0.05$ .

Correlation among values from different parameters was calculated using Pearson's correlation coefficient.

<sup>1</sup> Immunoglobulin (radial immune diffusion).

FEC remains an important parameter for evaluating the intensity of parasitic infection, however, if it is used as the only one parameter it may lead to incorrect conclusions. In this study, the FEC in animals from the homeopathy group was 50% lower than the FEC in the control and anthelmintic groups.

The mean FEC for the anthelmintic group baseline, on 18, 38 and 68 days were 729, 886, 1271 and 1229, respectively, demonstrating the low effectiveness of the product. These results are similar to those described in other flocks of sheep and goats in Northeast Brazil.<sup>22,23</sup>

In the present study, the mean reduction in the number of *H. contortus* larvae in the homeopathy group was highly significant in relation to the control group ( $p < 0.01$ ), suggesting a decrease in egg laying and a control of parasitism via increased immune response.

There was not significant reduction in the haematocrit and Hb concentrations during the peak period of parasitism. Hb concentration is the best parameter for monitoring the degree of anaemia. A highly significant correlation between FEC and haematocrit ( $r = -0.656$ ) and between FEC and Hb ( $r = -0.893$ ) was observed in the homeopathy group ( $p < 0.01$ ). In the control group, the correlation between FEC and haematocrit was  $r = -0.425$  ( $p < 0.05$ ) and the correlation between FEC and Hb was  $r = -0.624$  ( $p < 0.01$ ). The FEC correlations with haematocrit and Hb in the anthelmintic were very different than those in the

two other groups. The correlations coefficient between FEC-haematocrit and FEC-Hb ( $r = -0.412$  and  $-0.039$ , respectively) were not statistically significant.

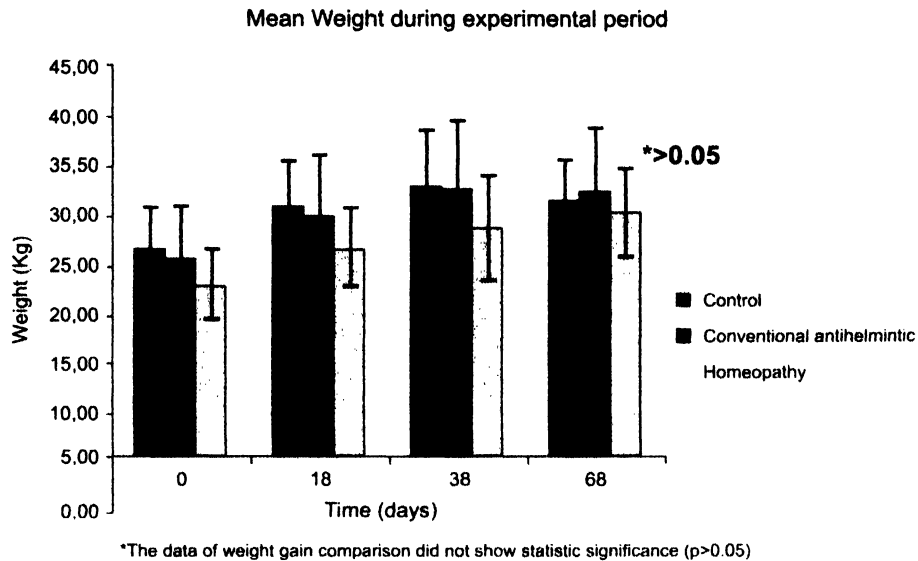
These results demonstrate the different responses to the homeopathic and anthelmintic treatments. Probably the homeopathic medicine acts by stimulating the entire body, while the conventional anthelmintic acts directly and exclusively on the nematodes. This led to a better recovery from haematopoiesis in the homeopathy group.

We observed a negative correlation between the number of eosinophils and FEC in the homeopathy group.

**Table 2** Differences between baseline and 68th day in leukocytes, IgG, immunoglobulin (IgG) ELISA and live weight gain

	Groups		
	Homeopathy	Anthelmintic	Control
Leukocyte	$4.63 \times 10^3$	$2.7 \times 10^3$	$4.34 \times 10^3$
IgG	693.57 mg/dL	601.85 mg/dL	488 mg/dL
Anti- <i>H. contortus</i> IgG (ELISA)	0.199 O.D.	0.081 O.D.	0.064 O.D.
Live weight gain	8.45 kg	7.90 kg	5.03 kg

Results are arithmetic mean of experimental groups and 68 day after treatment. Homeopathy group *Arsenicum album* and *Ferrum phosphoricum* alternately for a period 10 days, then they received *Calcarea carbonica* twice a day for 10 days, conventional anthelmintic doramectin (1 mL/50 kg, Dectomax<sup>®</sup>, Pfizer) and control group not treated.



**Fig. 2** Mean weight during experimental period. Homeopathy group, conventional antihelminthic group and control group after treatment on 18, 38 and 68 days. The animal body weight was also recorded before the first daily meal on the same day. The data of weight gain comparison did not show statistical significance.

suggesting that the homeopathic medicine stimulated the production of circulating eosinophils. Eosinophilia is one of the criteria for the selection of nematode resistant sheep.<sup>24</sup> EOSs can adhere and immobilize the invasive L3 larval stage of *H. contortus* in *in vitro* cultures in the presence of specific antiparasite antibodies.<sup>25</sup>

Although there were no significant differences in the concentration of total and specific IgG against *H. contortus* among the three groups, the animals of the homeopathy group showed higher values of IgG than the control and antihelminthic groups. Total immunoglobulins in this group presented a positive correlation with the globulins ( $r = 0.610$ ), while the other groups did not demonstrate a significant correlation, suggesting that the immune response was better in the homeopathy group. Immunity to parasitic infection may occur against the three stages of the nematode life cycle in the host. According to Gill and Husband,<sup>26</sup> 18-month-old sheep, genetically resistant to *H. Contortus*, have IgA and IgG antibody production peaks 2–4 times higher than non-resistant animals. There is a negative correlation between FEC and IgA and IgG levels, suggesting that these antibodies are directly responsible for the prevention of larvae establishment and participate indirectly in larvae elimination. In the present work, the results obtained in homeopathy group, suggest that the reduction of FEC and LPGF depends, at least in part, on plasma IgG levels.

The mean values of total serum proteins and albumin were similar in the two treatment groups and are consistent with normal values in sheep: 6.0–7.5 g/dL for protein and 2.4–3.0 g/dL for albumin. In this experiment the infected animals didn't show any decrease in blood protein level during any phase, even during the peak FEC periods.

Weight gain is an important parameter for evaluating the body condition of the animals when infected by helminthes. Economic losses are related to productivity indexes, in particular to decrease in body weight that can range from

20 to 60%.<sup>27–29</sup> The daily weight gain of the animals in the homeopathy group was higher than in the other groups. Our results showed that antihelminthic treated sheep gained 24.5% of weight compared to the animal control group; the homeopathy group gained 31%. These results would have a considerable impact in sheep flocks bred on a commercial scale.

Estimates of the financial burden of disease are beneficial in deciding priorities for control. The cost benefit analysis, showed a favourable trend for homeopathy compared to other groups. It has been suggested that homeopathy medicine may improve the efficiency of feed conversion and maximize investments.

## Conclusions

Treatment with homeopathic preparations of *Arsenicum album* and *Ferrum phosphoricum*, alternately, and *Calcarea carbonica*, showed favourable results in terms of parasitic, haematological values and weight gain compared to standard treatment and no treatment in lambs raised in Northeastern Brazil. Additional studies with more animals are required in order to confirm the results, to evaluate the homeopathic preparations and their separate effects.

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