Original Research

Oxfendazole in Combating Gastrointestinal Nematodes of Sheep and Goats

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Abstract

The environment and the farm practices of tropical and subtropical countries are congenial for various parasite infestations with reduced productivity in sheep and goats. The sulphoxide metabolite of fenbendazole, oxfendazole gains peak blood levels slowly, assuring maintenance of effective concentrations for a longer time. This improves the efficacy against immature larvae. The present study deals with the safety and efficacy of oxfendazole in sheep and goats. The reduction in egg per gram (EPG) count in treated and control groups was used to measure efficacy. No serious adverse events were observed in the study animals. Oxfendazole was effective in reducing the EPG by over 90% within 7 days of treatment denoting its efficacy in combating the parasitic infestation.

Key words: Efficacy, Goats, Nematodes, Oxfendazole, Sheep

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Introduction

The conventional farm practices and climatic stress in tropical and subtropical countries like India will result in increased parasite infestation. The increased parasitic burden subsequently causes reduced weight gain, reproductive performance and offspring production. Loss of protein by parasitic infestation stimulate the synthesis of replacement proteins by bypassing the proteins those are channeled into the production of wool, meat, and milk (FAO working group, 2004). The most important helminthic species found in various animals in India are- liver flukes, schistosomes, amphistomes, cestodes and gastrointestinal nematodes (Agrawal and Banerjee, 2007).

Oxfendazole belongs to benzimidazole group of anthelmintics and chemically it is methyl-5(6)-phenylsulfinyl-2-benzimidazole carbamate. As it is the sulphoxide metabolite of fenbendazole, it is responsible for the efficacy spectrum of fenbendazole. The pro-benzimidazole, febantel, also becomes fenbendazole, when it is metabolized and, finally, to oxfendazole. Oxfendazole is administered orally for treatment and control of gastro-intestinal roundworms, lungworms, and tapeworms in animals. By reaching peak blood levels rather slowly, oxfendazole maintain effective concentrations for a longer time in both the serum and the intestinal tract and broadens its efficacy against immature forms. Oxfendazole was reported to exhibit efficacy at a dose of 5.0 mg per kg of body weight (Baker *et al.*, 1978; Miller *et al.*, 1988; Bradley, 1989; Couvillion *et al.*, 1989). The efficacy of oxfendazole in cattle and buffaloes when administered at a dose of 5 mg per kg body weight was reported by Reddy *et al.* (2017). The product technical bulletin by European Medicines Agency (2004) reports its toxicity, tolerance, and field safety studies indicating its safe use in pregnant animals. Keeping in view of the above points, a field clinical study was planned to investigate the safety and efficacy of oxfendazole marketed by Indian Immunologicals Limited in sheep and goats.

Material and Methods

Animals and Treatments

The animals from villages surrounding Proddatur were enrolled in the study. The animals were reared in extensive system, where after grazing in the nearby fields, clean drinking water was provided at the farm. Mineral and vitamin supplements were provided to the young and pregnant animals. Not less than 40 sheep and goats above 3 months of age with worm burden were enrolled in the study. To minimize bias and variation, the animals having worm infestation, as denoted by Eggs per Gram (EPG) count of around 150 were enrolled in each study group (FAO Working Group, 2004). If any animals dewormed 12 weeks prior to the study and negative animals for any internal parasitic infestation were excluded from the study. Oxfendazole tablets manufactured and marketed by Indian Immunologicals Limited, Hyderabad (OXFENVET; Batch no. OXF 152 -150 mg) were used in the study. Oxfendazole was administered orally @ 5 mg/Kg body weight to all animals. The main parameters studied were safety of oxfendazole after administration and deworming efficacy, which was indicated by reduced EPG count after oxfendazole administration. The preferred method to evaluate the effectiveness in field studies is egg count/larval identification (VICH GL12, 1999).

Materials and Methods

Enrolled sheep and goats were randomly divided into two groups, one control (10 no. of animals) and second treatment group (30 no. of animals) per species based on faecal egg counts (EPG). The control

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(untreated) group was used for monitoring of natural changes in egg counts during the study period. As per VICH GL7 (2000), the controls animals should equal a minimum of 25% of the test product treated animal numbers. Two days before enrolment, dung samples were screened and animals exhibiting the inclusion/exclusion criteria were enrolled in the study. The general health status of the animals was recorded. The dung samples were analyzed by various methods like direct smear examination, sedimentation technique and floatation technique. At day 0, the selected animals were administered with oxfendazole according to the study design mentioned above. All the animals were monitored for adverse events during the study period. Dung samples were collected on 0^{th}, 3^{rd}, 7^{th}, 14^{th} and 21^{st}, days. All dung samples were processed and analyzed by McMaster egg counting technique for EPG counts at our laboratory for antiparasitic activity.

Evaluation of Efficacy

The efficacy was confirmed by the reduction of eggs per gram of faeces (EPG) count by more than 90 percent within 14 days of treatment.

Statistical Analysis and Interpretation of Data

From EPG counts at different time intervals, the geometric mean and percentage reduction were calculated. The more appropriate estimate of central tendency for EPG counts is geometric mean as it has less potential for misinterpretation than the arithmetic mean. In the case where some animals showing EPG counts is equal to zero, then the geometric means were calculated by adding 1 to all values in the group and later subtracting 1 from mean. The percentage reduction was calculated by the equation-

$$100(1-Xt/Xc)$$

Where, *Xt* was the mean egg count of the treated group and *Xc* was that of control group.

Efficacy was considered if the percentage reduction in egg counts was more than 90 percent.

Safety Evaluation

All animals observed for any adverse events and recorded the adverse events during the first 30 minutes to 1 hour after drug administration. The events, which were observed or reported during the entire study period, were also evaluated for safety. The adverse event was considered as a Serious Adverse Event (SAE) when the reaction resulted in death, was life-threatening, resulted in significant disability or incapacity or which resulted in permanent or prolonged signs in the animals treated with the drug under study. Apart from SAE, the animals were also observed for any systemic reactions like excessive salivation, diarrhoea, fever, loss of appetite (anorexia), restlessness and unsolicited systemic adverse events etc.

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Result and Discussion

Animal Demographics

Sheep

Total of 90 animal samples were screened for worm infestation out of which 50 were positive and 40 were included in study. The summary of demographics of sheep included in the study is presented below.

Table 1: Demographics of Sheep enrolled in the study

Group	No. of Animals	Breed	Mean Age (months) (Range)	Mean Weight (Kg) (Range)
1	30 (M-9; F-21)	Nellore-8; N.Jodipi-16; ND-6	18.7(6-36)	18.4 (9-35)
2	10 (M-2; F-8)	Nellore-2; N.Jodipi-6; ND-2	18.7(5-36)	18.2 (9-35)

Goats

Total of 100 animal samples were screened for worm infestation out of which 55 were positive and 40 were included in study. The summary of demographics of goats included in the study is presented below.

Table 2: Demographics of Goats enrolled in the study

Group	No. of Animals	Breed	Mean Age (months) (Range)	Mean Weight (Kg) (Range)
1	30 (M-10; F-20)	Non-Descript (ND)	17.6(6-36)	17.3 (8-35)
2	10 (M-2; F-8)		17.4(6-36)	17.7 (8-31)

Safety Results

Table 3: Summary of adverse events observed in sheep during the trial

Adverse Events	G1 (N=30)	G2 (N=10)
Systemic		
Salivation	0	0
Diarrhoea	2	0
Fever	0	0
Loss of appetite	0	0
Restlessness	0	0
Unsolicited systemic events	0	0

Two sheep of group 1 exhibited diarrhea 2 days after drug administration which was subsided later with symptomatic treatment.

Note

i. There were no SAEs observed in the trial in sheep.
ii. There were no SAEs or AEs observed in goats.

Efficacy

From different screening methods performed, we could able to find eggs in floatation technique in majority of the positive samples indicating the presence of gastro intestinal nematodes in the region. The major

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nematode species eggs found in the study were belonged to genera namely, *Trichostrongyle, Ostertegia, Haemonchus, Cooperia, Paracooperia and Nematodirus*. Hence, further analysis was performed by floatation technique to find out EPG count. Summary of the EPG counts in different species of animals is presented below.

Table 4: Mean (geometric) EPG counts of sheep on different days

Group	Day 0	Day 3	Day 7	Day 14	Day 21
1	461.9	416.6	39.5 (92.0%)	7.1 (98.7%)	4.3 (99.3%)
2	427.3	467.8	491.1	558.8	630.1

Table 5: Mean (geometric) EPG counts of goats on different days

Group	Day 0	Day 3	Day 7	Day 14	Day 21
1	435.7	406.2	18.1 (95.4%)	5.8 (97.9%)	2.8 (99.0%)
2	436.2	476.4	391	270.8	286

Values in brackets indicate percent reduction in EPG compared to control group

The study agent oxfendazole, manufactured and marketed by Indian Immunologicals Limited, has not shown any adverse events in sheep and goats during the study period. Further, the drug oxfendazole is effective in reducing EPG by above 90% by 7th day of treatment, and the antiparasitic effect increased till 21st day demonstrating the efficacy of oxfendazole against nematodes in sheep and goats.

Conclusion

From the study it can be concluded that the oxfendazole, manufactured and marketed by Indian Immunologicals Limited, Hyderabad is safe and effective in controlling gastrointestinal nematode parasites in sheep and goats.

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