

Efficacy of Oxfendazole against Gastrointestinal Nematodes in Cattle and Buffaloes: A Clinical Study

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Abstract: In tropical and subtropical countries, the husbandry practices and the environment is ideal for parasite infestation and subsequent reduced productivity in cattle. The most important parasites are liver flukes, schistosomes, amphistomes, cestodes and GI tract nematodes. Oxfendazole is the sulphoxide metabolite of fenbendazole and responsible for that efficacy spectrum of fenbendazole. Oxfendazole reaches peak blood levels more slowly, thereby maintaining effective concentrations for a longer time, which increases the efficacy against immature and inhibited larvae. In the present study safety and efficacy of oxfendazole marketed by Indian Immunologicals Limited was studied in cattle and buffaloes. The efficacy was determined by measuring the Egg per gram (EPG) count in treated and control animals at different time intervals after administration of oxfendazole. No adverse events were observed in the animals. Oxfendazole was found efficacious in reducing EPG by above 90% by 7th day. The antiparasitic effect increased and continued till 21st day indicating its efficacy in controlling the parasitic infestation.

Keywords: Buffaloes, cattle, efficacy, nematodes, oxfendazole,

I. Introduction and background

In mixed farming and extensive grazing systems practiced in tropical and subtropical countries, the environment is usually ideal for parasite infestation. This causes reduced productivity in terms of reduced weight gain, delayed and weak oestrus and lower calving rates and even greater impact is the lost production potential. The major effects are due to reduced feed intake and altered protein metabolism. Protein losses caused by parasites stimulate the synthesis of replacement proteins at the cost of energy and protein, which would normally be channeled into the production of meat and milk [1]. A large number of helminthic species are found in various animals in India, of which the most important are *liver flukes*, *schistosomes*, *amphistomes*, *cestodes* and gastrointestinal nematodes [2].

Oxfendazole is chemically methyl-5(6)-phenylsulfinyl-2-benzimidazole carbamate belongs to benzimidazole group of anthelmintics. It is the sulphoxide metabolite of fenbendazole and it is possible that efficacy spectrum of fenbendazole is due to its metabolite, oxfendazole. The pro-benzimidazole, febantel, when it is metabolized, also becomes fenbendazole, and finally oxfendazole. Oxfendazole administered orally to animals for treatment and control of gastro-intestinal roundworms, lungworms and tapeworms. Oxfendazole reaches peak blood levels more slowly from the intestinal tract than many of the older benzimidazoles, thereby maintaining effective concentrations for a longer time in both the serum and the intestinal tract. The persistence of effective concentrations increases the efficacy, particularly against immature and inhibited larvae. From various global efficacy studies the highest efficacy was seen at a dose of 5.0 mg oxfendazole/kg [3], [4], [5], [6]. Toxicity, tolerance, and field safety studies were reported for oxfendazole. A product technical bulletin by European Medicines Agency [7] stated that no effects on the foetus were reported following maternal exposure to oxfendazole during pregnancy in animals. Hence a field clinical study is planned to investigate the safety and efficacy of oxfendazole marketed by Indian Immunologicals Limited in cattle and buffaloes.

II. Material and Methods

2.1 Animals

All the animals enrolled in the study were from villages surrounding Proddatur. Not less than 40 numbers of animals for each species above 3 months of age with worm burden were enrolled in the study.

2.1.2 Inclusion Criteria

In order to minimize bias, only animals, which have worm infestation, as diagnosed by Eggs per Gram (EPG) count of around 150 were enrolled in each study group [1].

2.1.3 Exclusion Criteria

Animals underwent deworming treatment 12 weeks prior to the study and animals negative for any internal parasitic infestation were excluded.

2.2 Test Products and administration

Oxfendazole boli manufactured by Indian Immunologicals Limited, Hyderabad (OXFENVET; Batch nos. OXF 2201 (2200 mg) were used in the study. Oxfendazole was administered orally @ 5mg/Kg body weight to all animals. The main parameters studied were safety of oxfendazole after administration in animals and during the study period and deworming efficacy (as indicated by reduced EPG count) of oxfendazole. The preferred method to evaluate the effectiveness in field studies is Egg count/larval identification [8].

2.3 Study Design

Enrolled animals of each species were randomly divided into two groups one control (10 no. of animals) and one treatment group (30 no. of animals) per species of animals based on faecal egg counts. The control (untreated) group was used to allow for monitoring of natural changes in egg counts during the test period. The control animals should equal a minimum of 25% of the test product treated animal numbers [9].

2.4 Procedures

At base line (2 days before enrolment), dung samples were screened and animals meeting 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 enrolled 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 0th, 3rd, 7th, 14th and 21st, days. All dung samples were processed and analyzed by McMaster egg counting technique for EPG counts at our laboratory for antiparasitic activity.

2.5 Evaluation of efficacy

The effectiveness is confirmed if it could reduce the concentration of eggs per gram of faeces (EPG) by more than 90 percent within 14 days of treatment.

2.6 Statistical Analysis and Interpretation of data

From EPG counts at different time intervals, the geometric mean and percentage reduction were calculated as geometric mean is a more appropriate estimate of central tendency for EPG counts and has less potential for misinterpretation than the arithmetic mean. In the case where some animals showing EPG counts=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 = $100(1-X_t/X_c)$

Where X_t is the mean egg count of the treated group and X_c is that of control group.

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

2.7 Safety evaluation

Safety evaluation performed by observing and recording the adverse events observed 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.

2.7.1 Adverse Events (AEs)

The animals were observed for any systemic reactions like excessive salivation, diarrhoea, fever, loss of appetite (Anorexia), restlessness and systemic adverse events etc.

2.7.2 Serious Adverse Events (SAEs)

The adverse event was considered as a 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.

III. Results

3.1 Animal Demographics

3.1.1 Cattle:

Total of 110 animal dung samples were screened for worm infestation out of which 57 were positive and 40 were included in study. The summary of demographics of cattle included in the study is presented below.

Group	No of animals	Breed	Mean Age (months) (Range)	Mean Weight (Kg) (Range)
1	30 (M-9; F-21)	HF cross-18; Jersey cr-5; Ongole-7	36.2(4-72)	289.2 (70-500)
2	10 (M-3; F-7)	HF cross-8; Ongole-2	32.4 (6-60)	262.0 (90-450)

M-Male; F-Female; HF- Holstein Friesian

3.1.2 Buffaloes

Total of 150 animal samples were screened for worm infestation out of which 58 were positive and 52 were included in study. The summary of demographics of buffaloes included in the study is presented below.

Group	No of animals	Breed	Mean Age (months) (Range)	Mean Weight (Kg) (Range)
1	32 (M-7; F-25)	Graded Murrah	33.0(4-72)	274.4 (90-500)
2	10 (M-3; F-7)	Graded Murrah	31.5 (5-72)	288.5 (75-500)

M-Male; F-Female

3.2 Safety results

There were no AEs or SAEs observed in cattle and buffaloes during the study.

3.3 Efficacy

From different screening methods performed, we could find eggs in floatation technique in majority of the positive samples indicating the presence of gastro intestinal nematodes in the region. The major nematode species eggs found in the study belonged to genera namely, *Trichostrongyle*, *Ostertagia*, *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.

Mean (Geometric) EPG counts on different days in cattle

Group	Day 0	Day 3	Day 7	Day 14	Day 21
1	340.3	302.4	7.7 (97.9%)	2.8 (99.2%)	2.7 (99.3%)
2	353.8	335.8	362.4	358.7	374.8

Mean (Geometric) EPG counts on different days in Buffaloes

Group	Day 0	Day 3	Day 7	Day 14	Day 21
1	320.3	295.6	9.1 (97.4%)	3.7 (99.0%)	2.9 (99.2%)
2	333.2	340.7	353.4	354.3	356.3

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

IV. Discussion and conclusion

Oxfendazole, manufactured and marketed by Indian Immunologicals Limited, has not shown any adverse events in two species of the animals under study. The oxfendazole treatment group was efficacious in reducing EPG by above 90% by 7th day. The antiparasitic effect increased and continued till 21st day indicating the efficacy of oxfendazole against nematodes in cattle and buffaloes. 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 cattle and buffaloes.

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