

Research Article



Comparative Efficacy of Triclabendazole, Oxytoclozanide and Nitroxylin against Bovine Fasciolosis in Gomal Zam Dam Command Areas of District Tank, Khyber Pakhtunkhwa

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Abstract | The objective of this investigation was to assess the efficacy of three distinct anthelmintics; oxytoclozanide, nitroxylin and triclabendazole, in the treatment of *Fasciola hepatica* species in cattle that have contracted the disease naturally at a dairy farm in district Tank, Khyber Pakhtunkhwa. The trial involved the selection of 40 dairy cattle, which were divided into three treated groups and one untreated control group. A single anthelmintic drug was administered to each cohort on day zero. Fecal samples were collected from each animal in the groups on the first, seventh, fourteenth, twenty-eighth, sixty-fifth and eightieth days following treatment. The efficacy of the anthelmintics was determined by the percent reduction in fecal egg count, which was conducted using the McMaster technique. The fecal egg count was reduced by 100% on the 28th day post-treatment and oxytoclozanide and nitroxylin treated groups exhibited high efficacy against *Fasciola hepatica*. Simultaneously, triclabendazole group demonstrated lower efficacy levels in this trial, with a maximal reduction in fecal egg count (93.74%) and a mean value of 90.23% post-treatment. Nitroxylin and oxytoclozanide were more effective against the *Fasciola hepatica* species than triclabendazole, as indicated by these results. The results of the triclabendazole study indicated that the *Fasciola hepatica* species in dairy cattle in the Tank Area are developing resistance to the drug.

Keywords | *Fasciola hepatica*; Nitroxylin; Oxytoclozanide; Triclabendazole.

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INTRODUCTION

Pakistan is an agricultural country in which the livestock sector occupies a significant portion of the economy. According to the 2022-23 economic survey conducted by the Ministry of Finance of the Government of Pakistan, livestock account for 62.68 % of the agricultural sector and

14.36 % of the overall GDP, with a growth rate of 3.78 % (Government of Pakistan, 2023). The economy of Pakistan is ultimately adversely affected by the negative impact of a variety of helminth parasites on livestock, particularly ruminants, which adversely affect feed intake, growth rate, fiber growth, reproductive performance, milk yield, and carcass quality and quantity (Batool et al., 2022).

Fasciola hepatica is one of the most prevalent parasites that infect dairy cattle worldwide (Hamel et al., 2024). It is geographically widespread in Asia, Africa, Europe, Americas and Oceania, as well as other temperate countries and regions (Mas-Coma et al., 2005). The consistent administration of fasciolicidal medications is a control strategy for fasciolosis in ruminants (Castro-Hermida et al., 2021).

The probability of resistance development against a drug, such as trichlabendazole or any other anthelmintic, is increased when the same drug is administered on a regular basis on the same dairy farm (Olaechea et al., 2011). Triclabendazole has been reported to be the most effective fasciolicidal drug so far against both infantile stage flukes (93–98%) and mature flukes (up to 100%) (Boray et al., 1983). Nevertheless, resistance to triclabendazole is arising. This phenomenon was initially observed in Australia (Overend and Bowen, 1995), Netherlands (Borgsteede et al., 2005; Moll et al., 2000) and also in Spain, where resistance to triclabendazole and other members of the benzimidazole group was reported (Alvarez-Sa'ñchez et al., 2006). The efficacies of the fasciolicidal drug nitroxynil in dairy cattle against adult stages of *Fasciola hepatica* were 99.1% (Richards et al., 1990) and 100% (Rapic et al., 1988). Oxytoclozanide is also efficacious against adult stages of triclabendazole-resistant flukes (Coles et al., 2000; Coles and Stafford, 2001; Moll et al., 2000).

To preserve anthelmintic efficacy and prevent production losses, it is recommended to identify dairy animals or herds with helminth-induced production losses and target anthelmintic treatment to these subgroups in response to the recent rise in anthelmintic resistance reports worldwide (Charlier et al., 2014).

In Gomal Zam Dam command area of the Tank district, the objective of the present investigation was to evaluate the efficacy of commercially available fasciolicide medications against *Fasciola hepatica* and the resistance that *Fasciola hepatica* has developed.

MATERIAL AND METHODS

ETHICAL APPROVAL

Ethical approval of study was granted by the Station Director, Veterinary Research Institute, Dera Ismail Khan, vide Notification No. VR&DIC/DIK/ATRP/2022-23.

STUDY AREA

The study was conducted in the Gomal Zam Dam command area of Tank District, characterized by its humid climate and limited annual rainfall (approximately 121.11 mm). This area is critical for local agriculture, influencing both forage availability and livestock health. The region ex-

periences mild winters (average temperature around 4°C) and extremely hot summers (average temperature up to 42°C), conditions that can affect the lifecycle and transmission dynamics of *Fasciola hepatica*.

STUDY PERIOD

The investigation spanned from July 2022 to June 2023, with sample collections during the colder months of January and February and spring months of March and April. This period coincides with significant lifecycle stages of *Fasciola hepatica*, expected to peak following the rainy season, influencing the prevalence and detectability of infection.

ANIMALS SELECTION AND MANAGEMENT

Forty dairy cattle exhibiting symptoms of *Fasciola hepatica* infection were selected irrespective of their reproductive status (dry, milking, or pregnant). Management practices, including diet (green forage like berseem and barley, wheat straw, vanda (concentrate), and mineral supplements), were standardized across groups to minimize variations in nutritional status which could affect drug efficacy.

EXPERIMENTAL DESIGN AND PROCEDURE

Fecal samples were collected directly from the rectum of all animals at the dairy farm prior to the commencement of drug application. The samples were stored at 4°C in individual screw-capped plastic bottles that were labelled, transported and examined under a 40X microscope in the laboratory at the Veterinary Research Center Tank. The egg count was conducted and recorded using the McMaster technique, which involves counting eggs in a fixed volume of fecal suspension. This technique is standardized by presenting the egg count per 4 grams of feces to improve the accuracy and reliability of the parasite burden estimate. It is recommended to use 4-5 grams of feces for a standard fecal examination (for reference, a Hershey's Kiss weighs approximately 4.6 grams). While accurate fecal flotations can be performed with a minimum of 1 gram of feces, using less than this amount may reduce the ability to detect parasites effectively.

Forty animals that were positive were chosen. The positive animals were divided into four groups, with ten animals in each cohort. The control group was Group 1. The control group did not receive any treatment. trichlabendazole, oxytoclozanide and nitroxynil were administered as individual drugs to Groups 2, 3 and 4, respectively. Fecal samples were collected on 1st, 7th, 14th, 28th, 56th and 84th days following treatment. The McMaster technique was employed to conduct the fecal egg count of *Fasciola hepatica* on each occasion.

In the study, specific days for sampling were chosen based

on the expected action of the anthelmintics and the life-cycle of the parasite, *Fasciola hepatica*. Day 1 served to establish a baseline immediately after treatment. By Day 7, the drugs would have been absorbed and begun affecting the parasites, allowing early assessment of their efficacy. Sampling on Day 14 offered insights into the sustained effects of the treatments, checking if the drugs continued to suppress or eliminate the parasite load effectively. Each of these points helped to evaluate the initial and ongoing response to the anthelmintics used in the study.

STATISTICAL ANALYSIS

The data was verified for validity following the data collection process. Subsequently, the laboratory examination results were meticulously documented in well-organized format. The data generated from this study was stored in Microsoft Excel (2010), and statistical analysis was done using SPSS version 20.0. Statistical significance was set at $p < 0.05$.

The statistical methodologies employed in the trial included calculating the mean, standard error mean (SEM) and efficacy percentages for all treatment groups. The p -values were calculated to determine the statistical significance of differences observed between the groups. A one-way ANOVA followed by Tukey's post hoc test was performed to compare the means of different groups at various time points. The efficacy of the anthelmintic was assessed based on the percentage reduction in fecal egg count, calculated using the formula:

$$\text{Efficacy (\%)} = \frac{(\text{Pre-treatment EPG} - \text{Post-treatment EPG})}{\text{Pre-treatment EPG}} \times 100$$

RESULTS

The mean fecal egg count (EPG) was assessed at the following time points: the 1st day, 7th day, 14th day, 28th day, 56th day and 84th day, following treatment with three distinct anthelmintics: Nitronil, Oxcyclosanide and Triclabendazole. On the first day, there was no statistically significant difference in EPG between the control group and the treated groups ($p > 0.05$). This suggested that the anthelmintics had not yet begun to have a significant impact on the fecal egg counts. The EPG of all treated groups was significantly lower than that of the control group by the seventh day ($p < 0.05$). Oxcyclosanide, triclabendazole, and nitroxynil each reduced the EPG to 3.1 ± 0.2 , 3.5 ± 0.3 and 9.8 ± 1.2 , respectively, indicating their efficacy in reducing egg counts. The significant decrease in EPG for all treated groups persisted on the 14th day ($p < 0.05$). The EPGs

were further reduced to 0.2 ± 0.2 for nitroxynil, 0.8 ± 0.3 for oxcyclosanide and 5.1 ± 0.5 for triclabendazole. The ova were completely eliminated by nitroxynil and oxcyclosanide on the 28th day ($\text{epg} = 0$), while the count was reduced to 4.6 ± 0.3 by triclabendazole. The disparities persisted ($p < 0.05$). The treatments' efficacy was sustained through the 56th day, as EPGs remained low in all treated groups ($p < 0.01$). Triclabendazole exhibited a slightly higher count of 6.5 ± 0.3 , while nitroxynil and oxcyclosanide continued to exhibit extremely low counts of 2.1 ± 0.3 and 1.1 ± 0.4 , respectively. EPG in all treated groups showed a modest increase by the 84th day, but they remained significantly lower than the control group ($p < 0.01$). Nitroxynil's EPG was 4.4 ± 0.7 , oxcyclosanide's was 2.7 ± 0.4 and triclabendazole's was 9.9 ± 0.6 . These findings indicated that all three anthelmintics were efficacious in reducing fecal egg counts, with nitroxynil and oxcyclosanide demonstrating slightly higher efficacy than triclabendazole. (Table 1).

The efficacy of all three anthelmintics was 0% on the first day, suggesting that there was no immediate effect ($p > 0.05$). All treated groups exhibited substantial efficacy by the 7th day ($p < 0.05$). Efficacy was attained by nitroxynil at 96.0%, oxcyclosanide at 94.48% and triclabendazole at 86.65%. The efficacy of nitroxynil, oxcyclosanide and triclabendazole further improved on the 14th day ($p < 0.05$). the 28th day showed the highest efficacy ($p < 0.05$), with both nitroxynil and oxcyclosanide achieving 100% efficacy. On 56th day, the efficacy of nitroxynil, oxcyclosanide and triclabendazole decreased marginally ($p < 0.01$), but it remained high at 97.23%, 98.26%, and 91.15%, respectively. On the 84th day, the efficacy percentages for nitroxynil, oxcyclosanide and triclabendazole were 94.32, 95.75 and 86.53%, respectively ($p < 0.01$). The results of this study underscored the high efficacy of oxcyclosanide and nitroxynil in reducing fecal egg counts, as they achieved complete elimination on the 28th day. Triclabendazole was also effective, although its efficacy was marginally lower than that of the other two drugs. Nitroxynil and Oxcyclosanide were the most effective anthelmintics in this study, demonstrating consistent and high efficacy throughout the treatment period (Table 2).

DISCUSSIONS

In most global regions, fasciolosis is one of the most prevalent and significant helminthic diseases affecting ruminants. The infection rate of *Fasciola hepatica* in cattle is primarily chronic and significant. The severe liver damage caused by the infection leads to reduced feed intake, weight gain, milk production, and reproductive performance, which has a substantial economic impact.

The efficacy of the drugs triclabendazole, oxcyclozanide,

Table 1: The mean fecal egg count per 4 grams of feces following the administration of the three anthelmintic

Post-Treatment Days	Control	Nitroxynil (EPG)	Oxyclosanide (EPG)	Triclabendazole (EPG)	p-value
1 st day	68.6±3.7	77.6±3.1	63.5±3.8	73.5±3.6	0.132
7 th days	67.2±2.6	3.1±0.2	3.5±0.3	9.8±1.2	0.004*
14 th days	65.0±2.2	0.2±0.2	0.8±0.3	5.1±0.5	0.028*
28 th days	63.1±2.5	0	0	4.6±0.3	0.019*
56 th days	66.0±2.44	2.1±0.3	1.1±0.4	6.5±0.3	0.001*
84 th days	68.5±1.8	4.4±0.7	2.7±0.4	9.9±0.6	0.001*

* p<0.05

Table 2: Efficacy percentages of three anthelmintics against fasciolosis.

Post-Treatment Day	Nitroxynil - Efficacy %	Oxyclosanide - Efficacy %	Triclabendazole - Efficacy %	p-value
1 st day	0	0	0	1.00
7 th days	96.0	94.48	86.65	0.047*
14 th days	99.74	98.74	93.06	0.040*
28 th days	100.0	100.0	93.74	0.029*
56 th days	97.23	98.26	91.15	0.001*
84 th days	94.32	95.75	86.53	0.001*
Average efficacy	97.46	97.45	90.23	0.001*

* p<0.05

and nitroxynil was assessed on a dairy farm located in the Gomal Zam Dam command area of Tank District in the present study. Cattle treated with triclabendazole showed a maximum reduction of 93.74% in eggs per gram (EPG) on the 28th day and a minimum reduction of 86.53% on the 84th day against *Fasciola hepatica*. Bulent et al. (2006) reported similar results, with efficacy ranging from 98.5% to 100%. Keyyu et al. (2006), Hassan et al. (2012), and Sanabria et al. (2013) also reported efficacy against naturally occurring *Fasciola hepatica* infections in sheep and cattle. Rapic et al. (1988) found an efficacy of 96.5%, while Lecuyer et al. (1985) reported a slightly lower efficacy of 90% in cattle. Mooney et al. (2009) observed 49–66% efficacy of triclabendazole in sheep on a hill farm in western Ireland, which was interpreted as an indication of developing resistance to triclabendazole (Coles et al., 2000). Additionally, Coles and Stafford (2001) confirmed resistance of adult liver flukes to triclabendazole.

The efficacy values for triclabendazole in the current study are lower compared to the other two anthelmintics and previous studies. This discrepancy may be attributed to the development of resistance in *Fasciola hepatica*. Triclabendazole is commonly provided at no cost to local farmers at civil veterinary hospitals, which may contribute to its frequent use in the region. On the 28th day, the oxyclozanide-treated group achieved a 100% reduction in eggs per gram (EPG), similar to the results reported by Shokier et al. (2013) and Athar et al. (2011). Paraud et al. (2009) found oxyclozanide to be 95.9% effective against liver

flukes, and Mooney et al. (2009) reported over 98% efficacy in sheep against *Fasciola hepatica*. However, the efficacy values observed in the oxyclozanide-treated group did not align with those of Babiker et al. (2012) and Khan et al. (2017), who reported efficacy values ranging from 64.57% to 86.16% and 80.40%, respectively.

On the 28th day post-treatment, the nitroxynil-treated group also demonstrated a 100% reduction in EPG count. Durrani et al. (2007) and Khanam et al. (2015) reported efficacies of 93.88% and 83.04%, respectively, for nitroxynil against liver flukes. Similar results have been observed in cattle by other researchers, such as Asaduzzaman (2008) and Wahaab et al. (2019). The EPG count results for the untreated control group remained virtually unchanged, with only minor fluctuations in egg counts throughout the study.

The study’s results have significant implications for local farmers and veterinarians in managing bovine fasciolosis. The findings indicate that oxyclozanide and nitroxynil are highly effective against *Fasciola hepatica*, making them preferable treatment options in areas where triclabendazole resistance is a concern. This insight can aid in selecting the most effective anthelmintics, potentially reducing the incidence of fasciolosis and improving livestock health and productivity. Additionally, the results underscore the importance of regular monitoring for drug resistance to ensure the sustainable use of anthelmintics in local veterinary practices.

The study demonstrated that oxclozanide and nitroxylnil are highly effective against *Fasciola hepatica*, showing near-complete efficacy with no evidence of drug resistance. In contrast, triclabendazole exhibited diminished efficacy, likely due to the development of resistance in the local *Fasciola hepatica* population. Consequently, oxclozanide and nitroxylnil are recommended as the preferred treatments for this condition.

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CONFLICT OF INTEREST

There are no conflicts of interest.

NOVELTY STATEMENT

This study provided comparative analysis of the efficacy of three anthelmintics; triclabendazole, oxclozanide, and nitroxylnil, against bovine fasciolosis in Ditrit Tank, Khyber Pakhtunkhwa. The research uniquely highlighted the emerging resistance of *Fasciola hepatica* to triclabendazole, a commonly used fasciolicide, while demonstrating the superior efficacy of oxclozanide and nitroxylnil. This study is the first of its kind in this region, offering critical insights into effective fasciolosis management practices and guiding local veterinarians and farmers in selecting the most appropriate treatments to combat this pervasive parasitic infection.

AUTHOR'S CONTRIBUTION

Akhtar Ali conceptualized and supervised the study, Imtiaz Khan conducted the investigation, Umme Aimen and Waseem Ullah analysed the data, Arsalan Khan and Qamar Ullah compiled the data and helped in writing the original draft.

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