

COMPARATIVE STUDY ON IVERMECTIN PLUS CLORSULON AND NITROXYNIL IN TREATMENT OF FASCIOLIASIS IN CATTLE

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ABSTRACT

A controlled trial was conducted to compare the current efficacy of ivermectin plus clorsulon (Alfamectin super®) and nitroxy nil (Tronex®) against *Fasciola gigantica* in naturally infested cattle. This trial was conducted in Sharkia Province. Twenty four male Frezian cattle, (18-24) months old and ranged from (150-180) kgm /animal were selected based on finding eggs of *F. gigantica* in their faeces. The cattle were weighted and randomly allotted into four groups each of 6 animal and treatments were as follows: Group 1 served as non-infested non-treated control. Group 2 was naturally infested with *F. gigantica* and non-treated. Group 3 was infested and treated with ivermectin plus clorsulon at dose level of 1ml/ 50 kg bwt. administered subcutaneously (SC), and Group 4 was infested and received nitroxy nil at dose level of 1ml/25 kg bwt by SC injection. Individual faecal samples were collected before treatment (zero day) and on 1st, 2nd, 3rd and 4th week post treatment (PT), while blood samples were collected before treatment on zero day and on 7th, 14th and 28th day post treatment. The drug efficacy was assessed as a percentage of egg reduction (faecal egg count reduction percent FECR %). Body weight was recorded on zero day and on 2nd, 4th, 6th and 8th week PT. Biochemical, haematological findings and body weight gain were recorded relative to the infested untreated control. The present results showed that FECR% of group 3 was 69.1 ± 2.3 , 87.3 ± 0.6 , 94.5 ± 0.2 , and 100% while group 4 showed that FECR% was 73.2 ± 0.6 , 90.2 ± 0.3 , 97.6 ± 0.1 and 100% on 1st, 2nd, 3rd and 4th week post treatment (PT) respectively. There were no significant differences between the two drugs on liver and kidney functions as well as blood picture. In contrast, ivermectin plus clorsulon treated group showed more significant increase in body weight than nitroxy nil treated group.

INTRODUCTION

Fascioliasis is one of the most important parasitic debilitating diseases in ruminants. It is primarily a zoonotic disease caused by four species of trematodes, caused chiefly by *Fasciola gigantica* and *Fasciola hepatica* in the main bile duct⁽¹⁾. It has world wide distribution and high incidence in endemic areas.

It is a sequence of acute parenchymal hepatitis and chronic cholangitis, characterized by loss of weight, anemia, oedema and eosinophilia. It attacks all classes of grazing sheep and cattle causing extensive financial wastes. Economic losses result from inefficient conversion of food, retardation of growth, deaths, condemnation of infested livers, reduced meat and milk production in addition to predisposition of other diseases. Both the immature and mature liver flukes infection cause serious damage to the host liver producing liver hypertrophy and hepatic cirrhosis⁽²⁾. Infestation usually takes place by the ingestion of encysted metacercaria with the grass or drinking water⁽³⁾. It has been recorded that cattle infested with *F. hepatica* showed a decrease in RBCs, haemoglobin (Hb), packed cell volume (PCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and iron concentration⁽⁴⁾. An increase in the activity of serum transaminases (AST, ALT), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT) and WBCs counts was also recorded. Significant decrease in total serum proteins and albumin was recorded, while a significant increase in total globulins were observed⁽⁵⁾.

The development of new anthelmintics for use in live stock has been probably the most rapidly expanding area in the field of pharmaceutical research of recent years.

Ivermectin is an avermectin used for elimination of internal and external parasites in cattle, sheep, goats and camels. It is a fermentation product of *Streptomyces avermitilis*. It acts as a GABA agonist, causing paralysis of susceptible arthropods and nematodes; it also inhibits the enzymes implicated in the glycolytic pathway, the primary source of energy in flukes⁽⁶⁾. Clorsulon is a compound belonging to the benzenesulphonamide family given per os as a suspension for infections with (mainly) adult liver flukes in sheep and cattle and as a SC injection for cattle in combination with ivermectin. In plasma, clorsulon is bound to protein and when ingested by liver flukes, inhibits enzymes of the glycolytic pathway. Although its safety margin is wide, clorsulon is not licensed for use in lactating dairy cows producing milk for human consumption⁽⁷⁾.

Ivermectin plus clorsulon combination (Alfamectin super®), each ml contain 10mg ivermectin and 100 mg clorsulon, is widely used in the field as endectocide, used for elimination of external and internal parasites including liver flukes in cattle, sheep, goat and camels⁽⁸⁾.

Nitroxy nil (Tronex®) is a halogenated phenol, used as a fasciolicide, acting by uncoupling oxidative phosphorylation. It acts mainly on mature flukes and less on immature ones⁽⁹⁾.

This study was undertaken to compare the efficacy of ivermectin plus clorsulon, and Nitroxy nil in treatment of cattle naturally infested with *Fasciola gigantica* with special reference to their effects on liver and kidney functions, haematological changes, body weight and % reduction in faecal egg count in treated animals.

MATERIALS AND METHODS

Materials:

Animals:

The present study was performed on 24 male Frizian cattle aged from 18-24 months and weighed (150-180) kg/animal, they were fed on concentrated ration and tiben. They were belonged to Elbetar farm in Kafr saker, Sharkia province.

Drugs:

- 1- Ivermectin plus clorsulon (Alfamectin super)[®] is an injectable solution for the treatment of ecto and endo parasites in cattle, sheep and camel, manufactured by Arabcomed Com., each ml contains 10 mg Ivermectin and 100 mg clorsulon, its dose is 1 ml/50 Kg bwt, injected SC.
- 2- Nitroxylin (Tronix 25%)[®] is injectable solution for the treatment of fascioliasis (*F. hepatica* and *F. gigantica*) in cattle, and sheep, manufactured by Kahira Pharm. and Chem. Ind. Co., the standard dosage is 10 mg Nitroxylin/kg Bwt (1 ml Tronix /25kg bwt) injected SC.

Experimental design:

Animals used in this study were grouped into four equal groups (6 animal/each): 1st group (G1) was non-infested non-treated, 2nd group (G2) was naturally infested with *F. gigantica* and non treated, 3rd group (G3) was naturally infested with *F. gigantica* and treated with ivermectin plus clorsulon (1ml/50kg bwt SC), 4th group (G4) was naturally infested with *F. gigantica* and treated with nitroxylin (1ml/25kg bwt SC).

Specimens:

Individual faecal samples were collected before treatment (zero day) and on 1st, 2nd, 3rd and 4th week post treatment (PT), while blood samples were collected on zero day and on 7th, 14th and 28th day post treatment. Faecal samples were collected from each animal directly from the rectum in poly-ethylene sacs and examined for detection of the eggs of *F. gigantica* and counting the eggs to determine the severity of infestation. Faecal samples were examined by direct smear concentration method and egg count by (McMaster technique).

Blood samples were collected for biochemical and haematological findings (heparinized for

and kidney function tests).

Animals were weighted at the beginning of experiment and on 2nd, 4th, 6th and 8th week post-treatment.

Methods:

- 1) Faecal examination include direct smear method according to⁽⁹⁾ and McMaster technique⁽¹⁰⁾.
- 2) Haematological studies include: blood cell count⁽¹¹⁾, blood haemoglobin⁽¹²⁾, packed cell volume (PCV)⁽¹³⁾, red blood indices⁽¹⁴⁾ and they include Mean corpuscular volume (MCV) and Mean corpuscular haemoglobin (MCH) and Mean corpuscular haemoglobin concentration (MCHC).
- 3) Biochemical studies include: serum transaminases (AST and ALT)⁽¹⁵⁾, gamma-glutamyl transpeptidase (GGT)⁽¹⁶⁾, and serum alkaline phosphatase (ALP)⁽¹⁷⁾.

Determination of transferrin according the method of Mancini⁽¹⁸⁾, total and direct serum bilirubin⁽¹⁹⁾, serum total proteins⁽²⁰⁾, albumin⁽²¹⁾ while serum globulins were determined by subtracting serum albumin from the amount of total serum proteins and albumin/globulin ratio was also calculated. Determination of serum urea level and creatinine were determined according to the method of Chaney and Marbach⁽²²⁾ and Husdan and Rapoport⁽²³⁾ respectively.

Statistical analysis:

Data were collected, summarized and analyzed by using one way anova (F test), the comparison between mean by using LSD (least significant difference) according to SPSS⁽²⁴⁾.

RESULTS AND DISCUSSION

The efficacy of tested drugs on cattle naturally infested with *F. gigantica*:

The present results illustrated in table (1) showed that the pre-treatment egg count per gram faeces (epg) in infested groups was 3249.0 ± 192.9.

Faecal egg count reduction % (FERC %) of ivermectin plus clorsulon treated group (G3) was 69.1 ± 2.3, 87.3 ± 0.6, 94.5 ± 0.2, and 100% respectively, while in group 4 FERC% was 73.2 ± 0.6, 90.2 ± 0.3, 97.6 ± 0.1 and 100% on 1st, 2nd, 3rd and 4th week (PT) respectively.

Table (1). The efficacy of Ivermectin plus clorsulon (1ml/50kg bwt, SC) and Nitroxylin (1ml/25kg bwt, SC) on faecal egg count reduction percent (FERC%) and egg count per gram faeces (epg) in cattle naturally infested with *Fasciola gigantica* [(Mean ± SE.) n=6]

Group	Time	Zero time (before treatment)		Weeks post treatment							
		epg	FERC%	1 st		2 nd		3 rd		4 th	
				epg	FERC%	Epg	FERC%	epg	FERC%	epg	FERC%
Ivermectin plus clorsulon (G3)		3249.0	0.0	1025.2	69.1	124.5	87.3	148.5	94.8	0	100%
		± 192.9	%	± 14.5	± 2.3	± 18.7	± 0.6	± 4.8	± 0.2		
Nitroxylin (G4)		3249.0	0.0	971.8	73.2	258.8	90.2	57.3	97.6	0	100%
		± 192.9	%	± 3.1	± 0.6	± 7.96	± 0.3	± 3.02	± 0.1		

These results were similar to that obtained previously⁽²⁵⁾ who found that both ivermectin plus clorsulon (ivomec-super) and nitroxylin (itrodax 35%) was highly effective in treatment of Ayrshire cattle naturally infested with *F. gigantica* in Tanzania, while nitroxylin efficacy in cattle naturally infested with *F. hepatica* was 95%⁽²⁶⁾. It has been found that the efficacy of clorsulon was 97.9% in cattle infested with *F. hepatica* compared with some commercial compounds in naturally infested cattle⁽²⁷⁾.

Büscher et al.⁽²⁸⁾ recorded that the efficacy of clorsulon and nitroxylin against *F. hepatica* infection in cattle was 99.0% and 99.1% respectively.

The efficacy of ivermectin plus clorsulon combination at dose of (2mg/kgmBwt clorsulon and 200 microgm/kgmBwt ivermectin) was 100% against

mature liver fluke in cattle infested with *F. hepatica* in Mexico⁽²⁹⁾, while efficacy of clorsulon was 84.2% against mature flukes of *F. hepatica* in naturally infested cattle in Turkey during the spring (the time of year when liver fluke infestation is endemic) and it is the highly effective compound on them⁽³⁰⁾.

Effect of tested drugs on liver and kidney function:

These results were illustrated in table (2). ALT is an enzyme produced in hepatocytes, the major cell type in the liver, the level of ALT in the blood is increased in conditions in which hepatocytes are damaged. AST is an enzyme similar to ALT but less specific for liver disease as it is also produced in muscle and can be elevated in other conditions. All types of hepatitis cause hepatocyte damage leading to elevation of serum ALT and AST⁽³¹⁾.

Table(2): Effect of Ivermectin plus clorsulon(1ml/50kg bwt,SC) and Nitroxylin (1ml/25 kg bwt,SC) on liver and kidney function of cattle infested with *F. gigantica* [(Mean ± S.E.) (n=6)]

Parameter	Group	Control Non infested (G1)	Control Infested (G2)	Ivermectin plus clorsulon (G3)			Nitroxylin (G4)		
				7days PT	14 days PT	28 days PT	7days PT	14 days PT	28 days PT
AST (U/L)		36.6 ^c ± 0.2	62.2 ^{ll} ± 0.5	54.8 ^b ± 0.8	47.9 ^b ± 0.2	39.9 ^c ± 0.2	57.1 ^b ± 0.5	50.1 ^b ± 0.4	41.4 ^c ± 0.1
ALT (U/L)		30.3 ^d ± 0.4	66.5 ^a ± 0.9	59.2 ^b ± 0.5	54.2 ^c ± 0.6	49.9 ^b ± 0.2	61.9 ^b ± 0.4	57.9 ^c ± 0.2	50.7 ^b ± 0.4
ALP (kind and king)		28.6 ^d ± 0.2	57.1 ^a ± 0.4	38.1 ^c ± 0.4	31.9 ^{bc} ± 0.2	28.9 ^c ± 0.3	39.1 ^c ± 0.2	35.9 ^b ± 0.8	30.0 ^b ± 0.1
GGT (U/L)		20.4 ^d ± 0.5	67.5 ^a ± 0.8	59.4 ^b ± 0.4	53.8 ^b ± 0.4	40.8 ^b ± 0.4	58.3 ^b ± 0.2	52.7 ^b ± 0.3	41.7 ^b ± 0.3
Total bilirubin mg/dl		0.6 ^c ± 0.1	1.9 ^a ± 0.03	1.6 ^b ± 0.1	1.3 ^b ± 0.03	1.02 ^b ± 0.01	1.4 ^b ± 0.1	1.2 ^c ± 0.02	0.9 ^b ± 0.04
Direct bilirubin mg/dl		0.3 ^d ± 0.1	0.9 ^a ± 0.1	0.6 ^b ± 0.02	0.4 ^b ± 0.04	0.3 ^b ± 0.04	0.6 ^b ± 0.03	0.4 ^b ± 0.1	0.3 ^b ± 0.02
Transferrin mg/dl		264.1 ^d ± 1.2	197.3 ^d ± 1.5	211.3 ^c ± 1.5	226.2 ^b ± 1.6	235.7 ^b ± 0.4	219.6 ^b ± 0.9	229.9 ^b ± 0.6	238.3 ^b ± 0.4
Total proteins gm/dl		7.6 ^a ± 0.1	4.9 ^c ± 0.04	5.7 ^{bc} ± 0.2	6.3 ^b ± 0.1	7.2 ^a ± 0.1	5.5 ^{cb} ± 0.2	6.1 ^b ± 1.02	6.9 ^b ± 0.1
Albumin gm/dl		4.02 ^b ± 0.1	2.3 ^d ± 0.1	3.1 ^c ± 0.1	3.4 ^c ± 0.2	3.9 ^b ± 0.4	3.1 ^c ± 0.2	3.2 ^c ± 0.1	4.01 ^b ± 0.04
Globulin gm/dl		3.6 ^d ± 0.1	2.3 ^c ± 0.1	2.7 ^{bc} ± 0.2	3.2 ^b ± 0.2	3.5 ^u ± 0.1	2.8 ^b ± 0.1	3.2 ^b ± 0.1	3.2 ^b ± 0.1
A/G ratio %		0.9 ^c ± 0.03	0.8 ^c ± 0.02	1.6 ^a ± 0.1	1.2 ^a ± 0.1	1.1 ^b ± 0.1	1.3 ^b ± 0.1	0.8 ^b ± 0.2	1.3 ^a ± 0.04
Urca mg/dl		42.9 ^a ± 0.3	20.2 ^d ± 0.3	34.8 ^b ± 0.4	35.2 ^b ± 0.4	35.9 ^b ± 0.2	28.7 ^c ± 1.2	31.8 ^c ± 0.8	36.8 ^b ± 0.8
Creatinine mg/dl		0.8 ^c ± 0.01	1.2 ^a ± 0.04	1.2 ^a ± 0.1	1.1 ^b ± 0.1	0.8 ^b ± 0.2	1.1 ^b ± 0.03	1.01 ^b ± 0.04	0.9 ^b ± 0.03

Means within the same column carrying different letters are significant at P < 0.05

Duncan *et al.*⁽³²⁾ reported that alkaline phosphatase (ALP) is an enzyme, or a family of related enzymes, produced in the bile ducts, intestine, kidney, placenta and bone. An elevation in the level of serum ALP, especially in the setting of normal or only moderately elevated ALT and AST activities, suggests disease of the bile ducts or bile duct obstruction.

In this study, cattle naturally infested with *F. gigantica* showed a significant increase in AST, ALT and ALP, these results were reinforced with those previously obtained by ^(4, 32, 33), who detected a significant elevation in the activities of serum AST, ALT and ALP in infested cattle and sheep (table 2).

Liver damage is the most important cause of the increase in serum ALT activity in the infested cattle. ALP is known to be excreted via the bile duct; its elevation may have synchronized with the arrival of the flukes to the bile duct^(33, 34).

Both G3 and G4 showed a significant decrease in AST, ALT, and ALP levels on 7th, 14th and 28th day (PT) with no difference between them except ALP in G3 on 14th and 28th day (PT) which showed more decrease in ALP level than that of G4 compared with infested non-treated group.

GGT is an enzyme produced in the bile ducts that like ALP, may be elevated in the serum of animals with bile duct diseases. Elevations in serum GGT, especially along with elevations in ALP, suggest bile duct disease. These enzymes were previously found to be good indicators of hepatic damage^(35, 36).

It has been noticed that cattle naturally infested with *F. gigantica* showed a significant increase in GGT level, the present results were in the same direction with that obtained before^(4, 37) (table 2).

Duff *et al.*⁽³⁸⁾ found that GGT levels were elevated in infested lambs due to hepatic toxicity and necrosis. Raadsma *et al.*⁽³⁹⁾ reported that the elevation in GGT levels 10 weeks post-infestation was an indicator of epithelial damage in the bile duct of sheep infested with *F. hepatica*.

In the present study, both G3 and G4 showed a significant decrease in GGT serum level within the same range on 7th, 14th and 28th day (PT).

Bilirubin is found in the bile, it is the major product of the destruction of old red blood cells and removed from the blood by the liver. Any affection of the liver lead to elevation of bilirubin level in the blood⁽⁴⁰⁾.

Moreover, Amer *et al.*⁽³⁹⁾ reported that the secretion of bile pigments due to progressive cirrhosis and blocking of the bile ducts by mature flukes in cattle and sheep infested with *F. hepatica* led to the increase in serum bilirubin.

Cattle infested with *F. gigantica* in this study showed a significant increase in total and direct bilirubin these results were in agreement with those previously reported that total serum bilirubin increased in sheep at 6 weeks post-infestation and remained elevated at 8-14 weeks. This elevation may be attributed to the increase of production of bilirubin as a

result of hemolytic toxins produced from liver fluke (table 2)^(32, 41)

The treated groups (G3 and G4) showed a significant decrease in total and direct bilirubin level on 7th, 14th and 28th day (PT) with no variation between the two drugs, this may be attributed to their potent fasciolicidal effects on liver flukes.

Transferrin, is an iron transport protein and liver is the primary site of its synthesis⁽⁴²⁾. Its main function is the transport of ferric ion from intestine to the sites of synthesis of haemoglobin and other iron containing protein⁽⁴³⁾.

Cattle infested with *F. gigantica* showed a significant decrease in transferrin level (table 2). Lotfallahzadeh *et al.*⁽⁴⁴⁾ reported that the decrease in transferrin level was due to reduced synthesis in liver diseases.

G3 and G4 showed a significant increase in transferrin level on 7th, 14th and 28th day (PT) with non-significant difference between them except on 7th day (PT) where G4 showed more significant increase than G3. This might be due to their effects on *F. gigantica*.

The liver is of considerable importance in protein metabolism, any damage to its cells caused by liver flukes will be reflected on the total serum proteins depending on the severity of infestation. Albumin is the major protein that circulates in the blood stream, it is synthesized by the liver and secreted into the blood. Low serum albumin concentrations (hypoalbuminemia) indicate poor liver function⁽⁴⁵⁾.

The present results showed that cattle infested with *F. gigantica* have a significant decrease in total proteins, albumin and globulins, with no significant effect on A/G ratio (table 2). These results were similar to that obtained before⁽⁵⁾. On the other hand, Salimi-Bejestani, *et al.*⁽⁴⁴⁾ found that globulins levels increased in infested cattle with a decrease in total proteins and albumin levels.

Mohamed⁽⁴⁶⁾ and Matanović *et al.*⁽⁴⁶⁾ mentioned that hypoproteinaemia due to severe infestation of the liver leading to destruction of liver parenchyma resulting in drastic alteration in protein values. Likewise, no significant changes in albumin levels in *F. gigantica* infested sheep⁽³³⁾.

On 7th day, PT total proteins level showed no significant increase, while albumin level was significantly increased in both G3 and G4 within the same range but globulins level was increased in G4 only.

On 14th and 28th day PT total proteins, albumin and globulins were significantly increased, total proteins and globulins in G3 were nearly normal compared with infested non-treated group.

Ammonia is the major nitrogen-containing metabolic product of protein catabolism, converted to urea in the liver by the action of urea cycle enzymes. In advanced liver damage, there is a tendency for the blood urea nitrogen to be low⁽⁴⁷⁾. Creatinine is a non protein nitrogenous substance formed during muscle metabolism of creatine and phosphocreatine, it is excreted by glomerular filtration as urea, the rate of excretion is influenced by glomerular filtration rate

Cattle naturally infested with *F. gigantica* in this study showed significant decrease in urea level and a significant increase in creatinine level, these results were similar to that previously reported⁽⁴⁷⁾. On the other hand, Doaa et al.⁽⁴⁹⁾ found that serum urea and creatinine levels were significantly higher in infested than the control. The increase in serum urea may be due to the failure of detoxification of ammonia and other nitrogenous substances by cirrhotic liver⁽⁴⁶⁾.

Ahmed et al.⁽³³⁾ recorded that urea and creatinine levels in sheep infested with *F. gigantica*

significantly increased on 7th, 14th and 28th day PI but in G3 urea level was more significantly increased than G4 on 7th and 14th day PI. While creatinine level on 7th day PI was significantly decreased in G4 only while on 14th and 28th day PI the two groups showed a significant decrease in creatinine level.

Haematological results:

Results showed that RBCs counts, Hb concentration, PCV % and blood indices (MCV, MCH, MCHC) were significantly decreased than the control group (table 3). The present results were supported by numerous prior investigators^(1, 13, 40)

Table (3): Effect of Ivermectin plus clorsulon (1ml/50kg bwt,SC) and Nitroxynil (1ml/25 kg bwt,SC) on blood picture of cattle infested with *F. gigantica* [(Mean ± S.E.) (n=6)]

Parameter	Control Non infested (G1)	Control Infested (G2)	Ivermectin plus clorsulon (G3)			Nitroxynil (G4)		
			7days PI	15 days PI	30 days PI	7days PI	15 days PI	30 days PI
RBCs (10 ⁶ x cu mm)	7.1 ^a ± 0.1	2.8 ^d ± 0.2	4.4 ^c ± 0.1	4.9 ^c ± 0.03	5.9 ^b ± 0.2	4.1 ^c ± 0.1	5.4 ^b ± 0.2	6.1 ^b ± 0.1
WBCs (10 ³ x cu mm)	8.1 ^c ± 0.1	9.9 ^a ± 0.2	9.5 ^{ab} ± 0.1	8.9 ^b ± 0.1	8.2 ^c ± 0.1	9.43 ^b ± 0.1	8.8 ^b ± 0.1	8.7 ^b ± 0.1
Haemoglobin gm%	11.7 ^a ± 0.1	6.9 ^d ± 0.2	8.7 ^c ± 0.1	9.1 ^b ± 0.1	9.6 ^b ± 0.1	9.3 ^b ± 0.1	9.5 ^b ± 0.1	9.9 ^b ± 0.1
PCV %	34.4 ^a ± 0.1	24.7 ^c ± 0.8	27.9 ^{cb} ± 0.1	28.9 ^c ± 0.1	30.1 ^c ± 0.3	29.1 ^b ± 0.1	31.1 ^b ± 0.2	32.4 ^b ± 0.2
MCV (cu u)	48.6 ^a ± 0.5	45.1 ^c ± 0.3	46.6 ^b ± 0.1	46.9 ^b ± 0.1	47.6 ^b ± 0.2	46.1 ^b ± 0.1	46.6 ^b ± 0.1	46.9 ^b ± 0.03
MCH (u ug)	20.6 ^a ± 0.4	16.6 ^c ± 0.3	17.6 ^b ± 0.1	18.0 ^b ± 0.04	18.6 ^b ± 0.1	17.5 ^b ± 0.1	18.4 ^b ± 0.1	18.6 ^b ± 0.1
MCHC %	39.4 ^a ± 0.3	34.04 ^d ± 0.3	36.5 ^b ± 0.1	37.3 ^b ± 0.1	38.2 ^b ± 0.1	38.6 ^c ± 0.2	36.2 ^c ± 0.1	36.9 ^c ± 0.2

Means within the same column carrying different letters are significant at P < 0.05

Table (4): Effect of Ivermectin plus clorsulon (1ml/50kg bwt,SC) and Nitroxynil (1ml/25 kg bwt,SC) on body weight of cattle naturally infested with *F. gigantica* [(Mean ± S.E.) (n=6)]

Group	Time	Before treatment (zero day)	2 nd week post treatment		4 th week post treatment		6 th week post treatment			8 th week post treatment			Specific Growth rate		
			Mean ±S.E.	Gain /kg	Gain %	Mean ±S.E.	Gain /kg	Gain %	Mean ±S.E.	Gain /kg	Gain %	Mean ±S.E.		Gain /kg	Gain %
Ivermectin plus clorsulon (G3)		165.8 ^a ± 3.1	180.8 ^a ± 3.1	14.9 ± 0.6	6.8 ± 0.6	193.7 ^a ± 3.1	27.8 ± 0.4	12.6 ± 0.9	205.8 ^a ± 3.2	40.0 ± 0.8	18.0 ± 0.9	231.2 ^a ± 3.6	65.5 ^a ± 0.9	39.7 ^a ± 0.9	0.9 ^a ± 0.02
		163.3 ^a ± 2.5	172.7 ^a ± 3.2	9.3 ± 0.8	4.5 ± 0.9	180.5 ^b ± 2.7	18.9 ± 0.7	9.0 ± 0.3	185.8 ^b ± 2.8	22.6 ± 0.9	11.0 ± 0.7	199.2 ^b ± 3.03	36.3 ^b ± 0.6	22.3 ^b ± 0.5	0.5 ^b ± 0.01

Means within the same column carrying different letters are significant at P < 0.05

Lofly *et al.*⁽⁵⁰⁾ and Omran and El-Kholany⁽⁵¹⁾ reported that the severe anemia in cattle infested with *F.gigantica* may be due to a chronic liver inflammation, which causes depression of erythropoiesis.

The reduction in RBCs counts, Hb and PCV in this study may be attributed to the acute loss of blood by sucking activity of the flukes or extensive leakage of blood from the bile duct to the intestine, which results in iron deficiency^(52, 53).

Moreover, in the present study, infestation of cattle with *F.gigantica* caused marked increase in WBCs count. Similar results were previously recorded^(51, 53). The changes in WBCs or its differential counts may be obtained as a mean of body defense against Fasciola obstructive effects or due to the toxin mediated lesion of the bone marrow⁽⁵⁴⁾.

In a similar study Donn *et al.*⁽⁴⁹⁾ and Gebeyehu Ganga. *et al.*⁽⁵⁵⁾ recorded a decrease in Hb, PCV%, total erythrocyte counts, blood indices (MCH, MCHC, MCV) and appearance of reticulocytes in the blood of the buffaloes infested with *F.gigantica* suggested regenerative anemia.

The tested drugs showed a significant increase in RBCs count in both G3 and G4 on 7th, 14th and 28th day PT, but G4 showed more significant increase than G3. Haemoglobin content showed a significant increase in G3 and G4 on 7th, 14th and 28th day PT. PCV % showed a significant increase in G4 on 7th, 14th and 28th day PT, while in G3 a significant increase was noticed in PCV% on 14th and 23th day PT.

Blood indices were significantly increased on 7th, 14th and 28th day PT in G3 and G4.

On the other hand, WBCs count in G3 was not affected on 7th day PT while on 14th day PT its level was significantly increased and become nearly normal at 28th day PT. In G4 a significant increase was noticed on 7th, 14th and 28th day PT.

Concerning The effect of tested drugs on body weight, table (1) showed that G3 revealed more significant increase in body weight, gain /kgm, gain % and specific growth rate than that obtained by G4.

These results were supported by Davies *et al.*⁽⁵⁶⁾, who found that cattle infested with fascioliasis showed retardation in growth and when treated with ivermectin give the highest growth rate.

Chick *et al.*⁽⁵⁷⁾ recorded that beef cattle infested with *F.hepatica* showed retardation in growth rate and lower feed conversion rates in fattening cattle compared with non infested animals.

In a similar study DeRosa *et al.*⁽²⁾ reported that cattle infested with liver fluke and treated with clorsulon drench was heavier and had higher condition scores.

The increase in body weight in treated animals compared with infested animals might be attributed to their potent fasciolicidal effect.

CONCLUSION

It could be concluded that the efficacy of ivermectin plus clorsulon and nitroxyuil on cattle naturally infested with *F.gigantica* was 100% at the

than ivermectin plus clorsulon during the experiment. Also their effects on liver and kidney function and on blood picture were nearly similar, while on body weight ivermectin plus clorsulon treated group showed more significant increase in body weight, gain/kgm, gain % and specific growth rate.

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دراسة مقارنة لتأثير أيفرمكتين مع كلورسولون ونيتروكسيفيل على الديدان الكبدية في العاشية

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أحرقت التجربة مقارنة فعالية مركب أيفرمكتين مع كلورسولون (الفاكتين سوبر) وسبروكسيفيل (تروكس 25%) ضد الديدان الكبدية في مائة مصابة بشكل طبيعي وقد أحرقت هذه التجربة في مررة في محافظة الشرقية استخدم في هذه التجربة أربع وعشرين بقر أفرير بل من مختلف أصنافهم من (12-18) شهر ، ووزن من (150-180) كيلو جرام لكل حيوان في اليوم الأول تم أخذ عينات دم وروث من الحيوانات وتم تحليل الروث لتحديد درجة الإصابة وأيضا تم تحليل الدم وأظهرت نتائج التحليل الدموية للحيوانات المصابة انخفاضاً معنوياً في عدد كرات الدم الحمراء وتركيز الهيموجلوبين وحمم الخلايا المضغوطة وكذلك كان هناك زيادة معنوية في عدد كرات الدم البيضاء . أوضح التحليل الفيو كيميائية لمصل الدم لبعض الحيوانات وجود اختلافات معنوية في وظائف الكبد والكلى حيث أظهرت النتائج زيادة معنوية في كل من AST و ALT و ALP و GGT و البيلوروبين . وأيضا تراكبتين مع وجود نقصاً معنوياً في تركيز البروتين الكلى والبرال و الأمينو جلوتامين وأيضا تركيز اليوريا كما أوضح النتائج أن التغييرات الدموية والكيميائية في الحيوانات المصابة ما هي إلا انعكاساً لنتائج أنسجة الخلايا المصابة.

تم تقسيم الحيوانات إلى أربع مجموعات كل مجموعة تتكون من 6 حيوانات على النحو التالي : المجموعة الأولى غير مصابة وغير معالجه (الضابطة) ، المجموعة الثانية مصابة وغير معالجه ، المجموعة الثالثة مصابة ومعالجه بالأيفرمكتين مع كلورسولون (1 مل 50 كجم وزن) حفا تحت جلد الرقبة ، والمجموعة الرابعة مصابة ومعالجه بالنيتروكسيفيل (1 مل 25 كجم وزن) حفا تحت جلد الرقبة . تم جمع عينات روث قبل العلاج وبعد 7 ، 14 ، 28 يوم وأيضا تم وزن الحيوانات بعد 2 و 4 و 6 و 8 أسابيع بعد العلاج وأيضا عصبت دم قبل وبعد العلاج ب 7 ، 14 ، 28 يوم وأيضا تم وزن الحيوانات بعد 2 و 4 و 6 و 8 أسابيع بعد العلاج لمتابعة تطور الحالة بعد العلاج ، بعد انتهاء التجربة تم تقييم فعالية الأدوية كنسبة مئوية من الحد من عدد البويضات (الديدان الكبدية) في روث الحيوانات المصابة والمعالجه (FECR %) وأظهرت نتائج الدراسة أن FECR % في المجموعة الثالثة كان (69.1 + 2.3 ، 87.3 + 0.6 ، 94.5 + 0.2 و 100) على التوالي بينما في المجموعة الرابعة FECR % كان (73.2 + 0.6 ، 90.2 + 0.3 ، 97.6 + 0.1 و 100) على التوالي بعد العلاج ب 1 ، 2 ، 3 و 4 أسابيع . بالنسبة لتأثير العقارين على وظيفة الكبد والكلى ، بالإضافة إلى صورة الدم كشفت النتائج أن كلا من مركب أيفرمكتين مصافا إليه كلورسولون و نيتروكسيفيل (تروكس 25%) قد أتوا إلى نفس هذه الوظائف بالمقارنة بالمجموعة المعالجه والغير معالجه دون اختلافات كبيرة بينهما ، أما عن تأثيرهما على وزن الجسم للحيوانات فقط أظهرت النتائج أن أيفرمكتين مصافا إليه كلورسولون أظهر زيادة معنوية في وزن الحيوانات المعالجه مقارنة بتأثير سبروكسيفيل