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Pharmacology

Efficacy of Tylvalosin Aganist Mycoplasma Gallisepticum in Broilers and its Effect on Performance, Hematological and Biochemical Parameters

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ABSTRACT:

Tylvalosin tartrate is a macrolide antibiotic that has antibacterial activity against Gram-positive, some Gram-negative organisms and mycoplasma. It acts by inhibiting protein synthesis in the bacterial cell. Mycoplasma gallisepticum causes chronic respiratory disease (CRD) of domestic poultry, especially in the presence of management stresses and/or other respiratory pathogens. Disease is characterised by coryza, conjunctivitis, sneezing, and by sinusitis, particularly in turkeys and game birds. It can result in loss of production and downgrading of meat-type birds, and loss of egg production. In the current study, effect of tylvalosin on performance parameters (body weight gain, feed consumption as well as feed conversion ratio), hematological and biochemical profile were studied. A total of 24 fourteen-day old broiler chicks were divided into 3 equal groups. G1; control (-ve) group, G2; control (+ve) group that experimentally infected by mycoplasma gallisepticum at 30th day of age by intraocular/intranasal and intra tracheal rout, G3; experimentally infected by mycoplasma gallisepticum at 30th day of age by intraocular/intranasal and intra tracheal rout then received 25 mg/kg of tylvalosin per os for five consecutive days beginning from the 7th day of infection. In conclusion, treatment with tylvalosin at dose 25 mg/kg for consecutive 5 days was significantly improved growth performance (increased weight gain and feed utilization efficiency) with hematological and biochemical alteration and at least alleviate or partially reduce the severity of chronic respiratory disease (CRD) induced by Mycoplasma gallisepticum in broiler chickens.

Keywords: Broiler chickens, CRD, *Mycoplasma gallisepticum* and Tylvalosin tartrate.

INTRODUCTION

Tylvalosin tartrate is a macrolide antibiotic that has antibacterial activity against Gram-positive, some Gram-negative organisms and mycoplasma. It acts by inhibiting protein synthesis in the bacterial cell. Macrolides interfere with protein synthesis by reversibly binding to the 50S ribosome subunit. Macrolides are generally considered bacteriostatic and mycoplasmastatic (EMEA, 2009). *Mycoplasma gallisepticum* infection is particularly important in chickens and turkeys as a cause of respiratory disease and decreased meat and egg production (Bradbury, 2001; Ley, 2003). It can also cause upper respiratory disease in game birds. More recently MG has been recognised in North America in house finches as a cause of conjunctivitis (Luttrell et al., 1996). In poultry the infection is spread vertically through infected eggs and

horizontally by close contact; the MG nucleic acid has been identified in environmental samples (Marois et al., 2002). The clinical signs of MG in infected poultry can vary from subclinical to obvious respiratory signs including coryza, conjunctivitis, coughing and sneezing. Mycoplasma gallisepticum may be associated with acute respiratory disease in chickens and turkeys, especially in young birds, with the turkey being more susceptible. The severity of the disease is greatly affected by the degree of secondary infection with viruses such as Newcastle disease and infectious bronchitis, and/or bacteria such as Escherichia coli. This study was conducted to evaluate the efficacy of tylvalosin and its effect on performance parameters (body weight gain, feed consumption as well as feed conversion ratio), hematological and biochemical profile.

MATERIAL AND METHODS

Drug

Aivlosin(As tylvalosin tartrate 625 mg/g.) granules for use in drinking water for chickens and turkeys.

Chickens

A total of 24fourteen day old apparently healthy broiler chicks were used. All chicks were housed separately in cagesand were fed on balanced drug free ration for two weeks to ensure complete excretion of any drugs from their bodies. Water was supplied *ad-libitum*.

Experimental design

A total of 24fourteen-day old broiler chicks were divided into 3 equal groups.G1; control (-ve) group, G2; control (+ve) group that experimentally infected by *mycoplasma gallisepticum* at 30^{th} day of age by intraocular/intranasal and intra tracheal rout,G3; experimentally infected by *mycoplasma gallisepticum* at 30^{th} day of age by intraocular/intranasal and intra tracheal rout then received 25 mg/kg of tylvalosin per osfor five consecutive days beginning from the 7^{th} day of infection. At the age of 30^{th} day, *mycoplasma gallisepticum*free chickens were inoculated by intraocular/intranasal route with 0.1 ml containing 10^7 colony forming unit (CFU) of MG culture and received an additional inoculum by intratracheal route with 0.1 ml as described by (Gharaibeh and Hailat, 2011). The chickens were observed for 7 days till the appearance of the clinical signs asconjunctivitis, sneezing and sinusitis.

Determination of performance parameters:

The chicks of each group were individually weighted at 14^{th}, 28^{th}, 35^{th}, 40^{th}, and 47^{nd} days of age then body weight gain (WG) and feed conversion ratio (FCR) were calculated and recorded according to (Brady, 1968) using the following formulas:-

- Weight gain= Final weight - Initial weight
- Feed conversion ratio= Feed consumption (g) / Weight gain (g)

Determination of hematological and biochemical parameters:

At the 40^{th} and 47^{th} day of age, blood samples were collected from four randomly selected birds from each group. Blood samples were collected from wing veins and each blood sample was taken into two portions. The 1^{st} portion was collected in a small labeled dry and clean vial containing EDTA for hematological studies. The 2^{nd} portion was collected in plain clean dry and sterile non heparinized centrifuge tubes (10 ml capacity) and left to clot, then centrifuged at 3000 rpm for 15 minutes to separate serum samples. Serum samples were collected and kept separately in clean dry bottles in deep freeze (-20^{o}C) until biochemical analysis.

Histopathological examinations:

At the 40^{th} and 47^{th} day of age, chickens were slaughtered and organ was collected (liver,lung) for histopathological examination.

Statistical analysis:

The data were calculated as mean ± standard deviation. All statistical analysis was carried out according to (Berly and Lindgren 1990).

RESULTS:

Determination of performance parameters:

The chicks of each group were individually weighted at 14^{th}, 28^{th}, 35^{th}, 40^{th}, and 47^{nd} days of age then body weight gain (WG) and feed conversion ratio (FCR) were calculated and

recorded (**Table 1**). In tylvalosin treated infected group which infected experimentally with *Mycoplasma gallisepticum* at 30th day of age then received 25 mg/kg of tylvalosin per os beginning from the 7th day of infection for consecutive 5 days had exhibited a significant increase in the feed consumption (FC) and weight gain (WG) with imorovement in feed conversion ratio (FCR) compared with control (+ve) group.

Parameters		Control (-Ve)	Control (+Ve)	Tylvalosin treated group
At 14th day	B.Wt	497 ± 1.58	498 ± 1.18	503 ± 0.98
	AWG	-------	-------	-------
	FC	550	550	550
	FCR	1.1 ± 0.05	1.1 ± 0.07	1.09 ± 0.11
At 28th day	B.Wt	1570.25 ± 6.34	1540.50 ± 4.32	1570.50 ± 2.37
	AWG	1073.25 ± 3.54	1042.50 ± 2.04	1067.50 ± 1.50
	FC	2250	2250	2250
	FCR	1.43 ± 0.12	1.46 ± 0.22	1.43 ± 0.43
At 35th day	B.Wt	2131.25 ± 5.45	1760.0 ± 3.33	1776.15 ± 3.04
	AWG	561± 2.04^{a}	219.50 ± 1.84^{d}	205.65 ± 2.11^{cd}
	FC	3300^{c}	2950^{a}	2980^{b}
	FCR	1.54 ± 0.15^{b}	1.67 ± 0.20^{a}	1.67 ± 0.17^{a}
At 40th day	B.Wt	2435 ± 2.20	1859.15 ± 1.29	1979.50 ± 1.47
	AWG	303.75 ± 1.54^{a}	99.15 ± 0.91^{b}	203.35 ± 0.75^{c}
	FC	4250^{b}	3200^{c}	3300^{a}
	FCR	1.74± 0.37^{b}	1.72± 0.19^{a}	1.66± 0.32^{c}
At 47th day	B.Wt	3070 ± 5.623	1906.50 ± 4.325	2394.0 ± 2.371
	AWG	635 ± 3.78^{a}	47.35 ± 3.18^{b}	414.50 ± 2.17^{c}
	FC	5450^{d}	3500^{a}	4200^{b}
	FCR	1.77± 0.41^{c}	1.83± 0.57^{a}	1.75± 0.67^{b}

Determination of hematological parameters:

Table (1). Comparison of growth performance of Control (-ve) group, Control (+ve) group andTylvalosin treated infected group.

At the 40th and 47th day of age, blood samples were collected from four randomly selected birds from each group. Blood samples were collected from wing veins and each blood sample was taken into two portions for hematological and biochemical studies. At 40th day of age, tylvalosin treated group showed a significant increase in (RBCs, Hb and Lymphocyte) and a significant decrease in (PLTs, Neutrophil, Eosinophil and N/L ratio) without any significant effect on (PCV, TLC and Monocyte) in comparison with control (+ve) group.

At 47th day of age, it showed a significant increase in (RBCs, Hb and Lymphocyte) with a significant decrease in (PCV, PLTs, TLC, Neutrophil, Hb, Eosinophil, N/L ratio and Monocyte) in comparison with control (+ve) group (**Table 2**).

Determination of biochemical parameters:

In a comparison of biochemical parameters oftylvalosin treated infected group with control (+ve) group, it showed a significant decrease in (ALT, AST, Urea, Creatinine, Uric acid and MDA) with a significant increase in GSH at both 40th and 47th day of age (**Table 3**).

Table (2). Comparison of hematological parameters of Control (-ve) group, Control (+ve) group andTylvalosin treated infected group.

Parameters		Control (-Ve)	Control (+Ve)	Tylvalosin treated group
At 40th day	ALT(U/l)	19.00±2.00^{b}	26.67±2.96^{a}	22.33±1.67^{ab}
	AST(U/l)	14.67±0.33^{c}	23.6±2.33^{a}	21.00±2.65^{ab}
	Urea (mg/dl)	20.00±1.00^{c}	28.33±1.33^{a}	27.67±2.19^{ab}
	Creatinine (mg/dl)	0.43±0.03^{b}	0.75±0.16^{a}	0.70±0.11^{ab}
	Uric acid (mg/dl)	4.57±0.27^{b}	8.93±0.73^{a}	7.17±1.07^{c}
	GSH (U/ml)	1330±33.33^{ab}	1088±19.65^{d}	1166±2.57^{c}
	MDA (nmol/g)	5.52±0.26^{c}	6.27±0.19^{a}	5.72±0.01^{c}
At 47th day	ALT(U/l)	22.33±0.33^{b}	28.67±1.20^{aa}	25.00±0.58^{ab}
	AST(U/l)	19.00±1.00^{b}	27.67±1.86^{a}	19.67±1.45^{b}
	Urea (mg/dl)	20.57±1.29^{d}	35.00±1.00^{a}	30.23±2.04^{b}
	Creatinine (mg/dl)	0.74±0.02^{b}	1.20±0.10^{a}	0.87±0.03^{ab}
	Uric acid (mg/dl)	4.10±0.20^{b}	8.30±0.38^{a}	5.40±1.45^{b}
	GSH (U/ml)	1264.0±34.5^{a}	1152±32.17^{b}	1204±25.00^{ab}
	MDA (nmol/g)	5.57±0.28^{b}	6.07±0.22^{a}	5.74±0.37^{b}

Histopathological examinations:

Control (+ve) group:-

Lung tissue:-

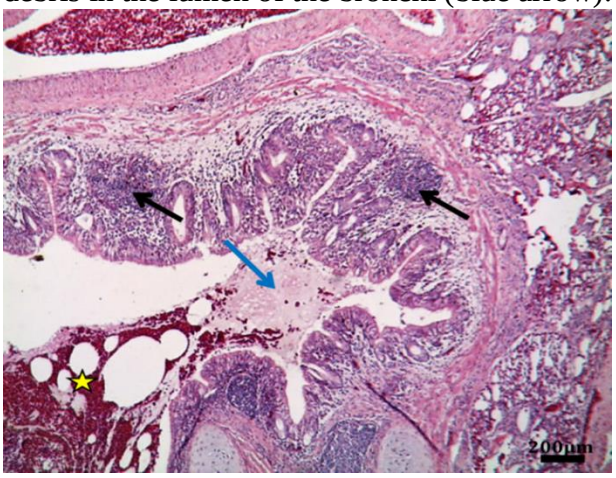
Photomicrograph of lung tissue of broiler chicken infected with mycoplasma scarified at 40th and 47th day showing focal aggregations of inflammatory cells (mononuclear cells predominantly lymphocytes and heterophils) in the

Table (3). Comparison of biochemical

Parameters		Control (-Ve)	Control (+Ve)	Tylvalosin treated group
At 40th day	RBCs (x10^{6}/µl)	3.67±0.12^{a}	2.63±0.18^{c}	3.02±0.39^{bc}
	PCV (%)	43.13±0.19^{d}	44.13±0.19^{c}	44.07±0.29^{c}
	Hb (g/dl)	9.73±0.07^{a}	7.53±0.24^{c}	8.53±0.24^{b}
	PLTs (x10^{3}/µl)	2.73±0.03^{cd}	3.00±0.01^{b}	2.86±0.03^{c}
	TLC (x10^{3}/µl)	19.93±0.30^{c}	20.33±0.83^{c}	20.60±0.32^{c}
	Neutrophils (%)	31.33±1.45^{a}	28.33±1.33^{abc}	26.33±1.33^{cd}
	Lymphocyte (%)	57.66±1.45^{c}	62.00±2.00^{bc}	64.66±1.33^{ab}
	N/L ratio (%)	0.54±0.04^{a}	0.46±0.04^{b}	0.41±0.03^{c}
	Eosinophils (%)	3.33±0.33^{c}	3.00±0.01^{a}	2.33±0.33^{b}
	Monocytes (%)	7.67±0.33^{b}	6.67±0.67^{a}	6.67±0.33^{a}
At 47th day	RBCs (x10^{6}/µl)	3.73±0.09^{a}	3.20±0.10^{c}	3.33±0.28^{bc}
	PCV (%)	46.07±1.15^{a}	44.47±0.26^{ab}	44.07±0.29^{b}
	Hb (g/dl)	9.83±0.07^{a}	7.90±0.06^{c}	8.33±0.12^{b}
	PLTs (x10^{3}/µl)	2.70±0.10^{b}	3.03±0.03^{a}	2.8±0.07^{ab}
	TLC (x10^{3}/µl)	19.57±0.17^{b}	22.23±0.27^{a}	20.63±0.53^{b}
	Neutrophils (%)	29.00±1.00^{a}	28.33±0.666^{b}	26.67±0.67^{ab}
	Lymphocyte (%)	59.33±0.33^{b}	61.33±1.33^{b}	64.67±0.33^{a}
	N/L ratio (%)	0.49±0.017^{a}	0.46±0.02^{a}	0.41±0.01^{b}
	Eosinophils (%)	3.66±0.33^{a}	3.66±0.33^{a}	2.33±0.33^{bc}
	Monocytes (%)	8.00±1.00^{b}	6.67±0.33^{bc}	6.33±0.67^{c}

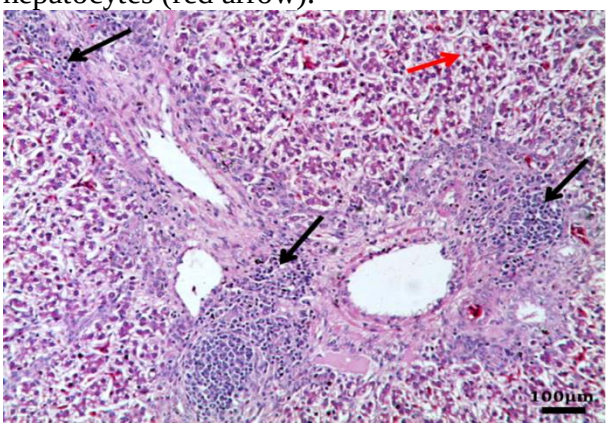
parameters of Control (-ve) group, Control (+ve) group andTylvalosin treated infected group.

bronchial epithelium (black arrows), bloody exudate (star) and edematous fluid with cellular debris in the lumen of the bronchi (blue arrow).



Hepatic tissue:

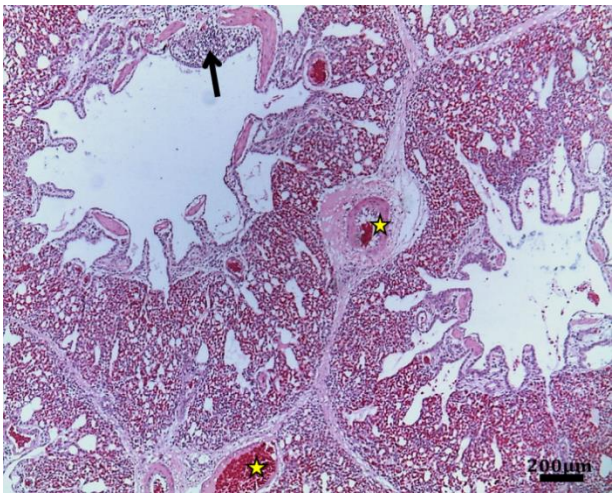
Photomicrograph of Liver tissue of broiler chicken infected with mycoplasma scarified at 40th and 47th day showing heavy aggregations of inflammatory cells in the portal area (black arrows) and hydropic degeneration of most hepatocytes (red arrow).



Tylvalosin treated infected group:-

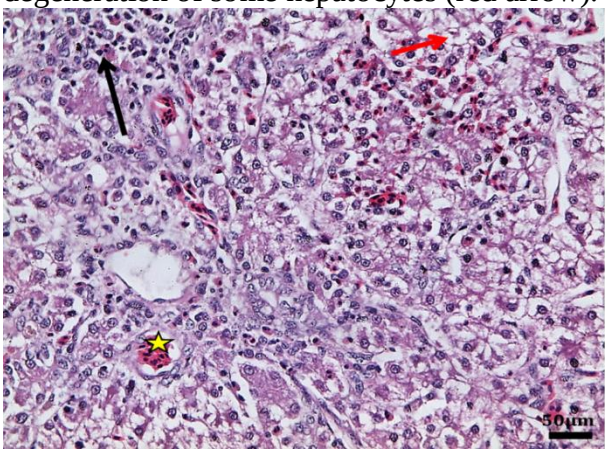
Lung tissue:-

Photomicrograph of lung tissue of broiler chicken infected with mycoplasma and treated by tylvalosin scarified at 40th and 47th day showing mild aggregations of inflammatory cells in the parabronchial lumen (black arrow) surrounded by normal air and blood capillaries and congestion of interstitial blood vessels (stars).



Hepatic tissue:

Photomicrograph of Liver tissue of broiler chicken infected with mycoplasma and treated by tylvalosin scarified at 40th and 47th day showing mild congestion (star), mild aggregation of inflammatory cells around central vein (black arrow) and hydropic degeneration of some hepatocytes (red arrow).



DISCUSSION

In this study, tylvalosin treated infected group had exhibited a significant increase in the feed consumption (FC) and weight gain (WG). This finding is in agreement with previous reports in pigs (Pallarés et al., 2015;Rodriguez et al., 2020), in broilers (Garces-Narro et al., 2013), in pheasants (Tasker et al., 2011). FCR showed a significant decrease at 40th day which was agreed with that reported in broiler (Garces-Narro et al., 2013), in pigs (Vyt et al., 2012; Rodriguez et al., 2020).

Hematological parameters of tylvalosin treated infected group compared with control (+ve) group showed a significant increase in (RBCs, Hb and Lymphocyte) but a significant decrease in (PLTs, Neutrophil, Eosinophil and N/L ratio) without any significant effect on (PCV, TLC and Monocyte) at 40th day of age which disagreed with that reported in tilmicosin in chickens (Elsayed et al., 2014). At 47th day of age, it showed a significant increase in (RBCs, Hb and Lymphocyte) with a significant decrease in (PCV, PLTs, TLC, Neutrophil, Hb, Eosinophil, N/L ratio and Monocyte) in comparison with control (+ve) group. This finding is in agreement with previous reports in broiler (Abo El-Ela et al., 2016) which showed a significant decrease in (TLC, Neutrophil, Eosinophil and Monocyte) but disagreed with lymphocyte and also agreed with that reported in chickens (Shwaish et al., 2021) which showed a significant decrease in (TLC, Eosinophil). Also like those reported in rabbits (Altunok et al., 2002) after administration of tilmicosin which induced a significant decrease in TLC. Azithromycin and clarithromycin have also been reported to lower the number of TLC in humans (Fujii et al., 1995; Ohtsuka et al., 1996).

In a comparison of biochemical parameters of tylvalosin treated infected group with control (+ve) group, it showed a significant decrease in (ALT, AST, Urea, Creatinine, Uric acid and MDA) with a significant increase in GSH at both 40th and 47th day of age. This finding is disagreed with previous reports in broiler (Abo El-Ela et al., 2016) which showed a non-significant difference in ALT and AST but like those reported in tilmicosin in chickens (Elsayed et al., 2014) that showed a significant decrease in ALT.

CONCLUSION:

Results of this work clearly show that supplementation with tylvalosinat dose 25 mg/kg per os for consecutive 5 days was significantly improved growth performance (increased weight gain and feed utilization efficiency) and at least alleviate or partially reduce the severity of chronic respiratory disease (CRD) induced by Mycoplasma gallisepticum in broiler chickens.

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