

**Interaction between Marbofloxacin and Flunixin in Treatment of Pneumonia in Lambs**

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**Abstract**

Nasopharyngeal swabs were collected from 100 lambs aging 9 -12 months (30 healthy and 70 pneumonic lambs for bacteriological examination. Overall, 25% were positive for *P. multocida*. Antibiogram study of the isolates revealed that marbofloxacin was the highest effective against *P. multocida*. Forty lambs (20 healthy and 20 naturally infected with *P. multocida*) were divided into 8 groups (5, each), the 1<sup>st</sup> group: healthy lambs (control), 2<sup>nd</sup> group: healthy received marbofloxacin, 3<sup>rd</sup> group: healthy received flunixin meglumine, 4<sup>th</sup> group: healthy received marbofloxacin and flunixin meglumine together, 5<sup>th</sup> group: infected non treated, 6<sup>th</sup> group: infected treated with marbofloxacin, 7<sup>th</sup> group: infected treated with flunixin meglumine and 8<sup>th</sup>: group infected treated with marbofloxacin and flunixin meglumine together. Hemato-biochemical changes at 1<sup>st</sup>, 7<sup>th</sup> and 14<sup>th</sup> day post treatment were studied. All clinical sign disappeared and *P. multocida* microorganisms were not reisolated in group post treated by marbofloxacin alone or together with flunixin meglumine. Healthy lambs received marbofloxacin or flunixin meglumine either alone or together showed significant decrease in RBCs, Hb, PCV%, T protein, albumin, globulin,  $\alpha$ ,  $\beta$ ,  $\gamma$  globulin and significant increase in WBCs, AST, ALT, ALP, GGT, urea and creatinine at 1<sup>st</sup> and 7<sup>th</sup> day post injection. Pneumonic lambs showed significant reduction in RBCs, Hb, PCV% T. protein, albumin, total globulin,  $\alpha$ ,  $\beta$  globulin and significant increase in WBCs, AST, ALT, ALP, GGT,  $\gamma$  globulin, urea and creatinine all over the experimental period. Pneumonic lamb treated with marbofloxacin alone or with flunixin meglumine resulted in complete disappearance of these clinical signs at 1<sup>st</sup> day post treatment but these clinical signs remained in flunixin meglumine alone lambs. It is concluded that, pasteurellosis in lambs resulted in adverse effect in hematobiochemical parameters. Using marbofloxacin alone or together with flunixin meglumine in treatment of diseased lambs lead to improve clinical signs and hemato-biochemical parameters at 7<sup>th</sup> day post treatment.

**Keywords:** Marbofloxacin, Flunixin, Treatment, Pneumonia, Lambs

**Introduction**

Respiratory infections represent in diseases lambs cause high economic losses. Pneumonic pasteurellosis is one of the most economically infectious diseases of lambs with a wide prevalence throughout the continents [1]. *Pasteurella multocida* comprises 5 capsular serogroups and 16 somatic serotypes [2]. Many efforts were done for controlling and prevent disease through medication, so continuous research for new drugs for controlling the disease is a necessity [3]. Marbofloxacin is a 3<sup>rd</sup> generation synthetic bactericidal drug belonging to fluoroquinolones acts by inhibition of DNA gyrase. It is effective against a wide range of Gr +ve & Gr-ve bacteria as *pasteurella multocida* [4]. It is used for treatment of respiratory and urinary diseases [5].

Flunixin meglumine is a member of non steroidal antiinflammatory drugs inhibit is production of body prostaglandins and other chemicals stimulate bodys inflammatory response. Flunixin meglumine works quickly, with pain relief and fever reduction starting within one to two hours [9].

The present study was carried out to evaluate the effect of marbofloxacin, flunixin meglumine and their combination on healthy and pneumonic lambs caused by *pasteurella multocida* beside study the effects of *pasteurella multocida* and drugs on some hemato-biochemical parameters in lambs.

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## Material and Methods

### Drugs

Marbofloxacin 10% (Marbocyl 10%)<sup>R</sup> produced by Vetoquinol S.A., (France) is a synthetic broad spectrum antibacterial agent from the flouroquinolone class of chemotherapeutic agents. Flunixin meglumine (Finadyne<sup>®</sup>) is a product of Schering-Plough animal health Segre –France.

### Isolation and identification

A total of 100 Nasopharyngeal swabs (30 apparently healthy lambs and 70 pneumonic lambs showed clinical sign as fever, bilateral nasal discharge, congested mucous membranes, moist cough, abnormal respiratory sounds, dyspnea and recumbency) 9 -12 month old were obtained from private farms at Abou Hamad city, Sharkia Governorate. All samples were collected aseptically and inoculated into nutrient broth aerobically at 37<sup>0</sup>C over night, subculturing on nutrient agar and MacConkey agar plates was performed for 24h at 37<sup>0</sup>C, colonies were identified [6]. Pathogenicity and virulence of isolated *P. multocida* to mice [7].

### Antibiotic sensitivity test

Susceptibility of *P. multocida* to different chemotherapeutic agents was tested by disc diffusion method [8].

### Experimental lambs

forty lambs aged from 9 -12 month old at a private farm in Abou Hamad city, Sharkia Governorate were involved in this investigation (20 clinically healthy and 20 pneumonic lambs). Lambs were reared under hygienic measures feed on barseem and dry ration and water was supplied *ad libitum*. Pneumonic lambs showed clinical sign include fever, congested mucous membranes, bilateral nasal discharge, moist cough, dyspnea, abnormal respiratory sounds and recumbency.

### Experimental design

Lambs were classified into 8 equal groups (5 Lambs in each), 1<sup>st</sup> group healthy lamb non treated (control), 2<sup>nd</sup> group healthy lamb received 10mg/kgm b.wt. marbofloxacin [9] 3<sup>rd</sup> group healthy lamb received 1.1 mg/kgm bwt flunixin meglumine [10], 4<sup>th</sup> group healthy lamb received marbofloxacin and flunixin meglumine together by same dose. 5<sup>th</sup> group

infected lambs with *pasteurella multocida* non treated. 6<sup>th</sup> group infected lambs treated by marbofloxacin by same dose, 7<sup>th</sup> group infected lambs treated by flunixin meglumine by same dose and the 8<sup>th</sup> group infected lambs treated with marbofloxacin and flunixin meglumine together by same dose. Treatment was I/M in all groups for 5 consecutive days.

### Sampling

Two blood samples were taken from all lambs from jugular vein on 1<sup>st</sup>, 7<sup>th</sup> & 14<sup>th</sup> days post injection. The first sample was collected in test tube contain EDTA for estimation hemogram and total leukocytic count according to [11]. While, the second sample was collected in centrifuge tubes and serum was separated for measuring total proteins [12]. Protein fractions were performed using cellulose acetate electrophoresis test [13], estimation of aspartate aminotransferase (AST), alanine aminotransferase (ALT) [14], Gamma glutamyl transferase (GGT) [15], alkaline phosphatase (ALP) [16], urea [17], creatinine [18].

### Reisolation of *Pasteurella multocida*

Nasopharyngeal swabs were taken aseptically from all groups post treatment then inoculated into nutrient broth aerobically at 37<sup>0</sup>C over night followed subculturing on selective media for 24h at 37<sup>0</sup>C, suspected colonies were identified according to colonial morphology, microscopically by gram's stain and biochemically [6].

**Statistical analysis:** obtained data were analyzed [19].

## Results and Discussion

Bacteriological examination of nasopharyngeal swabs from pneumonic lambs revealed the predominant isolates were *pasteurella multocida*, *Streptococcal spp*, *E. coli* and mixed infection. Similar pathogens were isolated from pneumonic lambs [20]. Also, Morad *et al.*, [21] isolate *pasteurella multocida* from pneumonic different animals. These results are agreed with these obtained by El-Dahshan and Elham [22] isolate *pasteurella multocida* and *E. coli* from pneumonic sheep.

The present study by using the disc-diffusion test showed that marbofloxacin was

the highest effective on *P. multocida* than other tested drugs. These results are agreed with Valle *et al.*, [23] who stated that marbofloxacin was very active against bovine respiratory tract pathogen as *Pasteurella multocida*. Also, our results coincide with those obtained by Thomas *et al.*, [4] they recorded that marbofloxacin has been approved for treatment of respiratory disease

in cattle, pigs, dogs, and cats. Pneumonic lambs showed clinical signs as fever, bilateral nasal discharge, congested mucous membranes, moist cough, dyspnea and recombency. Typical clinical signs were recorded by Zeitoun [24] in pneumonic sheep, Hussein *et al.*, [25] in pneumonic lamb, Ali *et al.*, [26] in Friesian calves. These signs may be due to bacterial infections and its toxins [27].

**Table 1: Types and percentage of isolated bacterial spp. from collected nasopharyngeal swabs in lambs**

Total number of nasopharyngeal swabs	Types of isolated bacteria	bacterial isolate		
		-ve	+ ve	%
Healthy lambs	30	--	--	----
Diseased lambs	<i>Pasteurella multocida</i>		25	25%
	<i>Streptococcal spp</i>	---	10	10%
	<i>E. coli</i>	---	9	9 %
	Mixed infection	---	9	9 %

The present investigation revealed that significant healthy lambs received marbofloxacin and flunixin meglumine either alone or together for 5 consecutive days displayed significant decrease in RBCs, HB and PCV % beside significant leukocytosis on 1<sup>st</sup> and 7<sup>th</sup> day post injection accompanied with insignificant effect in blood picture on 14<sup>th</sup> day post injection when compared with non infected non treated lambs. This finding may be due to suppressive effect of fluoroquinolones on growth and differentiation

of hematopoietic cells like erythroid precursors [28]. Also, the present changes in blood picture may be attributed to deleterious effect of drug on bone marrow resulted in bone marrow dysfunctions [29]. Our results are compatible with Elmeleh [30] stated that marbofloxacin produced significant decrease in RBCs, HB and PCV %. Our findings were in accordance with that of Carrick *et al.*, [31] and McIlwraith *et al.*, [32] they recorded that Flunixin induced significant decrease in RBCs, HB and PCV % and leucocytosis.

**Table 2: In-vitro susceptibility of *pasterulla multocida* to marbofloxacin and other commonly used antimicrobial agents by disc diffusion method.**

Drug	Mark	(Potency (ug)	Standerd inhibition zone	Mean Zone of Inhibition(mm)
Marbofloxacin	MAR	5	≤ 20 mm	25 mm
Florfenicol	FF	30	≤ 18 mm	20 mm
Doxycycline	DX	30	≤ 14 mm	19mm
Streptomycin	St	10	≤ 18 mm	18 mm
Gentamycin	Gm	10	≤ 15 mm	15 mm
Neomycin	NM	30	≤ 17 mm	15 mm
Spectinomycin	Sp	100	≤ 23 mm	13 mm

The present work revealed that pneumonic lambs showed significant reduction in RBCs, HB, PCV% and significant increase in WBCs throughout the experimental period. Reduction

in erythrogram parameters as a result to the *Pasteurella multocida* infection in lambs may be attributed to bacterial endotoxins which cause intravascular destruction of erythrocytic

cells and consequently lead to hemolysis with breakdown of hemoglobin [33]. The change in blood picture in infected lambs come from Dagmar *et al.*, [34] stated that infected bacteria produced cell damaging protein toxin (hemolysin) causes changes in cell membrane permeability and formation of surface lesions causes RBCs destruction. Such data go hand in hand with those reported by Salh and El-Bably [35] in pneumonic sheep

Healthy lambs received marbofloxacin and flunixin meglumine either alone or together for 5 consecutive days showed the side effect of drugs resembles the effect of the disease significant increase in serum AST, ALT, GGT, ALP, urea and creatinine on 1<sup>st</sup> & 7<sup>th</sup> day post treatment associated with insignificant

increase on 14<sup>th</sup> days post treatment. Our finding clearly confirmed by those obtained by Clark *et al.*, [36] who reported that fluoroquinolones had hepatotoxic effect. Increase in liver enzymes, urea and creatinine may indicate a degenerative changes and hypofunction of liver and kidney [37]. Same changes in liver enzymes were reported by Novert [27] who stated that marbofloxacin induce of degeneration and necrosis of hepatocytes leading to elevation in AST, ALT and ALP in rats. Elevations in liver enzymes in our study may be due to alteration of membrane permeability or damage of hepatic cells by direct effect of the drugs resulting in escape of these enzymes to the plasma [38].

**Table 3: Effect of marbofloxacin and flunixin meglumine on blood picture in healthy and pneumonic lambs (n=5)**

Groups	Erythrogram									T.LC (x 103/ ml)		
	RBCs (x 10 <sup>6</sup> /ml)			Hb gm/dl			PCV %			1 <sup>st</sup> d	7 <sup>th</sup> d	14 <sup>th</sup> d
	1 <sup>st</sup> d	7 <sup>th</sup> d	14 <sup>th</sup> d	1 <sup>st</sup> d	7 <sup>th</sup> d	14 <sup>th</sup> d	1 <sup>st</sup> d	7 <sup>th</sup> d	14 <sup>th</sup> d			
Gp(1)	11.5± 0.84	11.53± 0.95	11.41± 0.28	9.53 ± 0.91	9.40 ± 0.27	9.66 ± 0.48	27.94± 0.98	27.88± 0.89	27.87± 0.84	9.47 ± 0.64	9.66 ± 0.51	9.46± 0.27
Gp(2)	7.96 ± 0.98*	8.07 ± 0.77*	9.90± 0.94	7.34± 0.40*	8.16 ± 0.50*	8.66 ± 0.69	24.09± 0.83*	24.13± 0.82*	26.16± 0.85	12.35± 0.86*	11.04± 0.31*	10.34± 0.83
Gp(3)	7.77 ± 0.95*	8.90 ± 0.60*	9.94± 0.95	6.06 ± 0.82*	6.99 ± 0.80*	8.99 ± 0.57	24.35± 0.69*	24.43± 0.82*	25.56± 0.85	12.56± 0.79*	12.04 ± 0.63*	10.60± 0.95
Gp(4)	7.85 ± 0.78*	8.58 ± 0.40*	9.85± 0.97	6.14 ± 0.88*	7.05 ± 0.77*	8.96 ± 0.47	23.49± 0.98*	23.62± 0.99*	25.86± 0.95	12.14± 0.92*	12.44 ± 0.96*	10.03± 0.65
Gp(5)	8.06± 0.47**	8.65 ± 0.10**	8.80± 0.68**	6.03± 0.71**	6.25 ± 0.63**	6.23± 0.8**	24.23± 0.98**	24.16± 0.35**	25.06± 0.30**	12.84± 0.42**	12.80 ± 0.56**	12.90 ± 0.35**
Gp(6)	8.54 ± 0.57*	9.90± 0.98	10.29± 0.83	6.95 ± 0.25*	7.89 ± 0.96	9.64± 0.56	24.06± 0.70*	25.05± 0.80*	26.21± 0.99	12.05± 0.82*	10.02 ± 0.92	9.62 ± 0.50
Gp(7)	8.12 ± 0.44*	8.13± 0.83*	8.99 ± 0.78*	6.72 ± 0.37*	6.99 ± 0.81*	6.90± 0.92*	24.25± 0.66*	24.30± 0.93*	25.46± 0.36*	12.21± 0.79*	12.13 ± 0.81*	12.12 ± 0.91*
Gp(8)	8.38 ± 0.57*	9.95± 0.98	10.19± 0.92	6.74 ± 0.24*	8.68 ± 0.66	9.64± 0.35	24.76± 0.45*	26.73± 0.84	26.98± 0.57	9.47 ± 0.64	9.66 ± 0.51	9.46 ± 0.27

\*Significant at p < 0.5

\*\* Significant at p<0.1

Increase of liver enzymes may be due to damaging effect of anti-inflammatory on liver [39]. The above mentioned results were supported by previous studies of Valberg [40] who stated that flunixin meglumine induced significant increase in liver enzymes.

Our results demonstrated that pneumonic lambs showed significant increases in liver enzymes (AST, ALT, GGT and ALP), urea and creatinine all over the experimental period. Pneumonia induced elevation in liver enzymes urea and creatinine [27]. Similar results were reported by Kodary and Abdalla

[41] and El-Shabiny *et al.* [42] in pneumonic animals.

Healthy lambs received marbofloxacin and flunixin meglumine either alone or together for 5 days displayed significant reduction in serum total protein, albumin, globulin  $\alpha$ ,  $\beta$ ,  $\gamma$  globulin and significant increase in alpha globulin on 1<sup>st</sup> and 7<sup>th</sup> day post injection beside non significant effect in A/G ratio on 1<sup>st</sup> and 7<sup>th</sup> day post injection. Reduction in serum total

protein and albumin may be due to impaired albumin synthesis by liver due to harmful effect of drugs on hepatic cells [43]. Same change was reported by Elmeleh [30] who stated that marbofloxacin induced significant decrease in total protein, albumin,  $\alpha$   $\beta$  and  $\gamma$  globulin. These results are reinforced by Ahmed [44] who stated that hypoproteinemia and hypoalbuminemia were evident in levofloxacin treated rats.

**Table 4: Effect of marbofloxacin and flunixin meglumine on protein profile in healthy and pneumonic lambs (n=5)**

Group	total protein (gm/dl)			albumin (gm/dl)			total globulin (gm/dl)			A/G ratio		
	1 <sup>st</sup> d	7 <sup>th</sup> d	14 <sup>th</sup> d	1 <sup>st</sup> d	7 <sup>th</sup> d	14 <sup>th</sup> d	1 <sup>st</sup> d	7 <sup>th</sup> d	14 <sup>th</sup> d	1 <sup>st</sup> d	7 <sup>th</sup> d	14 <sup>th</sup> d
Gp(1)	6.51±	6.46 ±	6.43±	3.50 ±	3.45 ±	3.53±	3.01±	3.01 ±	1.16±	1.16±	1.15±	1.21 ±
	0.16	0.24	0.35	0.14	0.15	0.32	0.10	0.10	0.11	0.03	0.08	0.03
Gp(2)	5.55±	5.25 ±	6.32±	2.53±	2.52 ±	3.40 ±	2.62±	2.73±	2.83±	0.97±	0.92±	1.20 ±
	0.29*	0.42*	0.44	0.36*	0.32*	0.31	0.07*	0.02*	0.05	0.05	0.04	0.02
Gp(3)	5.67 ±	5.65 ±	6.12±	2.97 ±	2.89 ±	2.88 ±	2.70 ±	2.76 ±	2.74 ±	1.10±	1.05±	1.05±
	0.25*	0.30*	0.24	0.15*	0.13*	0.23	0.06*	0.03*	0.06	0.07	0.08	0.04
Gp(4)	5.30 ±	5.43 ±	5.46±	2.54 ±	2.64 ±	2.70 ±	2.75 ±	2.70 ±	2.76±	0.92±	0.98±	0.98±
	0.36*	0.29*	0.14	0.21*	0.31*	0.21	0.05*	0.05*	0.09	0.05	0.06	0.05
Gp(5)	5.07 ±	5.13±	5.02±	2.27 ±	2.32 ±	2.24 ±	2.80±	2.80 ±	2.70 ±	0.79±	0.83±	0.83±
	0.49*	0.39*	0.46*	0.43*	0.42*	0.32*	0.01*	0.04*	0.01*	0.07	0.04	0.06
Gp(6)	5.83 ±	5.40 ±	6.16±	2.64 ±	2.92 ±	3.23 ±	2.74±	2.78 ±	2.93±	0.96±	1.05±	1.08±
	0.49*	0.16	0.33*	0.30*	0.24	0.19	0.05*	0.05*	0.09	0.08	0.09	0.07
Gp(7)	5.28 ±	5.05 ±	5.46±	2.62 ±	2.33 ±	2.69 ±	2.66±	7.72 ±	2.77±	0.98±	0.86±	0.97±
	0.49*	0.42*	0.23*	0.36*	0.41*	0.13*	0.03*	0.06*	0.03*	0.04	0.07	0.05
Gp(8)	5.155±	6.06 ±	6.21±	2.75 ±	3.17 ±	3.36 ±	2.76±	2.81±	2.95±	0.99±	1.14±	1.14±
	0.38*	0.37	0.14	0.33*	0.27	0.14	0.02*	0.04	0.06	0.06	0.07	0.09

\* Significant at p < 0.05

\*\* Significant at p<0.01

Close similarity was seen between our finding and those obtained by Carrick *et al.*, [31] they found significant decrease in total protein and gamma globuline and insignificant decrease in total globulin in foal received flunixin meglumine for 5 days. This result may be due to drug toxicity and immunosuppressive effect of flunixin meglumine [45]. This observation was previously recorded by Stegelmeir *et al.*, [46] who stated that flunixin meglumine induced hepatocellular damage and

decrease total proteins and serum globulin in dog.

Infected lambs with *Pasteurella multocida* showed significant decrease in total protein, albumin, total globulin,  $\alpha$ ,  $\beta$  globulin beside significant increase in serum  $\gamma$  globulins and insignificant effect in A/G ratio thought out the experimental period. Reduction in serum total proteins and albumin may be due to destructive effect of bacteria and its toxins on liver cells [47]. Another explanation for hypoproteinemia post bacterial infection come

from El-Bealawy [48] who reported that hypoproteinemia met with post bacterial infection may be due to amino acid utilization as defense against pathogens. Our data clearly reinforced by Doxey [49] who stated that hypoproteinemia in pneumonic lambs may be due anorexia and inability of the liver to synthesis proteins. Our result was in complete harmony with those reported by Novert [27] who stated that pneumonic calves showed significant increase in serum  $\alpha$  and  $\gamma$  globulins level. Treatment of infected lambs with *P. multocida* by marbofloxacin and flunixin meglumine either alone or in combination for 5 consecutive days aid in disappear once of clinical symptoms and ameliorates the adverse effects and providing largely returns,

erythrogram, total protein, albumin, globulin, liver enzymes urea and creatinine to nearly normal levels. Our results were in accordance with results obtained by Schneider *et al.*, [50] who mentioned that fluoroquinolones had potent antimicrobial activity at very low concentrations when compared with other classes of antimicrobial agents. Also, Rougier *et al.*, [51] mentioned that marbofloxacin was potentially good in treatment of upper respiratory tract disease. Marbofloxacin improve of the clinical signs of respiratory disease [52]. Our finding was in agreement with those obtained by Weingarten [53] stated flunixin is commonly used for relief of pain and control of inflammation and pyrexia associated with diseases of different origin.

**Table 5: Effect of marbofloxacin and flunixin meglumine on protein fractions in healthy and pneumonic lambs (n=5)**

Groups	Alpha			Beta globulin			Gamma		
	1 <sup>st</sup> d	7 <sup>th</sup> d	14 <sup>th</sup> d	1 <sup>st</sup> d	7 <sup>th</sup> d	14 <sup>th</sup> d	1 <sup>st</sup> d	7 <sup>th</sup> d	14 <sup>th</sup> d
Gp(1)	0.97±0.03	0.96±0.04	0.91±0.04	0.99±0.04	0.97±0.06	0.96±0.02	1.05±0.06	1.08±0.04	1.03±0.05
Gp(2)	1.07±0.03*	1.09±0.06	0.92±0.05	0.76±0.03*	0.74±0.08	0.93±0.08	0.79±0.06*	0.90±0.04*	0.95±0.09
Gp(3)	1.06±0.02*	1.04±0.04	0.87±0.06	0.83±0.03*	0.87±0.04	0.84±0.06	0.81±0.08*	0.85±0.06*	1.01±0.06
Gp(4)	1.07±0.02*	0.99±0.05	0.93±0.08	0.88±0.03*	0.85±0.07	0.82±0.07	0.80±0.09*	0.86±0.06*	1.01±0.08
Gp(5)	0.89±0.01*	0.85±0.02*	0.93±0.01*	0.82±0.06*	0.89±0.04*	0.81±0.01*	1.19±0.02*	1.17±0.02*	1.14±0.05*
Gp(6)	0.92±0.05	0.91±0.05	0.91±0.06	0.81±0.05*	0.85±0.03*	0.99±0.05	1.04±0.05	1.02±0.04	1.02±0.09
Gp(7)	0.87±0.03*	0.86±0.02*	0.86±0.04*	0.80±0.04*	0.83±0.04*	0.90±0.01*	0.99±0.10	1.03±0.09	1.01±0.08*
Gp(8)	0.92±0.08	0.91±0.05	0.96±0.04	0.84±0.06*	0.85±0.08	0.96±0.07	1.04±0.09	1.03±0.14	1.03±0.18

Significant at  $p < 0.05$

\*\* Significant at  $p < 0.01$ \*

## Conclusion

It could be concluded that, pasteurellosis infection in lambs resulted in change in hemato-biochemical parameters which lead to economic losses in lambs. Marbofloxacin and flunixin meglumine either alone or together for 5 consecutive days treatment helped in controlling of the infection by *P. multocida*.

## Conflict of interest

The authors declare no conflict of interest.

## References

- [1] Callan, R.; Gunch, T. and Mock, R. (1991): Development of pneumonia in sheep after exposure to a flock of exotic wild and domestic sheep. *J Am Vet Ned. Ass.* 198 (6)152-155 .
- [2] Rimler, R. and Rhoades, K. (1989): *Pasteurella multocida*. In Adlan, C.; Rutter, J, Ed *Pasteurella and Pasteurellosis*. London, Academic Press, 37-73.

- [3] Gilmour, N. and Angus, K. (1993): Pasteurellosis In: Diseases of Sheep; Black well Scientific Publications, Oxiford., 3-8.
- [4] Thomas E, Caldow G, and Davot J(2001): efficacy and tolerance of marbofloxacin in treatment of bovine respiratory disease. J Vet Pharm Ther. 24 (5)53-58 .
- [5] Meunier, D.; Acar, J. and Vall, M. (2004): survey of susceptibility to marbofloxacin of bovine pathogenic strains from eight European countries. Inter J of Anti Ag, 24:70.
- [6] Abd El. Aliem, Nabila (1999): Immunotoxic effect of flunixin meglumine and isoflupredone acetate in rabbits. J Egypt Vet Med Ass 59:61-87.
- [7] Cruickshank R, Duguid J, Marmin B and Swain R (1975): Medical Microbiology. (2)Practice of Med Microb. 12<sup>th</sup>Ed Churchill Livingstone, London.
- [8] Okerman L, Spanoghe L and De Bruycker R (1979): experimental infection of mice with p. milt strain isolated from rabbits.J. Comp. Path.89:51-55.
- [9] Quinn P, Markery B , Carter M , Donnelly W and Leonard F(2002): Veterinary Microbiology and Microbial Diseases. Block well Sci Ltd.
- [10] Anadon, A; Martinez M and Castelna, V (2002): Pharmacokinetic and tissue residues for marbofloxacin in chicken. Am. J.Vet. Res 63(7) 27-33 .
- [11] Jain, N.C. (1986): Schalm's Veterinary Hematology. 4th Ed, Lea and Fibiger, philadelphia, U.S. A. PP. 834.
- [12] Doumas, B.; Carter, R.; Peers, T. and Schaffier, R. (1981):A candidate reference method for determination total protein serum. Clin Chem 27, 64.
- [13] Henry, R.; Cannon, D. and Winkelman, J. (1974): Clinical Chemistry: Principals and Techniques p. 437-440, Harper and Row, Hagrstown.
- [14] Reitman, S. and Frankel, S. (1957): Calorimetric determination of transaminases activity, Am. J. Clin. Path. (28)56.
- [15] Kaplan, L and Pesce, A (1992): Clinical Chemistry 2<sup>nd</sup> Ed St. Louis.,CV Mosby Comp.
- [16] John, D. (1982): Clinical laboratory mothed for determination of alkaline phosphatase. 9th Ed. 580-581.
- [17] Fawcet, J. and Scott, J. (1960): Determination of urea. J. Clin. Path. (13) 156.
- [18] Husdan H and Rapoport, A (1968): Estimation of creatinin Clin Chem (14) 22.
- [19] Petrie A and Watson P (1999): Statistics for Veterinary and Animal Science 1st Ed. 90-99, the Blackwell Science LTd, United Kingdom.
- [20] Abdalla O. & Emam .E. (2005): Effect of marbofloxacin and isofluerdone acetate as therapy of pneumonia associated with *pasteurela multocida* in lambs.4<sup>th</sup> Scentific Conf. of Fac of vet. Med. Mansoura Univ. 283-301.
- [21]Morad, M; El-Amrousi, S. and El. Allawy, T. (1980): Experim- ental studies of some strains of P. multocida from different animals. Assiut Vet. Med. J.,(7)342-350.
- [22]El-Dahshan E and Elham I. (2006): bacterial agents isolated from pneumonic sheep. 8<sup>th</sup> Sci. Vet. Med. Zag. , Conf.
- [23] Valle M; Schneider, M and Woehrl F (2012): Pharmacokinetic and pharmacodyna- mic of marbofloxacin administered as a single injection for the treatment of bovine respiratory disease. J Vet Pharm Ther.; 35 (6)19-28.
- [24]Zeitoun, A. (2001): Clinical study of pneumonic mycoplasmosis and pasturellosis in commercial sheep flock. Assiut, Vet Med. J. 45: 89 162-17.
- [25] Hussein, E, Alam, T and Masoud, E (2006): studies on clinical, haemato- biochemical changes in pneumonic lamb with trials of treatment. Mansoura Vet Med. J 8 (1) 81-97
- [26] Ali M., Ibrahim I. and Zaid M. (2017): Green Tea as a Supportive Treatment for

- Respiratory Disorders in Calves  
Alexandria J of Vet Sci ; 52(1) 118-124.
- [27] Novert, M. (2004): Bacteriological and mycoplasmal studies on lung infections in calves. J Egypt Vet Med. Ass.62, 4:89-94.
- [28] Axel, D. and Itamar, S. (2003): Immunomodulatory effects of quinolones. Lancet Infect Dis 3(6) 359–371.
- [29] Yeates, F. and March, D. (1980): adrenal cortex. in medical physiology(54) 85.
- [30]Elmeleh, A. A. (2008): some pharmacodynamic effects of marbofloxacin. MVSc Thesis (pharmacology) Fac. of Vet Med Benha Univ.
- [31]Carrick, J., Popich, M. and Townsend, H. (1989): Clinical and pathological effects of flunixin meglumine in neonatal foals.Can.F Vet Res. 53 (2) 95– 101.
- [32]McIlwraith, C.; Frisbie, D. and; Kawcak, C. (2001): Non steroidal Anti-Inflammatory Drugs. Proc. AAEP (47): 182-187.
- [33] Abdullah F, Osman A, Adamu L. Saad M, Saharee A (2013): Haematological and Biochemical Alterations in Calves Following Infection with *Pasteurella multocida* Type B: 2, Bacterial Lipopolysaccharide and Outer Membrane Protein Immunogens . Asian J of Anim and Vet Adv, 8: 806-813.
- [34] Dagmar, J.; Muhsin, O. and Ntondo, B. (2002): Production and characterization of E coli enterohemolysin and structure effects of erythrocyte membranes. Cell Biolo Inter 26(2)75-86.
- [35]Salh, L. and El. Bably, M. (1998): Hygienic studies for control of pneumonia in buffaloe calves with special reference to its Clinico-Laboratory diagnosis. 8<sup>th</sup> Sci, Fact, Vet. Med. Assiut Univ. Egypt 173-187.
- [36]Clark, L.; Deborah, V.; and Saad, A. (2001): Profiles of hepatic and dysrhythmic cardiovascular events post use of fluoroquinolone: Experience from large cohorts from drug safety research unit prescription monitoring database. Drug Safety 24:43-54.
- [37]Kaplan. M. (1987): Primary biliary cirrhosis. N. Engl. J. Med.316 (9) 21–28.
- [38]Hanafy, A. (1993): Some adverse effects of norfloxacin in male rats. Thesis presented to Fac. of Vet. Med., Edfina, Alex. Univ. for the degree of MVSc.
- [39]Er, A., Dik, B., and Cetin, G. (2013):Cardiac safety of diclofenac at a single dose in ram. The Scientific World J 2013: 808731.
- [40]Valberg, S. (2002) A review of the diagnosis and treatment of rhabdomyolysis in foals. American Asso of Equine 48,17–21.
- [41]Kodary, R. and Abdalla, O.(2001): Evaluation of tilmicosin as a treatment for pneumonia in ewes. Beni- Suef Vet.Med, J, 11 (28)53-63.
- [42]El-Shabiny, M. Laila; Agag, B. and El-Ebeedy, A. (2001): Contagious caprine pleuropneumonia in goats. 6th Soci for Cattle Dis, , Assuit, Egypt.
- [43]Kaneko, J. (1989): Clinical biochemistry of domestic animals 4<sup>th</sup>Ed., Academic.
- [44]Ahmed, A (2017): protective effect of some antioxidants on adverse effects of levofloxacin in albino rats. M Sc. Thesis Fac. Vet. Med. Zag Univ.
- [45]Cheng, Z.; Nolan, A. and McKellar, Q. (1998): Measurement of cyclooxygenase inhibition in vivo of two non-steroidal antiinflammatory in sheep. Inflamm. 22:53–66.
- [46]Stegelmeir B; Bottoms, G and Reed, W (1988): Effect of Flunixin meglumine in dogs post experimentally induced enterotoxaemia. Cornell Vet. 78: 221–230.
- [47]Radostits, O, Gay, C, Hinchcliff, K and Constable, P. (2007): Veterinary Medicine. A textbook of diseases of cattle, sheep and horses, W.B. Saunders Co.68-77.
- [48]El-Bealawy, M. (2003): Haematological and biochemical studies on pneumonia in



- new born calves. Egypt. J Agric. Res. 81(1) 23.
- [49] Doxey, D (1971): Veterinary Clinical Pathology. 1<sup>st</sup>Ed. Bailliere tindal, London .
- [50] Schneider, M; Thomas, V and Deleforge, J (1996): marbofloxacin Pharmacokinetics in dogs after oral administration. J Vet Pharm. Ther. 19, 56–61.
- [51] Rougier S; Galand D; and Vall, M (2006): Epidemology and susceptibility pathogenic bacteria responsible for respiratory tract infections in rabbits. Vet Micr.; 9(3)54-66.
- [52] Waxman, S.; Vicente, M. and Andres, M. (2001): marbofloxacin Pharmacokinetic after I/V and I/M injection in adult goats. J. Vet. Pharmac. 20 (6) 75-78.
- [53] Weingarten, A. J. (2009): Mechanisms of action and role of antiinflammatory in treatment of bovine respiratory disease. Proceedings of symposium on best practices in BRD treatment:. European Buiatrics. Marseille, pp 6-15.

### المخلص العربي

#### التداخل الدوائي بين كلا من المربوفلوكساسين والفلونيكسين لعلاج الالتهاب الرئوي في الحملان

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تم تجميع عدد ١٠٠ مسحة من الانف والقصبية الهوائية لحملان عمر ٩-١٢ شهر (٣٠ حمل بصحة جيدة و٧٠ حمل مريضه ويظهر عليها اعراض تنفسية) للفحص البكتريولوجي. وبعد الفحص البكتريولوجي وجد ميكروب الباستريلا مالتوسيدا في عدد ٢٥ عينة (٢٥%). ويعمل اختبار الحساسية للمعزولات وجد أن الماربوفلوكساسين أكثر المضادات الحيوية المستخدمة تأثيراً على الباستريلا مالتوسيدا المعزولة عن باقي المضادات الحيوية المستخدمة. تم استخدام عدد ٤٠ حمل عمر ٩-١٢ شهر (٢٠ حمل بصحة جيدة و٢٠ حمل تعاني من وجود التهاب رئوي) تم تقسيمهم إلى ٨ مجموعات متساوية (٥ بكلا منها) الأولى: مجموعة ضابطة الثانية: حملان بصحة جيدة وتم حقنها عضلياً باستخدام ١٠ مجم / كجم من الوزن الحي ماربوفلوكساسين لمدة ٥ أيام متتالية. الثالثة: حملان بصحة جيدة وتم حقنها باستخدام ١,١ مجم / كجم من وزن الجسم فلونكسين مجلومين لمدة ٥ أيام متتالية. الرابعة: حملان بصحة جيدة وتم حقنها بالماربوفلوكساسين والفلونكسين مجلومين معا بنفس الجرعة والمدة الخامسة: حملان مصابه اصابه طبيعيه بالباستيريلا مالتوسيدا ولم تعالج السادسة: حملان مصابه اصابه طبيعيه بالباستيريلا مالتوسيدا وتم علاجها باستخدام الماربوفلوكساسين بنفس الجرعة والمدة السابعة: حملان مصابه اصابه طبيعيه بالباستيريلا مالتوسيدا وتم علاجها باستخدام الفلونكسين مجلومين بنفس الجرعة والمدة الثامنة: حملان مصابه اصابه طبيعيه بالباستيريلا مالتوسيدا وتم علاجها باستخدام الماربوفلوكساسين والفلونكسين مجلومين معا بنفس الجرعة والمدة السابقة. تم دراسة التغيرات الهيماتولوجية والبيوكيميائية عند اليوم الاول والسابع والرابع عشر من نهاية العلاج. تم اخذ عينتين دم من كل حمل عند نهاية اليوم الاول والسابع والرابع عشر من نهاية العلاج ، الأولى لدراسة تأثير الماربوفلوكساسين والفلونكسين مجلومين والباستيريلا مالتوسيدا على صورة الدم والعينة الثانية لفصل المصل وذلك لقياس بعض المؤشرات البيوكيميائية. أظهرت النتائج بعد تحليلها إحصائياً أن الماربوفلوكساسين والفلونكسين مجلومين سواء منفردين او معا اديا الى حدوث نقص معنوي في العدد الكلي لكرات الدم الحمراء، تركيز الهيموجلوبين، حجم خلايا الدم المرصوصة، البروتين الكلي، الزلال، الجلوبيولين الكلي، وجاما جلوبيولين وزيادة معنوية في العدد الكلي لكرات الدم البيضاء الفا وبيتا جلوبيولين . الإصابة بالباستيريلا مالتوسيدا أدى إلى وجود نقص معنوي في العدد الكلي لكرات الدم الحمراء، تركيز الهيموجلوبين، حجم خلايا الدم المرصوصة البروتين الكلي، الزلال، الجلوبيولين الكلي وبيتا جلوبيولين وزيادة معنوية في العدد الكلي لكرات الدم البيضاء طوال مدة التجربة. علاج الحملان التي تعاني من وجود التهاب رئوي باستخدام الماربوفلوكساسين والفلونكسين مجلومين سواء منفردين او معا بالجرعة المستخدمة كان له أثر فعال في اختفاء الاعراض وتحسن صورة الدم والوظائف البيوكيميائية الى وضعهم الطبيعي عند اليوم الرابع عشر من نهاية العلاج عند مقارنتها بالمجموعة الضابطة. من كل ما سبق نلاحظ أن استخدام الماربوفلوكساسين منفردا او الماربوفلوكساسين والفلونكسين مجلومين معا بالجرعة العلاجية لة تأثير فعال في علاج الإصابة بالباستيريلا وأدى إلى اختفاء الأعراض الظاهرية وعودة هذه الوظائف إلى المستوى الطبيعي ولكن استخدام العقارين معا كان له أثر ايجابي أكثر من استخدام الماربوفلوكساسين منفردا.