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COMPARATIVE EFFICACY OF TILMICOSIN AND TULATHROMYCIN FO R THE CONTROL OF BOVINE RESPIRATORY DISEASES IN CALVES

By

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ABSTRACT

A total number of twenty calves aged (4-6 months) weighing (80-120 kg) was used for this study. Calves were divided into 4 equal groups. The first group (clinically healthy) was kept as normal control group, the second group (pneumonic calves) was kept as infected non treated group, the third group (pneumonic calves) was treated with Tilmicosin (10 mg/kg B.wt. S/C single injection), the fourth group (pneumonic calves) was treated with Tulathromycin (2.5 mg/kg B.wt. S/C single injection). All calves were clinically observed for 7 days with collection of nasal swabs at zero day and standard bacteriological techniques were used for isolation and identification of Pasteurella multocida. Specific identification of purified suspected ten isolates biochemically identified as *P. multocida* strains, only four were confirmed as *P. multocida* by polymerase chain reaction (PCR), of which two strains harbored the virulence gene tbpA and pfhA. Two blood samples were collected from each calf of all groups at 2nd day and 7th day post treatment. Infected non treated group showed significant increase in alanine transaminase (ALT) and aspartate transaminase (AST) activities, C- reactive protein (CRP) concentration and Malondialdehyde (MDA) and significant decrease in reduced glutathione (GSH) along the whole experimental period. Tilmicosin administration evoked significant increase in MDA and significant decrease in GSH. Tulathromycin-treated group showed significant increase in ALT and AST activities and significant decrease in GSH. Recovery rate of calves suffered from pneumonia caused by *P.multocida* was determined as 100% in Tulathromycin-treated group and 80% in Tilmicosin-treated group.

Keywords:

Tilmicosin, Tulathromycin, Pneumonia, Calves.

INTRODUCTION

Pasteurella multocida is a commensal in the upper respiratory tract of many animals and does not usually cause serious disease, but it can be a significant pathogen if associated with other bacteria, viruses, or mycoplasma as predisposing factor when calves are stressed. **Ewers *et al.* (2006)** showed that some genes, including PfhA, tbpA and dermonecrotoxin encoding gene (toxA), play a role in the virulence of bacteria. Among these genes, PfhA and tbpA are associated with bovine diseases. Respiratory affections, particularly bronchopneumonia constitute one of the most important problems for the practicing veterinarians and at the same time threaten a great deal of animal health, also morbidity and mortality rates are considerably high. Death losses are sometimes dramatic and well recognized **(Soliman and Ayad, 2014).** Unrecognized losses due to chronic respiratory diseases may be even greater because of decreased feed efficiency, lowered weight gain and permanent stunted growth of animals that never reach their optimum level of production **(Gunn and Stott, 1998).** Also, the harmful impact of this disease is exaggerated through impaired liver and kidney functions **(Abd-Alla, 1997). Svensson *et al.* (2006)** reported a high mortality rate of calves (1-6 months) due to respiratory diseases and pneumonia symptoms after calves necropsy. **Seker *et al.* (2009)** reported that *P. multocida* are normal inhabitant nasal bacterial microflora. They are opportunistic pathogens waiting for a chance to invade and proliferate under stressful conditions in calves between 1-6 months of age. **Crosier *et al.* (1996)** mentioned that Tilmicosin has been approved for treatment of the bovine respiratory disease in beef cattle and nonlactating dairy cattle associated with Pasteurella and Mycoplasma species**.**

Prescott(2000) stated that Tilmicosin is a broad-spectrum bacteriostatic macrolide which is synthesized from tyrosine, it is overwhelmingly effective against Pasteurella *sp.*, Mycoplasma *sp.*, and some Gram-positive organisms and for that it has been widely utilized to treat respiratory problems in swine, cattle and sheep **(El-Komy and Abubakr, 2020). Fajt *et al.* (2003)** studied the effects of danofloxacin and tilmicosin on neutrophil function and lung consolidation in beef heifer calves with induced *P. haemolytica* pneumonia and found that Danofloxacin and tilmicosin have no clinically significant effects on neutrophil function or apoptosis. **Schunicht *et al.* (2007)** demonstrated that Tulathromycin, administered once, SC, at the rate of 2.5 mg/kg BW, is more effective than florfenicol, administered once for the treatment of undifferentiated fever in feedlot calves, SC, at the dosage of 40 mg/kg BW, due to its lower first undifferentiated fever relapse and overall mortality rates. **Aytekin *et al.* (2010)** indicated that Tulathromycin, administered once, SC, at the dosage of 2.5 mg/kg body

weight (BW), is more effective for the treatment of the respiratory system diseases in cattle than tilmicosin, administered once, SC, at the dosage of 10 mg/kg BW, due to its higher recovery rates. **Burette (2010)** indicated that clinical concentrations of tilmicosin and other macrolides may induce neutrophil apoptosis, and that, this effect exhibits at least some degree of drug specificity.

Therefore, the current research was created to detect the most causative bacterial agent in the examined pneumonic calves before and after treatment and to evaluate the efficacy of tilmicosin and Tulathromycin to control pneumonia and to limit mortality rate via its effect on *multocida,* leukogram, liver enzymes, kidney function and protein profile, oxidative stress (MDA and GSH) and CRP in pneumonic calves treated with tilmicosin and Tulathromycin.

MATERIAL AND METHODS

Drugs:

Tilmicosin: (Tilmoject® 30% injectable solution; Arabcomed).

Tilmicosin main route of application in large ruminants is subcutaneously in the neck, at a dosage of 10 mg/kg b. wt. once **(Bishop, 2005).**

Tulathromycin: (Drainer 100 mg/mL injectable solution; Pfizer Animal Health).

Tulathromycin main route of application in large ruminants is subcutaneously at a dosage of 2.5 mg/kg b. wt. "Once in the neck" **(Ball *et al.* 2019).**

Experimental design and treatment:

This study was conducted in a private farm in Kafr El-Ziat, Gharbia Governorate. Twenty Calves aged 2-6 months weighing 80-120 kg were housed outdoors in concrete-floored pens with open front sheds as shelter, and they were fed milk replacer (free of antimicrobial substances twice daily) and non-medicated creep feed *ad libitum* with free access to clean drinking water. To enable the collection of blood samples, the animals were shaved over jugular vein .Twenty Calves were involved in this investigation. The calves were divided into 4 equal groups (five of each). The first group (clinically healthy) was kept as negative control group and was not given any treatment. The other three groups (pneumonic calves) suffering from signs of respiratory troubles including dyspnea, bilateral mucoid to mucopurulent nasal discharges with moist painful cough,fever,congested mucous membranes, lacrimation, and abnormal lung sounds, the second group (pneumonic calves) was kept as infected non-treated control, the third group (pneumonic calves) was treated with therapeutic

doses of Tilmicosin and the fourth group (pneumonic calves) was treated with therapeutic doses of Tulathromycin.

Sampling:

Nasal swabs:

At 0 day of the experiment, twenty nasal swabs were taken (5 of each 4 groups). Nasal swab was passed through nares after cleaning the discharge by spirit swab. Samples were taken using sterile polystyrene cotton swabs soaked in nutrient broth then penetrated into nostrils and rotated firmly and smoothly **(Barnum *et al.*, 1969).**

Within 1-2 hours of collection, swabs were transported to the lab for bacteriological analysis.

Blood samples:

At the 2nd and the 7th day of the experiment, two types of blood samples were collected from each of the twenty calves from the Jugular vein using vacuum tubes, the first blood samples were collected in vacationer tubes (Venoject, Terumo) containing Ethyl-enediaminetetraacetic acid (EDTA) as an anticoagulant for leukogram, once daily at the 2nd and the 7th days post drugs administration. Total leukocyte counts and granulocyte/agranulocyte ratios were determined by standard methodsthe second blood sample was left to clot and then centrifuged at 3000 rpm for 20 minutes for separation of serum. The sera were then stored frozen at -20°C until the biochemical analysis which include determination of AST, ALT, total protein, albumin, creatinine, uric acid,estimation of antioxidant status(GSH and MDA)and C-reactive protein.

Bacteriological Examination:

Isolation and identification:

Nasal swabs were inoculated at the same day of its collection into nutrient broth and incubated at 37ºC for 24 hours aerobically, then a loopful of the incubated broth was sub cultured onto selective sheep blood agar and incubated aerobically at 37º C for 24 hours to check any bacterial growth.The developed colonies of *P. multocida* isolates were morphologically identified by Gram stain and biochemical tests according to **(Quinn *et al*. 2002).**

Antimicrobial susceptibility testing:

The obtained bacterial isolates were tested in vitro for their susceptibility to the following antimicrobialdiscs:amoxicillin-Clavulanic (AMC)30µg,Cefotaxime (CTX)30µg,ciprofloxacin (Cip) 5 µg,Erythromycin (E)15µg,Gentamicin (CN)10µg,Tulathromycin(Tul)30 µgand Tilmicosin (Til) 15 µg according to **Plair *et al* (1970)** and the degree of sensitivity was interpreted according *to* **NCCLS (2002).**

Detection of virulence genes in *P. multocida:*

Extraction of bacterial DNA:

DNA was extracted from the isolated *P .multocida* using QIAamp DNA mini kit. It was applied on 10 isolates. PCR Master Mix and cycling conditions of the primers during PCR was prepared according to Emerald Amp GT PCR master mix (Takara) kit. Oligonucleotide primers used in PCR have specific sequence and amplify a specific product as shown instable (1). DNA samples were amplified in a total volume of 25µl as follows: 12.5 µl of Emerald Amp GT PCR master mix, 1 µl of each primer of 20 pmol concentrations, 4.5 µl of water and 6 µl of template DNA. The reaction was performed in a Biometra thermal cycler. Temperature and time conditions of the PCR were applied as shown in (Table 1). Aliquots of amplified PCR products were electrophoresed in 1.5 % agarose gel (ABgene) in 1x TBE buffer at room temperature. For gel analysis, 15 µl of PCR products were loaded in each gel slot. A 100 bp DNA ladder (QIAGEN Inc., Valencia, CA, and USA) was used to determine the fragment sizes. The gel was photographed by a gel documentation system and the data was analyzed through computer software.

Table (1): Primer sequences of primers used for the detection *P. multocida* virulence genes.

Target agent	Target gene	Primers sequences (5'-3')	Amplified segment (bp)	Reference
P. multocida	*Kmt1*	5`-ATC-CGC-TAT-TTA-CCC-AGT-GG-3`	460	OIE (2012)
		5`-GCT-GTA-AAC-GAA-CTC-GCC-AC-3`		
	*tbp*A	5`-GCTATCCGTGGCGTTGATAAA-3`	296	Eakins and Niven (2002)
		5`-GTTTTTTGAAGTATAGCCGGTTTTAGA-3`		
	*pfh*A	5`-TAAGCCTATCGGTTCAAGTCG-3`	830	Sarangi *et al*. (2014)
		5`-GATAAATCTACCCCGTCCTCT-3`		

Experimental protocol:

Clinical Examination:

All calves were examined once a day for 7 days(0 day till 7th day of treatment or till resolution of respiratory symptoms). Body temperature and respiratory rate were recorded daily.

Biochemical analysis:

Serum biomarkers were pinpointed using a commercial kit as directed by manufacturers. All parameters were measured spectrophotometrically by using standardized test-kits. Activities of

serum aspartate amino transferase (AST) and alanine amino transferase (ALT) were assessed according to the technique described by **Reitman andFrankel(1957)**.Uric acid and creatinine were determined according to **Newman and Price (1999)** using kits of Biodignostic, Cairo, Egypt.Serum total protein and albumin were assessed by the technique of **Henry (1964)** and **Westgard andPoquette (1972)**.Lipid peroxides formation was assessed as Malondialdehyde (MDA) according to the methods described by **Jentzsch *et al.* (1996)** and Glutathione **(**GSH) according to the method described by **Beutler *et al.* (1963).**C-reactive protein (CRP) was assessed according to the methods described by **Dolores *et al.* (2005).**

Statistical Analysis:

The obtained data was analyzed by analysis of variance and the mean values were compared by Duncan's Multiple Range test using the method cited by **Petrie and Watson (1999)** and computerized using **SPSS 20 (2011).** The results are given as mean ± SE.

RESULTS AND DISCUSSION

Identification of the isolated *P. multocida*:

Morphological examination showed that suspected isolates *P. multocida* colonies were which agreed with the description of **Adlam and Rutter (1989).**These colonies appeared under micros cope as Gram negative, non-motile, coccobacilli. Biochemically, isolates strains were nidol, H_2S production; oxidase and catalase positive while Voges Proskauer observed as smooth, rough or mucoid with light grayish color of 1-2 mm diameter colonies, urease, hydrolysis, methyl red and lactose fermentation negative so the primary identification was *P. multocida* **(Olsen *et al.* 2003).**

Prevalence of *P. multocida* from the examined samples:

According to phenotypic and biochemical identification, a total of 10 isolates of Pasteurella were recovered from twenty examined samples. Such result was in agreement with that of **Hussein and Eisa 2004 and with Aytekin *et al.* (2010**) who reported that, the main causative microorganisms that had the highest isolation rate in the tested animals was *Pasteurella spp*.

Antibiotic sensitivity test results:

The in-vitro sensitivity tests (Table 2) revealed that, the isolates were highly susceptible to Tulathromycin and Tilmicosin (100%) followed by erythromycin, gentamycin, ciprofloxacin, Amoxicillin-Clavulanic and Cefotaxime (93.33%), (86.66%), (80%), (80%) and (66.66%) respectively. Nearly identical outcomes were obtained by **Catry *et al.* (2007), Thomas *et al.* (2002), Mohammad *et al*. (2006) and Anwar *et al*. (2000).**

Table (2): In-vitro antimicrobial sensitivity testing of *P. multocida* isolates.

Antimicrobial disc	Code	Concentration	Sensitive		Intermediate		Resistant		AA
			No.	%	No.	%	No.	%	
Amoxicillin clavulanic	AMC	30 µg	12	80	3	20	0.0	0.0	S
Cefotaxime	CTX	30 µg	10	66.66	5	33.33	0.0	0.0	S
Ciprofloxacin	Cip	5 µg	12	80	3	20	0.0	0.0	S
Erythromycin	E	15 µg	14	93.33	1	6.66	0.0	0.0	S
Gentamycin	CN	10 µg	13	86.66	2	13.33	0.0	0.0	S
Tulathromycin	Tul	30 µg	15	100	0.0	0.0	0.0	0.0	S
Tilmicosin	Til	15 µg	15	100	0.0	0.0	0.0	0.0	S

AA: Antibiogram activity

Detection of some virulence genes of *P. multocida* by PCR:

P. multocida isolates were confirmed by polymerase chain reaction (PCR) using genus specific primer sequences (*Kmt*1). The result revealed that only 4 isolates from the examined 10 isolates harbored (K*mt*1) Fig. (1) and (Table 1).

Of four isolates of *P. multocida* examined for detection of pathogenic virulence associated genes; transferrin binding protein A (*tbp*A) and Pasteurella filamentous haemagglutinin A (*Pfh*A) only two isolates harbored these genes Fig. (2). these genes play an important role in pathogenicity of *P. multocida.* The obtained results were in agreement with **Doughty *et al.* (2000)**, **Ewers *et al.* (2006) and Ahmed *et al.* (2014)** who reported that *P. multocida* is one of the causative agents of calf pneumonia especially that had virulence genes *tbpA* and *pfhA* with other virulent genes as *tox*A gene.

The rate of recovery of animals with pneumonia was calculated as 80% in the group that was given tilmicosin and 100 % in the group that was given Tulathromycin as all clinical parameters including characters of respiration,nasal discharge,depression and rectal temperature were gradually improved in all treated animals, those results were very close to such results recorded by **Godinho *et al.* (2005) and Aytekin *et al.*, (2010)** whom found that recovery rate of pneumonic animals was 80% in the group treated with tilmicosin and 85% in the group treated with Tulathromycin.

Leukogram:

Table (3) represented leukocytosis in group 2 (infected non-treated group) which is due to neutrophilia and monocytosis; such increase could be due to infective micro-organisms and damaged cells **(Coles, 1986)**. These findings were supported by the results recorded by

Praveen *et al.* (2010). Calves received tilmicosin (group 3) showed non-significant change in total and differential leukocytic counts when compared to control normal group throughout the whole experiment. These findings agreed with **Fajt *et al*. (2003) and Yazar *et al.* (2004)** while **Altunok *et al.* (2002)** reported temporary decrease in white blood cell count in rabbits and such difference might be due to the difference in species, doses and molecular structure of the drug**.** Group 4 which was treated with Tulathromycin showed non-significant changes in total and differential leukocytic counts when compared to normal control group; these findings agreed with those of **Ayse *et al.*, (2011a).**

Biochemical analysis:

Table (4) revealed that infected non-treated calves showed significant increase in ALT and AST activities along the whole experimental period indicating hepatocellular damage caused by *P. multocida* toxins **(Dwivedi and Charan 2001)** and these findings agreed with that of **Sami *et al.* (1995).**

ALT and AST enzymes activities findings in tilmicosin-treated group revealed no significant changes when compared to normal control group. These findings coincided with the previous study of **Altunok *et al.* (2002).** While Tulathromycin-treated group showed a significant increase e in ALTactivities after1week from Tulathromycin administration and AST activities showed significant increase all over the experimental period which was in agreement with **Sambo *et al.* (2009) and El-Ashmawy *et al.* (2014)** while these findings disagreed with those of **Ayse *et al.* (2011a and 2011b).**

Transient significant increase in creatinine level was observed in infected non-treated group after two days, a result that agrees with that of **El-Sawy *et al. (*2017)**. No significant change was observed in creatinine levels in both tilmicosin treated groups and Tulathromycin treated a result that agrees with that obtained by **Xie *et al*. (2011).**

Our findings regarding uric acid level in infected non-treated group, tilmicosin treated group and tulathromycin treated group were significant increase in uric acid level all over the experiment when compared to normal control group and these findings agreed with **Ragbetli *et al.* (2010) and Gheith *et al.* (2015) and El-Sawy *et al.* (2017)** and disagreed with **Elsayed *et al.* (2014).** This difference may be due to the difference in species and doses of the drugs.

Our findings regarding infected non-treated group revealed significant decrease in total protein. Also albumin levels raised along the whole experimental period that rise may be due to liver affection and protein loss due to hemorrhage. Such result agreed with that of **Sami *et al.***

(1995) and Rasha *et al.* (2018) and disagreed with those of **Praveena *et al.* (2007)**. However, such difference may be due the difference in species.

Along the experimental period, serum total protein and albumin showed significant decrease in tilmicosin treated group when compared with normal control group >A result that was coincided with those of **Braun *et al.* (2010) and Yazar *et al.* (2004).**

Tulathromycin treated group showed significant decrease in serum total protein and albumin All over the whole experimental period as compared to normal control group which may be associated with hepatocellular dysfunction induced by severe inflammation.

Oxidative status:

Table (5) revealed that infected non-treated group showed significant elevation in MDA and significant decrease in GSH throughout the whole experiment a finding that may be due to *P. multocida* endotoxins which lead to oxidative stress; these findings were in agreement with those of **El-Sheik (2015).**

Tilmicosin administration evoked a significant increase in MDA in addition to a significant decrease in GSH. MDA that was formed during the oxidative degeneration as a product of free oxygen radicals **(Valenzuela, 1990)** referring to lipid peroxidation **(Neilsen *et al.*, 1997).** The increase of MDA level demonstrated the free radicals generated by tilmicosin which lead to oxidative injury **(Cetin *et al.*, 2011).** These findings were in agreement with the results of **Yazar *et al.* (2004), Yapar *et al.* (2006), Kart *et al.* (2007a), Kart *et al.* (2007b), Cetin *et al.* (2011) and El-Sheikh (2015).**

Tulathromycin injection evoked significant decrease in GSH besides non-significant changes in MDA. These findings agree with those of **El-Sheikh (2015).** Tulathromycin is one of triamilide subclass of macrolides which cause oxidative stress **(Ayse *et al.*, 2011a).**

Table (6) showed that tilmicosin and tulathromycin had depressing effect on CRP levels; tulathromycin has more expressed anti-inflammatory effects than tilmicosin.These findings are in agreement with **Ayse and Yazar (2012)**.

CONCLUSIONS

It could be concluded that tulathromycin is more effective for the treatment of pneumonia in calves than tilmicosin as it showed more recovery rates and more anti-inflammatory effects than tilmicosin.

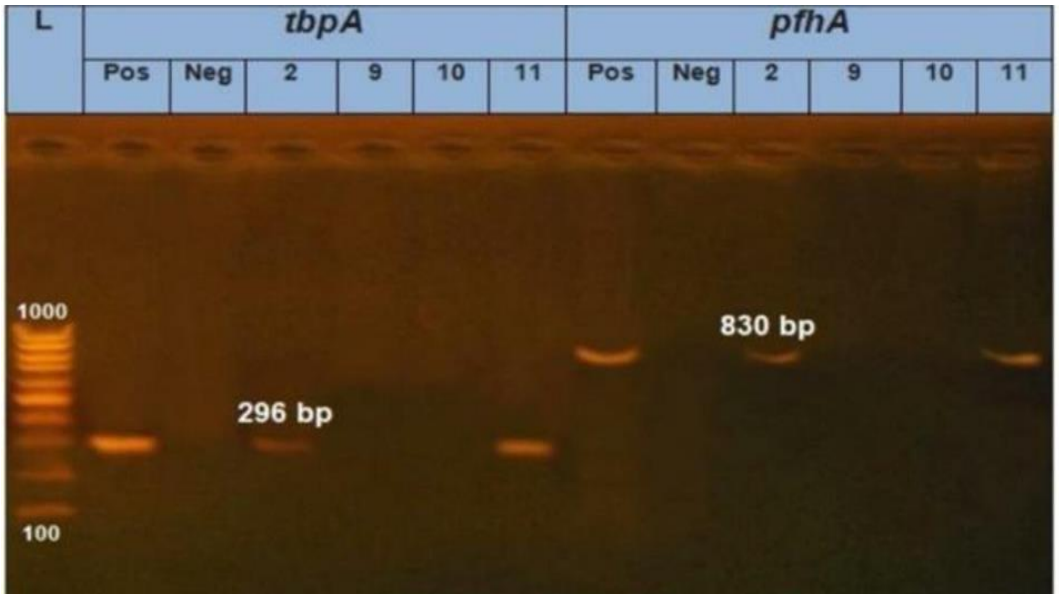

Fig. (1): Agrose gel electrophoresis pattern of PCR for detection of *tbpA* and *PfhA* genes of *P. multocida*: Lanes (2 and 11) positive amplification of tbpA gene at 296 bp fragment and *PfhA* gene at 830 bp fragment, L: ladder from 100 bp to 1000 bp, Pos: positive control, Neg: Negative control.

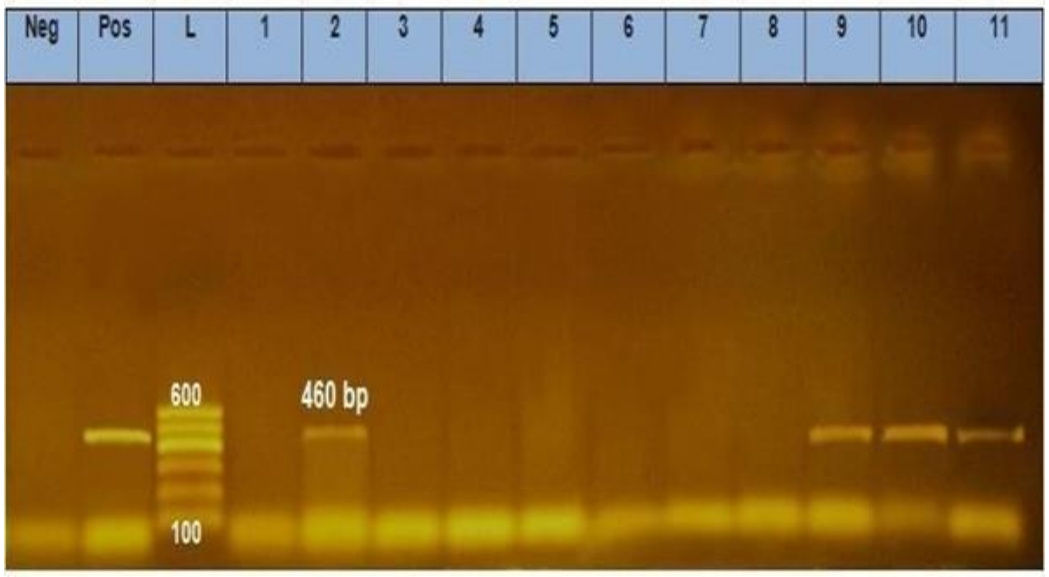

Fig. (2): Agrose gel electrophoresis pattern of PCR for detection of (*Kmt1*) gene of *P. multocida*: Lanes (2, 9, 10 and 11) positive amplification of (*Kmt1*) gene at 460 bp fragment. L: ladder from 100 bp to 600 bp, Pos: positive control, Neg: Negative control.

Table (3): Leukogram (mean ± SE) of pneumonic Calves treated with tilmicosin and tulathro mycin once. (n=5).

	Group	2 D post treatment	1 W post treatment
Total leukocytic count (10^3)	**GP 1**	**11.7 ± 3.3 [b]**	**11.6 ± 3.4 [b]**
	GP 2	**12.1 ± 2.5[a]**	**12.5 ± 1.6[a]**
	GP 3	**11.9 ± 2.2[b]**	**11.1 ± 3.1[b]**
	GP 4	**11.3 ± 1.9[b]**	**11.7 ± 2.7[b]**
Lymphocyte (10^3)	**GP 1**	**6.9 ± 2.5 [b]**	**6.3 ± 0.6 [b]**
	GP 2	**7.3 ± 3.1 [a]**	**7.8 ± 2.2 [a]**
	GP 3	**6.7 ± 1.2 [b]**	**6.1 ± 1 [b]**
	GP 4	**6.5 ± 0.7 [b]**	**6.3 ± 0.4 [b]**
Monocyte (10^3)	**GP 1**	**2.1 ± 0.8 [b]**	**2.3±1.3 [b]**
	GP 2	**2.7 ± 1.3 [a]**	**2.9 ± 1.4 [a]**
	GP 3	**2.3 ± 0.5 [b]**	**2.2 ± 0.9 [b]**
	GP 4	**2.4 ± 1.1 [b]**	**2.3 ± 0.7 [b]**
Neutrophil (10^3)	**GP 1**	**2.5 ± 1.8 [b]**	**2.6 ± 3.7 [b]**
	GP 2	**3 ± 2.1 [a]**	**3.3 ± 0.8 [a]**
	GP 3	**2.6 ± 1.3 [b]**	**2.8 ± 1.4 [b]**
	GP 4	**2.7 ± 1.1 [b]**	**2.7 ± 2.1 [b]**
Eosinophil (10^3)	**GP 1**	**0.2 ± 0.1 [b]**	**0.2 ± 0.2 [b]**
	GP 2	**0.3 ± 0.3 [a]**	**0.4 ± 0.2 [a]**
	GP 3	**0.2 ± 0.3 [b]**	**0.2 ± 0.1 [b]**
	GP 4	**0.2 ± 0.2 [b]**	**0.2 ± 0.2 [b]**

Results are represented as mean ± standard error.

For each type means within same column carrying different letters are significantly different at P≤ 0.05

GP 1: Control, GP 2: Infected non-treated, GP 3: Infected treated with Tilmicosin, GP 4: Infected treated with Tulathromycin.

Table (4): Serum biochemical parameters (mean ± SE) of pneumonic Calves treated with tilmicosin and tulathromycin once. (n=5).

	Group	2 D	1 W
Alanine transaminase (IU/ml)	**GP 1**	**14.7±2.2 ^{b}**	**18.3±0.88^{c}**
	GP 2	**35.3±3.5^{a}**	**35.3±3.5^{a}**
	GP 3	**18.7±0.67^{b}**	**23±0.58^{bc}**
	GP 4	**20.3±0.88^{b}**	**27.3±1.8^{b}**
Aspartate transaminase (IU/ml)	**GP 1**	**44.67±2.9 ^{c}**	**42.33±0.88 ^{c}**
	GP 2	**62±1.1 a**	**62±1.2 a**
	GP 3	**49.67±1.2bc**	**54±1b**
	GP 4	**52±1.7 b**	**55.67±1.2 b**
Creatinine (m/dl)	**GP 1**	**0.95±0.08 b**	**1.1±0.14 a**
	GP 2	**1.4±0.09 a**	**1.3±0.09 a**
	GP 3	**0.88±0.09 b**	**1.1±0.06 a**
	GP 4	**1.09±0.07 b**	**1.2±0.05 a**
Uric Acid (m/dl)	**GP 1**	**8.17±0.14 b**	**8.23±0.18 b**
	GP 2	**9.10±0.15 a**	**9.10±0.15 a**
	GP 3	**9±0.03 a**	**9.23±0.08 a**
	GP 4	**8.87±0.08 a**	**8.97±0.03 a**
Total Protein (g/dl)	**GP 1**	**6.73±0.33a**	**6.87±0.13a**
	GP 2	**4.66±0.08c**	**4.66±0.08c**
	GP 3	**5.46±0.27b**	**5.06±0.06b**
	GP 4	**4.90±0.05bc**	**4.73±0.03c**
Albumin (g/dl)	**GP 1**	**3.37±0.13a**	**3.23±0.08a**
	GP 2	**2.30±0.12b**	**2.30±0.11b**
	GP 3	**2.66±0.15b**	**2.40±0.06b**
	GP 4	**2.77±0.19 b**	**2.43±0.03b**

Results are represented as mean ± standard error.

For each parameter means within same column carrying different letters are significantly different at P ≤ 0.05

GP 1: Control, GP 2: Infected non-treated, GP 3: Infected treated with Tilmicosin, GP 4: Infected treated with Tulathromycin.

Table (5): Glutathione and Malondialdehyde (mean ± SE) of pneumonic Calves treated with tilmicosin and tulathromycin once. (n=5).

Parameter	Group	2 Days	1 Week
Reduced glutathione (mmol/ml)	**GP 1**	**21.87±01.16 [a]**	**23.37±0.63 [a]**
	GP 2	**14.77±0.62[c]**	**14.76±0.62[b]**
	GP 3	**17.20±0.15[b]**	**16.63±0.32 [b]**
	GP 4	**18.40±0.40 [b]**	**17.90±0.32 [b]**
Malondialdehyde (mmol/ml)	**GP 1**	**11.03±0.64 [c]**	**13.33±0.63 [c]**
	GP 2	**21.83±1.47 [a]**	**21.83±1.47 [a]**
	GP 3	**15.46±0.38 [b]**	**16.40±0.60 [b]**
	GP 4	**12.00±0.40 [c]**	**12.87±0.19 [c]**

Results are represented as mean ± standard error.

For each parameter means within same column carrying different letters are significantly different at P ≤ 0.05.

GP 1: Control, GP 2: Infected non-treated, GP 3: Infected treated with Tilmicosin, GP 4: Infected treated with Tulathromycin.

Table (6): C Reactive Protein (mean ± SE) of pneumonic Calves treated with tilmicosin and tulathromycin once. (n=5).

Parameter	Group	2 Days	1 Week
C Reactive Protein (mg/dl)	**GP 1**	**1.93±0.35 [b]**	**1.93±0.35 [b]**
	GP 2	**72±24[a]**	**72±24[a]**
	GP 3	**20.00±4[b]**	**5.10±0.49 [b]**
	GP 4	**9.40±2.60[b]**	**3.03±0.35 [b]**

Results are represented as mean ± standard error.

Means within same column carrying different letters are significantly different at P ≤ 0.05 GP 1: Control, GP 2: Infected non-treated, GP 3: Infected treated with Tilmicosi GP 4: Infected treated with Tulathromycin.

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مقارنة تأثير التلميكوزين و التولاثرومايسين في السيطرة على الأمراض التنفسية في العجول

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الملخص العربي

أجريت هذه التجربة على عدد 20 عجل (4 - 6 شهور) وزن (80 – 120 كجم)، و قد قسمت العجول إلى 4 مجموعات بالتساوي. المجموعة الأولى سليمة إكلينيكيا تركت كمجموعة ضابطة طبيعية للتجربة، المجموعة الثانية (عجول مصابة بالتهاب رئوي) تركت كمجموعة مصابة غير معالجة، المجموعة الثالثة (عجول مصابة بالتهاب رئوي) تم حقنها تلميكوزين تحت الجلد بمعدل 10 مجم / كجم من وزن الحيوان، المجموعة الرابعة (عجول مصابة بالتهاب رئوي) تم حقنها تولاثرومايسين تحت الجلد بمعدل 2.5 مجم / كجم من وزن الحيوان. تم متابعة العجول إكلينيكيا لمدة 7 أيام وتم تجميع مسحات أنفية و إجراء فحص بكتريولوجي لعزل الميكروب المسبب للالتهاب الرئوي والتعرف عليه. بالتعرف الخاص لمستخلص البكتريا المعزولة المحتملة باستخدام جهاز PCR وجد أن الميكروب المعزول هو باستيريلا مالتوسيدا لديها اثنان من الجينات الممرضة tbpA و pfhA. تم سحب عينتين من الدم من جميع العجول عند اليوم الثاني والسابع بعد العلاج للفحص الهيماتولوجي وكيمياء الدم و قد أظهرت النتائج ما يلي: المجموعة الثانية المصابة غير معالجة أظهرت زيادة معنوية في نشاط إنزيم ألانين ترانسفيريز، البروتين المتفاعل C وكذلك مالون داي ألدهيد مع نقص معنوي في مستوى الجلوتاثيون طوال فترة التجربة. المجموعة الثالثة المعالجة بالتلميكوزين أظهرت زيادة معنوية في مستوى مالون داي ألدهيد مع نقص معنوي في مستوى الجلوتاثيون. المجموعة الرابعة أظهرت زيادة معنوية في نشاط إنزيم ألانين ترانسفيريز و إنزيم أسبرتات ترانسفيريز مع نقص معنوي في مستوى الجلوتاثيون. معدلات الشفاء للعجول المصابة بالالتهاب الرئوي بسبب باستيريلا مالتوسيدا كانت 100% في المجموعة المعالجة بالتولاثرومايسين و 80% في المجموعة المعالجة بالتلميكوزين.