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Long Term Use of Flunixin Meglumine and Ketoprofen in Arabian Horses and Their Digestive and Cardiac Injuries (Biochemical, Hematological and Endoscopic Findings)

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Abstract: The present study was conducted in order to evaluation of hematologic, biochemical and endoscopic findings in horse following long period use of non-steroid anti inflammatory drugs. About 36 heads male Arab horses were divided to 3 groups consisted of 12 horses with an identical feeding, management and activity conditions. Physiological serum, 1.1 mg kg^{-1} flunixin meglumine and 3.3 mg kg^{-1} ketoprofen were injected intra muscular for 10 days, respectively for group 1-3. On zero time (before injection), days of 2, 4, 6, 8 and 10 bloods sampling was done from the horses' vena cava and the samples' serum was separated by centrifuging then the serums were freezed. Hematologic tests and some of biochemical tests were done on blood samples followed by endoscopic tests on horses for evaluating gastric viscera and gastric ulcers. Hematologic changes such as red and white blood cells count and haematocrit percentage were not meaningful in three groups. In groups 2 and 3 the average level of total protein, albumin, creatinine and urea serum levels demonstrated a meaningful increase with increasing of drug using period ($p<0.05$). The heart troponin serum level in group had a meaningful increasing since 6 and 8th day in groups 2 and 3, respectively ($p<0.05$), this increasing level was multifold in both groups on 10th day. The average level of CK, ALP, ALT, AST and GGT enzymes serum concentration in understudying horses had a meaningful increase by increasing the period of the used drug ($p<0.05$). Based on endoscopic findings all horses of group one had healthy gastric viscera after 10th day but 8 horses in group 2 had healthy gastric viscera, 3 horses suffered from I grade gastric ulcer and one horse suffered from II grade gastric ulcer. About 6, 4, 1, 1 horses of the 3rd group had healthy gastric viscera, I grade gastric ulcer, II grade gastric ulcer and III grade gastric ulcer, respectively. The result is that the use of flunixin meglumine in long time causes to increase total protein, albumin, creatinine and urea, heart troponin and CK, ALP, ALT, AST, GGT but there is no meaningful change in hematologic findings and causes to horse gastric viscera injury. Therefore, liver, renal and digestive injuries are some of long term influences of the drugs on horse.

Key words: Horse, flunixin meglumine, ketoprofen, biochemical, hematological, endoscopic

INTRODUCTION

The advantage of non steroid anti-inflammatory drugs compared with corticosteroids is due to glococorticoids. Because of the many side effects in human this issue has especial importance in human medicine. Most of non steroid anti-inflammatory applied their effects by controlling cyclooxygenase activity followed by controlling the production of prostaglandins (Tan *et al*., 2005; Yeh *et al*., 2010). Although, most of non steroid anti-inflammatory percent locotrins formation, some of them, ketoprofen and ibuprofen, control lipooxygenase and prevent locotrin production. Non steroid anti-inflammatory decrease the pain caused by inflammation but considered as inefficient analgesics and unable to relieve the visceral pain like stomachache or sever body pain like bone fracture and hurt pain (Burrows, 1981; Meschter *et al*., 1990; Messer *et al*., 1995; Morris and Garcia, 1985; Mozaffari *et al*., 2009). The role of non steroid anti-inflammatory in creating of gastric ulcer has been well known (Coenen, 1990; Geo *et al*., 1989; Tarnawski *et al*., 1985; Vernimb and Hennessey, 1977). The role and place of these kinds of drugs in producing gastric ulcers is so clear that researchers

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sometimes enjoy these drugs in creating experimental ulcers (Akah *et al*., 2007; Ajeigbe *et al*., 2008; Kisaoglu *et al*., 2011). Phenylbutazone, for instance have a proved role in creating gastric ulcers beside its side effects like anemia aplastic (Nomreal *et al*., 2004). The other drug of this group is flunixin meglomin which has some roles in creating gastric ulcer in ponies which received 1.5 mg/kg/8 h for 6 days or 1.1 mg/kg/8 h for 7 days (Dionne *et al*., 2003; Nomreal *et al*., 2004). It must be noted that the prescription of these drugs, orally or injection can cause gastric ulcer. Furthermore, other problems such as epithelial necrosis and intestine epithelium inflation have been attributed to these drugs (Nomreal *et al*., 2004). Long term use of non steroid anti-inflammatory may have some effects on cardiac function (Houdeshell and Hennssey, 1977; Kauffman *et al*., 1980). The present study examines this issue by evaluating cardiac and digestive enzymes. The study aiming at evaluating hematologic, biochemical and endoscopic findings following long term use of non steroid anti-inflammatory in Arab horse which examines mainly their effects on cardiac and digestive functions.

MATERIALS AND METHODS

The present study is an experimental interventional one which was conducted on 36 male Arab horses of Tabriz stables. About 36 male Arab horses were divided to 3 groups of 12 horses with an identical feeding, management and activity conditions. Feeding dietary of all groups consisted of alfalfa, hay, bran and barley. Physiological serum, 1.1 mg kg^{-1} flunixin meglomin and 3.3 mg kg^{-1} ketoprofen were injected intra muscular (Colhan *et al*., 1999) for 10 days, respectively for group 1-3. On 0 day (before injection), days of 2, 4, 6, 8 and 10 the blood sampling was done from the horses' vena cava and the samples' serum was separated by centrifuging then the serums were freezed. Two blood samples were obtained; one of them with anti-coagulant for hematologic tests and another one without anti-coagulant for biochemical tests.

Hematologic tests consisted of red and white blood cells count and haematocrit percentage as well as biochemical tests consisted of total protein, albumin, CK, ALP, ALT, AST and GGT enzymes serum concentration, creatinine, urea and cardiac troponin. All of serum levels were measured by biochemical kits and cardiac troponin was measured by ELISA kit at Sina laboratory. Finally, the average level of the mentioned metabolites was calculated on the mentioned times. All horses were endoscoped for examining gastric epithelium and gastric ulcer. For analyzing the data were used of $SPSS_{13}$ and for comparison of means between groups and between different days of ANOVA test were used.

RESULTS AND DISCUSSION

Hematologic findings of three groups: Normal salin (group 1), flunixin meglumine (group 2) and ketoprofen (group 3) has been shown in Table 1. The changes in red blood cells count in control group are not meaningful from 0-10th day. Besides, these changes were not meaningful in groups 2 and 3. On the other hand, the difference among three groups isn't meaningful on any of sampling days. The average level difference of white blood cells and haematocrit was not meaningful from zero to 10th day as well and the observed changes aren't significant.

The average level of total protein serum had no meaningful difference from 0-10th day in group 1 but it was increased on the mentioned days in group 2 such that from 6th day afterwards the increase was meaningful ($p<0.05$). In group 3 there was increase in this parameter which was meaningful from 4th days afterwards ($p<0.05$). Furthermore, the average difference among three groups was meaningful on the 0 and 2nd days. The difference of ketoprofen average level was meaningful on 4th day ($p<0.05$) but the difference of flunixin meglomin was not meaningful and the averages difference among three groups was meaningful on 6th, 8th, 10th days ($p<0.05$). The average of serum albumin in group 1 was not meaningful difference among various days but has meaningful difference in groups 2 and 3 from 8th day afterwards ($p<0.05$). The average difference among groups

Table 1: Hematological effects of saline (group 1), flunixin meglumine (group 2) and ketoprofen (group 3) administration in Arabian horses in different times of sampling during (M±SE)

		Groups		
Factors	Day of sampling	Saline	Flunixin meglumine	Ketoprofen
RBC ($\times 10^6$ μL^{-1})	0	8.4±0.920^{Aa}	8.5±0.870^{Aa}	8.6±1.030^{Aa}
	2	8.1±1.040^{Aa}	8.2±0.660^{Aa}	8.0±0.960^{Aa}
	4	8.5±0.650^{Aa}	8.3±0.660^{Aa}	7.8±0.840^{Aa}
	6	8.0±0.740^{Aa}	7.9±0.420^{Aa}	8.1±0.310^{Aa}
	8	7.9±0.340^{Aa}	8.1±0.310^{Aa}	7.9±0.520^{Aa}
	10	8.4±1.110^{Aa}	8.0±0.240^{Aa}	7.6±0.260^{Aa}
WBC ($\times 10^3$ μL^{-1})	0	6.8±0.330^{Aa}	6.3±0.480^{Aa}	6.4±0.640^{Aa}
	2	6.6±0.650^{Aa}	6.5±0.750^{Aa}	6.7±0.420^{Aa}
	4	6.7±0.980^{Aa}	6.9±1.020^{Aa}	7.2±0.540^{Aa}
	6	6.8±0.560^{Aa}	6.7±0.080^{Aa}	7.1±0.790^{Aa}
	8	7.0±0.750^{Aa}	7.5±0.630^{Aa}	7.8±1.010^{Aa}
	10	7.1±0.770^{Aa}	7.9±0.420^{Aa}	7.2±0.490^{Aa}
PCV (%)	0	45.31±4.23^{Aa}	46.58±5.04^{Aa}	44.69±6.92^{Aa}
	2	44.53±6.87^{Aa}	49.50±8.43^{Aa}	48.34±3.82^{Aa}
	4	46.76±6.08^{Aa}	48.96±5.66^{Aa}	46.33±4.77^{Aa}
	6	44.64±5.50^{Aa}	46.87±6.43^{Aa}	44.51±5.39^{Aa}
	8	43.97±7.18^{Aa}	50.41±3.17^{Aa}	47.40±3.06^{Aa}
	10	44.69±3.28^{Aa}	49.53±3.96^{Aa}	51.16±4.10^{Aa}

$^{a-c}$In each row, only those means with different letters are significantly different ($p<0.05$); $^{A-C}$In each column, only those means with different letters are significantly different ($p<0.05$); RBC = Red Blood Cell, WBC = White Blood Cell, PCV = Packed Cell Volume, SE = Standard Error, values are shown as mean±SE

was not meaningful on 0 and 2nd days but it was meaningful on the other days ($p<0.05$). The average of serum creatinine in group 1 had not meaningful difference on various days but it was different from 6th day afterwards in group 2 and from 8th day afterwards in group 3 ($p<0.05$). The difference of the averages among groups on 0, 2nd and 4th days was not meaningful but it was meaningful on the other days ($p<0.05$). The average level of blood urea wasn't meaningful in group 1 on various days but it was meaningful in group 2 from 6th day afterwards and in group 3 from 8th day afterwards ($p<0.05$).

The difference of the average among all groups wasn't meaningful on 0, 2nd and 4th days but it was meaningful on the other days ($p<0.05$). The average level of cardiac troponin serum was not meaningful in group 1 on various days but it was meaningful in group 2 from 6th day afterwards and in group 3 from 8th day afterwards ($p<0.05$) such that the increase was significant on 10th day. The difference of the average among groups was not meaningful on 0, 2nd and 4th days but it was meaningful on the other days ($p<0.05$). The increase of cardiac troponin serum in group 2 was apparent on 10th day (Table 2).

The average of serum keratin kinase enzyme was not meaningfully different in group 1 on various days but it was different meaningfully in group 2 from 8th day afterwards and in group 3 from 4th day afterwards ($p<0.05$). The difference of the average among all groups was not meaningful on 0 and 2nd days but it was meaningful on the other days ($p<0.05$). The average of serum alkaline phosphatase enzyme was not different meaningfully in group 1 on various days but it was meaningful in group 2 from 4th day afterwards and in group 3 from 8th day afterwards ($p<0.05$). The difference of the average among all groups was not meaningful on 0 and 2nd days but it was meaningful on the other days ($p<0.05$). The average of serum alanine transferase was not meaningfully different in group 1 on various days but it was different meaningfully in groups 2 and 3 from 8th day afterwards ($p<0.05$). The difference of the groups' average was not meaningful on 0, 2nd and 4th days but it was meaningful on the other days ($p<0.05$). The average of serum aspartate amino transferase was not meaningfully different in group 1 on various days but it was different meaningfully in groups 2 from 4th day afterwards and in group 3 from 8th day afterwards ($p<0.05$). The difference of the groups' average was not meaningful on 0, 2nd days but it was meaningful on the other days ($p<0.05$). The average of serum γ glutamyl transferase was not meaningfully different in group 1 on various days but it was different meaningfully in groups 2 from 6th day afterwards and in group 3 from 8th day afterwards ($p<0.05$). The difference of the groups' average was not meaningful on 0, 2nd and 4th days but it was meaningful on the other days ($p<0.05$) (Table 3).

Table 2: Some biochemical effects of saline (group 1), flunixin meglumine (group 2) and ketoprofen (group 3) administration in Arabian horses in different times of sampling during (M±SE)

		Groups		
Factors	Day of sampling	Saline	Flunixin meglumine	Ketoprofen
Total protein (g dL^{-1})	0	6.91±1.070^{Aa}	7.13±0.960^{Aa}	7.01±1.140^{Aa}
	2	7.04±1.110^{Aa}	7.08±1.120^{Aa}	7.13±0.560^{Aa}
	4	7.12±0.890^{Aa}	7.21±0.770^{Aa}	8.69±0.680^{Bb}
	6	6.86±1.040^{Aa}	9.17±1.210^{Bb}	10.13±1.530^{Cb}
	8	7.00±0.860^{Aa}	9.32±0.970^{Bb}	9.54±1.060^{Bb}
	10	7.23±0.450^{Aa}	10.87±1.500^{Bb}	11.03±1.420^{Cb}
Albumin (g dL^{-1})	0	3.01±0.230^{Aa}	3.11±0.310^{Aa}	3.07±0.140^{Aa}
	2	3.15±0.540^{Aa}	3.22±0.220^{Aa}	3.16±0.340^{Aa}
	4	2.97±0.440^{Aa}	3.98±0.570^{Ab}	4.16±0.180^{Bb}
	6	2.88±0.210^{Aa}	3.76±0.650^{Aa}	3.98±0.830^{Ab}
	8	3.07±0.450^{Aa}	4.88±1.030^{Bb}	4.76±1.050^{Bb}
	10	3.10±0.550^{Aa}	4.52±1.110^{Bb}	4.91±0.870^{Bb}
Creatinine (mg dL^{-1})	0	0.87±0.040^{Aa}	0.93±0.020^{Aa}	0.91±0.140^{Aa}
	2	0.79±0.030^{Aa}	0.87±0.050^{Aa}	0.92±0.110^{Aa}
	4	0.88±0.100^{Aa}	1.04±0.100^{Ab}	0.89±0.070^{Aa}
	6	0.86±0.040^{Aa}	2.31±0.660^{Bb}	1.00±0.210^{Aa}
	8	0.91±0.040^{Aa}	2.75±0.440^{Bb}	1.12±0.500^{Bc}
	10	0.86±0.110^{Aa}	2.07±0.110^{Bb}	2.05±0.760^{Cb}
Blood urea nitrogen (mg dL^{-1})	0	17.81±2.170^{Aa}	18.04±4.060^{Aa}	16.94±0.190^{Aa}
	2	18.92±3.080^{Aa}	19.45±3.760^{Aa}	18.33±2.970^{Aa}
	4	20.05±3.650^{Aa}	22.14±3.310^{Aa}	19.87±2.650^{Aa}
	6	19.54±4.180^{Aa}	30.14±2.640^{Bb}	22.65±4.130^{Aa}
	8	18.76±3.850^{Aa}	33.79±3.070^{Bb}	35.59±4.180^{Bb}
	10	17.65±5.010^{Aa}	28.42±2.580^{Bb}	32.74±3.410^{Bb}
Cardiac troponin (mg mL^{-1})	0	0.078±0.01^{Aa}	0.075±0.00^{Aa}	0.081±0.01^{Aa}
	2	0.065±0.00^{Aa}	0.080±0.00^{Aa}	0.078±0.00^{Aa}
	4	0.066±0.01^{Aa}	0.082±0.02^{Aa}	0.076±0.02^{Aa}
	6	0.081±0.03^{Aa}	0.17±0.060^{Bb}	0.098±0.04^{Aa}
	8	0.082±0.00^{Aa}	0.86±0.050^{Bb}	1.50±0.120^{Bc}
	10	0.076±0.00^{Aa}	2.37±0.130^{Cb}	1.84±0.090^{Bb}

$^{a-c}$In each row, only those means with different letters are significantly different ($p<0.05$); $^{A-C}$In each column, only those means with different letters are significantly different ($p<0.05$), values are shown as Mean±SE

Based on endoscopic findings all horses of group one had healthy gastric viscera after 10th day but 8 horses in group 2 had healthy gastric viscera, 3 horses suffered from I grade gastric ulcer and one horse suffered from II grade gastric ulcer. About 6, 4, 1, 1 horses of the third group had healthy gastric viscera, I grade gastric ulcer, II grade gastric ulcer and III grade gastric ulcer, respectively (Table 4).

Now-a-days, non-steroidal anti inflammatory drugs have a high use in veterinary which are used in equine treatment as well. The present study aiming at evaluating the hematologic, biochemical and endoscopic findings in horse following long term use of non-steroidal anti inflammatory. The average of red blood cells count in both groups received flunixin meglumine and ketoprofen decreased from 0-10th days but the decrease was not

Table 3: Some enzyme effects of saline (group 1), flunixin meglumine (group 2) and ketoprofen (group 3) administration in Arabian horses in different times of sampling during (M±SE)

		Groups		
Factors	Day of sampling	Saline	Flunixin meglumine	Ketoprofen
CK	0	217.64±12.29^{Aa}	224.41±21.14^{Aa}	237.76±14.26^{Aa}
(U L^{-1})	2	220.76±11.65^{Aa}	231.54±13.23^{Aa}	240.64±20.14^{Aa}
	4	224.54±13.76^{Aa}	222.14±5.690^{Aa}	268.42±13.86^{Bb}
	6	216.65±5.970^{Aa}	236.45±12.43^{Ab}	238.54±18.95^{Ab}
	8	219.98±11.75^{Aa}	275.40±21.14^{Bb}	268.63±19.05^{Bb}
	10	223.45±13.24^{Aa}	266.84±13.76^{Bb}	273.43±20.41^{Bb}
ALP	0	387.23±24.29^{Aa}	379.41±39.14^{Aa}	411.43±19.27^{Aa}
(U L^{-1})	2	396.54±31.09^{Aa}	367.50±24.54^{Aa}	407.66±18.53^{Aa}
	4	376.64±16.76^{Aa}	496.75±20.37^{Bb}	417.28±21.95^{Aa}
	6	384.73±25.87^{Aa}	475.64±21.62^{Bb}	423.49±12.76^{Ab}
	8	392.87±19.13^{Aa}	523.64±31.18^{Cb}	530.64±41.86^{Bb}
	10	390.43±13.65^{Aa}	487.54±21.80^{Bb}	512.42±27.60^{Bb}
ALT	0	9.27±1.140^{Aa}	8.23±0.760^{Aa}	10.11±1.210^{Aa}
(U L^{-1})	2	9.05±1.650^{Aa}	8.54±1.050^{Aa}	9.28±0.860^{Aa}
	4	9.54±0.870^{Aa}	9.48±1.110^{Aa}	10.07±1.250^{Aa}
	6	8.95±1.580^{Aa}	8.97±0.890^{Aa}	10.21±1.130^{Ab}
	8	9.33±2.060^{Aa}	11.32±1.230^{Bb}	15.61±2.060^{Bc}
	10	9.24±1.100^{Aa}	14.07±1.400^{Cb}	14.79±1.680^{Bb}
AST	0	314.36±9.230^{Aa}	310.09±11.28^{Aa}	309.64±19.73^{Aa}
(U L^{-1})	2	320.14±10.13^{Aa}	314.57±21.60^{Aa}	317.57±9.280^{Aa}
	4	308.64±7.670^{Aa}	419.44±19.59^{Bb}	329.54±21.74^{Aa}
	6	311.34±11.18^{Aa}	426.60±12.54^{Bb}	336.75±17.80^{Aa}
	8	316.45±9.670^{Aa}	539.47±20.06^{Cb}	491.55±21.74^{Bc}
	10	310.65±17.65^{Aa}	571.54±18.65^{Cb}	544.42±18.53^{Bb}
GGT	0	26.39±2.170^{Aa}	25.54±3.210^{Aa}	28.60±1.200^{Aa}
(U L^{-1})	2	25.61±3.850^{Aa}	24.68±4.120^{Aa}	27.64±4.310^{Aa}
	4	29.02±4.620^{Aa}	28.47±3.070^{Aa}	30.53±3.400^{Aa}
	6	25.75±1.640^{Aa}	42.16±3.430^{Bb}	36.76±3.220^{Ab}
	8	26.08±4.110^{Aa}	40.54±2.870^{Bb}	45.52±5.410^{Bb}
	10	27.92±3.050^{Aa}	47.61±3.440^{Bb}	51.05±4.330^{Bb}

$^{a-c}$In each row, only those means with different letters are significantly different ($p<0.05$); $^{A-C}$In each column, only those means with different letters are significantly different ($p<0.05$), CK = Creatine Kinase, ALP = Alkaline Phosphatase, ALT = Alanine Aminotransferase, AST = Aspartate Aminotransferase, GGT = γ Glutamyl Transferase, SE = Standard Error; values are shown as Mean±SE

Table 4: The number of horses affected with different grades of gastric ulcer through endoscopic survey in three groups

	Grade of gastric ulcer				
Groups	0	I	II	III	IV
Saline	12	-	-	-	-
Flunixin meglumine	8	3	1	-	-
Ketoprofen	6	4	1	1	-

meaningful. Furthermore, the decrease of the haematocrit percentage was not meaningful. The average of white blood cell count in both groups increase with increasing the injection days which was not meaningful. The difference of hematologic parameters among three groups was not meaningful on any sampling days. The decrease of red blood cell count and haematocrit may associate with anemia caused by gastric ulcers in groups 2 and 3 (Radostitis *et al*., 2007). Lees reported an anemia in horse caused by gastric ulcer. Although, the increase of white blood cells was not meaningful but it can be due to inflation caused by gastric epithelium injuries because of long term use of non-steroidal anti inflammatory. It was characterized in the present study by endoscopic examinations that there were various degrees of gastric ulcer in epithelium after 10th day of the drugs using; 4 horses of group 2 and 6 horses of group 3. The role and place of these kinds of drugs in producing gastric ulcers is so clear that researchers sometimes enjoy these drugs in creating experimental ulcers. Phenylbutazone, for instance have a proved role in creating gastric ulcers beside its side effects like anemia aplastic (Nomreal *et al*., 2004). The other drug of this group is flunixin meglumine which has some roles in creating gastric ulcer in ponies which received 1.5 mg/kg/8 h for 6 days or 1.1 mg/kg/8 h for 7 days (MacAllister *et al*., 1993; Nomreal *et al*., 2004). In another study by Morris the negative influence of phenylbutazone on thyroidal hormones serum level has been proved; the thyroidal hormones of these horses increased immediately by TSH injection (Morris and Garcia, 1985). Goodrich *et al*. (1998) and Traub *et al*. (1988) has reported high gastric ulcer following the long term use of non steroidal anti inflammatory like phenylbutazone and flunixin meglomin. Long term uses of non steroidal anti inflammatory disable protective mechanisms of gastric epithelium against gastric juice due to limit the PGE2 synthesis and decrease the blood circulation in gastric epithelium (Roth and Bennett, 1987). The findings conform to findings of Goodrich *et al*. (1998) and Traub *et al*. (1988). Lack of appetite resulted from long term use of the drugs has been reported in 6 horses which is caused by gastric epithelium injuries (MacAllister *et al*., 1993). It was characterized in this study that the average level of serum total protein and albumin was increased meaningfully in groups 2 and 3 from 4 and 6th afterwards.

These changes can be resulted of gastroenteropathy. Gastric epithelium injury and gastric ulcer followed by increasing the serum level of total protein and albumin have been reported in a study conducted by McAllister and Sangiah (1993). In another study by Meschter *et al*. (1990) it was reported that horses with gastric ulcer suffered from hypoproteinemia and hypocalcaemia. The meaningful increase of blood creatinine and urea average level in groups 2 and 3 with increasing of using period of the drug can be resulted of renal injury which needs more evaluation. In the study conducted by Mozaffari on goats and Snow on ponies the issue has been confirmed and it has been mentioned that long term use of non steroidal anti inflamatorys resulted in renal injury and increasing blood urea and serum level of alkaline phosphatase and creatinine (Mozaffari *et al*.,

2009; Snow *et al*., 1979). It was characterized in this study that cardiac troponin serum level had a meaningful increase in group 2 since 6th day and in group 3 since 8th day which was tenfold in group 2 on 10th day. Now-a-days, the increase of cardiac troponin level is as a standard biochemical criterion for identifying myocardial injury and severs myocardial infarctions (Parmacek and Solaro, 2004; Schward *et al*., 2003). Cardiac troponin serum level increase can be resulted of long term use of the drugs followed by cardiac myocardial. Cornelisse *et al*. (2000) in a study reported that a horse with arterial rupture and ventricular tachycardia the cTnl serum level was 5.9 mg mL^{-1} on referral day and 4.3 mg mL^{-1} 5 days afterwards. Schwarzwald *et al*. (2003) showed the increased level of troponin in a horse with ventricular tachycardia and myocardial necrosis. Phillips *et al*. (2003) demonstrated in a study that cTnl serum level in competition horses was not meaningfully different compared with pasture horses. The average level of cTnl in both groups was 0.047±0.085 mg mL^{-1}. Begg *et al*. (2006) estimated by ADVIA the normal level of cTnl in Thoroughbred horses <0/15 μg mL^{-1}. It was shown in 2007 that in equine piroplasmosis the increase of cTnl serum level was associated with tachycardia and early complexes of ventricular polymorphism. CTnl level was estimated at 0.27 mg mL^{-1} in horses suffered from piroplasmosis and at 0.1-0.03 mg mL^{-1} in healthy horses (Diana *et al*., 2007). Nostell and Haggstrom (2008) showed that the horses had troponin <0.022 μg L^{-1} but it was decreased 1-2 h after competition like 10-14 h after that time.

The average level of serum concentration of CK, ALP, ALT, AST and GGT enzymes in understudying horses of groups 2 and 3 showed a meaningful increase with increasing the using period of the drugs. The increase of these enzymes can be resulted of liver injury which was mentioned by other researchers as well (Safarchi *et al*., 2010; Morris and Garcia, 1985). The increase of GGT following the use of Phenylbutazone past has been reported by Lees and Higgins (1987).

CONCLUSION

It is concluded that flunixin meglumine and ketoprofen cause to increase the total protein, albumin, creatinine, urea and cardiac troponin enzymes, CK, ALP, ALT, AST and GGT but cause no meaningful change in hematologic findings as well as cause the gastric epithelium injury in horse. So, liver, renal and digestive injuries are long term results of the drugs in horse.

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