INTERNATIONAL JOURNAL OF SCIENCE AND NATURE

www.scienceandnature.org

EFFECT OF THE TOXIC DOSE OF LEVAMISOLE ON SOME HEMATOLOGICAL PARAMETERS, LIVER AND KIDNEY FUNCTIONS IN LAMBS

[1]Alaa Kamal Mahmoud & [2]Zainab Alaa Ahmed
[1,2] Department of Internal and Preventive Medicine-College of Veterinary Medicine- University of Baghdad. Baghdad-Iraq

ABSTRACT
The aim of the present study was to determine the effects of levamisole, administrated at therapeutic and toxic doses, on some hematological and biochemical parameters in lambs. For this purpose ten lambs were used during the period from 22 October to 5 November 2016. Animals were distributed randomly into two groups (therapeutic and toxic groups). Levamisole was given orally at single doses of 7.5mg/kg for therapeutic group and 20mg/kg for toxic group. Blood samples were taken from the jugular vein prior to administrations of levamisole, then at 2, 24, 48, 96 and 144 hours post-administrations. Hematological and biochemical parameters were performed. Clinical follow-up of the lambs related to therapeutic group revealed mild and transient complications which did not interfere with animals health. In contrast harmful problems were noticed in toxic group such as neurotoxicity, paralysis, vomiting, diarrhea and difficult respiration. Hematological analysis showed that the levamisole was decreased the RBCs count and Hb and increased the levels of PCV and WBCs count in both groups which were significant ($P<0.05$) and more clear in toxic group. Liver enzymes, (ALT), (AST) and (ALP) showed significant increased ($P<0.05$) in both groups especially in toxic group. For the kidney function, urea and creatinine were estimated and they recorded an increment in their values mainly in toxic group. The conclusion of the study was that levamisole in therapeutic doses caused mild changes in studied parameters; further more toxic doses were evocated in serious changes in blood picture, liver and kidney functions which were life threatening to lambs health.

KEYWORDS: levamisole, hematological, biochemical, parameters, lamb.

INTRODUCTION

Levamisole is used as broad spectrum anthelmintic in animals against (gastrointestinal and lung nematodes) and other parasites (Várady *et al.*, 2011), also it act as immunomodulator and immunostimulant (Ravindra *et al.*, 2017). It eliminates parasites by neuromuscular activity or interferes with the metabolism of carbohydrates (sugars) in the worm. Within 1 to 3 hours after administration the worms are paralyzed and die or are expelled (Rehni and Singh, 2010). The dose of levamisole should be calculated carefully because toxic dose of levamisole one or two times therapeutic dose. For sheep and goats, a normal dose is 7.5 mg/kg (Ahmet *et al.*, 2004). Toxic and adverse effects can develop in most of the animal species. Sheep have been observed experiencing transient excitability while on levamisole such as neurotoxicity, depression, hyperesthesia, and salivation (Pancarci *et al.*, 2007). Other possible side effects can include vomiting, diarrhea, dyspnea, loss of consciousness, bradycardia and even death due to respiratory failure is possible (Amir *et al.*, 2013). Laboratory examinations following levamisole administration revealed decreased number of erythrocytes, hemoglobin and increased hematocrit, activity of liver enzymes, urea and creatinine levels in the serum (Gokce *et al.*, 2004). Thus the aims of study were to evaluate the effect of toxic dose of levamisole on hematological parameters, liver and kidney functions in lambs.

MATERIALS & METHODS

Experimental animals

Ten clinically healthy male lambs were used for the present experiment during the period from 22 October to 5 November 2016. All lambs at the same ages (3months) and weighing ranged (18-20) Kg. The animals were fed three times a day. Ear tagged were inserted for numbering the animals and allowed two weeks preliminary period for observation and adaptation prior to the commencement of the experiment. The lambs were divided homogenously and equally into two groups (n = 5) for each group as follow. First group was received single therapeutic dose of levamisole (7.5 mg/kg) B.W. The second group (toxic group), was received single toxic dose of levamisole at a rate of 20 mg/kg B.W. Both doses were given orally.

Parameter of the study

A. Clinical observation: The Clinical signs were monitored after administration of levamisole in therapeutic and toxic doses to observe any side effects evocated from both doses.

B. Hematological and biochemical parameters: For hematological and biochemical assay, blood samples (20ml) (10ml for each group) were collected aseptically by jugular venipuncture at zero time (to record normal data of the studied parameters) and then after administration of levamisole at (2, 24, 48, 96 and 144) hours. The blood samples were divided into two equal portions (5ml for each). The first sample (5ml) was collected in tubes with (EDTA) as anticoagulant for hematological parameters, and then the tubes were inverted several times to ensure proper mixing. These samples were used for estimation of (WBCs x10 ^{3}/mm^3),

(RBCs x10 ^{6}/ mm^{3}), (Hb mg/dl) and (PCV %) which were determined by a hemolyzer. The second blood sample (5ml) was collected in plain tube (without anticoagulant) for obtaining clear serum for estimation the activities of liver enzymes (ALT, AST and ALP) by special kit and Reflotron. Also Serum levels of urea and creatinine were estimated using spectrophotometer. Blood samples in plain tubes were centrifuged at 3000 rpm for 5 minutes, to obtain the sera which were frozen individually at -20°C until analyzed. Similar division of blood sample and parameters measurement was following for lamb's toxic group.

Statistical analysis

Statistical analysis of data was performed using SAS (Statistical Analysis System - version 9.1). Two way Analysis of Variance (ANOVA) and least significant differences (LSD) post hoc test were performed to assess significant differences among means. The P<0.05 was considered statistically significant (SAS.2010).

RESULTS

Clinical follow-up

The oral administration of levamisole to the lambs at therapeutic doses 7.5mg/kg, three lambs were reflected mild and transient signs including; nausea, vomiting, abdominal discomfort and fever. These sings were disappeared on the second day morning. While the remaining two lambs showed normal behavior without any harmful effects on health status. In contrary lambs received toxic dose 20mg/kg showed varying clinical signs which include, inappitance, salivation, neurologic excitement, and diarrhea. The most obvious sings reported in dosed lambs of toxic group were two lambs (40%) unable to stand and they showed hind limb paralysis and finally they became recumbent. In general, therapeutic group looked clinically better than toxic group. Furthermore, all lambs in both groups survived the experimental period (mortality was zero percent). A remarkable improvement in clinical conditions of the toxic lambs was observed at 4th day post-levamisole administration.

Hematological results

a. White blood cells: Data fixed in (table 1) reflected higher (P<0.05) WBCs values in therapeutic and toxic lamb groups at zero time thus it recorded (6.12 ±0.62) and (6.15 ±0.58) respectively with no significant differences (P>0.05) between them. Significant differences (P<0.05) were started between the two groups at 2 and 24 hours. After that and at (48, 96 and 144) hours, there were mild differences between the two groups with lack of significance.

TABLE 1. Mean values of WBC (10 ^{3}/ mm^{3}) in both groups.

Groups	Zero time M±SE	2hrs M±SE	24hrs M±SE	48hrs M±SE	96hrs] M±SE	144hrs M±SE
Therapeutic	A	AB	AB	B	B	B
	6.12± 0.62	8.43± 0.32	8.22± 1.62	7.92±1.11	7.47± 0.33	7.58± 0.36
	a	a	a	a	a	a
Toxic	A	B	B	B	B	B
	6.15± 0.58	7.13 ± 0.17	7.02 ± 0.28	7.17± 0.69	6.40± 0.55	6.91±0.11
	a	b	b	a	a	a
LSD	1.12					

Different small letters in the same column indicate significant difference (P<0.05) between groups

Different capital letters in the same column indicate significant difference (P<0.05) between the animals related to same group

TABLE 2. Mean values of RBC (10 ^{6}/ mm^{3}) in both groups

Groups	Zero time M±SE	2hrs M±SE	24hrs M±SE	48hrs M±SE	96hrs M±SE	144hrs M±SE
Therapeutic	A	A	A	A	A	A
	11.04 ± 4.23	11. 06± 1.83	11.22± 3.53	11.25± 4.63	11.53± 3.73	11.21± 4.23
	a	a	a	a	a	a
Toxic	A	A	B	B	C	C
	11.25± 2.29	11.04± 4.43	9. 44± 4.27	8.75± 2.21	7.18± 4.13	6.92± 4.46
	a	a	b	b	b	b
LSD	1.22					

Different small letters in the same column indicate significant difference (P<0.05) between groups.

Different capital letters in the same column indicate significant difference (P<0.05) between the animals related to same group.

b. Red blood cells The RBCs values showed significant differences (P<0.05) between the therapeutic and the toxic groups at 24,48,96 hours and it was clear at 144 hours in which the values reached to it low level (6.92± 4.46) at that time. Furthermore there were no significant changes in RBCs values among lambs related to therapeutic group. In contrary animals of toxic group reflected significant alteration among periods i.e. 2, 24, 48, 96 and 144 hours (Table 2).

c. Hemoglobin: Information in (table 4-3) showed the mean values of hemoglobin in both groups. In general the values decreased dramatically with the advancement of time in toxic group mainly at 96 hours (6.24 ±0.52) and at 144 hours (6.84 ±0.57). The significant differences (P<0.05) between the two groups were recorded at 48, 96 and 144 hours post levamisole administration. In contrast no significant differences were observed at zero, 2 and 24 hours. Furthermore the significance differences were observed between zero times and remaining periods in both groups.

TABLE 3. Mean values of Hb (mg/dl) in both groups

Groups	Zero time M±SE	2hrs M±SE	24hrs M±SE	48hrs M±SE	96hrs M±SE	144hrs M±SE
Therapeutic	A	AB	B	B	B	AB
	9.40±0.84	9.04±0.55	8.21±0.28	8.70±0.32	8.80±0.73	8.92±0.90
	a	a	a	a	a	a
Toxic	A	B	B	B	B	B
	10.12±0.18	8.56±0.50	7.78±0.30	7.15±0.47	6.24±0.52	6.84±0.57
	a	a	a	b	b	b
LSD	1.08					

Different small letters in the same column indicate significant difference (P<0.05) between groups
Different capital letters in the same column indicate significant difference (P<0.05) between the animals related to same group

d. Packed cell volume: The PCV values were elevated with the progress of experimental time.The significant differences (P<0.05) between the two groups were recorded at 96 hour thus it reached (32.77±4.28) and (35.88±2.88). Also at 144 hours (32.01±4.66) and (35.11±0.75) respectively. There were no significant differences among lambs related to therapeutic group at all periods. While in toxic group the significant differences reported between zero time (un-dosed lambs) and the remaining periods with the exception of time two hours (table 4).

TABLE 4. Mean values of PCV % in both groups

Groups	Zero time M±SE	2hrs M±SE	24hrs M±SE	48hrs M±SE	96hrs M±SE	144hrs M±SE
Therapeutic	A	A	A	A	A	A
	31.84±2.37	32.11±4.29	33.50±2.55	33.60±5.22	32.77±4.28	32.01±4.66
	a	a	a	a	b	b
Toxic	B	AB	A	A	A	A
	30.70±3.38	32.88±2.21	34.22±2.53	35.12±1.37	35.88±2.88	35.11±0.75
	a	a	a	a	a	a
LSD	2.44					

Different small letters in the same column indicate significant difference (P<0.05) between groups.
Different capital letters in the same column indicate significant difference (P<0.05) between the animals related to same group

Liver function

a. Alanine aminotransferase (ALT): There were an obvious increment (P<0.05) in ALT values in both groups mainly at 96 and 144 hours. The highest value (32.11±0.13) was observed at the end of experiment in toxic lambs group. In addition variation was detected among the animals of the therapeutic and toxic groups (table 5).

TABLE 5. Mean values of ALT (IU/L) in both groups

Groups	Zero time M±SE	2hrs M±SE	24hrs M±SE	48hrs M±SE	96hrs M±SE	144hrs M±SE
Therapeutic	D	CD	C	B	AB	A
	15.80±1.68	16.5 ± 1.08	19.11±0.33	23.04±0.36	25.20±1.72	28.21±0.06
	a	a	b	a	b	b
Toxic	D	D	C	B	A	A
	15.67±2 .11	18.12± 1.15	22.53±0.12	26.10±1.62	29.52±0.24	32.11±0.13
	a	a	a	a	a	a
LSD	3.21					

Different small letters in the same column indicate significant difference (P<0.05) between groups.
Different capital letters in the same column indicate significant difference (P<0.05) between the animals related to same group

b. Aspartate aminotransferase (AST): Data in table (6) clarified that the values of AST recorded significant differences (P<0.05) between the two groups started from 2 hours till the end of the experiment. The highest value was recorded at 96 hours thus it reached (82.21±3.38) and (98.34±2.52) in therapeutic and toxic groups respectively then it decreased sharply at the end of experiment. Also differences in certain period were detected in both groups.

TABLE 6. Mean values of AST (IU/L) in both groups

Groups	Zero time M±SE	2hrs M±SE	24hrs M±SE	48hrs M±SE	96hrs M±SE	144hrs M±SE
Therapeutic	D	CD	BC	A	A	B
	56.12±1.27	60.11±2.03	62.11±2.75	78.52±1.22	82.21±3.38	64.22±1.45
	a	b	b	b	b	a
Toxic	D	C	B	A	A	C
	58.31±1.25	64.75±1.09	89.42±2.18	94.38±3.04	98.34±2.52	67.51±1..27
	a	a	a	a	a	a
LSD	4.35					

Different small letters in the same column indicate significant difference (P<0.05) between groups.
Different capital letters in the same column indicate significant difference (P<0.05) between the animals related to same group

c. Alkaline phosphate (ALP): Serum activity of ALP showed remarkable (P<0.05) increases in both groups in all period. Normal values of the ALP were obtained from the un-dosed groups (zero time) which was not satisfactorily (P>0.05). With respect to the enzyme ALP and post levamisole administration, clearly increased the values of this enzymes (P<0.05) were observed in both test groups. Values seemed to be more elevated at the 96 hours. It reached to 26.50±1.24 in therapeutic group and 30.17±5.31 in toxic group (Table 7).

TABLE 7. Mean values of ALP (IU/L) in both groups

Groups	Zero time M±SE	2hrs M±SE	24hrs M±SE	48hrs M±SE	96hrs M±SE	144hrs M±SE
Therapeutic	CD	C	BC	A	A	AB
	16.13±4.84	17.50±2.63	20.08±2.21	24.01±2.57	26.50±1.24	22.37±2.23
	a	a	b	b	b	a
Toxic	C	C	B	A	A	B
	16.39±2.02	19.27±1.18	25.25±1.37	29.25±3.05	30.17±5.31	25.13±2.18
	a	a	a	a	a	a
LSD	3.52					

Different small letters in the same column indicate significant difference (P<0.05) between groups.
Different capital letters in the same column indicate significant difference (P<0.05) between the animals related to same group

4. Kidney function:

a. Urea concentration: Control urea concentrations at (zero time) showed no significant difference (P > 0.05) between the two groups. Similar findings noticed in remaining periods. In therapeutic group a significant difference (P<0.05) was presented between zero time and 96 and 144 hours. The later recorded higher urea level (8.21±0.19) and (8.20±0.36) respectively, similar outcome for toxic group (concerning the periods) (Table 4-8).

TABLE 8. Mean values of urea (mg/dl) in both groups

Groups	Zero time M±SE	2hrs. M±SE	24hrs. M±SE	48hrs. M±SE	96hrs. M±SE	144hrs. M±SE
Therapeutic	B	AB	AB	AB	A	A
	5.91±0.33	7.57±0.08	7.35±0.52	7.31±0.22	8.21±0.19	8.20±0.36
	a	a	a	a	a	a
Toxic	B	AB	AB	AB	A	A
	5.82±0.17	7.73±0.70	7.92±0.56	7.58±0.75	8.57±0.38	8.50±0.57
	a	a	a	a	a	a
LSD	2.18					

Different small letters in the same column indicate significant difference (P<0.05) between groups.
Different capital letters in the same column indicate significant difference (P<0.05) between the animals related to same group

Creatinine levels

Likewise, creatinine values showed significant (P<0.05) respective increased in both groups with the advancement of experimental time. These obvious increases concentrated at the periods 24 and 48 hours in both groups. The values were 33.17±3.62) and (40.12±3.52) and (38.25±2.18) and (43.57±4.33) at these times in therapeutic and toxic groups respectively. At the end of experiment values were dropped with no significant variation (P> 0.05) when comparing with the un-dosed control groups (zero time). Differences across periods were observed at 2, 24 and 48 hours in therapeutic group and at 48, 96 and 144 hours in toxic group (table 9).

TABLE 9. Mean values creatinine (mmol/L) in both groups

Groups	Zero time	2hrs	24hrs	48hrs	96hrs	144hrs
Therapeutic	C	C	B	A	B	C
	24.52±2.28	27.71±2.19	33.17±3.62	38.25±2.18	31.80±2.08	25.51±1.41
	a	b	b	b	b	a
Toxic	C	B	AB	A	B	C
	24.65±3.54	35.59±2.23	40.12±3.52	43.57±4.33	37.42±1.02	29.59±1.73
	a	a	a	a	a	a
LSD	5.02					

Different small letters in the same column indicate significant difference (P<0.05) between groups.
Different capital letters in the same column indicate significant difference (P<0.05) between the animals related to same group

DISCUSSION

Clinical follow-up

The administration of therapeutic dose of levamisole did not showed any harmful effects on the lambs. The clinical signs in toxic group of the current study reflected mainly nervous manifestation which may be ascribed to the neuro-toxicity of levamisole. Rehni and Singh, (2010) found that toxicity delays the closing of sodium channel; thus increase neuronal plasma membrane excitability by membrane depolarization. Tamang *et al*. (1991) and Khan *et al*. (2009) recorded similar nervous manifestations in goats which treated by cypermethrin dipping. The duration of nervous signs corresponding with Kol *et al*. (2007) and Shah *et al*. (2007), who reported that the nerve stimulation is started after 5-10 minutes and persisting for (30-90) minutes. Uncontrolled diarrhea in the present study probably occurs due to the sloughing of the epithelium of the intestines. Khan *et al.* (2009) was reported that diarrhea may be happened as a result of intestinal mucosal epithelium degeneration or desquamation of the intestine. All clinical signs noticed on studied lambs in the present trial were disappeared during the 4th day in both groups because levamisole eliminated from the body through kidney at that time.

Hematological findings

In regard to the WBCs count obtained in this study for both categories of animals there were increment in its count and it was very marked in toxic group's compaired with therapeutic group. This could be as a result of immunostimulatory activity of levamisole which have the ability to effect the maturation of leukocytes and stimulation of T-cell differentiation. This result was further confirmed by the report of Vojtic (1997) who found that Levamisole induced significant increase in leukocytes count (leukocytosis) in dairy cows this may be attributed to its immunological effect, which may lead to increasing in neutrophils and lymphocytes counts. In an experiment study in buffalo- calves, Sayed *et al.* (2002) showed a significant increase in total leukocytic count which may be explained by absolute neutrophilia, eosinophilia and monocytosis. Total leukocytic count was reported to increase in acute inflammatory diseases particularly those due to bacterial infections. This could be attributed to that infectious agents and products of tissue injury stimulate a variety of cells to release growth factors, cytokines, and other mediators of inflammation that act as prompt stimuli and are all interrelated in causing the increase in total WBCs count and more production, proliferation. In current trial, mean values of RBCs were decreased significantly ($p<0.05$) mainly in toxic group, this firstly due to an immune-mediated mechanism which might be responsible for the erythrocyte destruction. Second cause could be due to increased levels of activated complement products. This interpretation comes with the of Yousef *et al.*, (1998), Azab and Abdel-Maksoud (1999) in sheep.

In the present study, fell in Hb concentration was observed mainly in the toxic group at the end of the experiment in comparing with the range values obtained for therapeutic group. This might be attributed to positive correlation of Hb with RBCs. On another hand Daramola *et al.* (2003) noticed relatively high Hb values and this is an advantage in terms of the oxygen carrying capacity of the blood. However, Iriadam (2007) found no significant change in Hb concentration in does.

The values of PCV obtained from our study showed slight increase in therapeutic group. The toxic dose of levamisole reflected significant increase of (PCV) values. This may be related to negative correlation between RBCs and PCV in addition to increase in environmental temperature. This increase was in concordance with (Tambuwal *et al.*, 2002). Daramola *et al.* (2005) reported gradual increase of PCV values following ivermectin treatment. The PCV varies proportionately with serum total protein and this suggests that PCV is beneficial in assessing the protein status and possibly forecasting the degree of protein supplementation in goats at different physiologic states.

Liver function: The AST, ALT and ALP values in both groups of current study were significantly increased ($P< 0.05$). These findings may be related firstly to liver injury. When the liver is injured, the enzymes within the hepatocytes enter the bloodstream. Secondly the impaired liver function and thirdly to oxidative tissue damage. This outcome was in accordance with Woreta and Alqahtani, (2014).

Result of this study, showed that ALT, AST and ALP serum levels were higher than Iranian Ghezel sheep breeds and were consistent with those levels measured in Pakistani and Baluchi sheep breeds (Mojabi *et al.*, 2000; Seyed *et al.*, 2015). In an experimental trial in dogs, Gokce *et al.* (2004) showed on laboratory examinations that levamisole poisoning causes a significant increase in the activity of liver enzymes as well as metabolic alkalosis. Sharma (2006), reported normal range of ALT, AST, and ALP in cattle and there were no statistical significant differences and the same results were recorded by Jezek *et al.*, (2006) in calves.

In a study in lambs implicated a significantly high serum enzymatic activity of ALT and AST in the diseased group. These changes could be attributed to dysfunction of various organs including liver due to hepatic degenerative and necrotic changes caused by bacterial infection and toxins (Aytekin *et al.*, 2011). In cows with liver fasciolosis, the hepatic damages led to an increase in the AST levels. Thus, the high sensitivity and/or specificity of the AST test for hepatic disease is accompanied by severe tissue damage (Gajewska *et al.*, 2005).

Kidney function: In current study the values of urea revealed significant increase ($P<0.05$) in both groups and it was clear in toxic group, this outcome may be ascribed to acceleration of catabolism of body proteins and appears at long lasting diarrheas which appeared on studied lambs of toxic group. The present results agreed with results obtained by Choi *et al.*, (2011) in dogs.

The increase in serum creatinine in the present study might be attributed to kidney dysfunction after levamisole administration, this in agreement with Yousef *et al.*, (2003) in sheep. Also Puri and Kataria (2004) found that the values of creatinine tend to be higher in kids than the adults. The amount of creatinine secreted daily is a function of the muscle mass and is affected by diet, age, sex or exercise. Patel *et al.*, (2013) indicated that the two substances most commonly measured to assess kidney

function are urea and creatinine. Urea is a by-product of protein breakdown. It is produced in the liver and secreted from the body in urine. Creatinine is a by-product of muscle metabolism. Increased levels of creatinine indicating that kidney function is abnormally distress.

CONCLUSION

The present study indicated that the administration of an anthelmintic therapeutic dose of levamisole, did not result in any harmful effects on the lambs. While toxic dose resulted in a variety of adverse effects in clinical, hematological, liver and kidney functions parameters.

REFERENCES

Ahmet, A., Izzet, K. & Ibrahim, P. (2004) Effects of therapeutic and toxic doses of levamisole on thyroid hormones and some biochemical parameters in sheep. Cell biochemistry and function, 22: 281–286.

Amir, H.S., Mohammad, M.H., and Saiful, B.H. (2013) Hemato-biochemical profiles of indigenous goats at Bangladesh. Vet. World, 6: 789-792.

Aytekin, İ., Mamak, N. and Kalinbacak, A. (2011) Clinical, hematological, biochemical and pathological findings in lambs. Kafkas Univ. Vet. Fak. Derg., 17(3): 349-355.

Azab, M.E. and Abdel-Maksoud, H.A. (1999) Changes in some hematological and biochemical parameters during pregnancy and post-partum periods in Baladi goats. Small Rumin. Res., 34:77-85.

Choi, S.Y., Hwang, J.S., Kim, I.H., Hwang, D.Y. and Kang, H.G. (2011) Basic Data on the Hematology, Serum Biochemistry, Urology, and Organ Weights of Beagle Dogs. Lab. Anim. Res., 27, 283-291.

Daramola, J.O., Adeloye, A. A., Fatoba, T.A. and Soladoye, A.O. (2005) Hematological and biochemical parameters of goats. Livestock Res. for Rural Develop.,17(8): 22-27.

Daramola, J.O., Adeloye, A.A., Fatoba, T.A. & Soladoye, A.O. (2003) Hematological and biochemical parameters of West African Dwarf Goats. Dept. of Anim. Produc. University of Ilorin, Nigeria, Pp:1-9.

Gajewska, A.; Samga- Kozlowska, K. & Wisniewski, M. (2005) Pathological changes of liver in infection of *F. hepática*. Wild Parasitology, 51: 15-123.

Gokce, H. I, Gunes, V.; Erdogan, H. M.; Citil, M.; Akca, A. and Yuksek, N. (2004) The effects of levamisole poisoning on the hematological and biochemical parameters in dogs. Dtsch Tierarztl Wochenschr, 111: 81-85.

Iriadam, M. (2007). Variation in certain hematological and biochemical parameters during the peri-partum period in Kilis does. Small Rumin. Res., 73:54-57

Jezek,J.; Klopcic., M. and Klinkon, M.(2006) Influence of age on biochemical parameters in calves. Bull. Vet. Inst., 50:211-214.

Khan, A.; Faridi, H. A..; Ali, M.; Khan, M.Z.; Hussain, I. and Ahmad, M. (2009). Effects of cypermethrin on clinico-hemato-biochemical and pathological parameters in goats J. Exp. Toxicol. Pathol., 61(2):151-160 .

Kol, I. O.; Kaygusuz, K. and Mimaraglu, C. (2007). Intramuscular injection of organophosphate and synthetic parathyroid. Clin. Pract. Rev., 8: 298-292 .

Mojabi, A. A.; Ali, P.K.; Safi, M. and Sharifi, S. T. (2000). Evaluation of normal range of major serum biochemical parameters in apparently healthy Ghezel sheep breed. J. of Tehran University, School of Vet. Med., 55 (2): 19-27.

Pancarci, S.M.; Gungor, O.; Gurbulak, K.; Cenesiz, M. and Guzeloglu, A. (2007). Effects of levamisole on pregnancy in ewes. Bull. Vet. Inst., 51: 253-256.

Patel, S. S., Molnar, M.Z. and Kalantar-Zadeh, K. (2013) Serum creatinine as a marker of muscle mass in chronic kidney disease: results of a cross- sectional study and review of literature. J. Cachexia Sarcopenia Muscle, 4: 19-29.

Puri, G. & Kataria, N. (2004) Creatinine clearance in goats during water deprivation and rehydration, Indian J. Anim. Health, 43(1):1-5.

Ravindra, K.J., Anil, U. Bhikane, A.A., Bhosale, H.A., Shaikh, A. and Sunil, J. (2017) Acute Levamisole Poisoning in Bullocks. J. of Advan. Vet. Res., 7(1): 16-17.

Rehni, A.K. and Singh, T.G. (2010) Levamisole-induced reduction in seizure threshold: a possible role of nicotinic acetylcholine receptor-mediated pathway. Arch. Pharmacol., 382: 279-285.

Sayed, A. S., Ali, A.A., Mottelib, A.A. and Abd El-Rahman, A.A. (2002): Bronchopneumonia in buffalo-calves in Assiut governorate. Studies on bacterial causes, clinical hematological and biochemical changes associated with the disease. Assiut Vet. Med. J., 46(92): 138-155.

Seyed, H., Hashemi, Mehdi, J. and Dariush, S. (2015) Blood serum biochemical factors of Baluchi sheep. J. Appl. Envrimo. Biolo. Sci., 5 (95): 838-840.

Shah, M.K., Khan, A., Rizvi, F., Sidddique, M. and Ur-Rahman, S. (2007) Effect of cypermethrin on clinico-hematological parameters .Pak. Vet. J., .27(4):171-175.

Sharma, M.C., Kumar, P., Joshi, C. and Kaur, H. (2006) Status of serum Minerals and biochemical parameters in cattle of organized farms and unorganized farms. Asian J. of Anim. and Vet., 1:33-41.

Tamang, R.K., Jha, G.J. and Singh, K.K. (1991) Clinico-pathology of acute cypermethrin toxicity in goats. Indian J. Anim. Sci., 61:493-499.

Tambuwal, F.M., Agale, B.M. and Bangana, A. (2002) Hematological and biochemical values of apparently healthy Red Sokoto goats. Proc. 27th Annual Conf. Nig. Soc. Anim. Produc. Nigeria, Pp: 50-53.

Várady, M., Papadopoulos, E. and Königová, A. (2011) Anthelmintic resistance in parasites of small ruminants: sheep versus goats. Helminthology, 48(3): 137–144.

Vojtic, I. (1997) Immunomodulation of puerperal disorders in dairy cows with levamisole. Raxis-Veterinaria-Zagreb, 45: 245-250.

Woreta, T.A. and Alqahtani, S.A. (2014) Evaluation of Abnormal Liver Tests. Med. Clin. North Am., 98: 1-16.

Yousef, M.I., Ibrahim, H.Z., Yacout, M.H. and Hassan, A. (1998) Effect of cypermethrin on some physiological and biochemical parameters in sheep. Egyptian J. Nutr. Feeds, 1:41-52.

Yousef, M.I., El-Demerdash, F.M., Kamil, K.I. and Al-Salhen, K.S. (2003) Changes in some hematological and biochemical indices of rabbits induced by cypermethrin. Toxicology, J. Anim. Sci., 189:223-224.