Case Report

Selenium toxicity and treatment of lambs dosed orally daily with 0.12 mg/Kg.BW of Sodium selenite solution.

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Clinical symptoms , hematological picture , biochemical and enzyme changes associated with Selenium toxicity were studied in fifteen male Awassy lambs aged (4-6) months and their weight ranged between (16-26) Kg. were enrolled in a controlled experiment .The lambs were divided randomly into three groups of (5) lambs. The 1st and 2nd groups   dosed orally daily with 0.12 mg/ Kg.BW of Sodium selenite solution (1g /L of distil water) for (16) weeks.After the 16th weeklambs of the 1st group treated by N-acytileL-cystine at a rate of (70) mg /kg.BW.divided into four daily doses orally for (2) weeks by working solution prepared by melting (20) grams of N-acytileL-cystinein one litter of distilled water. The 3rd group was left as a control.

The lambs were watched daily for (4-6) hr. and clinical symptoms (pulse , respiratory rate , temperature and body weight were taken according to (1) ,blood   samples

were examined every two weeks (2). Serum samples were used to examine: total serum protein(TSP), total serum albumin (TSA),Acid phosphatase (ASP), Alkaline phosphatase (ALP), Serum glutamic oxalacetic transaminase (SGOT) andSerum glutamic pyruvic transaminase (SGPT)   by using specific kits and spectrophotometer. Data were analyzed using statistical analysis system – SAS, to study the effect of groups and weeks in the difference traits. Least significant difference (LSD.) test was used to compare the significant difference between means.

Lambs of the 1st and 2nd groups showed the clinical signs after (8) weeks of sodium salenite administration, the clinical signs seems to be accumulative due to time's length of toxin administration. These signs characterized by: severe loss of weight to reach a mean of (17and18Kg.) in the (16th) week of administrations in the 1stand 2nd groups respectively .While the mean body weight of the control group was (44 kg.).An increased in the means ofpulse rate (93and 98/min.)and respiratory rate (50 and 48 /min.) in the 1st and 2nd groups respectivelywas significantly different (P< 0.05) incomparison with the control group,while means of temperature in all groups were within the normal range (39.0-40.0C®). All these results were in agreement with (3,4,5,6,7), due to accumulative toxicity sequel.Other clinical signs in the toxicated groups includepica , lambs eating the field floor and the wool of each other, severe emaciation, dullness, lack of vitality, and signs of anemia present because they couldn't eat or drink to survive so starvation shock may appear, all these data were in agreement with (8,4,9).

The P.C.V. in the1st and 2nd groups reached (16 and17%) respectively in the (16th) week , on the other hand, lambs of the 3rd group remained within the normal levels (ranged between 38 – 42%), which was significantly different (P<0.5),this decrease in P.C.V. may be due to selenium- hemolytic anemia (10,11,12).In the 1st and 2nd groupsthe means of RBCs count reach (7-8×10^6/μl) in the (16th) week. On the other hand lambs of the 3rd group remain within normal value (12 -15×10^6/μl), thiswas because the majority of the glutathione peroxidase is incorporated into red blood cells at the time of erythropoieses, so a complete response of glutathione peroxidase activity and selenium in whole blood to selenium supplementation will, therefore, require a time span equal to the average lifespan of the RBCs which is approximately (90 to 120) days, (4) and selenium in erythrocytes is distributed between glutathione peroxidase and hemoglobin and selenite is taken up by red blood cells within several minutes, and transferred to the liver (13). On the other hand, the toxicity changes appeared in blood picture in which RBCs vitiated in itsshape from oval to stellar shape due to toxin.Poikilocytosis, and anisocytosiswere seen in blood smears from lambs in the 1st and 2nd groups.The large cells are most likely immature and presence of reticulocytes which indicate early release from the bone marrow (8).The means of Hb concentration of the 1st and 2nd groups decreased gradually from (11-6 and 11-7) g/dl respectively. On the other hand, the lambs of the 3rdgroup showed a slight increase (10-14)g/dl due to good feeding and handling, whilethe Hb decrease was due to selenium – induced hemolytic anemia . The decline in the Hb levels could be due to the inhibition of delta- amino levulinatedehydratase, a key enzyme required for the Hbsynthesis.There was a significant difference compared with the 3rd control group (P< 0.05).

There was a significant decrease in the means of TSP in the lambs of the 1st and 2nd groups reached (4.2 and 4.4)g/dl respectively. On the other hand, the lambs of the 1st group had normal values which ranged between (6 – 8 g/dl). These results were in agreement with (2,14,15). The alterations in TSP are dependent upon an understanding of the various physiological and pathological factorsthat might cause such alterations. TSP decreased in animals having liver disease, since the majority of the decreases is direct reflection of hyper albuminemia (2).

There were significant (P<0.05) decrease in means of TSA in toxicity groups (2 and 2.1)g/dl respectively, in the (16th week) . These low serum albumin concentrations present in starvation and malnutrition, as well as, deficient synthesis of albumin occurs most commonlyin association with chronic hepatic diseases. A decrease in the concentration of albumin has been reported to occur in hepatitis, livercirrhosis, andhypoalbuminemia (12).

Significant increase in ACP and AKPappeared in the 1st and 2nd groups (P < 0.05), to reach means of ACP (2.9 and 2.8 μ/L) and AKP (260 and 290 μ/L)in the (16th) week compared with the 3rd group in which ACP ranged between (1 – 1.9μ/L) and AKP ranged between (70 - 90 μ/L). These results were comported with (16,14), they concluded that the activities of ACP and AKP should have

been increased because of tissue necrosis due to selenium toxicity. Elevations of ACP activity indicate cholestasis ,andAKP increased in suppurative hepatic necrosis and sever anemia which occur in chronic selenium toxicities.

SGOTof lambs in the 1st and 2nd groupswere (240 and 245 U/L) respectively, during the (16th) week of toxicity ,while(SGOT) of lambs in the 3rd group remain within the normal values (60 – 191 U/L),which was significantly different (P< 0.05) than the toxicated groups.(5,14)indicated that the increase in SGOT activity suggest a liver effect, and increase serum activity of these enzymes indicate hepatocellular damage.(2)reported that SGOT levels may be increased with liver disease in all species but cannot be considered as a specific test for liver damage. The same significantly highmeansofSGPTin the1st and 2nd groups(59 and 58 U/L) respectively during the (16th week) of the experiment, at that time, lambs of the 3rd group remain within normal values (22 – 38 U/L).(16,17,14)reported that the increase in this enzyme activity suggest a liver effect, and increase in the serum activity of both enzymes indicate hepatocellular damage activities and histopathological responses may be related to a variety of factors, including mechanisms and rates of injury and repair, organ adaptation, health and nutritional status, age of the animal, and exposureto a high concentration ofselenium.

Lambs of the 1st group showed significant differences after treatment with N-acyytile L-cystine for two weeks started on the (17th week) of the study, as signs oftoxicity started to disappear gradually, the means of body weight increased to (21 Kg.),pulse and respiratory ratesdecreased (83 and35/min)respectively and lambs became more active. Progressive increase in the means of RBCs count (9×10^6 /µL), PCV (15%),Hb concentration (10g/dl),and a significant increase in the means of TSP (6.2 g/dl), TSA (3.1 g/dl) while the ACP andALP,SGOT and SGPT decreased to (2.0 and 210 U/L) and (195and 42 µ/L) respectively (Tables 1,2and3).(1)reported that N-acytile L-cystine therapy regenerate glutathione, increases interacellular stores of glutathione, increases glutathione conjugation, and decreases the concentrations of reactive metabolites. As well as, supportive treatment (like multivitamins) improved (Vit. E) levels in the body, so normal active metabolisms, absorptions and excretion will take place, and all abnormal parameters were disappeared (18).

Table (1) Means and least significant difference (LSD) of Awassy male lambs Body weight, Pulse, Respiration and Body temperature pre and post toxicity and treatment.

Weeks	Body weigh Groups			Pulse Groups			Respiration Groups			Temperature Groups		
	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd
- 2	25	25	23	76	75	75	27	28	25	39.0	39.1	39.2
0(1)	26	25	24	75	75	76	27	25	26	39.2	39.3	39.2
2	25	24	25	79	77	73	30	30	24	39.4	39.2	39.5
4	25	24	27	80	78	72	35	30	27	39.3	39.4	39.6
6	25	23	29	80	79	72	37	34	25	39.5	39.4	39.6
8	24	23	31	81	80	76	38	36	28	39.7	39.5	39.6
10	23	22	31	84	85	77	40	39	26	39.6	39.5	39.7
12	21	22	32	86	88	75	41	40	29	39.7	39.5	39.6
14	21	21	38	90	91	75	45	42	30	39.7	39.5	39.6
16(2)	17	18	44	93	98	75	50	48	27	39.9	40.0	39.7
18	21	17	46	83	99	78	35	49	30	39.8	40.0	40.0
LSD	0.97*	1.20*	1.27*	1.46*	0.92*	0.92*	1.30*	2.15*	1.38*	0.212	0.204	0.127

* P < 0.05; (1) = Start of toxicity of the 1st and 2nd groups.;   (2) = Day of end of toxicity & start of treatment of the 1st group.

D

Table (2) Means and least significant difference (LSD) of Awassy male lambs RBC counts (x10$_6$/µL), P.C.V.%., Hb (g/dl), total serum protein (g/dl) and total serum albumin (g/dl) concentrations.

weeks	RBC (x10$_6$)			P.C.V.(%)			Hb (g/dl)			Serum protein (g/dl)			Serum albumin (g/dl)		
	Groups			Groups			Groups			Groups			Groups		
	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd
- 2	10	14	12	40	43	42	11	11	10	7.0	7.2	6.9	3.9	3.8	3.7
0[1]	12	15	14	42	44	43	12	14	11	7.1	7.0	7.3	3.8	3.7	3.8
2	11	14	13	38	39	43	11	13	10	6.8	6.9	7.1	3.7	3.6	3.7
4	9	10	14	30	32	41	8	9	11	6.6	6.7	7.2	3.5	3.6	3.8
6	8	9	13	26	29	40	7	8	10	6.4	6.1	7.1	3.4	3.5	3.7
8	8	9	12	22	25	38	7	8	12	6.3	6.1	7.1	3.3	3.2	3.9
10	8	8	14	20	22	39	7	7	13	6.1	5.9	7.3	3.1	3.1	3.8
12	7	8	13	17	20	38	6	7	13	5.6	5.2	7.2	2.8	2.9	3.9
14	7	8	13	17	19	40	6	7	14	4.6	4.5	7.0	2.4	2.5	3.7
16[2]	7	7	14	16	16	39	6	6	15	4.2	4.4	7.2	2.0	2.1	3.9
18	9	7	15	30	15	43	10	6	15	6.2	4.1	7.2	3.1	1.9	3.8
LSD	1.78*	1.82*	1.58*	5.03*	4.78*	3.49*	1.03*	1.05*	0.77*	0.17*	0.21*	0.12*	0.51*	0.36*	0.38 ns

(1) = Start of toxicity of the 1st and 2nd groups.; (2) = Day of end of toxicity & start of treatment of the 1st group.; * P < 0.05 for all LSD. Values except in the control group not significant (ns).

E

Table (3) Means of Acid phosphatase (ASP), Alkaline phosphatase (ALP), Serum glutamic oxalacetic transaminase (SGOT), and Serum glutamic pyruvictransaminase (SGPT) of Awassy male lambs in difference groups and weeks.

weeks	Acid phosphatase (U/L) Groups			Alkaline phosphatase (U/L) Groups			AST μ/L Groups			ALT μ/L Groups		
	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd
- 2	1.5	1.8	1.4	75	76	77	75	70	76	35	30	36
0(1)	1.6	1.5	1.7	74	78	76	79	80	82	30	32	35
2	1.6	1.4	1.8	76	79	80	89	92	75	32	34	32
4	1.7	1.6	1.4	85	82	72	96	99	79	35	34	35
6	1.8	1.9	1.5	93	90	79	120	115	85	36	35	34
8	2.0	2.1	1.7	100	98	82	145	144	89	38	36	29
10	2.1	2.4	1.6	160	150	75	170	175	89	40	39	36
12	2.5	2.6	1.7	200	210	80	185	190	76	48	42	30
14	2.7	2.5	1.5	210	250	85	210	205	90	52	54	35
16(2)	2.9	2.8	1.8	260	290	82	240	245	90	59	58	34
18	2.0	2.9	1.5	210	340	83	195	265	89	42	60	36
LSD	0.14*	0.13*	0.09*	16.84*	24.78*	4.27*	9.03*	11.14*	4.78*	3.02*	4.12*	2.78*

(1) = Start of toxicity of the 1st and 2nd groups.; (2) = Day of end of toxicity & start of treatment of the 1st group.   ; * P < 0.05 for all LSD. Values except in the control group not significant (ns).

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