IJBPAS, April, 2015, 4(4): 2295-2302

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

ELECTROLYTE CHANGES CAUSED BY PROLONGED INFUSION OF ISOFLUPREDOE ACETATE IN SHEEP

ELMI V[1] , HASSANPOUR A[2*], SAKHA M[3] , NADALIAN M[4] AND AMOGHLI TABRIZI B[5]

1: Postgraduate student of Large Animal Internal, Science and Research Tehran branch, Islamic Azad University, Tehran, Iran

2: Department of Clinical Sciences, Tabriz Branch, Islamic Azad University, Tabriz, Iran

3: Department of Clinical Sciences, Science and Research Tehran branch, Islamic Azad University, Tehran, Iran

4: Department of Clinical Sciences, Science and Research Tehran Branch, Islamic Azad University, Tehran, Iran

5: Department of Pathology, Tabriz Branch, Islamic Azad University, Tabriz, Iran

***Corresponding Author's: E Mail: Alihassanpour53@gmail.com; a_hasanpour@iaut.ac.ir**

ABSTRACT

Glucocorticoids are often used for the treatment of ketosis and Isoflupredone acetate and dexamethasone is commonly used for this purpose. In this study, 20 male lambs 12 -15 months that their weight and nutritional status were similar divided in 2 groups (10 cows), and for all of the 10 sheep in experimental group, 4 mg Isoflupredone acetate was injected in 4 days and all animals were sampled to measure biochemical parameters. After thawing frozen samples in the laboratory, sodium, potassium, chloride, calcium, phosphorus, magnesium were measured. Investigation of serum electrolytes of sheep in experimental and comparison with the control group showed increased levels of sodium, calcium, magnesium and decreased levels in potassium, chlorine and phosphorus of serum.

Keywords: Isoflupredone Acetate, Biochemical Parameters, Sheep

INTRODUCTION

Vetapredone is a potent corticosteroid hormone and its effects through experiment and determination the stability of glycogen in the liver of mice have been reported about ten times as prednisone, fifty times as hydrocortisone and sixty seven times as

cortisone. This drug penetrates from embryonic layer in to cytoplasm and connects to the specific receivers in cytoplasm, then these complexes enter in the core of cell, linked to DNA and actuate the generation process of messenger RNA and confirmation of various proteins such as enzymes subsequently and causing to glucocorticoid and mineralocorticoids effects. The balance between water and electrolytes through mineralocorticoids have been done, so that sodium transport in the distal renal tubular facilitate, therefore the reabsorption of sodium and excretion of potassium and hydrogen and water lock up within the body increase.

This drug have been used wide spreadly in treatment of ketosis, shock, stress, allergies, joint and tendon inflammation, all inflammation such as swelling and pain in the bones, spine and discs, low blood sugar, disorders of functions in liver, avoid of low blood calcium and magnesium and allergic skin diseases, rheumatoid arthritis, accelerate delivery, especially when delivery is delayed, mastitis, laminitis, Osteoarthritis, fatigue, cramps, depression, stress reduction resulting from the transport of livestock, inflammation and swelling of the conjunctiva, snakebite, milk fever and etc. in cattle. Glucocorticoids often used for the treatment of ketosis. Dexamethasone and Isofluoredone acetate is most commonly used. In the case of potassium deficiency symptoms, discontinue using corticotrophic and five per cent solution of potassium chloride is used as an intravenous drip infusion. Administration of glucocorticoids with reducing the levels of potassium in blood may increase the effects of nondepolarized neuromuscular blocking drugs, resulting in increased or prolonged respiratory weakness or even paralysis. Side effects and safety of drugs depends on the type of drug, their time, how to use, how much of the drug at a time, drug interactions with other medications and personal characteristics of the species. In other words, in medication of Adernocorticoids and corticotrophin, harms should be weighed against its benefits and then prescribe medication to be taken. Similarly, it should be used in recommended doses prescribing these drugs and must be avoided from medication overdose that the effect of drug had more confidence. As many of the complications is related to the prescription drugs over the limit value **(Radostits 2007)**.

METHODOLOGY

In this study, 20 male lambs weighing 12 - 15 months of age who were in a similar situation was purchased from a herd. All sheep had a similar diet (containing hay and straw and water) and anti-parasitic medication was prescribed for all sheep. After a few days the animals were

accustomed to the new environment were examined and divided into control and experimental groups and were numbered. On day zero all animals sampled for measuring biochemical parameters. The 10 cc syringe and needle # 18 of the jugular vein blood was taken and then were transferred to test tubes containing gel. The tubes were sent to the laboratory within 30 to 60 minutes and 2 ml of serum from blood samples were isolated by centrifugation and fizzed after transferring to plastic micro-tubes. In day one Isoflupredone acetate in a dose of 4 mg of drug per 10 sheep (test) was used intramuscularly. 24 hours after sampling, 4mg of drug Isoflupredone acetate was injected for second time. This process repeated until 4th day. After thawing frozen samples in the laboratory, sodium, potassium, chloride, calcium, phosphorus, magnesium were measured. Sodium and potassium of serum by flame surveying using flame photometer were measured and other parameters were measured using proprietary kits and with spectrophotometry method by autoanalyzer. After calibration samples entered in flame photometer then needle is inserted into the sample. A vacuum created in automyzer that material of sample is in it. After this material entered into the mixer and subsequently compressed air enter into the mixer. The material and compressed air have been suctioned above the flame and can cause to discoloration of the flame from burning metal. Flamephotometer measure the discoloration of light of metal directly. There are parameters that can affect the results, such as lubricate of samples, or samples are not completely separated from the clot or Sampler is unclear.

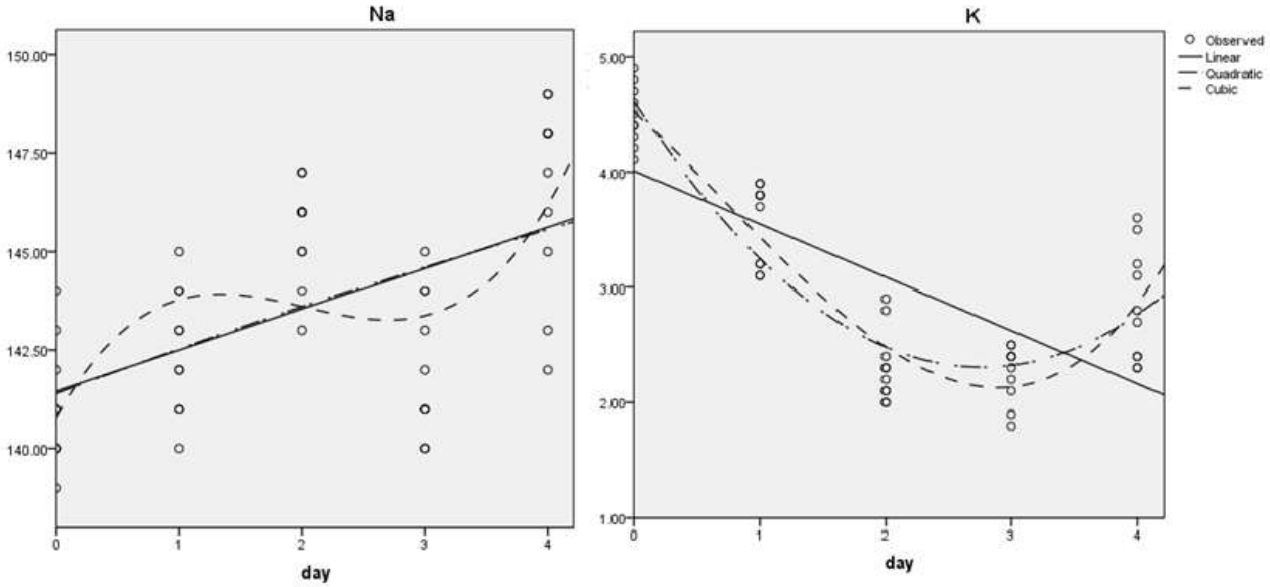
RESULTS

Mean value of any biochemical parameter in both treatment and control groups from day zero to four, have been calculated. The findings obtained from the analysis of serum electrolytes in animals showed the levels of serum sodium in the treatment group had a significant increase in the second and fourth days ($P < 0.01$) and this difference was not statistically significant on days zero and one and three. The levels of serum potassium in the treated group between days one, two and three and four have been reduced significantly ($P < 0.01$). The levels of chlorine in the treated group on days one and two had a significantly decreasing ($P < 0.05$) and on the third day this difference was highly significant ($P < 0.01$). However, no significant difference was observed on the fourth day. The levels of calcium in the treatment group had no significant difference in any day. The levels of magnesium in the treated group on day zero, one and two had a significant increase ($P < 0.05$) and on the third day this difference

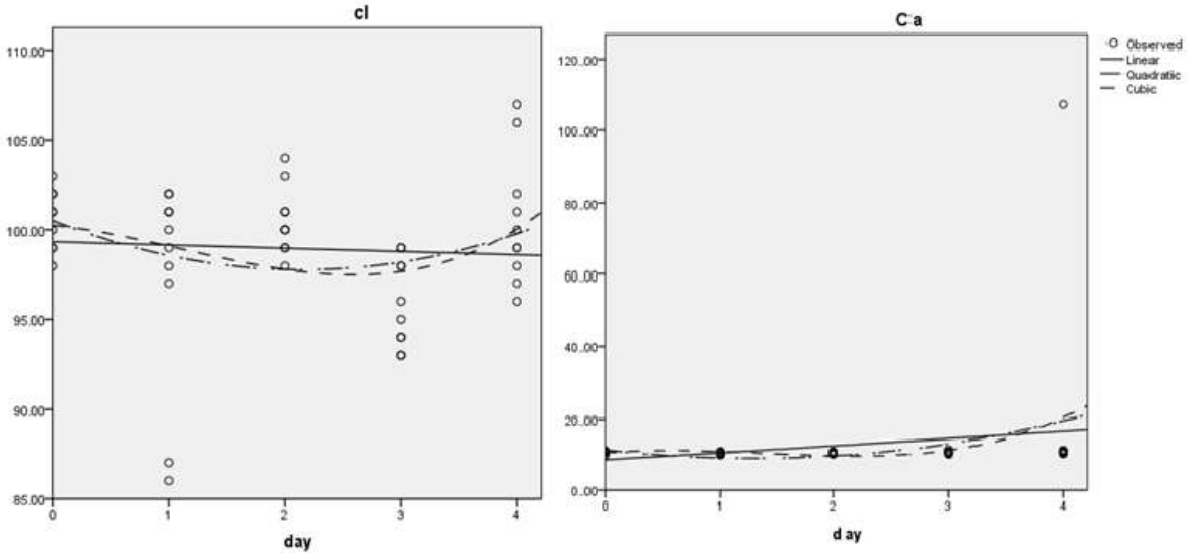
was very significant (P <0.01) but no significant difference was observed on the fourth day. Phosphate levels between the two groups in days one, three and four had a highly significant difference (P <0.01) and on the third day this difference was significant (P <0.05).

Table 1: Comparison of biochemical parameters between controls and patients at day zero to four

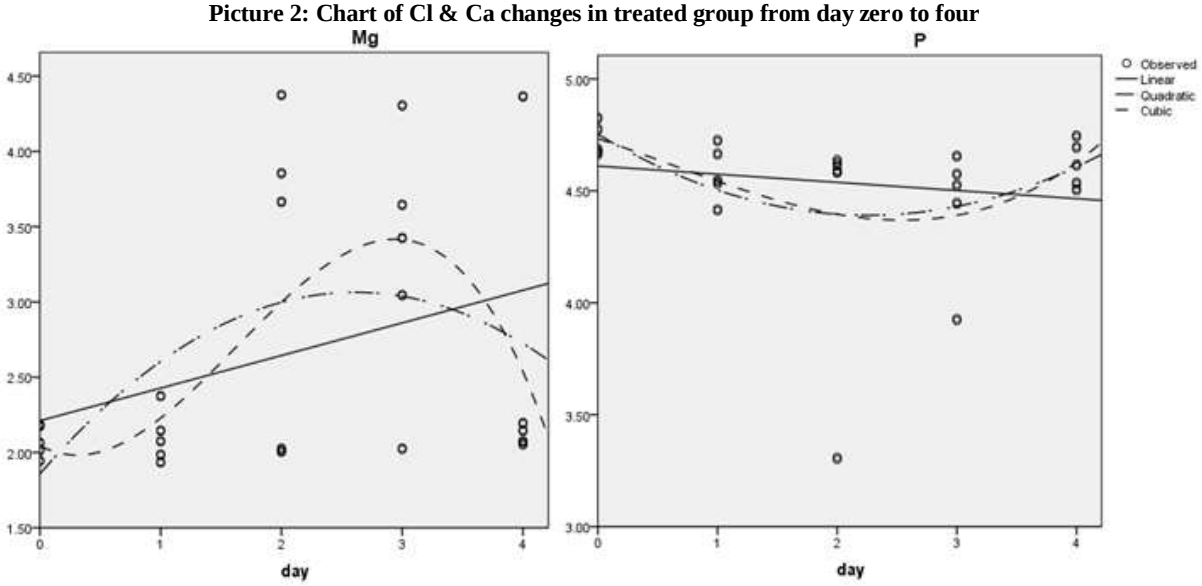
Day	Variant	Group	Count	Average±SD	T	P value
0	Na	Treated	10	141.10±1.52	0.998	0.331
		Control	10	141.90±2.02		
	K	Treated	10	4.49±0.26	0.169	0.868
		Control	10	4.51±0.26		
	Cl	Treated	10	100.70±1.63	2.18	0.042
		Control	10	102.10±1.19		
	Ca	Treated	10	10.83±0.47	0.676	0.508
		Control	10	10.97±0.49		
	Mg	Treated	10	2.07±0.09	2.5	0.022
		Control	10	2.39±0.39		
	p	Treated	10	4.72±0.06	1.59	0.128
		Control	10	4.76±0.04		
1	Na	Treated	10	141.10±1.52	0.998	0.331
	K	Treated	10	4.49±0.26	0.169	0.868
	Cl	Treated	10	100.70±1.63	2.18	0.042
	Ca	Treated	10	10.83±0.47	0.508	0.676
	Mg	Treated	10	2.07±0.09	0.022	2.5
	P	Treated	10	4.72±0.06	0.128	1.59
2	Na	Treated	10	145.5±1.26	4.76	<0.0001
	K	Treated	10	2.31±0.31	16.82	<0.0001
	Cl	Treated	10	100.50±1.84	2.30	0.033
	Ca	Treated	10	10.76±0.30	1.15	0.262
	Mg	Treated	10	3.18±1.03	2.25	0.037
	P	Treated	10	4.34±0.54	2.42	0.026
3	Na	Treated	10	142.10±1.79	0.234	0.818
	K	Treated	10	2.25±0.24	19.6	0.0001
	Cl	Treated	10	95.90±2.42	7.25	0.0001
	Ca	Treated	10	10.89±0.42	0.405	0.690
	Mg	Treated	10	3.28±0.79	3.19	0.005
	P	Treated	10	2.42±0.27	3.89	0.001
4	Na	Treated	10	146.50±2.46	4.56	0.0001
	K	Treated	10	2.83±0.49	9.44	0.0001
	Cl	Treated	10	100.50±3.62	1.32	0.202
	Ca	Treated	10	20.63±30.34	1.00	0.328
	Mg	Treated	10	2.56±0.94	0.530	0.603
	P	Treated	10	4.61±0.09	4.32	0.0001



Picture 1: Chart of Na & K changes in treated group from day zero to four



Picture 2: Chart of Cl & Ca changes in treated group from day zero to four



Picture 3: Chart of Mg & P changes in treated group from day zero to four

DISCUSSION

Investigation of serum electrolytes in sheep and comparison with the control group showed an increasing in levels of sodium, calcium, magnesium and decreasing in the levels of potassium, chlorine, phosphorus.

Coffer *et al*. (2007), had a study on 33 cattle that past 20 to 25 days of lactation. They injected dexamethasone and Isoflupredone acetate in cattle. Injections of both corticosteroid increased blood glucose and injection of Isoflupredone acetate solely decreased serum potassium levels significantly. Injection of Isoflupredone acetate in one dose decreased Potassium by 25% on the second day and in the cattle with severe hypokalemia Potassium concentration was less than 3.2 mEq per liter. Plasma concentration of potassium in cows that had received two doses of Isoflupredone acetate was 46% less than zero day. Three days later, five cattle were suffering from severe hypokalemia. In this study, after injection of three doses Isoflupredone acetate in sheep, a statistically high significant decrease was observed (P <0.01).

In another study by **Sielman *et al*., (1997)**, on 10 bovine with ketosis, were treated with Isoflupredone acetate, 8 vertices of them were hospitalized and two vertices were extremely weak, all cows were extremely Hypokalemic (Between 1.4 to 2.3 mEq per liter). Despite treatment with potassium, concentration of potassium in plasma only in six vertices of cattle was in normal range. Three cows dead and three vertices were killed and two vertices recovered and one cattle was leaved while crippling and one case was sent to the slaughterhouse without treatment.

In present study in order to reducing the levels of serum potassium the Isoflupredone acetate drug have been used. The levels of serum potassium in 10 sheep decrement to 2.1-2.5 mEq /lit. It should be noted that potassium excretion by the kidney through the discharge in the distal tube occurs. Aldosterone or other steroids with mineralocorticoid activity, exerting potassium from distal tubular by increasing permeability of the luminal membrane tubes and increasing the loss of potassium in the urine. Frequently using of Isoflupredone acetate, decrease the potassium concentration in plasma as much as 70 - 80 percent. The mean value of serum sodium level in sheep showed a significant increase in the treated group (p <0.01). Balance of water and electrolytes through mineralocorticoids is done, as Isoflupredone acetate facilitate transportation of sodium in the distal renal tubular so increasing reabsorption of sodium and excretion of potassium and hydrogen, resulting in retention of water in the body. There was a

statistically significant reduction in the mean value of the levels of serum chloride, this reduction can be related to anorexia and diet and water intake of the animals. Since many factors such as hyperlipidemia, hyperglycemia, and increased protein can affect the reduction of chlorine and Isoflupredone acetate increase blood sugar, so this reduction can be related to the performance of the drug. The mean value of serum calcium indicates that there is no statistically significant increase. It should be noted that Isoflupredone acetate prevents from decreasing serum calcium. Increasing the destruction and erosion of bone tissue, direct inhabitation osteoblasts and stimulates and osteoclasts, may be because of Isoflupredone acetate drug effects, leading to increased blood calcium and osteoporosis in animal subsequently. A statistically significant Increasing in the mean value of serum magnesium levels have been observed (P <0.05) . **Chou *et al.* (2007)** showed that magnesium deficiency is most often associated with hypokalemia. When there is magnesium deficiency, resonant hypokalemia occurs, so loss of potassium and secretion of potassium from distal tube increase. Increamentation in delivery of sodium in distal tube or high aldosterone leads to the intensification of hypokalemia in hypo magnesium. It is estimated that 50% of patients with hypokalemia are faced with magnesium deficiency. With respect to high levels of serum magnesium in present study, it can be related to the effects of Isoflupredone acetate drug because the drug can prevent low blood calcium and magnesium. Investigation of serum phosphate levels showed that there is a statistically significant reduction (p <0.01). Peek et al. studied 17 cases of sever hypokalemic cattle. In 4 cases hypophosphatemia and in 13 cases Hypochloremia was recorded. In **Sielman *et al.*** study, 40% of cows had hypophosphatemia associated with hypokalemic myopathy and weakness. In Sattler et al. study 35% of cows have been reported hypokalemic. Repeated using from drug Isoflupredone acetate, muscle weakness, unabsorbtion of phosphorous in increased levels of serum calcium and magnesium can be the major cause of hypophosphatemia in sheep in this study.

REFERENCES

[1] Chou-Long Huang and Elizabeth Kuo: Mechanism of Hypokalemia in Magnesium Deficiency. J Am Soc Nephrol 18: 2649–2652, 2007

[2] Coffer NJ, Frank N, Elliott SB, Young CD, van Amstel SR: Effects of dexamethasone and isoflupredone acetate on plasma potassium concentrations and other biochemical measurements in dairy

cows in early lactation. Am J Vet Res. 2006 Jul;67(7):1244-51.

[3] Peek SF, Divers TJ, Guard C, Rath A, Rebhun WC: Hypokalemia, muscle weakness, and recumbency in dairy cattle. Vet Ther. 2000 Fall; 1(4):235-44.

[4] Radostits OM, Gay CC, Blood DC, Hincliff KW: Veterinary Medicine. A textbook of the diseases of cattle, sheep, pigs, goats and horses. 2007. 10th edition. W. B. Saunders Co. Ltd.p.2057,77-80,1734.

[5] Sattler N, Fecteau G, Girard C, *et al*: Description of 14 cases of bovine hypokalemia syndrome. Vet Rec143:503–507, 1998.

[6] Sielman ES, Sweeney RW, Whitlock RH, *et al*: Hypokalemia syndrome in dairy cows: 10 cases (1992–1996). JAVMA 210:240–243, 1997.