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Effect of Intravenous (IV) and Intramuscular (IM) Injection of Oxytetracycline on Serum Calcium, Phosphorous and Magnesium in Cattle

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Abstract: This study was carried out to investigate the effect of oxytetracycline on blood serum Ca, P and Mg in cattle. The dose of 10mg/kg BW oxytetracycline was injected IV and IM in 8 cattle (4 cattle IV and the others 4 cattle IM) for four days. Oxytetracycline and Ca (ionized and total), P and Mg were measured in blood serum which were taken before and 1, 3, 6, 12 and 24 hours after IV injection and before, 6, 12 and 24 hours after IM injection.Oxytetracycline was measured by HPLC and Ca, P and Mg were measured by biochemical methods. The level of total and ionized calcium, P and Mg decreased by IV injection, but in IM injection only the level of total calcium decreased.

Key words: Oxytetracycline · Calcium · Phosphorous · Magnesium · Cattle

INTRODUCTION

Oxytetracycline (OTC) is one of the important members of the tetracycline group of antibiotics which is routinely used in animal husbandry [1]. It is a highly active, broad-spectrum antibiotic which is produced by a fermentation process by *Actinomycete*, *Streptomyces Rimosus* and widely used in veterinary medicine for the prophylaxis and treatment of respiratory and gastrointestinal infectious disease. It is used for the treatment of a great number of diseases since this antibiotic possesses a broad spectrum activity against many pathogenic organisms such as aerobic Gram-positive and Gram-negative bacteria, *Rickettsia*, *Mycoplasma* and *Chlamydia*. OTC can be used in veterinary formulations for the prevention and control of disease and added to feed for such a purpose [1,2]. Oxytetracycline passed the blood brain barrier, placental, intestinal, serous membrane and milk barriers and was excreted mainly by urinary and biliary systems [2]. It is licensed for use in a wide variety of food-producing animals such as cattle, pigs, sheep, poultry and it is a principal antibiotic used in fish farming too [1].

Calcium (Ca) is the major cation required in the mammalian diet and is the most abundant mineral element in the body. The skeleton, an articulated framework that facilitates locomotion and provides some support for the vital internal organs, contains about 98% of the body Ca as calcium phosphate. The remaining Ca, about 2%, is distributed in the extracellular and cellular fluids and has essential roles in metabolism, blood clotting, enzyme activation and neuromuscular function. The metabolism of Ca and phosphorus (P) is closely related and a deficiency or an excess of either one will interfere with the utilization and metabolism of the other. Phosphorus is second only to Ca in abundance in the body, with about 80% of the body P located in the skeleton, the remaining 20% having essential metabolic functions in cell contents and cell walls. Phosphorus functions as a component of the nucleic acids which are the basis of genetics and in nucleotides, such as adenosine triphosphate (ATP), which function in energy metabolism. Phosphorus is a component of both cell walls and cell contents as phospholipids and phosphoproteins. In addition, P functions in acid-base buffer systems of blood and body fluids, in cell differentiation and in maintaining the structural integrity of cells [3].

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There are some side effects for OTC. These include calcium chelation and tissue residues [1,2]. Many public health problems may arise from OTC residues. These include drug allergy, hypersensitivity, skin rashes and phototoxic dermatitis. The presence of OTC residues in feed may increase the bacterial resistance. The binding of tetracycline to calcium may result in inhibition of teeth development and skeletal growth [2].

The aim of the experiment presented here was to determine the calcium chelating side effect of OTC. There for this study was carried out in cattle to investigate the effect of intravenous (IV) and intramuscular (IM) injection of oxytetracycline on serum level of calcium, phosphorous and magnesium.

MATERIAL AND METHODS

Eight cross breed, non-lactating and non-pregnant cattle were used for this study. The dose of 10mg/kg BW oxytetracycline [4] was injected IV and IM in these cattle (4 cattle IV and the others 4 cattle IM) for four days.

Blood samples were taken before and 1, 3, 6, 12 and 24 hours after IV injection and before, 6, 12 and 24 hours after IM injection. Sera were stored at -20°C until analyzed.

The level of Oxytetracycline was measured by HPLC (Shimadzu Company, Japan) [5]. The level of Ca (ionized and total) measured by ion selective electrode potentiometry(Convergent Technologies Company, Germany), P and Mg were measured by commercial kits(Pars Azmoon and Zist Chemistry Company, Iran).

Statistical Analysis: Data were analyzed by a one-way analysis of variance (ANOVA) and LSD test with the confidence level 95% using soft ware SPSS version 16.

RESULTS

Results of Iv Injection: The results of IV injection showed in Table 1 and Figures 1 and 3.

The level of oxytetracycline increased immediately one hour after each injection and then reduced.

Serum total calcium levels decreased one hour after each injection of oxytetracycline and this trend continued up to 6 hours after injection and then decreased at 12 hours and reached to the level in before injection at 24 hours. The level of total calcium decreased from 9.8±0.26 mg/dl before the first injection to 9.22±0.22 mg/dl at 24 hours after the fourth injection.

Table 1: The level of total and ionized Ca, P, Mg and Oxytetracycline (mg/dl) in serum after the IV injection of Oxytetracycline

	IV Injection					
Day	Time	OTC	Total Ca	Ca ionized	p	Mg
1	0	0	9.8±0.26	3.78±0.11	6.96±1.11	2.47±0.15
	1	215.7±12.76	9.38±0.19	3.85±0.07	7.36±0.45	2.7±0.18
	3	180.91±9.06	9.46±0.15	3.8±0.2	6.76±0.7	2.76±0.23
	6	167.02±18.92	9.12±0.19	3.7±0.28	9.55±1.05	2.48±0.13
	12	130.67±17.87	9.6±0.1	4.09±0.19	9.07±0.8	2.83±0.28
	24	112.65±8.34	9.76±0.26	3.83±0.19	9.5±0.94	2.56±0.23
2	0	112.165±8.34	9.76±0.26	3.83±0.19	9.5±0.94	2,56±0.23
	1	178.33±15.98	9.12±0.14	3.57±0.18	7.34±0.93	2.55±0.25
	3	152.35±22.29	9.2±0.12	3.89±0.25	6.07±0.77	2.41±0.29
	6	147.43±10.32	8.62±0.26	3.67±0.19	5.27±0.78	2.13±0.14
	12	135.54±14.45	9.18±0.13	4.01±0.11	4.57±0.55	2.23±0.11
	24	129.41±13.96	9.7±0.26	3.61±0.17	4.31±0.49	2.3±0.3
3	0	129.41±13.96	9.7±0.26	3.61±0.17	4.31±0.49	2.3±0.3
	1	165.45±12.90	9.26±0.23	3.54±0.21	5.204±0.22	2.91±0.44
	3	134.56±6	9.26±0.15	3.6±0.2	4.71±0.49	2.83±0.21
	6	117.07±1.72	9.18±0.13	3.93±0.15	3.68±0.33	2.54±0.08
	12	115.54±20.67	9.4±0.17	3.9±0.12	4.09±0.54	1.93±0.19
	24	112.56±2.9	9.62±0.18	3.57±0.11	5.79±0.69	1.85±0.23
4	0	112.56±2.9	9.62±0.18	3.57±0.11	5.79±0.69	1.85±0.23
	1	143.07±44.14	9.64±0.25	3.97±0.14	5.43±0.34	1.64±0.1
	3	137.65±11.87	8.88±0.11	3.69±0.12	5.72±0.7	1.42±0.06
	6	132.67±17.34	9.02±0.05	3.92±0.13	4.93±0.44	1.56±0.12
	12	114.53±1.01	9.08±0.14	4.05±0.04	5.61±0.68	1.2±0.11
	24	115.3±0.11	9.22±0.22	3.52±0.3	5.29±0.67	1.32±0.15

Table 2: The level of total and ionized Ca, P, Mg and Oxytetracycline (mg/dl) in serum after the IM injection of Oxytetracycline

	IM injection					
Day	Time	OTC	Ca total	Ca ionized	p	Mg
1	0	0	9.3±0.8	2.47±0.14	8.45 ±.19	2.09±.0.19
	6	146.06±11.28	8.76±0.618	3.28 ±0.25	7.4 ±1.09	2.18±.0.23
	12	197.57± 26.48	8.98 ± 1.12	3.89 ±0.15	6.2 ±0.7	2.52±0.2
	24	187.74± 14.33	8.94 ±0.71	2.92 ±0.37	6 ± 0.89	2.35 ±0.18
2	0	187.74± 14.33	8.94 ±0.71	2.92 ±0.37	6 ±0.89	2.35 ±0.18
	6	168.71 ±17.06	9.16 ±0.59	3.3 ±0.21	5.16 ±0.64	2.58±.0.25
	12	180.31± 43.23	9.34 ±0.55	3.7 ±0.15	4.78 ±0.73	2.32±.0.09
	24	156.65± 13.36	9.36 ±0.66	3.2 ±0.19	6.63 ±0.36	2.38±.0.14
3	0	156.65± 13.36	9.36 ±0.66	3.2 ±0.19	6.63 ±0.36	2.38±.0.14
	6	196.07± 24.86	8.84 ±0.54	3.21 ±0.14	6.83±0.43	2.31±.0.28
	12	127.09± 5.41	8.78 ± 1.28	3.65 ±0.17	5.24 ±0.55	2.12±.0.43
	24	110.63± 2.43	9.1 ±0.7	2.5 ±0.27	7.25 ±0.44	2.35±.0.06
4	0	110.63± 2.43	9.1 ±0.7	2.5 ±0.27	7.25 ±0.44	2.35±.0.06
	6	184.55± 9.3	8.54 ±0.62	2.81 ±0.32	7.88 ± 0.26	3.16±.0.51
	12	130.32± 4.6	8.92 ±0.87	2.88 ±0.37	8.85 ±1.07	2.35±.0.06
	24	115.98± 5.09	9.22 ±0.64	2.98 ±0.35	8.7 ±0.65	2.22±.0.16

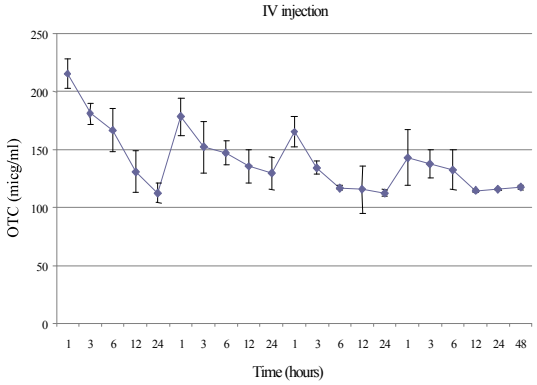

Fig. 1: The level of Oxytetracycline (mg/dl) in serum after the IV injection of Oxytetracycline

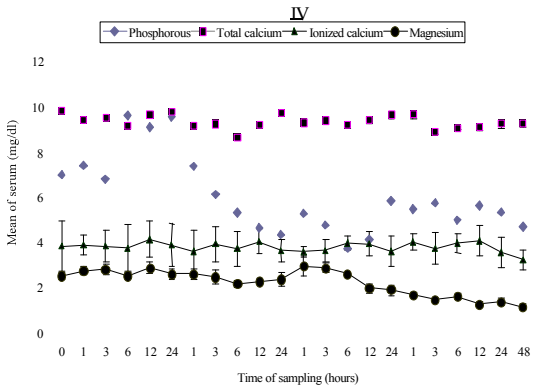

Fig. 3: The level of total and ionized Ca, P and Mg (mg/dl) in serum after the IV injection of Oxytetracycline

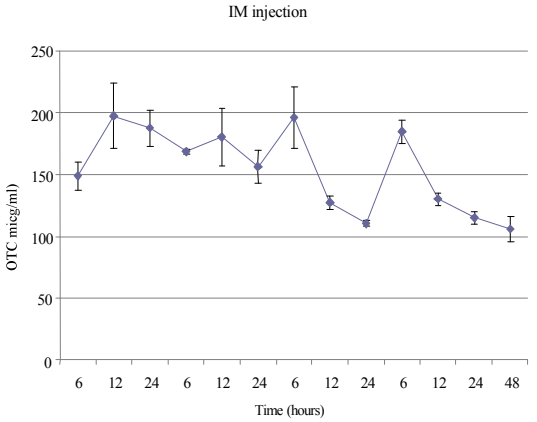

Fig. 2: The level of Oxytetracycline (mg/dl) in serum after the IM injection of Oxytetracycline

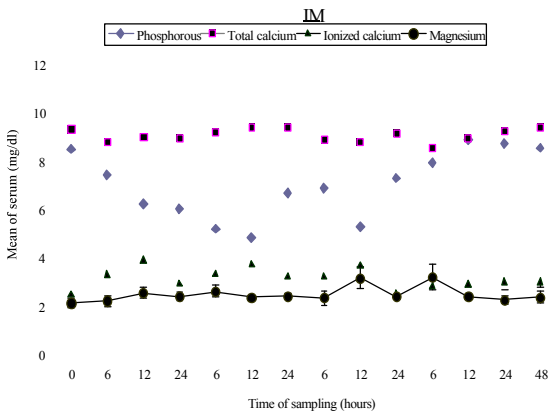

Fig. 4: The level of total and ionized Ca, P and Mg (mg/dl) in serum after the IM injection of Oxytetracycline

The level of ionized calcium decreased from 3.78±0.11 mg/dl before the first injection to 3.52±0.3 mg/dl at 24 hours after the fourth injection.

The level of P decreased from 6.96±1.11 mg/dl before the first injection to 5.29±0.67 mg/dl at 24 hours after the fourth injection.

The level of Mg decreased from 2.47±0.15 mg/dl before the first injection to 1.32±0.15 mg/dl at 24 hours after the fourth injection.

Results of Im Injection: The results of IV injection showed in Table 1 and Figures 2 and 4.

Oxytetracycline gradually absorbed after intramuscular injection. In the first two injections (days 1 and 2) the highest concentrations in serum were determined 12 hours after injection and in the third and fourth (days 3 and 4) injection the highest concentration were found at 6 hours after injection.

The level of total calcium decreased from 9.3±0.8 mg/dl before the first injection to 9.22 ±0.64 mg/dl at 24 hours after the fourth injection. But the level of ionized Ca, P and Mg increased at 24 hours after the fourth injection.

DISCUSSION

In this study the concentration of OTC was determined by HPLC method. This method would be useful for routine monitoring of oxytetracycline residues in ovine dairy milk [6] and edible tissue and meat of cattle [7, 8]. In the group of IV injection, the level of OTC increased immediately one hour after each injection and then reduced but in the group of IM injection, OTC gradually absorbed after intramuscular injection. In the first two injections (days 1 and 2) the highest concentrations in serum were determined 12 hours after injection and in the third and fourth (days 3 and 4) injection the highest concentration were found at 6 hours after injection.

After IV injection of OTC, serum total calcium levels decreased one hour after each injection and this trend continued up to 6 hours after injection and then decreased at 12 hours and reached to the level in before injection at 24 hours. The level of ionized calcium, P and Mg decreased at 24 hours after the fourth injection. After IM injection of OTC, only serum total calcium levels decreased at 24 hours after the fourth injection and the level of ionized calcium, P and Mg increased. Button and Mulders [9] showed intravenous injection of OTC in propylene glycol (PG), OTC in saline solution and PG alone in sheep had no significant effects on total plasma calcium concentrations over a 60-minutes period. In contrast, ionized calcium concentrations in whole blood were significantly decreased for approximately 3 minutes after injection of OTC in PG and OTC in saline solution. A slight depression of ionized calcium concentrations was noticed after injection of PG alone. Seemingly, calcium chelation by OTC may be a major factor in the collapse syndrome of ungulates given preparations containing OTC by rapid IV injection.

CONCLUSION

The result of this study showed IV injection of oxytetracycline had significantly effects on Ca, P and Mg. It is resulted from divalent metal ion chelating by oxytetracycline. It is concluded that in treatment with oxytetracycline, the level of blood serum Ca, P and Mg of patient must be noted.

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