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THE EFFECT OF INTRA MUSCULAR INJECTION OF SOME ANESTHETICS ON SERUM CREATINE KINASE ACTIVITY IN DOGS

(With 1Table)

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SUMMARY

In this study, xylazine and ketamine which are used as pre- and general anesthetics in dogs, were injected intramuscularly (I.M) to musculus semimembranosus and musculus longissimus dorsi muscles, then after the injection changes in plasma creatine kinase (CK) activity were observed. For this purpose six homeless dogs were used. Blood samples taken from dogs 1, 0.5 hours before the I.M injection and during the injection were used as control group values, whereas, samples taken at 0.25th, 0.5th, 1st, 2nd, 3rd, 4th, 6th, 8th, 10th, 12th, 24th, 48th, 72nd hours after the injection, were used as experimental group values. After the I.M injection of xylazine to m.semimembranosus and m.longissimus dorsi, CK activity of experimental group started to increase after 0.25. hour, reached to its peak at 4th hour ($p<0.001$) and returned to normal levels after 24th hour. After the I.M injection of ketamine to m.semimembranosus, CK activity of experimental group started to increase after 0,25. hour, reached to its peak at 4th hour ($p<001$) and returned to normal levels after 24th hour. After injection to m.longissimus dorsi, CK activity of experimental group started to increase after 0.25th hour, reached to its peak at. 4th hour ($p<001$) and returned to normal levels after 24th hour. As a result, it has been seen that, according to the properties of both anesthetic drugs and injection place, different muscle damage has occurred and serum CK enzyme activity has returned to normal levels after almost 24th hour.

Key Words: *Dogs, creatine kinase, muscles, xylazine, ketamine.*

INTRODUCTION

Creatine kinase (CK: EC 2.7.3.2), is an important high-energy transferring enzyme abundant in brain, skeletal muscle, heart and smooth muscle (Basson *et al.*, 1985, Hortobagyi, Denahan, 1989, Lang, Würzburg, 1982) If the integrity of muscle cell membrane is altered, CK leaks from cells. Serum CK has been the subject of various experimental and clinical investigations in dogs to establish a model for human myocardial, neuro-muscular and intestinal infarctions, and to verify that serum CK activity can be used in diagnosis of muscular diseases. However, in domestic animals including dogs, plasma or serum CPK activity can be used as an aid for detection of skeletal muscle disease (Aktaş, 1994; Cardinet, 1989; Hortobagyi, Denahan, 1989; Yasuda, Too,K., 1983).

It has been announced that, physical activity, especially running and exercise plays a role in changing plasma CK activity of dogs (Bjotvedt, *et al.*, 1984; Hinchcliff *et al.*, 1993; Ilkiv *et al.*, 1989; Snow *et al.*, 1988). It has been claimed by Yasuda and Too (1983) that, CK activity in animals with decubitis wounds was 12 times greater than normal levels and has also been claimed by Schimdt and Booker (1982) that enzyme activity has increased as a result of myopathy, surgical operation and wounds caused by firearms (Zheng *et al.*, 1988).

Researchers have shown that, by measuring plasma CK activity with periodic blood analysis, muscle degeneration and the level of degeneration could be determined (Heffron, *et al.*, 1976; Dibartola *et al.*, 1977).
Steines *et al.*, (1978) described that, increase in CK enzyme activity following I.M injection of a drug is associated with significant muscle damage and volume of muscle tissue. It was also revealed that, enzyme activity would change due to the properties of injected solution, local muscle binding capability of the drug, the damaging effect of injection and, local blood flow of the muscle (Hirzel *et al.*, 1977; Steines *et al.*, 1978).

In Europe and Turkey, for surgical purposes in dogs, intra muscular xylazine is applied as preanesthetic and ketamine is applied as general anesthetic. In most of the European countries, I.M injection in dogs is applied to dorsal region into the m.longissimus dorsi muscle, which is placed between L4-L6 (between 4th lumbal vertebra and 6th lumbal vertebra). However in Turkey, m.semimembranosus muscle, which is in hind limb, is preferred as I.M injection place.

Determining plasma CK activity in dogs after an I.M injection is important for clinical veterinary medicine to determine the level of muscular

degeneration level and the most suitable injection place. It can also give us an opportunity to differentiate the effect of injection from that of muscle and heart diseases in which the level of CK activity also increase.

For this purpose, the present study involved the IM injection of xylazine which is the mostly used preanesthetic in veterinary clinics and ketamine which is used commonly as a general anesthetic, to m.longissimus dorsi and m.semimembranosus, in homeless dogs for monitoring effects on plasma CK levels and to determine the most ideal injection places in both drugs.

MATERIALS and METHODS

In the study, 6 male, healthy, homeless dogs were used as experiment material. Average ages of the dogs were between 14-30 months, weights were between 15-21.5 kg and cidago heights were between 36-41 cm.

Xylazine hydrochloride (Xylazine, Bayer, Istanbul, Turkey) and ketamine (Ketalar, Eczacibasi, Istanbul, Turkey), were used as pre- and general anesthetics were injected intra muscularly to the dogs respectively 0.15ml/kg, 15mg/kg, into two different muscle groups (m.semimembranosus and m.longissimus dorsi) and with different time intervals. Injections of both anesthetics were carried out after the plasma CK enzyme activities return to normal levels. Blood samples were obtained from the dogs 1 and 0,5 hours before and during the injection from Vena jugularis, and plasma CK activity was determined, and these mean values were accepted as before injection (control group) values. After the injection, blood were taken at 0.25th, 0.5th, 1st, 2nd, 3rd, 4th, 6th, 8th, 10th, 12th, 24th, 48th, 72nd. hours and, were used as experimental group values. CK enzyme reagents were supplied by Sigma Diagnostics (Sigma Chemical Co. Ltd., Poole, Dorset, UK) and spectrophotometric assays were performed

For statistical analysis of differences between control and experimental groups variance analysis method was used.

RESULTS

Mean CK values obtained at 1, 0.5 hour before the I.M injection and during the injection (control group); mean values, which are determined 0.25, 0.5, 1, 2, 3, 4, 6, 8, 10, 12, 24, 48, 72 hour after the injection (experimental group); the comparison between the groups, and statistical results are all shown at Table-1.

When Table-1 is examined, it was found that plasma CK activity of the experimental group started to increase, 0.25th hour after i.m injection of xylazine to m.semimembranosus, reached its peak with a value of 354,98 IU/L at 4th hour, and when compared with the control group this value was found to be significant ($p<0.001$), and it returned to normal level after 24th hour. After i.m injection of xylazine to m.longissimus dorsi, it started to increase at 0.25th hour, reached its peak with a value of 363,98 IU/L at 4th hour, and when compared with the control group this value was found to be significant ($p<0.001$), and it returned to normal level after 24th hour.

After i.m injection of ketamine to m.semimembranosus, plasma CK activity started to increase at 0.25th hour, at 4th hour reached its peak with a value of 399,08 IU/L at 4th hour, and when compared with the control group this value was found to be significant ($p<001$), and it returned to normal level after 24th hour. After i.m injection of ketamine to m.longissimus dorsi, the plasma CK activity started to increase at 0.25th hour, reached its peak with a value of 359,48 IU/L, at 4th hour and when compared with the control group this value was found to be significant ($p<0.001$), and it returned to normal level after 24th hour.

DISCUSSION

Today, xylazine and ketamine are the commonly used preparations, as pre- and general anesthetics in Veterinary Medicine. In this study, by injecting xylazine and ketamine into both muscle groups, we tried to define the minimum muscle damage. Obtained values are discussed with other researchers results.

In the study, plasma CK levels of dogs, which are measured before the injection of xylazine and ketamine and are defined as control group, were showed correspondence to control values of plasma CK levels measured by other researchers in different ages and races of dogs (Aktaş, 1994; Dibartola, *et al.*, 1977; Heffron *et al.*, 1976).

It is well-known fact that some muscle damage occurs after intra muscular injection. Aktaş (1994), in a study involving intra muscular B vitamin injection, claimed that, plasma CK activities increased at 3rd and 4th hours, and at 48th and 72nd hours decreased to normal levels. When the same researcher applied imidokap and lidokain injection intra muscularly to dogs, he claimed, that plasma CK activities reached to the values of 373-1874 IU/L and 857-1894 at 3rd and 6th hours, and returned back to the normal levels at 48th and 72nd hours. These results showed correspondence

with, peak time and time of returning back to normal, of plasma CK levels which occurred after application of xylazine and ketamine to both muscle groups.

Steines *et al.*, (1978), proposed that, after injection of irritant drugs to humans and rabbits, plasma CK activity reached its peak at 4th hour, maintained significant till 24 hours, and finally returned to normal levels at 72nd hour. Because in the present study, the highest plasma CK activity is obtained after ketamine injection, ketamine is thought to be a more irritant anesthetic then xylazine. Lindena *et al.*, (1982) announced that CK activity changes depend on the muscle type, and claimed that CK activity in rapidly contracting muscles is greater than slowly contracting muscles. In our study, the highest plasma CK activity is also obtained from injection of ketamine to m.semimembranosus muscle and when compared to that after the injection to m.longissimus dorsi, significant differences (in basis of $p<0.5$) is detected at values of 6^{th}, 8^{th} and 10^{th} hours. Since m.semimembranosus is active compared to long m.longissimus dorsi, it seems natural to obtain such results. Steines *et al.*, (1978) pointed out that, the amount of CK released following an I.M injection of a drug is correlated with the mass of muscle that is damaged. They claimed that, this in turn is associated with the properties of the drug and the amount injected. In our study the amount of ketamine is more than the amount of xylazine injected to both muscle groups and, the plasma CK activity is higher when ketamine is used. So the results of the study mentioned above, show correspondence with our results. Wilson, (1976) and Cairns *et al.* (1977) reported that, besides changes among individuals, an individual change in its own is also important and these changes could vary between 13% and 35% due to many factors. In our study, individual changes are also observed after the injection.

In conclusion, after the I.M injection of xylazine and ketamine to m.semimembranosus and m.longissimus dorsi muscle groups, muscle damage occurred due to the properties of both anesthetics and the place they were used. Since the use of ketamine produced more damage compared to xylazine CK analysis shouldn't be done until 72nd hour following I.M injection or margin of error in CK analysis should be taken into consideration. M.longissimus dorsi muscle group should be chosen as I.M injection place like in the European countries.

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Table-1: Varying plasma CK activities before (control group) and after (experimental group) i.m injection of xylazine and ketamine to m.semimembranosus and m.longissimus dorsi, and statistical significance of differences between two groups.

Muscle / Anest.		Control	0.25	0.5	1	2	3	4	6	8	10	12	24	48	72
ML Xyl	X	42,7^{b}	45,4^{b}	53,96^{b}	101,18^{ab}	170,48^{ab}	242,93^{ab}	363,98^{a}	344,63^{a}	222,23^{ab}	162,83^{ab}	128,14^{ab}	53,96^{bc}	45,86^{b}	40,92^{b}
	Sx	± 2,11	± 1,62	± 1,97	± 8,38	7,58	9,37	6,21	9,57	5,05	5,03	3,01	2,31	3,11	2,73
ML Ket	X	36,12^{bc}	52,16^{bc}	62,95^{bc}	111,93^{abc}	187,08^{abc}	266,78^{abc}	378,46^{a}	359,48^{ab}	238,01^{abc}	174,58^{abc}	131,33^{abc}	50,44^{bc}	41,37^{bc}	43,46^{bc}
	Sx	± 2,63	± 2,27	± 2,37	± 3,63	± 3,58	± 7,08	± 9,33	± 11,52	± 6,20	± 5,19	± 3,08	± 6,01	± 5,29	± 5,61
			*	*											
MS Xyl	X	41,52^{b}	53,59^{b}	59,80^{b}	96,23^{ab}	174,98^{ab}	255,53^{ab}	354,98^{a}	327,53^{ab}	227,14^{ab}	160,13^{ab}	130,43^{ab}	63,40^{b}	52,56^{b}	43,17^{b}
	Sx	± 3,26	± 4,14	± 3,71	± 3,73	± 2,55	± 4,45	± 13,88	± 9,65	± 7,23	± 6,88	± 5,01	± 2,06	± 3,51	± 4,29
MS Ket	X	37,90^{b}	49,91^{b}	60,24^{b}	115,13^{ab}	199,28^{ab}	270,83^{ab}	397,73^{a}	399,08^{a}	253,75^{ab}	193,43^{ab}	138,53^{ab}	45,71^{b}	41,67^{b}	40,02^{b}
	Sx	± 3,00	± 3,46	± 3,65	± 6,29	± 5,80	± 4,33	± 10,58	± 8,23	± 4,12	± 5,10	± 4,76	± 3,01	± 2,05	± 2,73
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a,b,c: In each line, the differences between the means with different letters are significant ($p<0.05$).

*$p<0.05$, **$p<0.01$, ***$p<0.001$

ML: M.longissimus dorsi MS: M..semimembranosus Ket: Ketamine Xyl: Xylazine