

Haematological and biochemical alterations caused by epidural and intramuscular administration of xylazine hydrochloride in dromedary camels (*Camelus dromedarius*)

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Summary

This study was conducted in 16 healthy immature dromedary camels weighing 120-150 kg to evaluate and compare the effects of epidural and intramuscular injections of xylazine administered at 0.1 mg/kg and 0.2 mg/kg. Haematological parameters included haemoglobin, packed cell volume, total erythrocyte count and total leukocyte count. Biochemical parameters included alkaline phosphates, alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, creatinine and glucose. Parameters were measured at different intervals before (baseline) and after the administration of drugs. Our study showed that the effect of xylazine on haematological and biochemical parameters is dose-dependant and is also related to the route of administration. The low dose of xylazine administered using both intramuscular and epidural methods showed minimal effects, whereas high doses of the drug, especially when injected intramuscularly, caused greater changes in haematological and biochemical parameters.

Keywords

Biochemical, Camel, *Camelus dromedarius*, Dromedary camel, Epidural, Haematology, Injection, Intra-muscular, Iran, Xylazine.

Alterazioni ematologiche e biochimiche da somministrazione epidurale e intramuscolare di xilazina idrocloruro in dromedari (*Camelus dromedarius*)

Riassunto

Questo studio è stato condotto in 16 dromedari sani immaturi del peso di 120-150 kg per valutare e confrontare gli effetti di somministrazioni epidurali e intramuscolari di xilazina (0.1 mg / kg e 0,2 mg / kg). I parametri ematologici considerati comprendono emoglobina, volume di eritrociti condensati volume cellulare totale, conta degli eritrociti e conta dei leucociti; i parametri biochimici includono fosfati alcalini, alanina aminotransferasi, aspartato aminotransferasi, azoto ureico, creatinina e glucosio. I parametri sono stati misurati a differenti intervalli prima e dopo la somministrazione di

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farmaci. Il presente studio ha mostrato che l'effetto di xilazina sui parametri ematologici e biochimici dipende dalla quantità di dose somministrata ed è anche correlato alla modalità di somministrazione. La somministrazione di basse dosi di xilazina per via intramuscolare e epidurale ha evidenziato effetti minimi, mentre alte dosi del farmaco, soprattutto quando iniettato per via intramuscolare, hanno causato importanti cambiamenti alterazioni nei parametri ematologici e biochimici.

Parole chiave

Biochimica, *Camelus dromedarius*, Cammello, Dromedario, Ematologia, Epidurale, Intramuscolare, Iran, Somministrazione, Xilazina.

Introduction

Xylazine is an alpha-2 adrenergic receptor agonists (43), and it is often used to sedate or, in higher doses, restrain (recumbency and heavy sedation) ruminants (38). Of all domestic animals, ruminants are the most sensitive to xylazine (27). The use of xylazine in ruminants may be followed by moderate to severe cardiopulmonary depression (such as bradycardia, hypotension, hypoxaemia and tachypnea) (8, 9, 16). The dose-dependent cardiovascular side effects of xylazine are similar in different species and the most severe reactions occur after intravenous injection and during general anaesthesia (26). Xylazine has recently been used epidurally in induction of caudal analgesia in many species of animals, such as horses (29, 30), ponies (20), cattle (25), dogs (19), goats (1, 27, 28), sheep (5), buffalo (39, 41) and llamas (22). When xylazine is administered epidurally, good analgesia is achieved and cardiopulmonary effects are less in comparison to systemic administration (5, 19).

Nowadays, there are large populations of dromedaries (single hump) (*Camelus dromedarius*) living in tropical regions around the world, such as the Middle East, Africa and a smaller number in Australia (2). As a result, it seems necessary for veterinarians to broaden their knowledge of the treatment of this species. The systemic use of xylazine in camels has been described in the veterinary literature (14, 23). However, to the knowledge of the authors,

there are few reports on the epidural administration of xylazine and its systemic effects on dromedary camels (40). We undertook this study to evaluate and compare the haematological and biochemical alterations following epidural and intramuscular administration of xylazine in dromedaries.

Materials and methods

The experimental protocols were approved by the Research Ethics Committee of Shahid Bahonar at the University of Kerman in Iran. A total of 16 immature dromedary camels aged 4 to 6 months of both sexes and weighing 120-150 kg were selected for this study. The animals were housed in a pen and maintained on grass (hay), supplemented with concentrate. Drinkable water was made freely available. Camels were judged to be in good health based on clinical and haematological evaluations prior to the study. Food was withheld for 12 h and water for 8 h prior to the experiment. The trials were conducted in the morning hours of the day. During the course of the study, the ambient temperature fluctuated between 25°C and 27°C.

The animals were randomly placed into groups. They were treated with epidural injection (at a dose of 0.1 mg/kg [X1_e] and 0.2 mg/kg [X2_e]), and intramuscular injection (at a dose of 0.1 mg/kg [X1_{im}] and 0.2 mg/kg [X2_{im}]) of xylazine. Xylazine 2% (Alfasan, Woerden) was used for all camels. A full dose of xylazine was considered to be 0.2 mg/kg on the basis of normal sedative doses for camels (2).

The animals were restrained in sternal recumbency prior to each treatment. For epidural injections, the skin over the sacrococcygeal area was prepared surgically. The injections were administered into the extradural space through the first intercoccygeal space, using an 18 gauge 3.7 cm long hypodermic needle. The epidural space was confirmed by the hanging drop technique and lack of resistance to injection. Intramuscular injection was performed at quadriceps muscle sites routinely.

For haematological evaluation, a catheter was placed into the jugular vein and blood samples were taken and collected in clean, dry vials containing ethylenediaminetetraacetic acid (EDTA) before xylazine administration (baseline) and at 15, 30, 45, 60, 75, 90, 105, 120, 150 and 180 min thereafter. The haematological parameters considered in this study included haemoglobin (Hb), packed cell volume (PCV), total erythrocyte count (TEC) and total leukocyte count (TLC).

For biochemical evaluation, blood was collected in clot tubes, without anticoagulant, prior to xylazine administration (baseline) and at 30 min intervals thereafter until 180 min. Blood samples were transported on ice to the laboratory, and sera were separated immediately by centrifugation of blood at $1500 \times g$ for 15 min at room temperature and were kept at -20°C until use. The biochemical parameters measured in the serum included alkaline phosphates (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine and glucose (GLU).

Statistical analyses were performed using Statistical Package for Social Sciences software (SPSS, Version 16.0) (Chicago, Illinois). Data were analysed using two-way analysis of variance (ANOVA) for repeated measures followed by post-hoc Tukey HSD (honestly significant difference) test for the comparison of mean \pm standard deviation (SD) at different time intervals between the groups. A paired sample *t* test with Bonferroni correction was used to compare the mean at different time intervals with their baseline values within the group. A value of $p < 0.05$ was considered significant.

Results

In our study, haematological and biochemical parameters were recorded at different intervals; these are presented in Tables I and II, respectively. Baseline values for all variables were within normal limits for dromedary camels (10, 34).

Evaluation of haematological parameters revealed a decrease in the amount of Hb in all

groups. A significant decrease in Hb was observed from minute 60 to 150 in group X2_e and from minute 30 to 180 in group X2_{im}. Altered quantities of Hb were significant only at minute 60 in group X1_e and at minute 120 in group X1_{im}.

Although the PCV level decreased in all groups post administration of different doses of xylazine, the alteration was not significant.

A decrease in TEC was observed after the administration of xylazine in all groups and was significant from minute 30 to 105 in group X2_e, from minute 30 to 180 in group X2_{im}, and at minute 75 in groups X1_e and X1_{im}.

In addition, TLC decreased in all animals treated with xylazine. There was a significant decrease in TLC from minute 30 to 120 in group X2_e, from minute 30 to 180 in group X2_{im}, from minute 90 to 105 in group X1_{im} and at minute 105 in group X1_e.

Alterations in Hb and TEC values were significantly higher in group X2_{im} compared to groups X1_e and X1_{im}; furthermore, the alteration in TLC value in group X2_{im} was significantly higher in comparison to group X1_e during the 180-min study. A tendency to normalisation of haematological parameters was observed at the end of the experiment but the values never returned to the baseline level (Table I).

Biochemical analysis demonstrated that in all groups, the differences for ALP activity were not significant. Although AST, ALT, BUN and creatinine values increased during the post injection period in all groups, these changes were not significant. The serum glucose level increased after the administration of xylazine in all groups, but it was significant from minute 60 to 90 in group X2_{im} and at minute 60 in group X2_e (Table II).

Discussion

Despite the great advances that have been made in the use and understanding of sedative drugs in domestic animals, there have been few reports of their use in camels (21). The camel is a large animal and entails a risk of injury to personnel. Consequently, in camel

clinical practices, the use of drugs to produce sedation as well as analgesia is mandatory when conducting certain routine examinations and most surgical interventions. Analgesia is an important quality of alpha-2 agonists (18). The administration of alpha-2 agonist drugs are frequently recommended in the camel to ensure immobilisation and provide sedation (33). Intramuscular and intravenous administration of xylazine alone or in

combination with an anaesthetic agent, has been described extensively for use in camels (11, 46). Although much research work has been conducted on the clinical and physiological effects of epidural administration of xylazine in various animal species, it appears that there are few reports on the use of xylazine administered epidurally in dromedary camels (2, 35, 36, 40). The aim of our study was to compare the physiological effects of

Table I
Mean value ± (standard deviation) of haematological parameters after epidural and intramuscular administration of xylazine in dromedary camels

Parameter and group	Time interval (min)										
	0 (baseline)	15	30	45	60	75	90	105	120	150	180
Hb (g/dl)											
°X1 _{im}	13.1± 0.19	12.98± 0.11	12.36± 0.56	12.45± 0.78	12.35± 0.76	12.28± 0.7	12.13± 0.42	11.9± 0.51	11.81± 0.37*	12.1± 0.27	12.21± 0.36
X2 _{im}	11.97± 0.41	12.33± 0.55	11.47± 0.86*	11± 0.57*	10.97± 0.35*	10.83± 0.44*	11.01± 0.4*	11.17± 0.41*	11.38± 0.46*	11.45± 0.35*	11.85± 0.24*
°X1 _e	12.94± 0.43	12.92± 0.43	12.82± 0.32	12.69± 0.22	12.64± 0.23*	12.5± 0.27	12.5± 0.27	12.53± 0.31	12.66± 0.36	12.71± 0.37	12.84± 0.43
X2 _e	13.06± 0.57	13.01± 0.57	12.72± 0.58	12.13± 0.61	11.68± 0.54*	11.45± 0.51*	11.39± 0.37*	11.5± 0.38*	11.64± 0.36*	11.87± 0.29*	12.22± 0.22
PCV (%)											
X1 _{im}	26± 1.82	25.25± 1.5	24.5± 1.29	24.5± 1.29	24.25± 1.25	23.75± 1.7	23.5± 1.29	23.75± 1.7	24± 1.82	24.25± 1.5	24.5± 1.9
X2 _{im}	27.25± 3.3	26.25± 2.63	24± 2.3	23± 2.94	22.5± 2.38	22.5± 2.38	22.75± 2.21	23.7± 2.08	23.75± 2.21	24.5± 2.38	25.25± 2.63
X1 _e	27.75± 1.7	27.25± 2.06	25.25± 2.06	25.75± 1.7	25.25± 1.25	24.5± 1.29	24.5± 1.29	24.75± 1.5	25.75± 1.5	26.5± 1.29	26.75± 1.7
X2 _e	22.75± 1.7	25.25± 2.21	24.5± 2.08	23.5± 2.08	23.25± 1.89	23.25± 1.89	23.25± 1.89	23.5± 1.73	24.25± 2.21	24.25± 2.06	24.75± 1.7
TEC (×10⁶)											
°X1 _{im}	6.78± 0.59	6.62± 0.64	6.32± 0.53	6.22± 0.53	6.08± 0.46	6± 0.47*	5.97± 0.46	5.97± 0.6	6.15± 0.55	6.32± 0.37	6.45± 0.46
X2 _{im}	6.8± 0.29	6.4± 0.45	5.75± 0.42*	5.12± 0.29*	4.75± 0.31*	4.65± 0.23*	4.75± 0.23*	4.9± 0.32*	5.1± 0.58*	5.3± 0.51*	5.65± 0.44*
°X1 _e	6.69± 0.37	6.12± 0.25	6.05± 0.42	6.05± 0.45	5.77± 0.42	5.7± 0.4*	5.85± 0.27	6.12± 0.46	6.37± 0.38	6.49± 0.31	6.55± 0.35
X2 _e	6.75± 0.28	6.12± 0.62	5.75± 0.28*	5.62± 0.62*	5.25± 0.5*	5.12± 0.25*	5.25± 0.28*	5.5± 0.3*	5.9± 0.2	6.06± 0.12	6.19± 0.24
TLC (×10³)											
X1 _{im}	14.8± 0.42	14.6± 0.34	14.3± 0.39	14.1± 0.63	13.9± 0.46	13.8± 0.49	13.6± 0.31*	13.6± 0.45*	13.8± 0.48	13.85± 0.43	14.1± 0.33
X2 _{im}	15.2± 0.33	14.8± 0.26	14.3± 0.22*	13± 0.17*	12.9± 0.27*	12.9± 0.36*	12.9± 0.26*	13± 0.24*	13± 0.31*	13.4± 0.29*	13.8± 0.21*
°X1 _e	15.35± 0.77	15± 0.75	14.7± 0.68*	14.3± 0.61	14± 0.57	13.8± 0.52	14± 0.54	14± 0.4**	14.3± 0.43	14.4± 0.53	14.5± 0.67
X2 _e	15± 0.42	14.4± 0.33	13.7± 0.64*	13.3± 0.47*	13.1± 0.25*	13.3± 0.52*	13.35± 0.56*	13.7± 0.57*	13.8± 0.67*	14± 0.39	14.3± 0.33

In group X1_{im}, 0.1 mg/kg and in group X2_{im}, 0.2 mg/kg xylazine was administered intramuscularly
In group X1_e, 0.1 mg/kg and in group X2_e, 0.2 mg/kg xylazine was administered epidurally

Hb haemoglobin
PCV packed cell volume
TEC total erythrocyte count
TLC total leukocyte count

° significant difference compared to the group X2_{im} during 180-min study ($p < 0.05$)
* significant differences compare to the baseline ($p < 0.05$)

Table II
Mean value ± (standard deviation) of biochemical parameters after epidural and intramuscular administration of xylazine in dromedary camels

Parameter and group	Time interval (min)						
	0 (baseline)	30	60	90	120	150	180
ALP (U/l)							
X1 _{im}	131.25±26.91	125.75±29.17	123.75±34.49	126.75±23.6	128.25±22.11	128.5±21.49	131±29.2
X2 _{im}	128.25±33.69	121.5±24.28	120.75±29.09	118±31.82	119.5±24.85	120.5±27.38	118.75±28.58
X1 _e	134±29.68	132.5±30.96	128.5±30.26	130±20.56	131.75±24.98	127.5±25.12	130±28.62
X2 _e	125±27.36	119±25	117.75±24.86	118.75±23.41	120.75±21.42	120±33.21	122.25±33.19
ALT (U/l)							
X1 _{im}	13.37±2.21	13.96±2.19	14.17±2.42	14.31±2.69	14.5±2.65	14.11±2.21	14.26±2.39
X2 _{im}	14.41±1.48	15.12±1.75	15.54±1.78	15.96±1.84	16.06±1.56	15.71±1.61	15.71±1.85
X1 _e	13.66±1.98	13.85±1.98	13.92±1.91	14±2.25	13.77±2.08	13.6±2.3	13.67±2.09
X2 _e	13.54±1.77	13.59±1.87	13.8±1.95	13.98±2.07	14.01±1.95	13.81±1.98	13.72±1.97
AST (U/l)							
X1 _{im}	89.5±18.88	91.75±17.73	93.5±15.55	96.5±17.46	94.25±15.2	92.25±16.74	93.25±18.71
X2 _{im}	86.5±8.18	90.25±6.18	93.5±5.26	99.25±6.65	97.5±5.16	95.75±6.24	92.5±5.51
X1 _e	83.75±18.1	86±18.46	82.25±18.64	90.25±19.75	88±18.76	85.5±19.5	86.25±16.92
X2 _e	80±19.39	86.25±16.34	87.5±17.48	92.12±17.69	91±16.51	87.75±11.56	85±16.91
BUN (mg/dl)							
X1 _{im}	29±3.65	29.42±3.62	29.8±3.61	29.7±3.54	29.39±3.48	29.28±3.57	29.11±3.54
X2 _{im}	28.25±4.79	28.92±4.7	29.96±4.62	29.53±5.13	29.23±5.12	29.09±5.21	28.95±5.02
X1 _e	29.75±3.77	30.19±4.03	30.36±3.71	30.29±3.84	30.12±3.86	29.94±3.83	29.74±3.76
X2 _e	27.25±2.63	28.04±3.06	28.12±2.59	27.89±2.28	27.6±2.37	27.8±2.56	27.46±2.52
Creat (mg/dl)							
X1 _{im}	1.79±0.56	1.81±0.56	1.91±0.59	1.95±0.53	1.92±0.53	1.86±0.56	1.84±0.55
X2 _{im}	1.91±0.48	2.15±0.59	2.31±0.62	2.22±0.63	2.18±0.56	2.12±0.56	2.04±0.54
X1 _e	1.75±0.4	1.8±0.33	1.86±0.34	1.86±0.38	1.82±0.35	1.76±0.4	1.78±0.45
X2 _e	1.89±0.68	2.02±0.7	2.19±0.75	2.1±0.76	2±0.71	2.06±0.77	1.97±0.76
Glu (mg/dl)							
X1 _{im}	103.5±13.48	111±12.52	117.25±13.45	114±14.02	111.5±13	108±13.14	107.75±13.74
X2 _{im}	99.25±4.99	112.5±6.81	120±7.62*	119±7.53*	114.75±7.72	112.25±10.05	109±6.61
X1 _e	105.25±9.11	110.75±11.79	117.75±7.45	115.25±10.66	115.75±8.02	113±8.12	109.75±8.85
X2 _e	105.25±9.11	116.25±10.05	131.25±6.65*	122.5±7.14	116±7.35	111.75±6.95	108±7.39

In group X1_{im}, 0.1 mg/kg and in group X2_{im}, 0.2 mg/kg xylazine was administered intramuscularly
In group X1_e, 0.1 mg/kg and in group X2_e, 0.2 mg/kg xylazine was administered epidurally

ALP alkaline phosphates
ALT alanine aminotransferase
AST aspartate aminotransferase
BUN blood urea nitrogen
Creat creatinine
Glu glucose

* significant differences compare to the baseline (p<0.05)

epidural and intramuscular xylazine at different doses in dromedary camels.

Based on haematological evaluations, we observed changes in the quantities of Hb, TLC and TEC in all groups after intramuscular and epidural injection of different doses of xylazine and the effects were dose-dependent, so that the higher the dose of xylazine, the greater the alteration of haematological parameters.

It also appeared that intramuscular injection of xylazine was more effective on the haematological parameters in comparison to the epidural administration at the same dose, although the differences were not significant. In this study, the most intensive change in the haematological parameters occurred when a high dose of xylazine (0.2 mg/kg) was administered intramuscularly. Pooling of

circulating blood cells in the spleen and other reservoirs secondary to decreased sympathetic activity explain the decrease in haematological parameters (32). The decrease in Hb and PCV following injection of xylazine might be due to the fluid shifting from the extravascular compartment to the intravascular compartment in order to maintain normal cardiac output (45). A fall in the haematological parameters was also reported after epidural administration of xylazine in cattle (25), horses (42), buffalo (41), goats (27) and dogs (19).

Some studies have evaluated the use of intramuscular xylazine on some biochemical and haematological parameters in dromedary camels. Peshin *et al.* (35) and Ali *et al.* (4) reported that intramuscular injection of xylazine at a dose of 0.5 mg/kg was ineffective in changing haematological parameters after xylazine administration (4, 35). Bolbol and Ibrahim (12) showed that intramuscular xylazine (0.25 mg/kg) caused significant reduction in Hb, PCV, TEC and TLC (12). Sharma *et al.* (40) stated that Hb, PCV, TEC and TLC did not alter significantly following the epidural administration of three different doses (0.1 mg/kg, 0.2 mg/kg and 0.3 mg/kg) of xylazine in dromedaries (40).

The differences in alteration of haematological parameters between the results of present study and Sharma's might be attributed to the age of the animals. In our study, immature camels (aged 4-6 months) were used, while Sharma and colleagues examined older camels (40). It has been confirmed that there is a high correlation between the age of the animals and the clinico-physiological effects of anaesthetic drugs (37). Caulkett (15) explained that young calves are more sensitive to alpha-2 agonist agents, such as xylazine, compared to adult cows (15).

Biochemical evaluation in our study demonstrated that level of the serum enzyme activity (ALP, ALT and AST) did not change significantly following the epidural and intramuscular injection of xylazine in all groups. However, a slight increase was observed in serum levels of ALT and AST. Fani *et al.* (19) reported that the ALT and AST values increased after epidural injection of

xylazine in dogs (19). An increase in ALT value was reported after the administration of epidural xylazine in buffalo due to the stress produced by systemic absorption of xylazine (41). The increase in AST and ALT values might be due to the alteration in the cell membrane permeability which may enable these enzymes to leak from the cells with intact membrane. Stress or any damage to the liver cells cause enzyme leakage into the bloodstream and increase ALT and AST levels in the plasma (44).

Al-Busadah (3) reported that intravenous administration of xylazine at a dose of 0.5 mg/kg caused a significant increase in serum AST activity and a significant decrease in serum ALT activity in dromedaries. He stated that these changes could be related to various factors, such as changes in body temperature, haemodilution or excess leakage of cellular enzyme (AST) into the plasma (3). Ali *et al.* (4) explained that an intramuscular injection of 0.5 mg/kg xylazine did not alter plasma AST activity significantly (4). In our study, serum ALP activity did not change after the epidural administration of xylazine in any of the groups. A decline in serum level of ALP was recorded post injection of xylazine in buffalo (36) and camels (3).

In our study, a slight increase in serum BUN was recorded in all groups. Increase in BUN levels following epidural administration of xylazine has been recorded in buffalo (41), dogs (19). Fani *et al.* (19) stated that an increase in BUN value might be attributed to a temporary inhibitory effect of the drug on renal blood flow which, in turn, might have caused a rise in BUN (19). In addition, increased hepatic urea production from amino acid degradation could account for the increase in BUN values (17). In another study, Kinjavdekar *et al.* (27) suggested that subarachnoid administration of xylazine did not induce significant differences in BUN levels of goats (27).

We observed no significant increase in serum creatinine in all groups. It appears that the intramuscular injection of a high dose of xylazine was more effective in increasing the level of creatinine compared to the other

groups. Intravenous injection of xylazine (0.5 mg/kg) did not alter the creatinine level in the serum of dromedaries (3). Creatinine significantly increased following the epidural administration xylazine in buffalo (41) and goats (27), but no change was observed in dogs (19). The increase in creatinine values might be related to the temporary inhibitory effect of xylazine on renal blood flow which, in turn, may have caused a rise in creatinine (41). It is difficult to ascribe this to possible renal damage, as all reported values were within normal limits.

Serum glucose increased in animals of all groups, but it was significant from minute 60-90 in group X2_{im} and at minute 60 in group X2_e. There have been many investigations into the hyperglycaemic effect of xylazine in various species (13, 17, 24). The hyperglycaemic effects might be due to the results of alpha-2 adrenergic receptor inhibition of insulin release by the stimulation of alpha-2 adrenoreceptors in pancreatic β cells (7). It might also be attributed to the stress induced gluconeogenesis as a result of anaesthesia and increased production of glucose in the liver (41). Epidural administration of xylazine increased blood glucose in dogs (19), buffalo (41) and goats (27). An increase in serum glucose was recorded following intravenous (3), intramuscular (4, 35), and epidural injection (40) of xylazine in dromedaries.

In our study, as a result of slow systemic absorption of xylazine from the epidural space, epidural administration of xylazine had less effects on haematological and biochemical parameters compared to the intramuscular injection of the drug at the same dose. It has been confirmed that epidural administration of

xylazine exhibited minimal side-effects compared to the systemic injection of the drug (31).

Conclusions

Based on our findings, it can be concluded that effect of xylazine on haematological and biochemical parameters in dromedary camels is dose-dependant and is related to the route of administration. The low dose of xylazine administered using both intramuscular and epidural methods showed minimal effects on all of the parameters studied, whereas a high dose of the drug, especially when injected intramuscularly caused a more pronounced alteration in haematological and biochemical parameters. The haematological and biochemical changes caused by this drug were transient and improved in the latter half of the study as the drug effect wore off.

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