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Comparative Evaluation of Sedative and Hematologic and Biochemical Effects of Intravenous Administration of Xylazine, Detomidine, Medetomidine, and Dexmedetomidine in Caspian Miniature Horses

Seyed Mohammad Rahchamani[1], Amir Saeed Samimi[2], Ehsanollah Sakhaee[3*], Mohammad Mahdi Molaei[3] and Mohamad Zamani-Ahmadmahmudi[2]

[1] PhD Student of Large Animal Internal Medicine, Faculty of Veterinary Medicine, Shahid Bahonar University of Kerman, Kerman, Iran
[2] Associate Professor, Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Bahonar University of Kerman, Kerman, Iran
[3] Professor, Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Bahonar University of Kerman, Kerman, Iran

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Abstract

Pharmaceutical research on α2-adrenergic agonists in Caspian miniature horses, a breed native to Iran, is currently limited. So, the objective of the present study was to evaluate sedative and hematobiochemical effects of intravenous administration of xylazine, detomidine, medetomidine, and dexmedetomidine in Caspian miniature horses. The study involved the random assignment of six Caspian miniature horses (by drawing of lots), crossover design into five groups. Each horse received one of four α2-adrenoreceptor agonists or saline. The study employed a randomized crossover design with a minimum washout period of seven days. The horses received either intravenous treatments of 1 mg/kg xylazine, 20 µg/kg detomidine, 10 µg/kg medetomidine, 5 µg/kg dexmedetomidine, or 5 mL of 0.9% saline. The sedation scores and physiological responses, including heart rate, respiration rate, digestive motility, and rectal temperature, were assessed immediately prior to drug administration (0 min) and subsequently at intervals of 5, 10, 15, 30, 45, 60, 75, 90, 105, and 120 min post-administration. The results indicated that there were no significant differences in some mean sedation scores and incoordination (impairment of the ability to coordinate muscle movements) among the treatments examined. The findings showed that there were no significant differences in the mean heart rate among the treatments and control assessed at any of the time points; however, significant differences in the mean respiration rate, digestive motility, rectal temperature, and selected hematobiochemical parameters were observed at some measurement time points post-injection. In conclusion, these agents demonstrated potential for effective sedation in healthy Caspian miniature horses, though further studies are recommended.

Key words: Caspian miniature horse, Alpha 2 agonist, Sedation, Hematobiochemical effects

Introduction

The Caspian miniature horse is a unique equine breed known for its small stature and historical significance. This breed has endured through centuries of tumultuous historical events, maintaining its existence despite its limited population (Dalton, 2000). The Caspian miniature horse is recognized for its ancestral significance in the broader context of equine history. The average height of a Caspian miniature horse

[*] **Corresponding Author**: Ehsanollah Sakhaee, Professor, Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Bahonar University of Kerman, Kerman, Iran
E-mail: ehsan_sakhaee@yahoo.com

ranges from 100 to 120 cm at the withers. While they are comparable in size to small pony breeds, Caspian miniature horses are classified as small horses and exhibit a conformation similar to that of full-sized equine breeds. Their average body weight generally falls between 180 and 270 kg, influenced by factors such as age, gender, health, and overall physical condition (Dalton, 2000).

Xylazine, detomidine, medetomidine, and dexmedetomidine are classified as α_2 -adrenergic agonists, which are non-narcotic agents exhibiting both sedative and analgesic properties. The sedative and anti-nociceptive effects of these α_2 -adrenergic agonists have been documented in some species of Equidae (Gozalo-Marcilla et al, 2018). These pharmacological agents primarily exert their sedative effects by modulating noradrenergic neuron activity, leading to decreased sympathetic outflow and enhanced sedation. Furthermore, their analgesic effects are mediated through the activation of spinal α_2 -adrenergic receptors, which inhibit nociceptive transmission, thus providing effective pain relief without the associated risks of opioid use (Zeiler, 2015; Sajjadi et al, 2025). The most dependable sedative medications approved for use in horses are α_2 - agonists. These drugs also offer several additional advantages, such as pain relief, muscle relaxation, decreased need for anesthetic drugs during induction and maintenance, and a reduction in the stress response associated with pain and surgery. Furthermore, α_2 -agonists are utilized to sedate horses during transport, as part of pre-anesthetic medication for both surgical and non-surgical standing procedures, and as elements of pain management protocols (Vigani and Garcia-Pereira, 2014).

To the best of our knowledge, no published studies have evaluated the effects of α2-adrenergic agonists in Caspian miniature horses. Therefore, the present study aimed to assess the sedative and hematobiochemical effects of intravenous administration of xylazine, detomidine, medetomidine, and dexmedetomidine in this breed.

Materials and Methods

Animals

In the present study, six miniature Caspian horses were selected based on their height at the withers, approximately five years of age and representing both sexes (3 males and 3 females). Each horse had an estimated weight of 150 ± 25 kg and exhibited a moderate body condition score at the commencement of the experiment. All animals were maintained under uniform management conditions, receiving a diet tailored to meet their maintenance and physiological requirements. The composition of the diet remained consistent throughout the duration of the experiment. To enhance nutritional intake, rare mineral salts were incorporated into the feed at a concentration of 0.3% by weight. Food was provided ad libitum in two daily meals. Prior to the initiation of the experiment, all horses underwent a comprehensive broad-spectrum anti-parasitic treatment to mitigate any potential contamination from internal and external parasites. Furthermore, before the commencement of the research, a thorough clinical and laboratory evaluation was conducted on each animal. Only those horses that were determined to be clinically and laboratory healthy were included in the study. The animals were deprived of food for a duration of 12 hours and water for 8 hours.

Experimental design

Prior to the experiment, the approval were received from the animal welfare committee at the Faculty of Veterinary Medicine, Shahid Bahonar University of Kerman, Iran (institutional approval number: IR.UK.VETMED. REC. 1401. 022). The horses underwent a behavioral assessment and were trained to adapt to physical restraint using a halter. Their health was evaluated through clinical

assessments and para-clinical (hematological, biochemical, and fecal parasitological) tests. The experiment was conducted under controlled environmental conditions (The temperature and relative humidity in the environment during the experiment ranged from 18 to 24 ºC and 12 to 18%, respectively) and each horse was individually restrained in a quiet, and covered area, equipped with a soft pad.

The study involved the random assignment of horses (by drawing lots with random number table), into five groups, each receiving one of four distinct α_2 -adrenoreceptor agonists or saline, utilizing a randomized crossover design with a minimum washout period of seven days, as detailed in Table 1. The horses were administered intravenous (IV) treatments consisting of 1 mg/kg xylazine (Xyla; Interchemie Werken "De Adelaar" B.V., Venray, Holland), 20 µg/kg detomidine (Domosedan, Orion Corporation, Espoo, Finland), 10 µg/kg medetomidine (DorbeneVet; N-Vet AB, Uppsala, Sweden), 5 µg/kg dexmedetomidine (Dexdomitor, Orion Corporation), or 5 mL of 0.9% saline (Shahid Ghazi Pharmaceutical Company, Tabriz, Iran). Prior to administration, all sedatives were diluted with 0.9% saline to achieve a final volume of 5 mL, following aseptic preparation of the left jugular vein. The drugs were administered to standing horses using a 16-gauge needle. Following the administration of the sedative agents, the halter was removed from each horse to facilitate observation.

To enhance the reliability and validity of the observations (without blind assessment), three independent observers evaluated the level of sedation in each horse using a standardized 4-point sedation scale, as described by the previous researchers (Deupree et al, 2008; Dalton, 2000). The sedation scores were defined as follows: Score 1: No sedation (the horse is alert, sensitive to noise and environmental stimuli). Score 2: Mild sedation (characterized by reduced alertness with slight reactions to external stimuli, occasional stumbling, and easily able to continue walking). Score 3: Moderate sedation (indicated by drowsiness and lethargy, sporadic responses to external stimuli, a minor drop in the position of the head, lips, and upper eyelids, along with marked stumbling and significant ataxia during ambulation). Score 4: Deep sedation (evident lethargy, a pronounced drop in head position, lack of response to external stimuli, and potential recumbency or falling while walking). The assessment of sedation and other clinical signs was conducted immediately prior to drug administration (0 min) and subsequently at intervals of 5, 10, 15, 30, 45, 60, 75, 90, 105, and 120 min post-administration. Sedation scores were consistently evaluated before measuring other clinical variables to ensure accurate monitoring of the horses' responses

Table 1: The order in which six miniature Caspian horses were assigned to receive intravenous treatments consisting of either 1 mg/kg xylazine (Xyl), 20 µg/kg detomidine (Det), 10 µg/kg medetomidine (Med), 5 µg/kg dexmedetomidine (Dex), or saline (Sal), over five distinct testing days, ensuring a washout period of no less than seven days between each treatment. The study involved the random assignment of horses (by drawing of lots with random number table), into five groups, with a minimum washout period of seven days

Testing days	Horses No					
	1	2	3	4	5	6
1	Sal	Xyl	Det	Med	Dex	Sal
2	Dex	Sal	Xyl	Det	Med	Dex
3	Med	Dex	Sal	Xyl	Det	Med
4	Det	Med	Dex	Sal	Xyl	Det
5	Xyl	Det	Med	Dex	Sal	Xyl

Sedation scores and clinical signs

Two large animal internists conducted an assessment of the physiological responses, including heart rate (HR), respiration rate (RR), digestive motility (DM), and rectal temperature (RT). The HR was measured using a stethoscope (Classic II SE, Littmann Co, USA), with the bell positioned on the left side of the chest wall at the fourth intercostal space, behind the olecranon, for a duration of one min. The RR was determined through direct observation of

thoraco-abdominal movements over one min. The RT was recorded using a medical digital thermometer (FT09, Beurer GmbH, Ulm, Germany), which was inserted into the rectum. The DM was assessed by auscultating the four abdominal quadrants, left upper, left lower, right upper, and right lower, using the same stethoscope for four min on each quadrant (Samimi, 2020).

Hematologic and biochemical parameters

Blood samples (5 ml) were collected from each subject at three time points: before injection (baseline), 2 hours after injection, and 24 hours after injection. For serum biochemical analysis, blood was drawn into plain tubes (without anticoagulant). The samples were allowed to clot at room temperature and then centrifuged at 3000 g for 15 minutes to separate the serum. The serum was aliquoted and stored at - 20°C until analysis. For hematological analysis, blood was collected into tubes containing EDTA as an anticoagulant and was analyzed immediately to ensure accuracy.

Serum levels of blood urea nitrogen (BUN), creatinine (Cr), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transaminase (GGT), cholesterol, triglyceride, calcium, phosphorus, sodium, potassium, albumin, and total protein were measured using an automated clinical chemistry analyzer (Roche Diagnostics, Germany) according to the manufacturer's instructions. Hematocrit (HCT) and white blood cell (WBC) count was determined using an automated hematology analyzer (Sysmex XE-2100, Japan). For WBC differential, a manual count was performed on stained blood smears if required

Statistical analysis

The statistical analysis of the collected data was conducted using IBM SPSS software, version 27. Initially, descriptive statistics including indices such as mean, standard deviation, and standard error were calculated and reported for the studied variables. The normality of the data was assessed using the Kolmogorov-Smirnov test. For normally distributed data, repeated measures ANOVA was utilized to examine the effect of measurement times on the mean indices before and after drug administration, categorized by treatment groups. For the data that did not meet normality assumptions and non-parametric data, the Friedman test was applied. In cases where significant differences were detected, the Student's t-test for dependent groups was used for parametric data, while the Wilcoxon signed-rank test was employed for non-parametric data to determine differences between measurement times. Additionally, to compare parametric data with normal distribution among treatment groups at identical measurement times, one-way ANOVA and Tukey's post-hoc test were utilized. It is worth noting that throughout all stages of the analysis, a significance level of 0.05 was adopted for rejecting the null hypothesis (H0).

Results

Sedation scores and clinical signs

All animals successfully recovered following the sedation period, and no injuries were observed in any of the cases. The agreement among the observers was very good (k >0.81).

The results indicated that there were no significant differences (P>0.05) in the mean sedation scores and incoordination among the treatments examined at the time points prior to injection, as well as at 75, 90, 105, and 120 minutes post-injection. In contrast, significant differences (P<0.05) in the mean sedation scores among the treatments were noted at other measurement intervals (Figures 1 a and b)

Physiological signs

The test results revealed that there were no statistically significant differences (P>0.05) in the mean HH among the treatments assessed at the time points prior to injection, as well as at 105 and 120 minutes after injection. In contrast,

significant differences (P<0.05) in the mean HH among the treatments were noted at other measurement intervals (Figure 1 c).

Prior to conducting the statistical analysis of the results obtained, descriptive statistics, including count, mean, standard deviation, standard error, minimum, and maximum values, were calculated for the HR, RR, RT, and DM variables. These statistics were organized by the groups under investigation at both pre-injection and post-injection time points.

No statistically meaningful variation was observed (P>0.05) in the mean HR among the treatments and control assessed at any of the time points (Figure 1 d).

The results of the RR assessment indicated that there were no significant differences in the mean of RR among the treatments evaluated both prior to injection and at 5 minutes post-injection (P>0.05). However, marked differences (P<0.05) in the mean RR were observed at other time points, specifically at 10, 15, 30, 45, 60, 75, 90, 105, and 120 minutes (Figure 1 e).

No statistically meaningful variation was observed (P>0.05) in the average DM among the treatments assessed prior to injection. However, significant differences (P<0.05) among the treatments were observed at other measurement time points (Figure 1 f).

No statistically meaningful variation was observed (P>0.05) in the average RT across the various treatments at the time points prior to injection, as well as at 5, 15, 30, 45, 60, and 75 minutes post-injection. Conversely, significant differences (P<0.05) in average RT were observed at other measurement intervals (Figure 1 g).

Biochemical parameters

Marked differences were detected in mean BUN levels among the treatment groups: prior to injection (P<0.01), 2 hours post-injection (P<0.01), and 24 hours post-injection (P<0.01) (Figure 2 a). According to Tukey's post-hoc test, the Medetomidine and Dexmedetomidine groups exhibited significantly lower mean BUN values compared to the other groups. For creatinine, the results indicated no significant differences among groups before injection (P>0.05) or 2 hours after injection (P>0.05). However, a significant difference emerged at 24 hours post-injection (P<0.01) (Figure 2 b). Tukey's test showed that, at 24 hours, the Dexmedetomidine, Detomidine, and Xylazine groups had significantly higher mean creatinine levels than the Normal saline group.

No significant differences were found in the mean cholesterol levels among groups at any time point: before injection (P>0.05), 2 hours after (P>0.05), or 24 hours after injection (P>0.05) (Figure 2 c). Similarly, the mean triglyceride levels did not differ significantly among groups before injection (P>0.05), 2 hours after (P>0.05), or 24 hours after injection (P>0.05) (Figure 2 d).

Marked differences were detected in the mean AST levels among groups at all time points: before injection (P<0.05), 2 hours after (P<0.05), and 24 hours after injection (P<0.01) (Figure 2 e). Tukey's post-hoc analysis indicated that the Dexmedetomidine group had significantly higher mean AST levels at all time points compared to the Medetomidine group. No significant differences were observed in the mean ALT levels among groups at any time point: before injection (P>0.05), 2 hours after (P>0.05), or 24 hours after injection (P>0.05) (Figure 2 f). For GGT, there were no significant differences before injection (P>0.05). However, significant differences were observed at 2 hours (P<0.05) and 24 hours post-injection (P<0.05) (Figure 2 j). Tukey's post-hoc test indicated that at 2 hours, the Normal saline, Medetomidine, and Detomidine groups had significantly lower mean GGT levels than Dexmedetomidine (P<0.05), and at 24 hours, the Normal saline group was significantly lower than Dexmedetomidine (P<0.05).

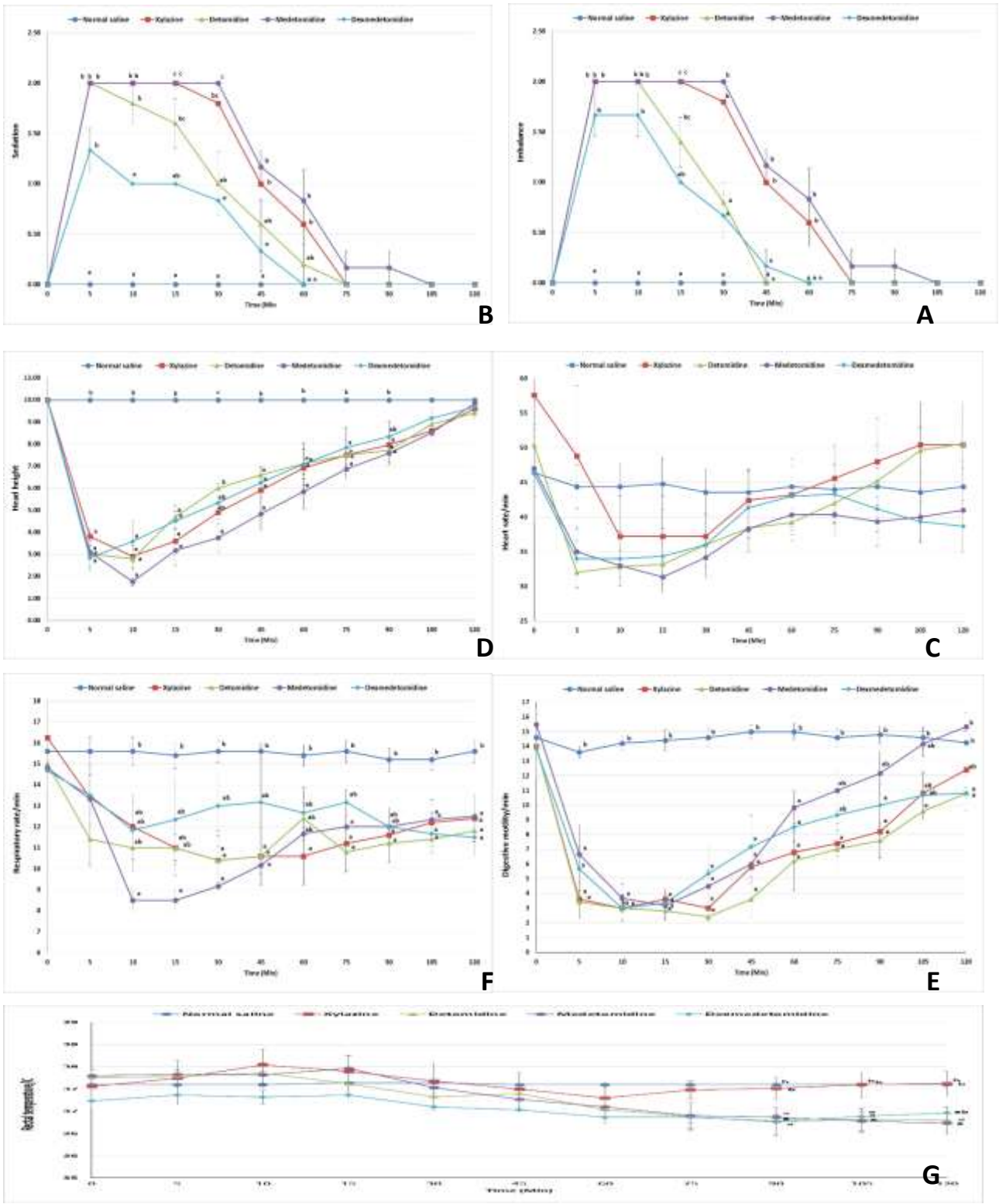


Figure 1: A: Sedation, B: incoordination, C: head height, D: hear rate, E: respiratory rate, F: digestive motility, G: rectal temprature (Mean ± standard error) before and after drug administration in treatment group (Red: Xylazine, green: Detomidine, purple: Medetomodine, light blue: Dexmedetomidine, and dark blue: control). One-way ANOVA and Tukey's post-hoc test were utilized Treatments that share similar letters do not have a statistically significant difference at the 95% probability level ($p<0.05$).

The observed significant changes in AST and GGT levels may indicate liver involvement or hepatocellular stress, which could be related to the pharmacological effects or toxicity of the administered drug. Understanding these alterations helps to better evaluate the safety profile and physiological impact of the treatment.

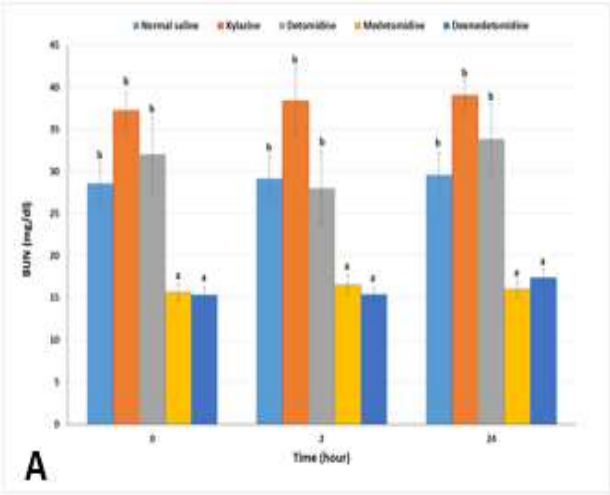
For calcium, no significant differences were found before injection (P>0.05) or 2 hours after (P>0.05). However, at 24 hours post-injection, a significant difference was detected (P<0.01) (Figure 2 g). Tukey's test showed that mean calcium levels at 24 hours were significantly lower in the Medetomidine and Detomidine groups compared to the Normal saline and Dexmedetomidine groups. Significant differences in the mean phosphorus levels were observed at all time points: before injection (P<0.01), 2 hours after (P<0.01), and 24 hours after injection (P<0.01) (Figure 2 h). Tukey's analysis revealed that before injection, the Medetomidine and Detomidine groups had significantly lower mean phosphorus levels than the Normal saline and Dexmedetomidine groups. At 2 hours post-injection, the Medetomidine, Detomidine, and Xylazine groups had significantly lower values than the Normal saline and Dexmedetomidine groups, and the Normal saline group was also significantly lower than Dexmedetomidine (P<0.05). At 24 hours, the Normal saline, Medetomidine, Detomidine, and Xylazine groups had significantly lower phosphorus levels than Dexmedetomidine, with the Detomidine group also significantly lower than the Normal saline (P<0.05).

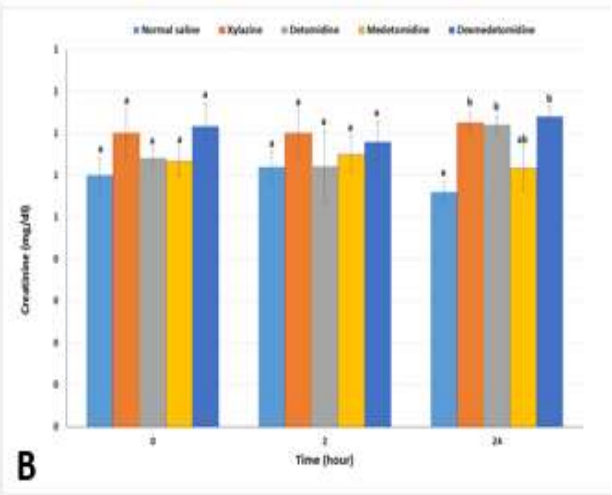
No statistically meaningful variation was observed in the mean albumin levels among groups at any time point: before injection (P>0.05), 2 hours after (P>0.05), or 24 hours after injection (P>0.05) (Figure 2 i). Similarly, no significant differences were found in mean total protein levels among groups before injection (P>0.05), 2 hours after (P>0.05), or 24 hours after injection (P>0.05) (Figure 2 m).

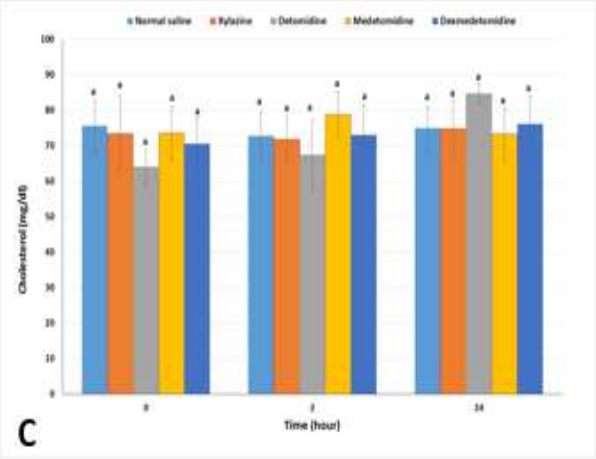
No statistically meaningful variation was observed in the mean sodium levels before injection (P>0.05) or 24 hours after (P>0.05), but a significant difference was found at 2 hours post-injection (P<0.05) (Figure 2 k). Tukey's test showed that at 2 hours, the Normal saline, Dexmedetomidine, and Detomidine groups had significantly lower sodium levels than the Medetomidine group. No significant differences were observed in the mean potassium levels among groups at any time point: before injection (P>0.05), 2 hours after (P>0.05), or 24 hours after injection (P>0.05) (Figure 2 l).

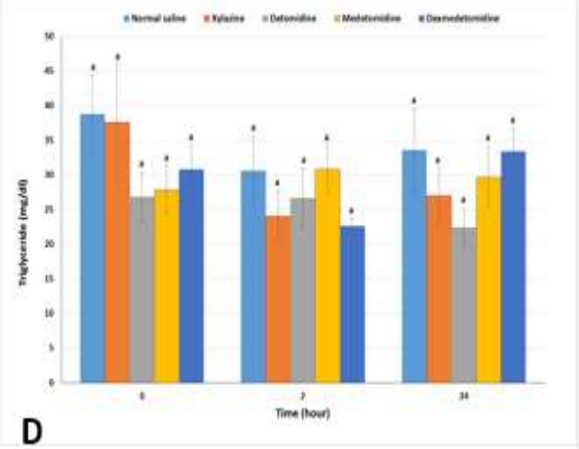
Hematological parameters

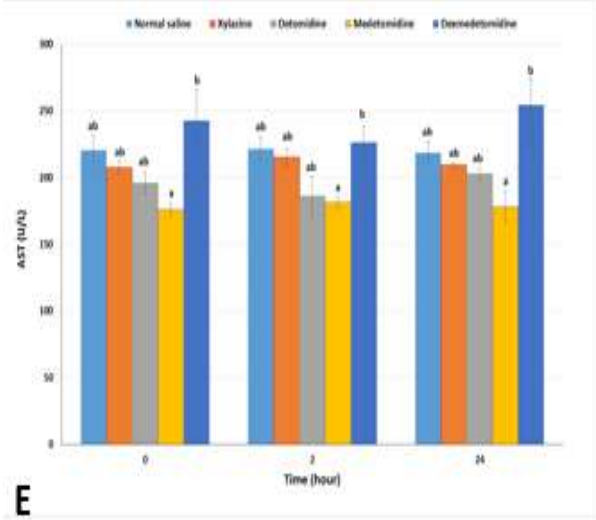
For WBC, no significant differences were observed at 2 hours (P>0.05) or 24 hours post-injection (P>0.05). However, a significant difference was found before injection (P<0.05) (Figure 2 n). Tukey's post-hoc analysis indicated that, prior to injection, the Detomidine group had significantly higher mean WBC counts than the Medetomidine group (P<0.05). Finally, no significant differences in the mean PCV were noted among groups at any time point: before injection (P>0.05), 2 hours after (P>0.05), or 24 hours after injection (P>0.05) (Figure 2 o).

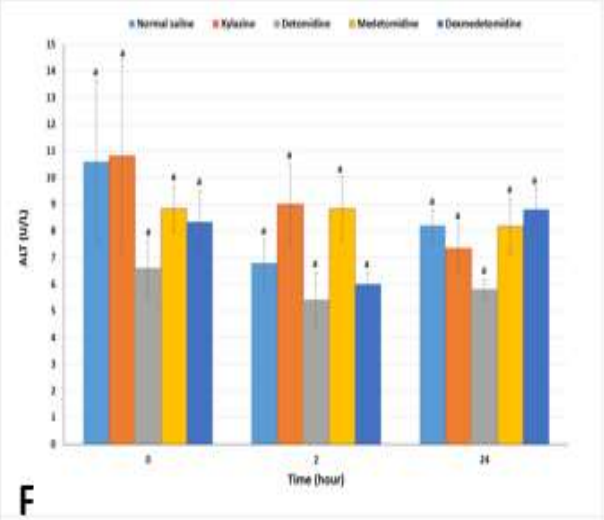

Normal saline
Xylazine
Detomidine
Medetomidine
Dexmedetomidine
BUN (mg/dl)
Time (hour)
A

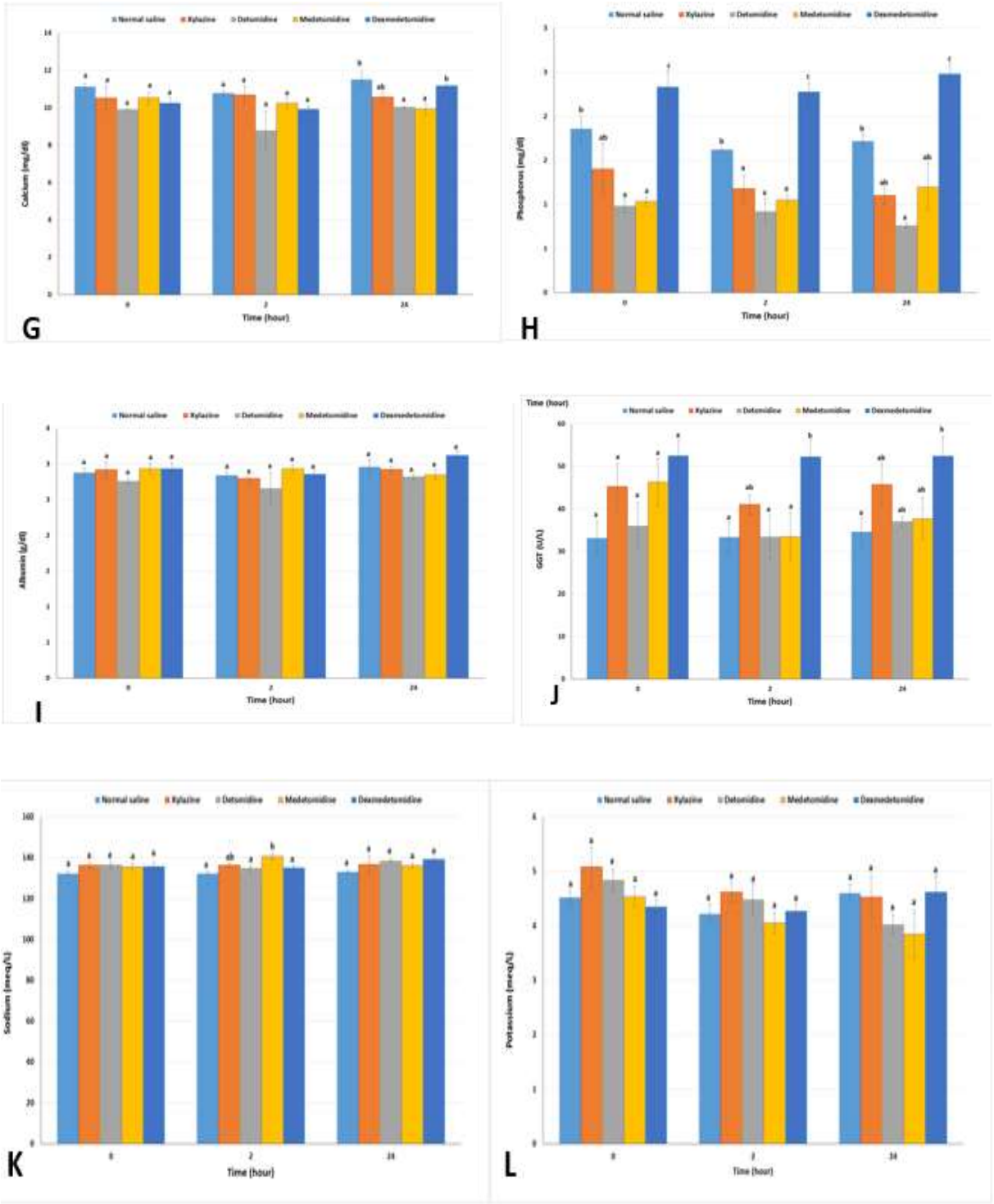

Normal saline
Xylazine
Detomidine
Medetomidine
Dexmedetomidine
Creatinine (mg/dl)
Time (hour)
B


Normal saline
Xylazine
Detomidine
Medetomidine
Dexmedetomidine
Cholesterol (mg/dl)
Time (hour)
C


Normal saline
Xylazine
Detomidine
Medetomidine
Dexmedetomidine
Triglyceride (mg/dl)
Time (hour)
D


Normal saline
Xylazine
Detomidine
Medetomidine
Dexmedetomidine
AST (U/L)
Time (hour)
E


Normal saline
Xylazine
Detomidine
Medetomidine
Dexmedetomidine
ALT (U/L)
Time (hour)
F


Normal saline
Xylazine
Detomidine
Medetomidine
Dexmedetomidine
Calcium (mg/dl)
Phosphorus (mg/dl)
Albumin (g/dl)
GGT (U/L)
Sodium (meq/L)
Potassium (meq/L)
Time (hour)
G
H
I
J
K
L

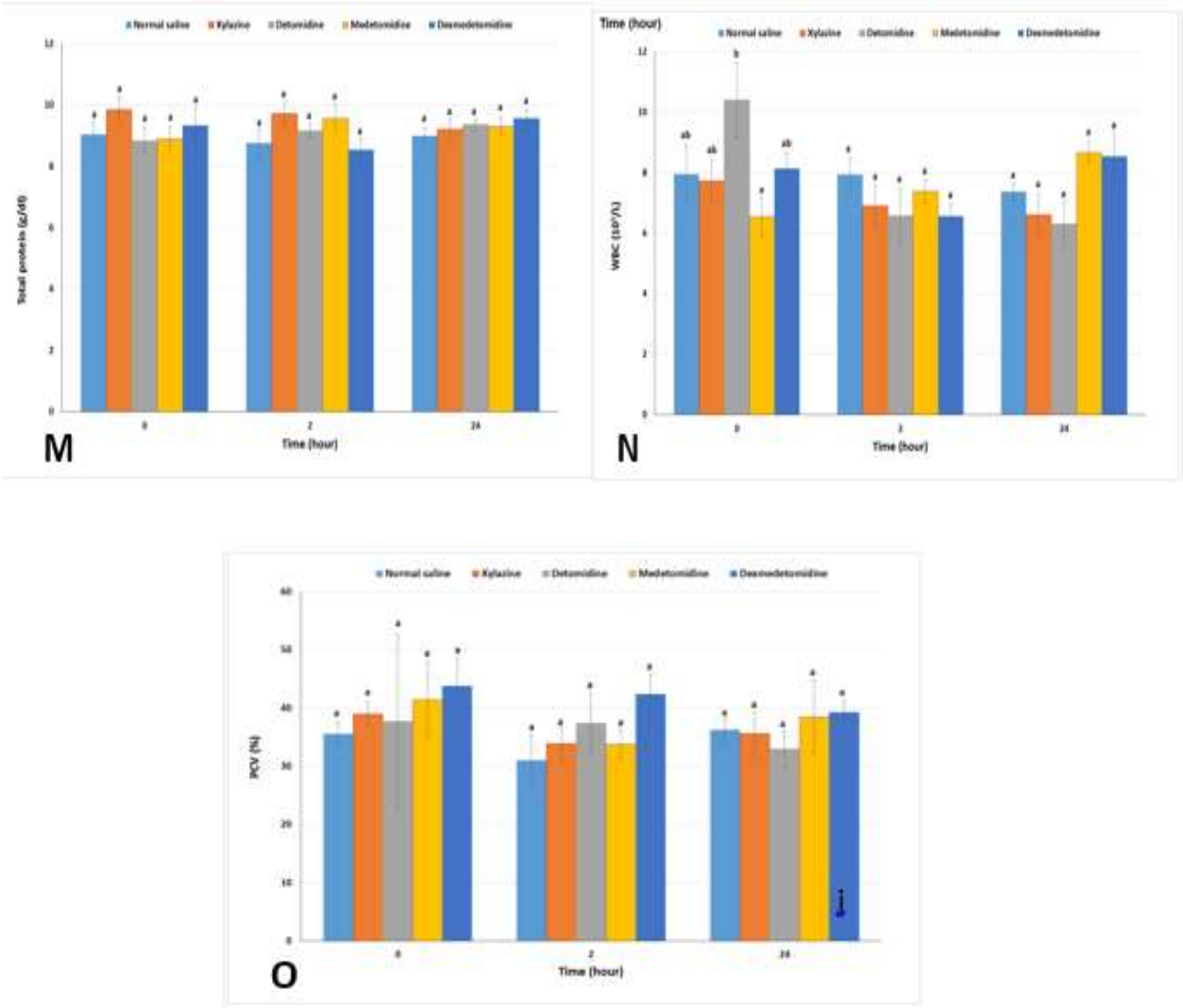


Figure 2. Trends in a: Blood Urea Nitrogen (BUN) levels, b: Serum Creatinine (Cr) levels, c: Serum Cholesterol levels, d: Serum Triglyceride levels, e: Serum AST levels, f: Serum ALT levels, g: Serum Calcium levels, h: Serum Phosphorus levels, i: Serum Albumin levels, j: Serum GGT levels, k: Serum Sodium levels, l: Serum Potassium levels, m: Serum Total Protein levels, n: WBC levels, and o: PCV levels (mean ± standard error) across experimental groups at pre- and post-drug injection time points. One-way ANOVA and Tukey's post-hoc test were utilized. At each time point, groups annotated with the same letter are not significantly different at the 95% confidence level ($p<0.05$).

Discussion

Research has extensively explored the effects of α_2-adrenergic drugs in horses; however, there is a notable absence of studies focusing on the Caspian miniature horse, a breed indigenous to Iran. This gap in the literature underscores the need for targeted research to elucidate the pharmacological effects of these agents within this specific equine population. Given that the Caspian miniature horse is a unique breed with distinct physiological characteristics, it is imperative to investigate how α_2-adrenergic agonists might influence its behavioral and physiological responses.

The findings within the designated time frame revealed that all four drugs administered significantly influenced HR, RR, RT and DM, thereby demonstrating their sedative effects on the equine subjects. Although certain signs of sedation were not consistently observed or were diminished at

specific time intervals throughout the study, overall, there was no statistically significant difference in the effectiveness of these drugs in eliciting sedative signs among the study groups (Gozalo-Marcilla et al, 2018, Yamashita et al, 2000).

α_2 - adrenergic receptor agonists have become integral components of contemporary anesthetic practices due to their capacity to induce sedation without significant respiratory depression. These agents contribute to cardiovascular stability and facilitate a reduction in the overall requirements for anesthetic agents. Their unique pharmacological profile allows for effective management of patients in various clinical settings, particularly in anesthesia, where maintaining hemodynamic stability is crucial while minimizing adverse effects associated with traditional anesthetics (Giovannitti et al, 2015).

The analysis of variance results with repeated measures indicated that the mean HR among the four groups exhibited statistically significant differences at various time points following drug administration. It was hypothesized that, due to the sedative properties of the administered drugs, the HR would decrease shortly after injection and subsequently return to baseline levels approximately one hour post-injection, contingent upon the specific characteristics of the drug utilized.

The stimulation of α_2 - adrenergic receptors may play a crucial role in mediating sedation, analgesia, and sympatholytic effects (Buerkle and Yaksh, 1998). Research has demonstrated that activation of these receptors inhibits adenylyl cyclase, leading to a reduction in cyclic adenosine monophosphate (cAMP) levels. This process results in hyperpolarization of noradrenergic neurons located in the medial dorsal pons, particularly within the locus ceruleus. As cAMP levels decline, potassium efflux through calcium-activated channels is facilitated, preventing calcium ions from entering the nerve terminal, which ultimately suppresses neural firing. This suppression inhibits norepinephrine release and diminishes the activity of ascending noradrenergic pathways, culminating in hypnosis and sedation. Furthermore, activation of this negative feedback loop may contribute to reductions in heart rate and blood pressure, as well as attenuation of the sympathetic stress response (Pichot et al, 2012).

One of the primary benefits of dexmedetomidine in comparison to other anesthetic agents is its negligible impact on respiratory function. This characteristic is particularly advantageous for patients who may have compromised airway patency, obesity, or restricted mobility, as dexmedetomidine facilitates effective sedation without endangering airway integrity or causing respiratory depression (Kaur and Singh, 2011).

The results of the present study indicate that the mean DM and RT across the four studied groups exhibited a statistically significant decrease at all-time points following injection, when compared to pre-injection measurements.

The previous research has shown that α_2-adrenoceptors play a complex role in regulating intestinal motility by modulating neurotransmitter release. Studies have demonstrated that α_2-agonists can reduce contractions in the equine jejunum, suggesting a potential therapeutic use for treating hyper motility in horses (Zullian, 2011).

Activation of α2-adrenoceptors in rodents induces hypothermia (Deupree et al, 2008). In humans, α2-adrenergic receptor agonists reduce energy expenditure and body temperature, promoting a drop in core temperature. Intravenous dexmedetomidine effectively lowers oxygen consumption, induces sedation, and suppresses shivering responses to induce hypothermia in healthy individuals (Callaway et al, 2024).

α_2 - adrenergic agonists are known to inhibit the activation of the brainstem

vasomotor center within the central nervous system (CNS). The sedative effects of these agents are linked to a reduction in sympathetic outflow from the CNS (Zullian, 2011). Our findings indicate that sedation levels were significantly higher at 15 minutes post-administration in Caspian miniature horses treated with various α_2 - adrenoreceptor agonists, as opposed to those receiving saline and dexmedetomidine shows a faster sedative effect compared to other medications.

The findings of this study reveal that symptoms such as head height (by an index), this measurement helps monitor the horse's response to sedative drugs by quantifying how much the head height changes during the sedation process, and incoordination, which are primary clinical indicators of sedation induced by the sedative agents under investigation, can present within 5 to 10 minutes following administration. The onset of these symptoms is contingent upon the specific sedative drug administered to the examined animals. Notably, there is no statistically significant difference in the onset timing of these symptoms across the various sedative agents evaluated. It is particularly noteworthy that both xylazine and dexmedetomidine demonstrated signs of incoordination slightly later than the other medications assessed.

The previous studies showed that following administration of α_2 - adrenergic agonists, responses such as HH and HR has been characterized as having a ceiling effect, where increasing the dose increases the duration of response but does not increase the magnitude. This ceiling effect is apparent when doses of 5, 20, 80, and 160 µg/kg of intravenous of detomidine were given to horses demonstrating that the HR decreased to values of low to mid-20 s for all three of the higher doses (Jochle & Hamm, 1986). The ceiling effect was also demonstrated for sedation, where the magnitude of sedation was similar for the three higher doses; however, the duration was longer with increasing doses, and animals remained standing even at the higher doses (Grimsrud et al, 2024).

So, it is recommended that future studies investigate the sedative effects of varying doses of the medications utilized in the present study on Caspian miniature horses. Furthermore, it would be beneficial to compare the results obtained from these investigations with those derived from administering the same drugs to horses.

Additional research is essential to comprehensively assess the cardiopulmonary effects associated with the doses utilized in this study. Specifically, investigations should focus on parameters such as stroke volume, blood pressure, pulmonary arterial pressure, and the partial pressures of arterial oxygen and carbon dioxide.

Significant alterations in blood urea nitrogen (BUN) and creatinine levels were observed following administration of the different agents. Both Medetomidine and Dexmedetomidine groups consistently exhibited lower BUN levels compared to other treatments at all measured time points, suggesting a potential renoprotective effect or altered renal handling of nitrogenous waste products. In contrast, at 24 hours post-injection, creatinine levels were significantly elevated in the Dexmedetomidine, Detomidine, and Xylazine groups relative to the Normal saline group. This delayed increase may indicate transient changes in glomerular filtration or altered muscle metabolism, which aligns with previous reports of alpha-2 agonists affecting renal hemodynamics.

The study also revealed significant changes in aspartate aminotransferase (AST) activity, particularly in the Dexmedetomidine group, which showed higher AST values compared to Medetomidine at all time points. This elevation could reflect mild hepatic stress or muscle enzyme leakage, a phenomenon occasionally reported with sedative administration, although additional

investigation is required to fully elucidate this issue. In contrast, alanine aminotransferase (ALT) levels remained stable across all groups, suggesting the absence of significant hepatocellular injury.

Alterations in calcium and phosphorus concentrations were also observed. Notably, at 24 hours post-injection, calcium levels were significantly lower in the Medetomidine and Detomidine groups compared to both Normal saline and Dexmedetomidine groups. This finding may be attributed to the pharmacodynamic effects of these agents on calcium homeostasis or renal excretion. Phosphorus levels exhibited a complex pattern, with Dexmedetomidine generally associated with higher values, suggesting a possible impact on phosphate metabolism or renal tubular handling.

Sodium levels showed a transient decrease at 2 hours post-injection in the Normal saline, Dexmedetomidine, and Detomidine groups compared to Medetomidine, but these differences were not sustained at 24 hours. Potassium and total protein levels, as well as albumin, remained unaffected, indicating that the observed effects were specific rather than generalized disturbances of fluid or protein balance. It seems that, changes in macro elements are temporary.

No significant changes were detected in cholesterol or triglyceride levels among the groups at any time point. This suggests that the acute administration of these sedatives does not markedly impact lipid metabolism in the short term, which is consistent with the previous studies.

White blood cell (WBC) counts and packed cell volume (PCV) were largely unaffected by the treatments, except for a higher baseline WBC in the Detomidine group compared to Medetomidine. This may reflect individual variability or a mild stress response, rather than a direct pharmacological effect. The stability of PCV across groups suggests that these agents do not induce significant hemoconcentration or hemodilution under the experimental conditions.

In conclusion, the intravenous administration of xylazine at a dosage of 1 mg/kg, detomidine at 20 µg/kg, medetomidine at 10 µg/kg, and dexmedetomidine at 5 µg/kg produced comparable levels of sedation in Caspian miniature horses. Consequently, any of the evaluated sedative agents may be considered effective options for sedation in healthy Caspian miniature horses, though further studies are warranted to confirm long-term safety and efficacy.

The study has several limitations, including a small sample size, the use of a specific breed, the lack of blinding procedures, and the absence of evaluation of long-term effects. These factors should be considered when interpreting the results.

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Conflict of interest

None of the authors of this paper possess any financial or personal affiliations with individuals or organizations that could potentially unduly influence or bias the content presented in this paper.

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ارزیابی مقایسه‌ای اثرات آرامبخشی، هماتولوژی و بیوشیمیایی تزریق وریدی زایلازین، دتومیدین، مدتومیدین و دکسمدتومیدین در اسبچه خزر

سیدمحمد راه‌چمنی[۱]، امیرسعید صمیمی[۲]، احسان‌اله سخائی[۳*] ، محمدمهدی مولائی[۳] و محمد زمانی‌احمدمحمودی[۲]

[۱] دانشجوی دکترای تخصصی بیماری‌های درونی دام‌های بزرگ، دانشکده دامپزشکی، دانشگاه شهید باهنر کرمان، کرمان، ایران
[۲] دانشیار گروه علوم درمانگاهی، دانشکده دامپزشکی، دانشگاه شهید باهنر کرمان، کرمان، ایران
[۳] استاد گروه علوم درمانگاهی، دانشکده دامپزشکی، دانشگاه شهید باهنر کرمان، کرمان، ایران

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چکیده

پژوهش‌های داروشناسی در زمینه آگونیست‌های گیرنده آلفا-۲ آدرنرژیک، در اسبچه خزر بسیار محدود است. بنابراین، هدف مطالعه حاضر ارزیابی اثرات آرام‌بخشی، هماتولوژی و بیوشیمیایی تزریق وریدی زایلازین، دتومیدین، مدتومیدین و دکسمدتومیدین در اسبچه خزر بود. در این مطالعه، شش اسبچه خزر به صورت تصادفی به پنج گروه تقسیم شدند و هر گروه یکی از چهار آگونیست گیرنده آلفا-۲ یا سرم فیزیولوژیک را دریافت کردند. داروها شامل تزریق وریدی ۱ میلی‌گرم به ازای هر کیلوگرم زایلازین، ۲۰ میکروگرم به ازای هر کیلوگرم دتومیدین، ۱۰ میکروگرم به ازای هر کیلوگرم مدتومیدین، ۵ میکروگرم به ازای هر کیلوگرم دکسمدتومیدین یا ۵ میلی‌لیتر سرم فیزیولوژیک ۰/۹ درصد بود. سطح آرام‌بخشی و پاسخ‌های فیزیولوژیک، از جمله ضربان قلب، نرخ تنفس، حرکات دستگاه گوارش و دمای رکتال، بلافاصله قبل از تزریق دارو (زمان صفر) و سپس در فواصل ۵، ۱۰، ۱۵، ۳۰، ۴۵، ۶۰، ۷۵، ۹۰، ۱۰۵ و ۱۲۰ دقیقه پس از تزریق ارزیابی شد. نتایج نشان داد که تفاوت معنی‌داری در میانگین سطح آرام‌بخشی و عدم تعادل بین برخی گروه‌های مورد بررسی وجود نداشت. همچنین یافته‌ها بیان‌گر آن بود که در هیچ یک از زمان‌های اندازه‌گیری شده، تفاوت معنی‌داری در میانگین ضربان قلب بین گروه‌ها و گروه کنترل مشاهده نشد؛ اگر چه در نرخ تنفس، حرکات دستگاه گوارش، دمای رکتال و برخی پارامترهای هماتولوژی و بیوشیمیایی خون، در برخی از زمان‌های اندازه‌گیری شده پس از تزریق، اختلاف معنی‌داری دیده شد.

کلمات کلیدی: اسبچه خزر، گیرنده آلفا-۲ آدرنرژیک، آرامبخشی، هماتولوژی، بیوشیمیایی

* نویسنده مسئول: احسان‌اله سخائی، استاد گروه علوم درمانگاهی، دانشکده دامپزشکی، دانشگاه شهید باهنر کرمان، کرمان، ایران
E-mail: ehsan_sakhaee@yahoo.com