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# Effects of intravenous xylazine versus dexmedetomidine premedication with ketamine-midazolam-isoflurane anaesthesia for castration in horses

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#### ABSTRACT

The objectives of this research was to study the sedation and anaesthetic characteristics of intravenous xylazine and dexmedetomidine combined with ketamine-midazolam-isoflurane and to evaluate the cardiopulmonary effects during the anaesthetic period. Stallions were premedicated with xylazine (1.1 mg/kg IV) in Group 1 and dexmedetomidine (3.5  $\mu$ g/kg IV) in Group 2. Sedation quality was evaluated and scored. General anaesthesia was achieved with ketamine (2.2 mg/kg IV) and midazolam (0.1 mg/kg IV) in both groups and anaesthesia was maintained with isoflurane inhalant in fresh oxygen gas flow (6-8 L/min). All the stallions underwent an orchiectomy by the half-closed method. Cardiovascular variables and pulmonary variables were recorded using multi gas vital sign monitor. Anaesthetic parameters, reflex status and quality of muscle relaxation were assessed. After the surgical procedure, recovery was monitored and scored on 6 point scale. Sedation score and quality was clinically better in Group 2. The difference in cardiopulmonary variables was statistically not significant. However, statistically significant changes were noticed between two groups with regard to some blood gas values during the intra-operative and at 15 min post anaesthetic period. Quality of muscle relaxation was better in group 2. Recovery was not significant. Overall quality of anaesthesia and recovery was almost similar in both the groups. In conclusion, both drug combinations produced satisfactory results for castration in the horses studied. In this study, dexmedetomidine at 3.5  $\mu$ g/kg and xylazine at 1.1 mg/kg sedative doses did not result in much significant changes compared to one other.

Keywords: Dexmedetomidine, Horses, Isoflurane, Ketamine, Midazolam, Xylazine

Alpha, adrenoceptor agonists such as xylazine and dexmedetomidine have strong dose-dependent cardiovascular effects. Monitoring these cardiovascular parameters during short surgical procedures in horses grouped under American Society for Anaesthesiologists (ASA) I category will help us to know the effect of these drugs over the cardiovascular system. Earlier studies with xylazine had reported an altered cardiovascular function, prolonged sedation and recovery time on dose-dependent basis (Wagner et al. 2008). Dexmedetomidine has a shorter half-life, rapid redistribution, potent peri-operative cardiovascular effects compared to xylazine. In this study, the sedative dose of dexmedetomidine was set at 3.5 µg/kg based on previous research (Marcilla et al. 2010, Gozalo-Marcilla et al. 2013). This dosage exhibited comparable sedation/antinociception effects to xylazine at 1.1 mg/kg in

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horses. The administered dose resulted in sedation lasting for 60 min, accompanied by brief antinociception lasting from 40 to 55 min (Lizarraga and Janovyak 2013).

Alpha<sub>2</sub> adrenoceptor agonists are frequently coupled with ketamine. The benefit of the combination are that ketamine counteracts the circulatory depression induced by alpha<sub>2</sub> adrenoceptor agonists and in turn alpha<sub>2</sub> adrenoceptor agonists decreases the ketamine induced muscular hypertonicity, resulting in a brief duration of safe anaesthesia in horses.

With the above-mentioned effects, the addition of a benzodiazepine-midazolam, reduces ketamine-induced muscle rigidity, increases the quality of sedation by making the animal gradually turn into sternal recumbency with limited or no ataxia. Furthermore, it provides good to excellent quality of induction without excitement, ideal surgical anaesthesia and smooth recoveries (Gozalo-Marcilla *et al.* 2013).

With the benefits discussed above, this study was carried out with the objectives to compare the sedation and anaesthetic characteristics of xylazine versus dexmedetomidine at equi-potent doses coupled with ketamine-midazolam under isoflurane maintenance in

horse castration and to study the cardiopulmonary effects of the above protocol during the anaesthetic period.

The hypothesis of this study was that dexmedetomidine at  $3.5~\mu g/kg$  will produce significant anaesthesia and cardiovascular stability in horses compared to routinely used xylazine at its equipotent dose of 1.1~mg/kg.

#### MATERIALS AND METHODS

The study was reviewed and approved by Tamil Nadu Veterinary and Animal Sciences University (TANUVAS).

Animals and instrumentation: Twelve client-owned stallions which had been referred for elective surgery were included in this study. The stallions were assigned randomly in to Group 1 (xylazine) and Group 2 (dexmedetomidine), six in each. Based on physical status and results of laboratory investigation all the stallions were found to be healthy and were categorised as American Society of Anesthesiologists (ASA) I. The age (in years) and body weight (in kg) (mean±SD) of selected stallions in Group 1 (two Thoroughbred and four Indian breeds) was 7.0±0.8 and 405±20.0 respectively and in Group 2 (three thoroughbred and three Indian breeds) was 6.8±0.7 and 411±25.9, respectively.

Feed was withheld for 12 h before anaesthesia and stallions had free access to water. Syringes containing sedative drugs were prepared by one of the qualified anaesthetist/co-author. Both the premedicants were diluted to 20 ml with normal saline. The anaesthetic procedures were evaluated by the same investigator who was blinded to the drugs given. Prior to surgery, all the stallions were administered once with flunixin meglumine (FLUMINE, 50 mg/ml, Biograde Organics Private Limited, Ludhiana) at the dose rate of 1.1 mg/kg intravenously in the preparation room.

Anaesthesia: Prior to administration of sedatives, the mouth was rinsed with water. The stallions in Group 1 were premedicated with xylazine (XYLO-B, 20 mg/ml, BRILLIANT Bio Pharma Private Limited, Telangana) at the dose rate of 1.1 mg/kg intravenously once and Group 2 animals with dexmedetomidine (DEXTOMID, 200 µg/2 ml, NEON Laboratories Limited, Mumbai) at the dose rate of 3.5 µg/kg intravenously once, over two min. Anaesthesia was induced with intravenous administration of ketamine (ANEKET, 50 mg/ml, NEON Laboratories Limited, Mumbai) at the dose rate of 2.2 mg/kg once and midazolam (Mezolam, 5 mg/ml, NEON Laboratories Limited, Palghar) at the dose rate of 0.1 mg/kg once, in both groups. The stallions were carefully transported to the operation theatre using overhead electronic rail. All stallions were positioned in right lateral recumbency and intubated with suitable size cuffed silicone endotracheal tubes connected to the large animal semi-closed anaesthetic system (SurgiVet, Model: 262-513-8500 INTL) with isoflurane vaporiser (Patterson Veterinary). Anaesthesia was maintained with isoflurane (SOSRANE, 250 ml, NEON Laboratories, Mumbai) in 100% fresh oxygen gas flow (8 L/min) and stallions were allowed to breath spontaneously. The inspired and end-tidal

isoflurane concentration was altered during anaesthesia to regulate the anaesthetic depth based on reflex status assessment.

Surgery: In the operation theatre, all the stallions underwent an orchiectomy by the half-closed method using a Serra emasculator. Intra-operatively, stallions received fluid support with the intravenous administration of Ringers' Lactate at the rate of 10 ml/kg/h for maintenance.

*Recovery*: After the surgical procedure, the stallions were ventilated with oxygen for 5 min, and transported to the padded recovery box by portable large animal bed and overhead electronic rail. Following extubation, stallions were left undisturbed; doors of the recovery box were closed, and monitored from outside.

### Parameters studied

Sedative characteristics: After administering xylazine and dexmedetomidine, the sedation quality was assessed based on temperament of stallions, response to environmental stimuli and nature of movements and scored according to Taylor *et al.* (2008).

Cardiovascular variables: Cardiovascular variables, such as heart rate (HR), pulse rate (PR), arterial blood pressure and electrocardiography were studied. The heart rate and pulse rate were recorded every 15 min by direct cardiac auscultation and palpation of external maxillary artery, respectively. Invasive arterial blood pressure (systolic, diastolic and mean arterial pressure) were recorded every 15 min by placing a 20G catheter in to the facial artery and connected to a standard calibrated pressure transducer at the level of heart. Electrocardiograph was recorded on lead II (position of the electrodes: green- over the apex beat of the heart, caudal to the left elbow joint, yellow - middle of the left scapula, black- on the ventral neck) during pre anaesthetic period (before sedation), at 15 min start of isoflurane maintenance and at 15 min post-operative period using multi gas vital sign monitor (TRUSCOPE Ultra-Q5 SCHILLER Private Limited, Switzerland).

Pulmonary variables: The studied pulmonary variables are respiratory rate, fraction of inspired oxygen, endtidal carbon dioxide, inspiratory and end-tidal isoflurane concentration and blood gas values. The respiratory rate (RR) and breathing pattern were recorded by direct observation of thoraco-abdominal movements during pre, intra and post-operative periods. The fraction of inspired oxygen (FiO<sub>2</sub>), end-tidal carbon di-oxide concentration (EtCO<sub>2</sub>), inspiratory and end-tidal isoflurane concentration, and saturated oxygen pressure (SpO<sub>2</sub>) were recorded using a multi gas vital sign monitor during the intra-operative period and at 15 min post-operative period. Arterial blood was collected in to heparin coated 2 ml syringes from the facial artery during the intra-operative and at 15 min post operative period. The samples were analyzed immediately after collection using an automated blood gas analyser (Siemens 0L085-RAPIDLAB 348). The values of blood pH, partial pressure of oxygen (PaO<sub>2</sub>) and carbon dioxide (PaCO<sub>2</sub>), bicarbonate concentration (cHCO<sub>3</sub>), base excess in blood [BE(b)] and extracellular fluid [BE(ecf)], electrolytes concentration (Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>+</sup>, Cl<sup>-</sup>), anionic gap (Agap), glucose and lactate concentration were recorded.

Anaesthetic parameters: Anaesthetic parameters, such as mean time for induction (time from ketamine administration to lateral recumbency), quality of induction, anaesthetic depth, reflex status and quality of muscle relaxation were studied. According to Casoni et al. (2015), the quality of induction was scored from 1 to 5. The anaesthetic depth was scored as -1, 0, 1, 2 and 3 according to Nannarone and Spadavecchia (2012). The quality of muscle relaxation was scored from 1 to 4 (Muir et al. 2000).

Recovery: The duration of lateral and sternal recumbency, numbers of attempts to successful stand, total time taken to stand, recovery score and quality were observed by the same anaesthetist. The recovery quality was assessed based on overall attitude, nature of movement to sternal recumbency, characteristics of sternal phase, transition to standing position, recovery strength, number of attempts, balance and co-ordination and presence of knuckling as suggested by Carregaro et al. (2020).

Statistical analysis: Results of the quantitative data (values) were expressed as mean±standard deviation (SD) and categorical data (scores) as both mean±SD and range. No difference with regard to various parameters such as sedative characteristics, cardiovascular variables, pulmonary variables, anaesthetic parameters and recovery parameters between the groups was considered as the null hypothesis. The quantitative (parametric) data collected in this study was analysed by means of a two-tailed unpaired student *t*-test and the qualitative (non-parametric) data with Mann Whitney U-test as appropriate. Significance and highly significance were set as p<0.05 and p<0.01 respectively. All the data collected during this study was entered onto a spread sheet (Microsoft Excel); statistical

analysis was performed using software IBM SPSS 23.0 for windows.

#### RESULTS AND DISCUSSION

Sedative characteristics: The quality of sedation was 'good' in all animals from the Group 1 and 'excellent' in all animals from the Group 2. (Supplementary Table 1).

Cardiovascular parameters: The mean ± SD values of various cardiovascular parameters recorded in this study are given in Table 1. Gradual reduction in the values of HR, PR, SAP, DAP and MAP were noticed during the intraoperative and at 15 min post-operative periods compared to pre-operative period. All the recorded values were within the clinical range and statistically not significant between two groups. Electrocardiograph configuration revealed no marked changes during the pre, intra and post-operative periods.

Pulmonary parameters: The mean±SD values of various pulmonary parameters recorded in this study are given in Table 2. The respiratory rate at 0 min, end-tidal carbon di-oxide values at 15 min. intra-operative period and post-operative EtCO2 were differed significantly between two groups. The other parameters such as FiO<sub>2</sub>, inspiratory and end-tidal isoflurane concentration were statistically not significant. The SpO2 and FiO2 range was 96-98% and 87-94.5%, respectively in both the groups. With regard to arterial blood gas values listed in the Table 3, intra-operative bicarbonate (cHCO, ) and base excess (ecf) concentration, and post-operative anion gap (Agap) and serum glucose concentration differed significantly between two groups. The intra-operative partial pressure of oxygen (PaO<sub>2</sub>) was highly significant between two groups. The post-operative partial pressure of oxygen, bicarbonate concentration, base excess (ecf) concentration and base excess (blood) concentration were significantly higher one compared to the other.

Table 1. Mean±SD values of cardiovascular parameters (HR, PR, SAP, DAP and MAP) during pre, intra and post-operative periods

Parameter	Group	Pre-operative		10 min Post-		
			0 min	15 min	30 min	operative period
Heart rate	I	41±3	38±4	34±2	31±1	35±3
(beats/min)	II	38±4	37±4	34±1	33±4	34±3
	t-value	$1.464^{NS}$	$0.198^{ m NS}$	$0.529^{\mathrm{NS}}$	$0.437^{\mathrm{NS}}$	$0.419^{\mathrm{NS}}$
Pulse rate	I	38±2	36±3	32±4	37±4	35±1
(beats/min)	II	37±6	37±5	33±3	41±12	34±3
	t-value	$0.172^{\mathrm{NS}}$	$0.322{}^{\rm NS}$	$0.380^{\mathrm{NS}}$	0.481 NS	$1.408^{\mathrm{NS}}$
SAP	I	150±22	$147 \pm 14$	126±21	130±26	126±10
(mmHg)	II	145±21	131±26	123±25	$129.20\pm23.31$	116±20
	t-value	$0.340^{\mathrm{NS}}$	$1.269^{\mathrm{NS}}$	$0.159^{\mathrm{NS}}$	$0.074^{\mathrm{NS}}$	1.028 NS
DAP	I	113±20	109±11	83±21	89±28	93±7
(mmHg)	II	103±18	92±22	85±25	83±23	82±21
	t-value	$0.933^{ m NS}$	$1.677^{\mathrm{NS}}$	$0.147^{\mathrm{NS}}$	$0.392^{\mathrm{NS}}$	1.209 NS
MAP	I	119±11	122±12	98±20	103±25	105±8
(mmHg)	II	112±21	107±22	99±25	100±24	94±19
	t-value	$0.632^{\mathrm{NS}}$	$1.466^{\mathrm{NS}}$	0.125 NS	$0.156^{\mathrm{NS}}$	$1.180^{\mathrm{NS}}$

SAP, Systolic Arterial Pressure; DAP, Diastolic Arterial Pressure; MAP, Mean Arterial Pressure. Means bearing similar superscripts do not differ significantly. \*\*, significantly different at  $P \le 0.01$ ; \*, significantly different at  $P \le 0.05$ ; No Significant at P > 0.05.

Table 2. Mean±SD values of pulmonary variables

Parameter	Group	Pre-operative period	Intra-operative period			15 min Post-
			0 min	15 min	30 min	operative period
Respiratory rate	I	14±22	13±1	10±1	8±1	9±2
(breaths/min)	II	13±2	12±1	8±2	8±1	10±2
	t-value	1.053 NS	2.355*	$1.584^{\mathrm{NS}}$	$0.000{}^{\rm NS}$	$0.327^{\mathrm{NS}}$
Fraction of inspired oxygen (FiO <sub>2</sub> ) (%)	I	-	90.33±7.31	$89.67 \pm 2.07$	$93.50\pm2.17$	94.50±1.05
	II	-	$87.67 \pm 4.18$	92.17±3.43	$93.60 \pm 1.52$	93.50±2.17
	t-value	-	$0.776^{\mathrm{NS}}$	1.529 NS	$0.087^{\mathrm{NS}}$	$1.017^{\mathrm{NS}}$
End-tidal carbon- dioxide concentration	I	-	38.50±7.26 5.13±0.96	46.67±5.61 6.22±0.74	45.55±7.78 6.07±1.03	47.83±8.75 6.37±1.16
$(EtCO_2)$ (mmHg) (kPa)	II	-	30.00±11.71 3.99±1.56	35.00±9.23 4.66±1.23	42.33±3.79 5.64±0.50	36.33±7.31 4.84±0.97
	t-value	-	1.511 NS	2.646*	$0.636^{\mathrm{NS}}$	2.470*
Inspiratory isoflurane	I	-	$1.77 \pm 0.67$	$1.80\pm0.33$	1.30±0.28	0.00
concentration (%)	II	-	$2.17 \pm 0.89$	1.78±0.54	1.13±0.76	0.00
	t-value	-	$0.878^{\mathrm{NS}}$	$0.064{}^{\rm NS}$	$0.286{}^{\rm NS}$	-
End-tidal isoflurane	I	-	$1.50\pm0.76$	$1.58\pm0.26$	$1.05\pm0.21$	0.00
concentration (%)	II	-	$1.90\pm0.96$	1.55±0.52	$0.97 \pm 0.65$	0.00
	t-value	-	0.801 NS	$0.140{}^{\rm NS}$	$0.169^{\mathrm{NS}}$	-
Saturated per cent of	I	-	98.1±1.7	96.1±2.2	95.0±1.4	96.0±1.0
oxygen $(SpO_2)$ (%)	II	-	95.6±3.1	97.6±1.8	95.6±3.2	97.1±2.5
	t-value	-	$1.709^{\mathrm{NS}}$	1.265 NS	$0.266^{\mathrm{NS}}$	1.025 NS

Means bearing similar superscripts do not differ significantly. \*\*, significantly different at  $P \le 0.01$ ; \*, significantly different at  $P \le 0.05$ ; Not Significant at P > 0.05.

Anaesthetic parameters: The mean  $\pm$  SD values of various anaesthetic parameters are listed in Supplementary Tables 2 and 3. The quality of induction was 'Excellent' and anaesthetic depth was ideal in both groups. The mean time for induction, quality of induction and anaesthetic depth was statistically not significant between two groups. The muscle relaxation quality was 'Good to Excellent' in Group 1 and 'Excellent' in Group 2. Statistically significant muscle relaxation was observed in Group 2. The total duration of anaesthesia was insignificant between groups. In both the groups, the MAC ranged from 1.0 to 1.5.

*Recovery parameters:* The mean  $\pm$  SD values of various recovery parameters are listed in Supplementary Table 4. All the values were statistically not significant between the groups. In Group 1, two out of six stallions had smooth, calm recovery in one attempt with no/mild ataxia of less than 5 min of duration, three out of six stallions had calm recovery with difficulty or weakness with 1-3 attempts and mild ataxia of 5-10 min of duration and only one stallion had unco-ordinated recovery (marked difficulty and weakness with less than 3 min and notable ataxia, stumbling for 10-20 min.). In Group 2, four out of six stallions had smooth, calm recovery in one attempt with no or mild ataxia of less than 5 min of duration and two out of six stallions had calm recovery with some difficulty or weakness with 1-3 attempts and mild ataxia for 5-10 min. However, recovery quality was not statistically different between two groups.

After administration of intravenous premedication, the characteristics signs of sedation such as lowering of head, dropping of ears and lips, shivering of limbs, relaxation of prepuce and protrusion of penis were noticed in both the groups. At peak sedation, Group 1 stallions were infrequently responded to external stimulation but Group 2 stallions stood calmly and were reluctant to move with minimal or no response to stimulation. However, both xylazine and dexmedetomidine at given sedative doses resulted in acceptable level of sedation (Nannarone *et al.* 2007 and Raheim *et al.* 2014) for castration in this study.

An excellent, rapid and smooth induction phase was observed by the anesthesiologist (within 17-22 s) after administration of ketamine in both groups. This effect was mainly due to the equipotent sedative and analgesic effects of xylazine and dexmedetomdine. Ketamine induced muscle rigidity, tremors, ataxia and excitement were absent after subsequent administration of co-induction agent midazolam. Both xyalzine and dexmedetomidine produced ideal anaesthetic plane with ketamine induction under isoflurane maintenance and was sufficient to complete the castration without any intra-operative complications (Nannarone et al. 2007, de vries et al. 2015). The excellent quality of muscle relaxation noticed in Group 2 was attributed to faster sedative and superior muscle relaxation property of dexmedetomidine when combined with midazolam (Rezende et al. 2014) than xylazine.

Table 3. Mean±SD values of arterial blood gas analysis during intra and post-operative periods

Period	Group I	Group II	t-value
Intra-operative	$7.31 \pm 0.08$	$7.32 \pm 0.05$	0.293 NS
Post-operative	$7.28\pm0.10$	$7.33 \pm 0.07$	1.004 NS
Intra-operative	$56.75 \pm 10.07$	$50.07 \pm 9.69$	$1.172^{\mathrm{NS}}$
	$7.56\pm1.34$	$6.67 \pm 1.29$	
Post-operative	$58.18\pm12.14$	47.99±12.11	1.457 NS
Intra-operative			3.516 **
Post-operative			3.623 **
•			2.800*
•			3.188 **
•	$1.6\pm1.9$	-1.1±2.1	2.328*
Post-operative	$2.9 \pm 2.0$	$-1.2\pm1.3$	4.160**
Intra-operative	119±7	112±5	1.768 NS
Post-operative	120±8	109±9	$2.064^{\mathrm{NS}}$
Intra-operative	$4.2 \pm 0.8$	$4.3 \pm 0.5$	$0.247^{ m NS}$
Post-operative	$4.3 \pm 1.0$	$3.9 \pm 0.9$	$0.760^{ m NS}$
Intra-operative	$0.91\pm0.19$	$0.84 \pm 0.12$	$0.786^{ m NS}$
Post-operative	$0.91 \pm 0.36$	$0.77 \pm 0.19$	$0.825^{\mathrm{NS}}$
Intra-operative	87±7	82±7	$0.959^{ m NS}$
Post-operative	89±9	81±7	$1.595^{\mathrm{NS}}$
-	4.17±1.83	5.33±3.08	$0.798^{ m NS}$
•	1.33±2.58	4.67±1.97	2.516*
•	$1.0\pm2.0$	-1.3±1.8	$2.091^{ m NS}$
•	1.9±1.9	-1.1±1.1	3.292**
•		135±20	$1.891^{\rm NS}$
•			2.358*
•			$0.185^{\mathrm{NS}}$
•			$0.322^{\mathrm{NS}}$
	Post-operative Intra-operative Intra-operative Intra-operative Post-operative Intra-operative Post-operative Intra-operative Intra-operative Intra-operative Intra-operative Intra-operative Intra-operative Intra-operative Post-operative Intra-operative Intra-operative Intra-operative Intra-operative Intra-operative	Intra-operative	Intra-operative   7.31±0.08   7.32±0.05   Post-operative   7.28±0.10   7.33±0.07   Intra-operative   56.75±10.07   50.07±9.69   7.56±1.34   6.67±1.29   Post-operative   58.18±12.14   47.99±12.11   7.75±1.61   6.39±1.61   Intra-operative   210.30±50.07   310.82±48.97   28.03±6.67   41.43±6.52   Post-operative   163.13±63.86   279.97±46.49   21.74±8.51   37.32±6.19   Intra-operative   27.98±0.90   25.02±2.43   Post-operative   29.77±3.17   24.73±2.22   Intra-operative   1.6±1.9   -1.1±2.1   Post-operative   119±7   112±5   Post-operative   120±8   109±9   Intra-operative   4.2±0.8   4.3±0.5   Post-operative   4.3±1.0   3.9±0.9   Intra-operative   0.91±0.19   0.84±0.12   Post-operative   87±7   82±7   Post-operative   87±7   82±7   Post-operative   4.17±1.83   5.33±3.08   Post-operative   1.04±0   -1.3±1.8   Post-operative   1.04±0   -1.3±1.8   Post-operative   1.0±0   -1.3±1.8   Post-operative   1.0±0.0   -1.3±1.8   Post-operative   1.0±0.0   -1.3±1.8   Post-operative   1.0±0.0   -1.3±1.8   Post-operative   1.0±0.0   -1.0±0.25   Post-operative   1.05±0.25   Post-

<sup>\*\*,</sup> significantly different at  $P \le 0.01$ ; \*, significantly different at  $P \le 0.05$ ; No. Not Significant at P > 0.05.

During the clinical trial, the values of HR and PR were slightly reduced during the intra and post-operative periods. Both the drugs produced similar cardiovascular changes and these changes were statistically not significant. The values of SAP, DAP and MAP were comparatively lower in Group 2 than in Group 1 due to more hypotensive effects of dexmedetomidine on cardiovascular system (Grimsrud *et al.* 2012, Ranheim *et al.* 2014, Duke-Novakovski *et al.* 2015) than xylazine. However, all the changes were maintained within clinical range (Sacks *et al.* 2017). Previous studies revealed that combination of alpha<sub>2</sub> adrenoceptor agonists with ketamine and midazolam, provided greater sedation and anaesthesia without eliciting significant cardiovascular or respiratory depression than using these drugs alone and same was observed in this study.

Respiratory rate (RR) was found to be slightly reduced during the intra and post-operative periods. In both the groups, FiO<sub>2</sub> and SpO<sub>2</sub> was maintained more than 80% and 90% respectively. Blood gas values were found to be good during the intra and post-operative periods with alpha, adrenoceptor sedation (Duke-Novakovski *et al.* 

2015). In this study, the range of MAC was 1.0-1.5 (Taylor and Clarke 2007) which was sufficient to complete the entire surgical procedure like castration with consistent anaesthetic depth (Yamashita *et al.* 2007, Marcilla *et al.* 2012). This combination of anaesthesia markedly reduced the end-tidal isoflurane concentration (ranged from 0.9 to 1.0%) in both the groups. Increased glucose concentration observed in this study was attributed to peculiar hyperglycemic effects of alpha<sub>2</sub> adrenoceptor agonists (Steffey *et al.* 2000). Both the groups resulted in reduced PaO<sub>2</sub> during the post-operative period and the reduction was clinically unremarkable. Overall, both xylazine and dexmedetomidine had minimal effects on respiratory parameters and the effects were within the clinical range.

Although time to standing could not be correlated with the recovery quality, total time to stand was comparatively shorter in Group 2 than in Group 1. Shorter duration of recovery with an excellent quality in Group 2 was attributed to shorter duration of action and rapid plasma clearance of dexmedetomidine as compared to xylazine (Grimsrud *et al.* 2012, Gozalo-Marcilla *et al.* 2013, Rezende *et al.* 2014). Post-operative complications such as recovery excitement,

hyperesthesia and ataxia were absent in both the groups, except one horse from Group 1 had an uncoordinated recovery. Hamed *et al.* (2010) noticed marked ataxia during recovery due to longer muscle relaxation property of midazolam, however, in the present study, midazolam at the dose rate of 0.1 mg/kg did not reveal any ataxia. Clinically, animals premedicated with dexmedetomidine at 3.5 μg/kg exhibited somewhat better recovery quality than with xyalzine at 1.1 mg/kg, but not statistically.

The study was conducted with different breeds of horses including thoroughbred and Indian breeds. Further studies with large number of homogenous populations, using same anaesthetic combination are required to evaluate further effects of above-mentioned agents on various vital parameters during short surgical procedures like castration.

In conclusion, both drug combinations produced satisfactory results for castration in the horses studied. In this study, dexmedetomidine at 3.5  $\mu$ g/kg and xylazine at 1.1 mg/kg sedative doses did not result in much significant changes compared to one other. However, comparing all the above facts, dexmedetomidine is considered a good sedative agent in healthy horses with potential advantages such as quick onset of action, excellent quality of sedation and analgesia, good muscle relaxation, minimal cardiopulmonary effects, shorter duration of action, good anaesthetic depth, and smooth, rapid coordinated recovery (1-2 attempts to stand) without any complications.

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