



## Comparative Efficacy of Xylazine, Detomidine and Romifidine as Epidural Anesthetics in Egyptian Goat (*Capra hircus*)

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**T**HE PRESENT study was carried out in order to evaluate the efficacy of xylazine (XYL), detomidine (DET) and romifidine (ROM) on analgesia, sedation and haematobiochemical parameters following epidural injection in Baladi Egyptian goats. Six goats were used; treatment consists of 200µg/kg xylazine, 40µg/kg detomidine, 50µg/kg romifidine administered in each group sequentially. Onset, duration and degree of analgesia, sedation and ataxia were recorded. Physical parameters (RR, RT, and HR), Hb, PCV%, DCL, serum glucose, urea, creatinine, ALT and AST were evaluated prior to injection and at 15, 45, 75, 120 min after injection. Onset of analgesia after epidural DET was significantly earlier ( $1.00 \pm 0.28$  min). The duration of analgesia was significantly longer with ROM ( $140.00 \pm 1.15$  min). Analgesia and sedation scores were higher after administration of ROM. Duration of sedation was significantly longer with ROM ( $130.00 \pm 1.15$  min). The duration of ataxia was significantly shorter with DET ( $70.00 \pm 0.00$  min), with most delayed onset. It was noticed that RR, RT and HR tends to decrease overall at various treated groups compared to baseline levels. Hb and PCV were within the physiological limits in all groups. There was significant increase in blood glucose level after administration of all tested drugs. The BUN levels were decreased significantly with the administration of DETO and ROM. XYL produced a significant increase in creatinine and AST levels. ALT values significantly declined with XYL. In conclusion, Epidural administration of XYL, DET or ROM proved to be an effective analgesic and sedative agents for goats without severe adverse effect. ROM induced a longer analgesic and sedative effects than XYL or DET.

**Keywords:** Epidural analgesia, Sedation, Xylazine, Detomidine, Romifidine, Goat.

### Introduction

Goats are the most widely spread domestic species in the world, 90% of goats are found in Asia and Africa. They play an important economical role in developing countries. Recently, in Egypt goats became an important aspect of animal production. Among ruminants, goats comprise 4.04 million in Egypt, which occupies the second largest position in livestock [1]. Epidural anesthesia is advisable for use more than general anesthesia in ruminants because this technique is simple, inexpensive and requires no complicated equipments [2]. It has been shown to have less cardiopulmonary and other systemic side effects than general

anesthesia and used for providing operative and postoperative analgesia [3]. Lumbosacral epidural analgesia can be used for surgery involving the hind limbs, caudal abdomen and pelvic region of goats [4]. Commonly used local analgesics as lidocaine, mepivacaine and bupivacaine have short duration. For prolongation of action different drugs have been used as opioids and alpha-2 adrenoceptor agonists, administered into the epidural space. Xylazine, detomidine and romifidine are  $\alpha_2$ -adrenoceptor agonists have been shown to produce increased duration of analgesia on epidural administration in comparison to conventional local anesthetics, but the onset of action is slower than lidocaine [5]. Epidural

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alpha-2 agonists induce analgesia by stimulation of alpha-2 adrenergic receptors in dorsal horn of spinal cord [6]. When the analgesic effects of epidurally and IM administered xylazine (0.3 mg/kg) or detomidine (40 µg/kg) in sheep were compared, the epidural administration of either drug produced a greater degree of analgesia in the tail, perineum, hind limbs, and flank region than did similar doses administered IM [7]. The use of romifidine at 50µg/kg produce moderate to complete analgesia of perineum and flank after epidural administration in goats. The analgesia could not be enhanced by increasing the dose to 75µg/kg while, ataxia, cardiopulmonary and haemodynamic side effects become more apparent [8]. The present study was designed to assess and compare the effects of epidural administration of xylazine, detomidine, and romifidine on the clinical, physiological and haematobiochemical parameters in goats.

### **Material and Methods**

#### *Animals*

The present study was carried out on six adult clinically healthy local breed Baladi Egyptian goats (randomly selected) aged between 2 and 3 years old and weighing 25–30 kg. Before elaboration of the study, all goats were subjected to complete physical and hematological examinations to exclude evidence of systemic disease. All study procedures were done in accordance to the Institutional Animal Care and Use Committee of Faculty of Veterinary Medicine, Alexandria University. Animals were prepared for aseptic injection using ordinary hypodermic needle (18 gauge, 5cm) at the lumbosacral space according to the technique described by Hall et al.[4]. The presence of the needle in the extradural space was confirmed by the hanging drop technique, loss of resistance and by ease of injection.

#### *Experimental design and evaluating parameters*

The study was conducted in three phases with interval 3-weeks washout period so, each goat was allocated into one of the three groups. The animals in group 1 were injected with 200µg/kg xylazine (xylaject®; Adwia Co., Egypt) (XYL), group 2 injected with 40µg/kg detomidine (Dormosedan®; Orion Corporation Farnos, Finland) (DET) and group 3 injected with 50µg/kg romifidine (Sedivet®; Boehringer Ingelheim Vetmadica, USA) (ROM). The doses of drugs were selected based on earlier pilot studies. The volume of all medication was adjusted to 1ml/8kg body weight by the use of distilled water. All

injections were done in standing position. The onset, duration and extension of analgesia were evaluated by detecting the response to pin prick stimuli at these sites using 22-gauge, 3cm-long needle. The intensity of analgesia was estimated according to the following scores; 0, no analgesia (normal strong reflect to pin prick); 1, mild analgesia (depressed moderate reflect to pin prick); 2, moderate analgesia (no reflect to pin prick at the level of skin); 3, complete analgesia (no response to pin prick test even into the muscle) [8- 10]. The signs and the degree of sedation were assessed depending on the behavioral and attitude changes on the animal (alertness, drowsiness and response to auditory stimuli, in addition to eye reflexes, position of head and ptosis of eyelids). It was scored as the following; 1, no sedation; 2, mild sedation (reduced alertness with slight drowsiness and response to stimuli); 3, moderate sedation (drowsiness, not response to stimuli, eyelid closed, drooping of the head and swaying of the animal); 4, extreme sedation (severe drowsiness, unable to stand) [8-10]. The motor and ataxic effect were evaluated using the following scale; 1, no ataxia (normal gait); 2, mild ataxia (able to stand but reduce coordination of hind limb); 3, moderate ataxia (sterna recumbent with movement of hind limb); 4, severe ataxia (lateral recumbent without any movement of hind limbs) [8, 9, 11, 12]. The degree and intensity of both analgesia and sedation in addition to the extent of ataxia were graded at 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 min after injection of drugs. Respiratory rate (RR), rectal temperature (RT) and heart rate (HR) were recorded 5 min before injection (baseline), 15, 45, 75 and 120 min after injection. Blood samples were collected for assessment of hemoglobin (Hb), packed cell volume (PCV %) and differential leukocyte count (DLC %). The remaining blood was centrifuged for plasma which used for assessment of plasma glucose, blood urea nitrogen (BUN), creatinine, alanine aminotransferase (ALT) and aspartate aminotransferase (AST).

#### *Statistical Analysis*

The data were calculated and analyzed using analysis of variance with SAS computer software package [13]. Data were grouped, analyzed and summarized as  $M \pm SE$ . In each analysis, differences were considered significant at  $p < 0.05$ .

### **Results**

#### *Analgesia, Sedation and Ataxia*

There were significant variation ( $p < 0.05$ )

in the onset and duration of analgesia among the three groups, which started at perineum and tail and extend cranially to the flank region in addition to scrotum in males. Onset of analgesia was rapid after administration of DET ( $1.00\pm0.28$  min) compared with XYL ( $2.00\pm0.57$  min) or ROM ( $4.00\pm0.57$  min). Duration of analgesia was prolonged after ROM injection ( $140.00\pm1.15$  min) than XYL ( $115.00\pm2.88$  min) or DET ( $80.00\pm1.15$  min). The analgesic scores that reflect the intensity of analgesic effect after each treatment showed gradual increase in each group with variable degrees. The higher intensity of prolonged analgesia was achieved with ROMI and continued to over 120 min after injection when compared with other drugs (Fig. 1).

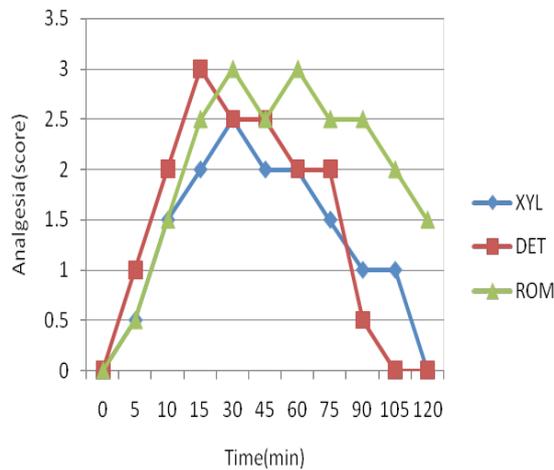


Fig. 1. Analgesic scores at perineum, tail, flank region and hind limb after epidural injection of XYL, DET and ROM in goats.

Onset of sedation was marked later than that of analgesia in all groups. Following XYL sedation was observed after ( $2.33\pm0.44$ min) and continued for ( $116.66\pm7.26$  min), with DET observed after ( $3.00\pm0.57$  min) and continued for ( $60.00\pm1.15$  min) while ROM was observed after ( $6.00\pm0.57$  min) and continued for ( $130.00\pm1.15$ min). Depth of sedation reached its apex- points between 30 and 45 min in all groups (Fig. 2) and ranged from mild to moderate with XYL, moderate with DET and reached to extreme sedation with ROM at 45 min and continued to 60 min. All animals showed marked signs of ataxia started in mild form with difficulty in maintaining standing position then recumbent with paddling movement of hind limbs (Fig. 3).

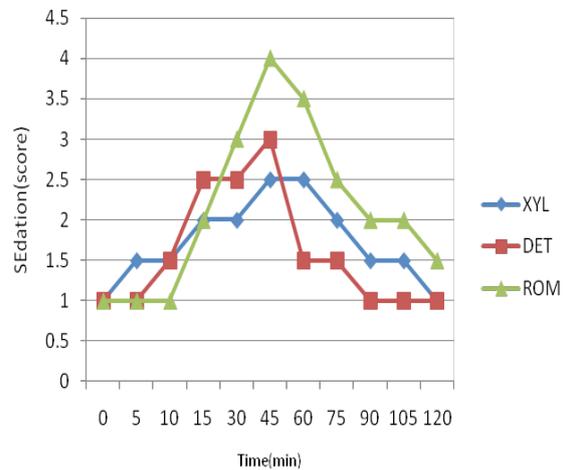


Fig. 2. Sedative scores after epidural injection of XYL, DET and ROM in goats.

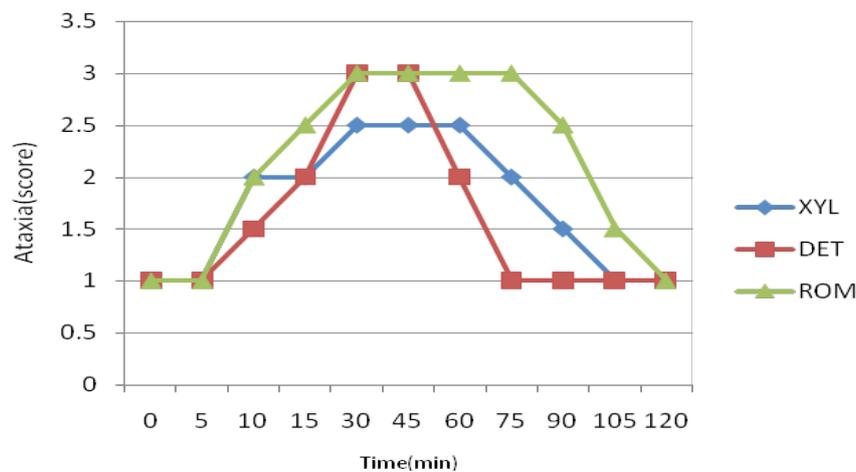


Fig. 3. Ataxia scores after epidural injection of XYL, DET and ROM in goats.

Ataxia was of shorter duration ( $70.00 \pm 0.00$  min) and of delayed onset ( $10.00 \pm 0.00$  min) following DET than other drugs (Table 1).

*Physical, hematological and biochemical effect*

The effect of XYL was associated with significantly decreased in RR at 45-75 min, this also observed in goats received ROM at (15-120 min). Significant decrease in RT was noticed with XYL at 45-120 min. Other drugs recorded no significant changes at all-time points. All groups showed significant decrease in HR and remained below the baseline up to 120 min (Table 2).

Hemoglobin and PCV% remained within the normal range throughout the period of observation in all the groups (Table 3), PCV% showed significant decrease with ROM at 75 min and returned to baseline at 120 min. There were significant variations in neutrophils at different time intervals. XYL showed significantly higher neutrophils at (15 and 45 min), DET and ROM

showed significantly higher neutrophils at (15, 45, 75 and 120 min). No significant changes recorded in eosinophils in all groups. Lymphocytes were increased significantly at 75 and 120 min following XYL and DET. And recorded significant decreased at different intervals of experiment with ROM. Monocytes showed significant decrease at 45, 75 and 120 min in XYL. (Table 3). The glucose levels showed marked significant increase in all groups up to end of experiment period. The urea levels were within the physiological limits and returned to baseline values by end of experiment. The serum levels of creatinine and AST were significantly increased after XYL with peak levels at 120 min. DET showed significant increases in creatinine at 15 min then returned to baseline with significant increase in AST at 15, 45 and 120 min. In comparison ROM did not show any significant changes in creatinine, ALT and AST. ALT was significant decreased with XYL at all intervals (Table 4).

**TABLE 1. Means  $\pm$  SE values of analgesia, sedation and ataxia after epidural injection of XYL, DET and ROM in goats.**

Drugs	Analgesia		Sedation		Ataxia	
	Onset (min)	Duration (min)	Onset (min)	Duration (min)	Onset (min)	Duration (min)
XYL	$2.00 \pm 0.57^B$	$115.00 \pm 2.88^B$	$2.33 \pm 0.44^B$	$116.66 \pm 7.26^A$	$6.00 \pm 1.08^B$	$100.00 \pm 7.36^A$
DET	$1.00 \pm 0.28^B$	$80.00 \pm 1.15^C$	$3.00 \pm 0.57^B$	$60.00 \pm 1.15^B$	$10.00 \pm 0.00^A$	$70.00 \pm 0.00^B$
ROM	$4.00 \pm 0.57^A$	$140.00 \pm 1.15^A$	$6.00 \pm 0.57^A$	$130.00 \pm 1.15^A$	$7.00 \pm 0.57^B$	$98.00 \pm 0.57^A$

Means within the same column carrying different letters are significantly different at ( $P < 0.05$ ).

**TABLE 2. Means  $\pm$  SE of respiratory rate (RR), rectal temperature (RT) and heart rate (HR) following epidural injection of XYL, DET and ROM in goats.**

Anaesthetic drugs	Time/min	(RR) (breath/min)	(RT) ( $^{\circ}$ C)	(HR) (beat/min)
XYL	baseline	$22.00 \pm 1.15$	$40.50 \pm 0.11$	$90.00 \pm 1.15$
	after			
	15 min	$27.00 \pm 1.15^*$	$40.40 \pm 0.11$	$64.00 \pm 1.15^*$
	45 min	$18.00 \pm 1.15^*$	$39.50 \pm 0.11^*$	$60.00 \pm 1.15^*$
	75 min	$16.00 \pm 1.15^*$	$38.50 \pm 0.11^*$	$70.00 \pm 1.15^* 80.00$
DET	baseline	$27.00 \pm 0.57$	$40.50 \pm 0.005$	$81.00 \pm 0.57$
	after			
	15 min	$31.00 \pm 0.57$	$40.30 \pm 0.005$	$73.00 \pm 0.57^*$
	45 min	$26.00 \pm 0.57$	$40.26 \pm 0.003$	$71.00 \pm 0.57^*$
	75 min	$25.00 \pm 0.57$	$40.00 \pm 0.005$	$67.00 \pm 0.57^*$
ROM	baseline	$25.00 \pm 0.57$	$40.50 \pm 0.005$	$85.00 \pm 0.57$
	after			
	15 min	$16.00 \pm 0.57^*$	$41.20 \pm 0.005$	$68.00 \pm 1.52^*$
	45 min	$14.00 \pm 0.57^*$	$40.80 \pm 0.005$	$64.00 \pm 0.88^*$
	75 min	$13.00 \pm 0.57^*$	$40.70 \pm 0.005$	$59.00 \pm 0.88^*$
	120 min	$16.33 \pm 0.57^*$	$40.63 \pm 0.003$	$69.66 \pm 0.88^*$

\* Means significantly different to the value before injection (baseline) ( $P < 0.05$ ).

**TABLE 3. Means  $\pm$  SE of Hb, PCV %, Neutrophil, Eosinophil, lymphocyte and Monocyte following epidural injection of XYL, DET and ROM in goats.**

Anaesthetic drugs	Time/min	Hb g/dl	PCV %	DLC %			
				Neutrophil	Eosinophil	Lymphocyte	Monocyte
XYL	baseline	11.0 $\pm$ 0.50	34.5 $\pm$ 0.50	37 $\pm$ 0.57	5 $\pm$ 0.67	62 $\pm$ 0.47	5 $\pm$ 0.50
	15 min	10.3 $\pm$ 0.58	34.6 $\pm$ 0.59	55 $\pm$ 0.55*	4 $\pm$ 0.50	63 $\pm$ 0.53	3 $\pm$ 0.59
	45 min	10.2 $\pm$ 0.51	34.8 $\pm$ 0.47	43 $\pm$ 0.51*	6 $\pm$ 0.55	65 $\pm$ 0.50	2 $\pm$ 0.52*
	75 min	10.4 $\pm$ 0.52	35.0 $\pm$ 0.37	40 $\pm$ 0.50	6 $\pm$ 0.52	67 $\pm$ 0.57*	2 $\pm$ 0.57*
	120 min	10.8 $\pm$ 0.57	34.8 $\pm$ 0.52	40 $\pm$ 0.57	7 $\pm$ 0.57	67 $\pm$ 0.54*	2 $\pm$ 0.53*
DET	baseline	12.5 $\pm$ 0.59	32.5 $\pm$ 0.59	43 $\pm$ 0.67	4 $\pm$ 0.37	53 $\pm$ 10.5	5 $\pm$ 0.47
	15 min	12.0 $\pm$ 0.50	32.7 $\pm$ .50	55 $\pm$ 0.47*	2 $\pm$ 0.55	53 $\pm$ 0.57	6 $\pm$ 0.59
	45 min	10.7 $\pm$ 0.54	32.8 $\pm$ 0.56	55 $\pm$ 0.37*	2 $\pm$ 0.50	55 $\pm$ 0.47	7 $\pm$ 0.52
	75 min	10.9 $\pm$ 0.57	33.0 $\pm$ 0.58	51 $\pm$ 0.47*	3 $\pm$ 0.57	59 $\pm$ 0.50*	8 $\pm$ 0.57*
	120 min	12.7 $\pm$ 0.59	32.8 $\pm$ 0.57	48 $\pm$ 0.50*	4 $\pm$ 0.51	66 $\pm$ 0.57*	8 $\pm$ 0.56*
ROM	baseline	9.1 $\pm$ 0.67	30.0 $\pm$ 0.57	39 $\pm$ 0.37	4 $\pm$ 0.67	56 $\pm$ 0.57	2 $\pm$ 0.57
	15min	8.3 $\pm$ 0.50	26.5 $\pm$ 0.57	46 $\pm$ 0.47*	6 $\pm$ 0.50	44 $\pm$ 0.45*	3 $\pm$ 0.45
	45 min	8.0 $\pm$ 0.53	26 $\pm$ 0.36	44 $\pm$ 0.57*	4 $\pm$ 0.58	49 $\pm$ 0.59*	4 $\pm$ 0.50
	75 min	8.1 $\pm$ 0.55	25 $\pm$ 0.57*	51 $\pm$ 0.45*	4 $\pm$ 0.59	40 $\pm$ 0.50*	6 $\pm$ 0.58*
	120 min	8.5 $\pm$ 0.57	29.3 $\pm$ 0.67	49 $\pm$ 0.57*	3 $\pm$ 0.57	39 $\pm$ 0.57*	5 $\pm$ 0.50

\* Means significantly different to the value before injection (baseline) ( $P < 0.05$ ).

**TABLE 4. Means  $\pm$  SE of glucose, urea, creatinine, ALT and AST following epidural injection of XYL, DET and ROM.**

Anesthetic drugs	Time/min.	Glucose	Urea	Creatinine	ALT	AST
XYL	baseline	120 $\pm$ 0.58	52 $\pm$ 0.67	1.79 $\pm$ 0.057	34 $\pm$ 0.47	56 $\pm$ 0.50
	after					
	15 min	171 $\pm$ 0.59*	51 $\pm$ 0.77	1.93 $\pm$ 0.054	24 $\pm$ 0.59*	60 $\pm$ 0.58*
	45 min	211 $\pm$ 0.51*	47 $\pm$ 0.97*	2.05 $\pm$ 0.058*	28 $\pm$ 0.55*	65 $\pm$ 0.50*
	75 min	213 $\pm$ 0.52*	58 $\pm$ 0.87*	2.08 $\pm$ 0.050*	26 $\pm$ 0.50*	61 $\pm$ 0.58*
	120 min	243 $\pm$ 32.8*	54 $\pm$ 0.47	2.20 $\pm$ 0.067*	26 $\pm$ 0.57*	66 $\pm$ 0.52*
DET	baseline	153 $\pm$ 32.8	47 $\pm$ 0.47	1.29 $\pm$ 0.055	32 $\pm$ 0.50	70 $\pm$ 0.50
	after					
	15 min	158 $\pm$ 0.37*	44 $\pm$ 0.67	2.29 $\pm$ 0.07*	32 $\pm$ 3.84	80 $\pm$ 0.47*
	45 min	160 $\pm$ 0.54*	32 $\pm$ 0.51*	1.50 $\pm$ 0.97	38 $\pm$ 0.59*	76 $\pm$ 0.59*
	75 min	178 $\pm$ 0.59*	50 $\pm$ 0.59	1.27 $\pm$ 0.59	30 $\pm$ 0.37	67 $\pm$ 0.37
	120 min	200 $\pm$ 0.50*	48 $\pm$ 0.50	1.41 $\pm$ 0.05	32 $\pm$ 0.50	85 $\pm$ 0.87*
ROM	baseline	113 $\pm$ 0.54	62 $\pm$ 0.67	2.18 $\pm$ 0.051	30 $\pm$ 0.59	60 $\pm$ 0.50
	after					
	15 min	167 $\pm$ 0.58*	58 $\pm$ 0.59	2.16 $\pm$ 0.054	31 $\pm$ 0.56	62 $\pm$ 0.58
	45 min	210 $\pm$ 0.50*	51 $\pm$ 0.54*	2.18 $\pm$ 0.055	29 $\pm$ 0.55	58 $\pm$ 0.47
	75 min	187 $\pm$ 0.77*	53 $\pm$ 0.55*	2.30 $\pm$ 0.053	30 $\pm$ 0.52	60 $\pm$ 0.51
	120 min	190 $\pm$ 0.67*	64 $\pm$ 0.58	2.20 $\pm$ 0.058	27 $\pm$ 0.51	61 $\pm$ 0.57

\* Means significantly different to the value before injection (baseline) ( $P < 0.05$ ).

## Discussion

Lumbosacral epidural analgesia is highly advisable to avert the need for general anesthesia in goats with providing long duration of analgesia and reduce surgical stress. Epidural administration

of xylazine, detomidine and romifidine resulted in analgesia due to stimulation of  $\alpha$ -2 adrenoceptors in the dorsal horn of the spinal cord resulted in analgesia in goats. This stimulation has been reported to inhibiting the central transmission of the afferent nociceptive impulses [6] by pre-

and postsynaptic membrane hyperpolarization and inhibiting the release of neurotransmitters, norepinephrine and substance-p, which is involved in pain sensation leading to reduce the neural activities and analgesia [8, 14,15, 16]. Results of the present study in group 3 indicated that romifidine produced moderate to complete degree of analgesia in the region of perineum, tail, flank and hind limbs in goats at dose of 50 $\mu$ g/kg [8, 9, 17]. The duration was significantly prolonged than that produced by xylazine or detomidine in spite of delayed response to onset of analgesia for romifidine [15]. This result may be attributed to that the mechanism of analgesic action of epidurally administered romifidine, like that of other alpha-2 adrenergic agonists as well as it inhibits impulse conducting in primary afferent nerve fibers as a result of the local anesthetic action of romifidine at spinal nerve roots [8]. Detomidine could present a greater cranial extension of the epidural block compared with xylazine thus produce most rapid onset of moderate to complete analgesic effect but with least duration while xylazine produce moderate degree of analgesia [18]. Other results by Pohl et al. [19] who compare the three drugs in dogs found that the time of sensory epidural block did not differ in any of the treated groups. However, the duration of the postoperative analgesia differed in xylazine lasting for up to 4 hours. Increasing the volume of the anaesthetic solution has been reported to produce more cranial migration of analgesics. In our present study, this variable was remained constant in all goats and therefore, any variation in the extent and depth of analgesia may be assigned to the potency of the drug itself, this agreed with result of Kinjavdekar et al. [11].

There was decrease in spontaneous activity in all goats after drugs administration with marked sedation characterized by lowering of head and salivation. The sedative action of  $\alpha$ 2-adrenergic agonists is due to inhibition of firing activity of locus coeruleus (LC) neurons in the pons of the lower brainstem which involved with physiological responses to stress and panic [20]. It may be also referred to rapid vascular or lymphatic absorption from the subarachnoid space [14]. No significant difference detected in the onset of sedation between XYL and DET, while the onset of ROM was significantly delayed than both of them, this result disagreed with the published investigation of Marzok and El-khodery [15] who observed that time to onset of sedation was significantly prolonged

following epidural detomidine (11.2  $\pm$  2.4 min) in comparison with epidural romifidine in buffalo (5.8 $\pm$ 1.1 min), this variation may be attributed to species difference. The duration of sedation was significantly prolonged with XYL and ROM than DET. Sedation reached its peak at 45 min after injection in all groups, at this time-point the goats were completely sedated in ROM and moderately sedated in DET while, in XYL they were mild to moderate degree of sedation [11].

Xylazine, detomidine, and romifidine are  $\alpha$ 2-adrenergic receptor agonist drugs, in addition to their analgesic effects; they have potent sedative and muscle relaxant effects that can result in profound stupor, ataxia and reluctance to move [21]. It was observed in this study that both XYL and ROM produced almost similar duration of ataxia but of different degrees. ROM created prolonged moderate ataxia and lack of hind limb coordination, this might refers to the inhibitory effects of romifidine on A- $\alpha$  nerve fibers which are responsible for motor function that was proved by, moreover it also might attributed to the local anaesthetic action of romifidine at the level of spinal nerve roots [8]. The ataxia produced by XYL in the present study may be related to its local anesthetic action on hind limb motor neurons probably due to structural similarity with lignocaine. Hind limb ataxia with DET might be due to its possible local action in the hind limb motor neurons [18].

Reduction of respiratory rate (RR) was recorded in all groups especially after epidural injection of ROM, this agreed with the results of Kinjavdekar et al. [8] and Amarpal et al. [9]. The adverse effect of epidural administration of  $\alpha$ 2-adrenergic receptor agonist on RR could be due to the depression of respiratory centers through alpha-2 adrenoceptor activity following systemic absorption of the drugs as reported by Amarpal et al. [9] and Prado et al. [22]. Alpha 2-Agonists have been announced to promote reduction of thermoregulation and depress the hypothalamic noradrenergic  $\alpha$ 2-receptors resulting in mild hypothermia. Moreover, the decrease in RT by  $\alpha$ 2-agonist is related to CNS depressing mechanisms [12]. The significant decrease in RT after XYL and insignificant decrease after DET injection agreed with those obtained by DeRossi et al. [14] and Malhi et al. [23]. On other hand, an insignificant increase in RT was recorded within 15 min of epidural injection of ROM in the present study. The same result was reported by Kinjavdekar

et al. [8], Amarपाल et al.[9] and Malhi et al.[23]. Hyperthermia also has been reported after IV administration of 120 µg/kg romifidine in dogs [24]. This observation was in agreement with the result of Pypendop and Verstegen [25] who detected significant decrease in body temperature in dogs received romifidine at a dose of 10µg/kg. These probably suggest that romifidine may affect central mechanisms of thermoregulation in a dose-dependent manner, so that the higher dose of romifidine may cause transit onset of hyperthermia.

In all groups there was a gradual decrease in HR after epidural administration of the drugs. A reduction in HR after epidural administration of xylazine has been reported in goats by Kinjavdekar et al. [11] and DeRossi et al.[14]. The decrease in HR in XYL might be attributed to the action on CNS after its systemic absorption from the venous sinuses in the epidural space. The decrease in HR following DET in goats was recorded by Khan et al. [26] and Onifade and Arowolo [27] while after ROM was observed by Kinjavdekar et al. [8] and Amarपाल et al. [9]. Cardiovascular effects induced by α<sub>2</sub>-adrenergic receptor agonist are the result of stimulation of peripheral or central alpha-2 adrenoceptors. This Stimulation results in inhibition of release of norepinephrine from peripheral nerve endings, which, in part, contributes to the bradycardiac effect of the drugs [14, 23], decreased sympathetic outflow from the CNS, direct depression of cardiac pacemaker and conduction tissue, increased vagal tone and a direct increase in the release of acetyl choline from parasympathetic nerves in heart [11].

The haemoglobin and PCV were probably within the physiological limits in all groups, with insignificant reduction after ROM administration. This agreed with the result of Kinjavdekar et al. [8] who mentioned that their reduction may attributed to the fluid shifting from the interstitial spaces to the intravascular space in order to maintain normal cardiac output or collecting of erythrocytes in the spleen or other reservoirs in the effect of reducing the sympathetic outflow after romifidine epidural injection in goats. The DLC% showed a rise in neutrophil count in all the groups and a decrease in lymphocyte count with DET and ROM, while increased with XYL. Similar findings were reported for xylazine [11,28], detomidine [29] and romifidine [30]. The changes in DLC% observed in the present study might be due to stress caused by the drugs and subsequent stimulation of adrenal

glands and the effect of glucocorticoid. Plasma glucose increased in all groups, similar effects have been reported after epidural administration of xylazine, detomidine [11,12] and romifidine [9]. The high glucose was probably the result of increased muscular activity and sympathetic stimulation caused during restraining of the animals, resulting in increased secretion of adrenocortical hormone. Hyperglycemia may also be attributed to α<sub>2</sub>-adrenergic-mediated inhibition of insulin release from the pancreatic β-cells [8] and increased glucose production in the liver. Comparison between the three treatments; the blood glucose level was sharply increased with XYL as compared to other groups [11]. In contrast Malhi et al. [23] reported that glucose level was lower with xylazine (0.2 mg/kg) as compared to detomidine (40µg/kg) after intravenous administration in sheep. The changes in BUN levels were non-significant [9] except at 75 min in first group was significantly increased which may be referred to increase amino acid degradation [12], then its level return to physiological limits. Decreases in the BUN levels were observed with the administration of detomidine and romifidine [31]. The observed decrease may be as a result of increase in renal function in response to the elimination of these drugs then returned to the physiological limits. Creatinine is a product of deamination of amino acids and its level increases when renal function is inhibited. Its blood levels are dependent upon the rate of urine formation and elimination. The significant increased in creatinine levels following xylazine in all time-point may be attributed to a temporary inhibitory effect on renal blood flow, which in turn might have caused a rise in creatinine level and not indicate renal damage [11,12]. The significant decrease of ALT in the goats received XYL might be attributed to the stress produced in first group because of systemic absorption of xylazine and changes in body temperature [32]. The significant increase of AST in XYL and DET received goats may be due to the possible hypotension and hypoxemia that may cause the release of these enzymes from the heart muscles or liver [31].

### **Conclusion**

Epidural administration of xylazine, detomidine and romifidine are produce a rapid, safe and reliable analgesia and sedation in the goats without critical variation in the physical, haematological and biochemical parameters. Romifidine produces more potent and prolonged

analgesia and sedation than xylazine and detomidine.

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#### Ethical approval

The research plan was approved from Alexandria University institutional animal care and use committee (AU-IACUC) with approval number ACU-013-18-11-29

#### Conflict of Interest

The author has no conflict of interests to declare regarding the publication of this paper.

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## الفعالية المقارنة للزيتون والديتوميدين والروميفيدين كمخدر فوق الأم الجافية في الماعز المصري (كابرا هيركوس)

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تم إجراء هذه الدراسة من أجل تقييم فعالية الزيتون (XYL) والديتوميدين (DET) والروميفيدين (ROM) وذلك من خلال دراسة التأثير التسكينى للألم والتأثير التهدئي لهم وكذلك التغيرات في صورة وكمياء الدم بعد الحقن فوق الأم الجافية في الماعز المصري. تم استخدام ستة من الماعز، يتكون العلاج من ٢٠٠ ميكروغرام / كيلو غرام زيتون ، ٤٠ ميكروغرام / كيلو غرام ديتوميدين ، ٥٠ ميكروغرام / كيلو غرام روميفيدين تدار في كل مجموعة بالتتابع.

تم تسجيل بداية ظهور ومدة ودرجة التسكين للألم في منطقة العجاني ، وكذلك التهدئة والترنج للحيوان. تم تقييم وقياس معدلات التنفس و الحرارة و النبض، و نسبة الهيموجلوبين في الدم و حجم الخلايا المنضغطة و نسب خلايا الدم البيضاء و جلوكوز الدم ، واليوريا ، الكرياتينين ، وكذلك وظائف الكبد ( ALT و AST ) قبل الحقن وعند ١٥ ، ٤٥ ، ١٢٠ ، ٧٥ دقيقة بعد الحقن.

أظهرت النتائج بداية ظهور التأثير التسكينى للألم بعد حقن الديتوميدين في وقت سابق بشكل ملحوظ عن باقي المجموعات، و كانت مدة التسكين أطول مع حقن الروميفيدين بدرجة تسكين وتهدئة أعلى من نظيراتها في المجموعتين الأخرين و مدة ترنج أقصر بكثير. وقد لوحظ أن معدل التنفس ، درجة الحرارة و معدل النبض يميل إلى الانخفاض بشكل عام في مختلف المجموعات المعالجة مقارنة بمستويات ما قبل الحقن. أما التغيرات في قيم و صورة الدم فكانت وقتية وفي اطار المستوي الفسيولوجي مع عدم وجود تأثيرات عكسية واضحة . في الختام ، أثبتت النتائج ان الحقن فوق الأم الجافية لـزيتون أو ديتوميدين أو روميفيدين لها تأثير تسكينى و تهدئي فعال للماعز دون تأثير ضار شديد، و أن التأثير الناجم عن الروميفيدين أطول بشكل ملحوظ من الزيتون والديتوميدين.