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Evaluation of the Sedative, Analgesic, Physiological and Haematological Effects of Intravenous Detomidine, Detomidine-Butorphanol, Romifidine and Romifidine-Butorphanol in Baladi Goats

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Abstract: The present study was aimed to clarify and determine the sedative and analgesic effects of intravenous injection of detomidine, detomidine-butrophanol, romifidine and romifidine-butorphanol in Egyptian Baladi goats and to evaluate the most efficient treatment regimen for induction of sedation and analgesia with the least adverse effects on clinicophysiological and hematological parameters. Six baladi goats, three males and three females weighing 25-35 kg were studied in prospective randomized experimental anaesthetic trial. Four intravenous treatments of detomidine, detomidine-butorphanol, romifidine and romifidine-butorphanol were administered to each goat using: 0.04 mg/kg body weight detomidine, 0.04 mg/kg body weight detomidine plus 0.03 mg/kg body weight butorphanol, 0.05 mg/kg body weight romifidine and 0.03 mg/kg body weight romifidine plus 0.05 mg/kg body weight butorphanol. The pulse rate, respiratory rate, rectal temperature, sedation, analgesia, ataxia, hemoglobin, packed cell volume percentage, differential leukocytic count, serum glucose, creatinine, urea, Aspartate aminotransferase and Alanine aminotransferase were evaluated. Marked sedation and complete analgesia was observed after detomidine-butorphanol and romifidine-butorphanol injections. Frequent urination and obvious watery salivation with tympany were observed in all treated goats. A significant reduction in pulse rate was observed in all goats compared to baseline value ($p<0.05$). Changes in clinicophysiological and haematological parameters were transient with no obvious systemic effects. Intravenous injection of 0.04 mg/kg body weight detomidine combined with 0.03 mg/kg body weight butorphanol or intravenous injection of 0.05 mg/kg body weight romifidine combined with 0.03 mg/kg body weight butorphanol showed a prolonged marked sedation and complete analgesia in Baladi goats than intravenous injection of detomidine or romifidine alone. The combination of butorphanol with detomidine or romifidine was induced bradycardia, which within acceptable value. The adverse effects on clinicophysiological and haematological values were mild, transient and within the physiological limits.

Key words: Sedative · Analgesic Effects · Detomidine · Romifidine · Butrophanol · Goats

INTRODUCTION

Detomidine is α_2-adrenergic agonists used for sedation in large animals. Although similar to xylazine, detomidine produces sedation and analgesia of greater magnitude and longer duration [1]. It produces prolonged and intense analgesia [2]. Nature of the analgesic effect appears to be wide, producing a reduced response to experimental stimulation and exhibiting a clinical effect in the horse with colic [3]. Detomidine can be used as a safe and effective pre anaesthetic resulting in smooth induction and recovery [4]. Romifidine is potent and selective α_2-agonists, that is chemically similar to clonidine, used for sedation and premedication [5]. Romifidine produces sedation, muscle relaxation, reluctance to move, reduced responsiveness to environmental stimuli, bradycardia and reduced respiratory rate [6]. Respiratory depression appears to be a secondary result of the central nervous system depression produced by α_2-adrenoceptor stimulation [7]. Body temperature may decrease in animals sedated with $\alpha_2$agonists which generally, could be attributed to C.N.S

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depression, in combination with reduction in muscular activity [8]. Varying dosages of opioids can produce depression, analgesia and sleep or in other species it induces excitement of the central nervous system. Combinations of opioids and α_2-agonists could be resulted in profound sedation and analgesia [9]. Detomidine is commonly combined with opioids to enhance sedation and analgesia [10]. Butorphanol is a kappa opioid (KOP)-receptor agonist and a mu opioid (MOP)-receptor antagonist [11]. Intravenous doses of butorphanol between 0.1 mg/ kg and 0.4 mg/ kg produce dose dependent sedative [12] and analgesic effects [13]. A combination of romifidine with butorphanol in horses greatly reduced response to stimuli compared with that following administration of romifidine alone. The addition of butorphanol did not influence the cardiovascular system any more than romifidine alone, but may increase respiratory depression [14]. Administration of α_2-agonist and opioid agonist combinations decrease hematological parameters including; red blood cell and white blood cell counts, packed cell volume and hemoglobin and total protein and albumin and increased glucose, cholesterol, blood urea nitrogen, creatinine and alanine aminotransferase. The changes in hematobiochemical parameters were transient and caused no marked systemic effects [15, 16]. The purpose of this study was to clarify and determine the sedative and analgesic effects of intravenous injection of detomidine, detomidine-butrophanol, romifidine and romifidine-butorphanol in Baladi goats and to evaluate the most efficient treatment regimen for induction of sedation and analgesia with the least adverse effects on clinicophysiological and haematological parameters.

MATERIALS AND METHODS

The present experimental investigation was approved by the Committee of Animal Welfare and Ethics at Alexandria University. Six Egyptian Baladi goats, three males and three females weighing 25-35 kg were studied. All goats were healthy and were housed in stalls in the Department of Surgery, Faculty of Veterinary Medicine at Alexandria University during the investigation period. Feeding was withheld 12 hours prior to experimentation, but each goat was allowed to drink water ad libitum. Intravenous treatments were applied to each goat via the left jugular vein for a minimum one week interval using: 0.04 mg/kg body weight detomidine (Domosedan®, Farmos-Orion Co., Finland); 0.04 mg/kg body weight detomidine plus 0.03 mg/kg body weight butorphanol (Torbugesic®, Fort Dodge Laboratories, Fort Dodge, IA, USA), 0.05 mg/kg body weight romifidine (Sedivet®, Boehringer ingelheim Vet medica, Inc., Saint Jseph, Mo, USA); and 0.03 mg/kg body weight romifidine plus 0.05 mg/kg body weight butorphanol Tranquilli *et al*. [44]. The site of the injection was aseptically prepared, clipped and scrubbed with povidine iodine solution. All parameters including; pulse rate (PR, pbm), respiratory rate (RR, Breath/min), rectal temperature (RT, °C), Sedation, Analgesia, Ataxia, Hemoglobin (Hb), Packed cell volume (PCV%), Differential leukocytic count (DLC%), glucose (mg/dl), creatinine(mg/dl), urea(mg/dl), Aspartate aminotransferase (AST, U/L) and Alanine aminotransferase (ALT, U/L) were evaluated 15 minutes before injection (baseline value) and at 15, 45,75, 120 minutes after drug administration. The PR was measured in beats/minute, the RR was evaluated by movement of the thoracic wall and RT was measured with a digital thermometer. Blood samples were collected at the previous intervals for hematological and biochemical evaluation. Analgesia was evaluated by deep muscle pricks through applying painful stimuli with 23-gauge needle inserted through the skin and the underlying tissues [17, 18]. The levels of analgesia for the tail, perineum, hind limbs, flank, abdomen, thoracic limbs and rib areas were determined using a scoring system of Skarda and Muir [19]. A score of 0 (no analgesia) indicated normal sensation in response to a painful stimulus, a score of 1 indicated a depressed reaction to painful stimulus, a score of 2 indicated moderate analgesia in response to a painful stimulus and a score of 3 indicated complete analgesia. Depth of sedation was rated by central effects produced by the drugs. The scale was as follows: 1, no sedative effect; 2, reduced alertness with no other signs; 3, mild sedation, drowsiness and slight drop of the head; and 4, marked drowsiness [18 and 20]. Motor effects were evaluated using the following score: one, no ataxia; two, mild ataxia, animal having difficulty remaining in a standing position, three, ataxia, animal recumbent but with hind limbs movement and four, severe ataxia, animal recumbent but with no hind limb movements.

Statistical Analysis: The data were calculated and analyzed using analysis of variance with SAS computer software package [21]. Data for the PR, RR, RT, sedation, analgesia, Hb, PCV, DLC, glucose, creatinine, urea, AST and ALT were grouped, analyzed and summarized as the mean plus or minus the standard deviation. In each analysis, differences were considered significant if $p < 0.05$.

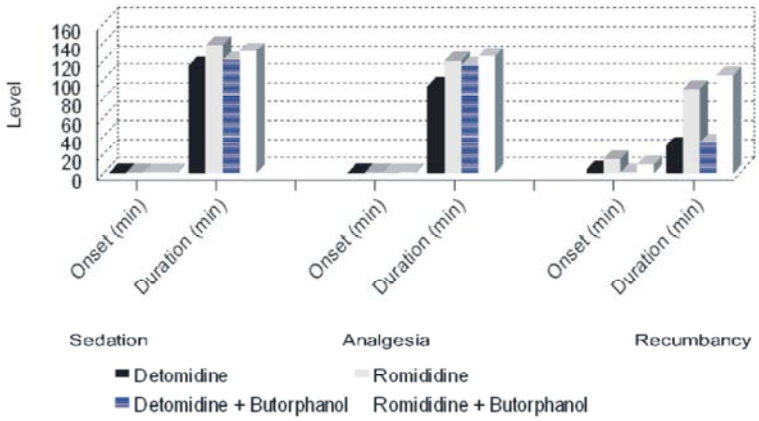

Fig. 1: Sedation, analgesia and recumbancy following IV injection of detomidine (0.04mg/kg), romifidine (0.05mg/kg), combination of butorphanol (0.03mg/kg) with detomidine (0.04mg/kg) and romifidine (0.05mg/kg) in goats.

Table 1: Means ± SD values of sedation, analgesia and recumbancy following IV injection of detomidine (0.04mg/kg), romifidine (0.05mg/kg), combination of butorphanol (0.03mg/kg) with detomidine (0.04mg/kg) and romifidine (0.05mg/kg) in goats

	Sedation		Analgesia		Ataxia	
Drugs	Onset (min)	Duration (min)	Onset (min)	Duration (min)	Onset (min)	Duration (min)
Detomidine	0.83 ± 0.39^{A}	115.00 ± 7.05^{D}	0.66 ± 0.39^{B}	93.33 ± 10.78^{D}	4.00 ± 0.63^{B}	29.33 ± 5.70^{D}
Romifidine	0.83 ± 0.39^{A}	137.33 ± 10.60^{A}	1.00 ± 0.39^{A}	120.00 ± 14.13^{C}	15.00 ± 2.15^{A}	90.00 ± 5.70^{B}
Detomidine + butorphanol	0.66 ± 0.39^{B}	120.33 ± 3.55^{C}	0.50 ± 0.19^{C}	115.00 ± 7.05^{B}	0.83 ± 0.39^{D}	33.00 ± 4.94^{C}
Romifidine + butorphanol	0.67 ± 0.34^{B}	130.66 ± 8.52^{B}	0.66 ± 0.39^{B}	125.00 ± 7.05^{A}	9.60 ± 2.15^{C}	105.00 ± 1.39^{A}

Capital letters indicated that: Means within the same column of different letters are significantly different at ($p < 0.05$).
No. of treated animals in each trial = 6

RESULTS

Sedative and Analgesic Effects: Marked signs of sedation were observed at 0.83 ± 0.39 minutes and continued for 115.00 ± 7.05 minutes. Analgesia was observed at 0.66 ± 0.39 minutes and continued for 93.33 ± 10.78 minutes, affecting nearly the whole body following detomidine injection. The animal became ataxic for a short period, after that it was recumbent at 4.00 ± 0.63 minutes, which continued for 29.33 ± 5.70 minutes. Marked sedation (A score of 4) was observed at 0.66 ± 0.39 minutes and continued for 120.33 ± 3.55 minutes after injection of detomidine-butorphanol. Complete analgesia (A score of 3) occurred at 0.50 ± 0.19 minutes and continued for 115.00 ± 7.05 minutes, affecting the whole body with a short period of ataxia, which observed at 33.00 ± 4.94 minutes. Marked signs of sedation were found at 0.83 ± 0.39 minutes and continued for 137.33 ± 10.60 minutes. Analgesia was observed at 1.00 ± 0.39 minutes and continued for 120.00 ± 14.13 minutes following intravenous injection of romifidine. The analgesia affected nearly the entire body of the goats which became ataxic, then recumbent at 15.00 ± 2.15 minutes for 90.00 ± 5.70 minutes. The intravenous injection of romifidine-butorphanol induced marked sedation (A score of 4) at 0.67 ± 0.34 minutes and continued for 130.66 ± 8.52 min. Complete analgesia (A score of 3) was induced in the whole body at 0.66 ± 0.39 min and continued for 125.00 ± 7.05 minutes. The animal became recumbent after 9.60 ± 2.15 minutes and continued for 105.00 ± 1.39 minutes (Table 1 and Fig. 1). Frequent urination and obvious watery salivation with tympany were found in all treated goats.

Clinicophysiological Effects: Intravenous injection of detomidine reduced RR significantly at 15 and 75 minutes, then it increased at 120 minutes, but it remains lower than the baseline value. The intravenous injection of detomidine-butorphanol increased RR significantly at 15 minutes followed by a significant decrease in RR at 45 minutes. Romifidine-butorphanol combination increased RR significantly at 15 minutes, after that it was decreased significantly at 45 minutes until the end of the experiment. Intravenous injection of detomidine was decreased RT significantly at 15 minutes after injection until the end of the experiment. Romifidine intravenous injection was decreased RT significantly during the entire observation period. Intravenous injection of detomidine-butrophanol

Table 2: Means ± SD of Respiratory rate, Rectal temperature and Pulse rate following IV injection of detomidine (0.04mg/kg), romifidine (0.05mg/kg), combination of butorphanol (0.03mg/kg) with detomidine (0.04mg/kg) and romifidine (0.05mg/kg) in goats

Anaesthetic drugs	Time/min	Respiratory Rate RR(breaths/min)	Rectal Temperature RT(°C)	Pulse Rate PR (bpm)
Detomidine	Base line	23.66 ± 4.53	39.86 ± 0.30	85.00 ± 3.73
	15 min	14.33 ± 4.18*	39.53 ± 0.08	76.00 ± 3.73*
	45 min	12.66 ± 3.88*	38.53 ± 1.48*	68.00 ± 3.73*
	75 min	10.66 ± 3.88*	38.03 ± 1.68*	74.00 ±3.73*
	120 min	15.66 ± 7.84*	38.03 ± 1.88*	80.00 ± 3.73*
Romifidine	Base line	25.00 ± 3.15	39.20 ± 1.12	90.00 ± 3.16
	15 min	15.00 ± 3.15*	38.40 ± 1.11*	70.00 ± 3.15*
	45 min	12.00 ± 3.15*	38.50 ± 1.11*	60.00 ± 3.15*
	75 min	10.00 ± 3.15*	37.50 ± 2.11*	68.00 ± 3.15*
	120 min	20.66 ± 2.66*	37.06 ± 0.06*	80.00 ± 3.15*
Detomidine +Butorphanol	Base line	21.66 ± 2.88	39.40 ± 0.05	81.00 ± 2.57
	15 min	26.66 ± 3.52*	39.20 ± 0.5	71.00 ± 3.56*
	45 min	16.66 ± 2.88*	38.90 ± 1.88*	69.00 ± 3.54*
	75 min	17.66 ± 2.88	38.70 ± 0.5*	63.00 ± 3.57*
	120 min	18.66 ± 2.88	38.80 ± 0.5*	73.00 ± 3.58*
Romifidine +Butorphanol	Base line	25.00 ± 3.57	39.50 ± 0.5	88.00 ± 3.57
	15 min	30.00 ± 3.00*	39.40 ± 0.5	72.00 ± 3.55*
	45 min	20.00 ± 3.55*	39.00 ± 0.5	64.00 ± 3.58*
	75 min	18.00 ± 3.54*	38.50 ± 0.5*	54.00 ± 3.57*
	120 min	17.00 ± 3.56*	38.53 ± 0.5*	80.00 ± 3.59*

* Significantly different to the value before injection ($p<0.05$).
No. of treated animals in each trial = 6

and romifidine-butrophanol was decreased RT significantly at 45 and 75 minutes, respectively until the end of the experiment. The PR decreased significantly at 15 minutes after injection of detomidine or romifidine, but did not return to the baseline value. The Combination of butorphanol with detomidine or romifidine was decreased PR significantly during the entire period of the experiment (Table 2).

Physiological and Haematological Evaluation: Intravenous injection of detomidine was decreased significantly Hb value until 75 minutes. Non significant changes in PCV% or eosinophils counts were observed. Neutrophils were increased at 45 minutes after injection, followed by a non significant reduction until the end of the experiment. Lymphocytes increased 15 minutes, followed by a non significant change until the end of the experiment. Monocytes were increased significantly at 15 and 45 minutes, after that it were returned to the baseline value at 75 minutes followed by a significant increasing again at 120 minutes (Table 3). Detomidine injection was increased the glucose significantly over the entire observation period. The ALT activities were increased significantly at 75 and 120 minutes post injection. A significant reduction in AST activities were observed over the entire observation period. Urea was decreased significantly until 45 minutes after injection and then it was increased significantly at 75 minutes followed by a slight reduction to reach the baseline value at 120 minutes. Creatinine was exhibited no significant changes after injection (Table 4). Both Hb and monocytes were increased significantly only at 15 minutes after romifidine injection, then Hb and monocytes were exhibited no significant reduction afterward. There was a significant reduction in PCV%, which continued until the end of the experiment. Neutrophils were increased significantly at 15 and 75 minutes after injection followed by a significant reduction until the end of the experiment. Lymphocytes were increased significantly at 15 and 45 minutes after injection and then it decreased significantly later on. Eosinophils were exhibited only significant increasing at 45 minutes after injection. No significant changes in PCV%, eosinophils and monocytes were observed along the entire period of the experiment (Table 3). Neutrophils were showed a significant increasing at 15 and 45 minutes after injection followed by a significant reduction afterward. Lymphocytes were decreased signifcantly at 15 and 45 minutes then it increased significantly later on. Glucose value and AST activities were increased significantly after romifidine injection. Urea, creatinine and ALT activities were showed no significant changes at the entire observation period. Both glucose and AST activities were increased significantly after detomidine-butorphanol injection. A significant increasing in urea

Table 3: Means ± SD of Hb, PCV %, Neutrophil, Eosinophil, lymphocyte and Monocyte following IV injection of detomidine (0.04mg/kg), romifidine (0.05mg/kg), combination of butorphanol (0.03mg/kg) with detomidine (0.04mg/kg) and romifidine (0.05mg/kg) in goats

				DLC %			
Anaesthetic Drugs	Time/min	Hb (g/dl)	PCV %	Neutrophil	Eosinophil	Lymphocyte	Monocyte
Detomidine	Base line	11.3±0.13	34 ± 1.66	35 ± 1.67	2 ± 1.58	64 ± 1.5	2 ± 1.57
	15 min	10.3±0.14*	34 ± 1.57	37 ± 1.50	4 ± 1.50	76 ± 1.57*	10 ±1.47*
	45 min	9.9 ± 0.15*	35 ± 1.56	44 ± 1.58*	2 ± 1.57	66 ± 1.50	8 ± 1.37*
	75 min	9.5 ± 0.15*	36 ± 1.73	35 ± 1.53	4 ± 1.51	67 ± 1.57	3 ± 1.50
	120 min	10.9±0.15	33 ± 1.37	39 ± 1.57	2 ± 1.57	68 ± 1.47	7 ± 1.57*
Romifidine	Base line	8.1 ± 0.15	38 ± 1.67	48 ± 1.67	3 ± 1.47	45 ± 1.57	2 ± 1.51
	15 min	9.1±0.15*	32 ± 1.47*	39 ± 1.59*	2 ± 1.50	73 ± 1.59*	7 ± 1.58*
	45 min	8.7 ± 0.15	31 ± 1.50*	38 ± 1.50*	7 ± 1.59*	50 ± 1.50*	4 ± 1.56
	75 min	7.9 ± 0.15	32 ± 1.52*	58 ± 1.53*	2 ± 1.52	37 ± 1.51*	2 ± 1.47
	120 min	8 ± 0.15	33 ± 1.57*	55 ± 1.55*	3 ± 1.57	34 ± 1.57*	4 ± 1.50
Detomidine+ butorphanol	Base line	10.8 ± 0.15	38 ± 1.57	41 ± 1.66	2 ± 1.50	56 ± 1.47	2 ± 1.67
	15 min	9.1 ± 0.15*	37.2± 1.57	54 ± 1.50*	1.6 ± 1.56	36 ± 1.50*	2 ± 1.50
	45 min	8.5 ± 0.15*	37.5± 1.57	54 ± 1.55*	2 ± 1.55	37 ± 1.52*	4 ± 1.59
	75 min	8.7 ± 0.59*	37 ± 1.57	31 ± 1.51*	2 ± 1.59	66 ± 1.53*	2 ± 1.37
	120 min	9.2 ± 0.16*	37.4± 1.57	21 ± 1.77*	2 ± 1.57	73 ± 1.50*	4 ± 1.53
Romifidine+ butorphanol	Base line	9.2± 0.15	32.6± 1.55	37 ± 1.70	4 ± 1.77	58 ± 1.67	2 ± 1.36
	15 min	7.5±0.17*	31.3± 1.50	45 ± 1.59*	7 ± 1.47	45 ± 1.58*	2 ± 1.50
	45 min	7.1±0.15*	30.5± 1.53	43 ± 1.50*	3 ± 1.50	50 ± 1.55*	4 ± 1.58
	75 min	6.8±0.15*	30.2± 1.53	49 ± 1.55*	3 ± 1.59	41 ± 1.77*	5 ± 1.56*
	120 min	7.1±0.15*	31.5± 1.54	54 ± 1.57*	2 ± 1.58	37 ± 1.67*	5 ± 10.59*

* Significantly different to the value before injection (p<0.05).

No. of treated animals in each trial = 6

Table 4: Means± SD of glucose, urea, creatinine, ALT and AST following IV injection of detomidine (0.04mg/kg), romifidine (0.05mg/kg), combination of butorphanol (0.03mg/kg) with detomidine (0.04mg/kg) and romifidine (0.05mg/kg) in goats

Anesthetic drugs	Time/min	Glucose (mg/dl)	Urea(mg/dl)	Creatinine(mg/dl)	ALT (U/L)	AST (U/L)
Detomidine	Base line	173 ± 1.57	50 ± 1.56	0.99 ± 0.15	30 ± 1.57	70 ± 1.50
	15 min	186±1.47*	45 ± 1.54*	1.04 ± 0.15	34 ± 1.15	55 ± 2.67*
	45 min	224±1.59*	44 ± 1.47*	0.72 ± 0.59	34 ± 1.11	60 ± 1.77*
	75 min	246±1.77*	55 ± 1.77*	1.09 ± 0.52	36 ± 1.55*	62 ± 1.59*
	120 min	253±0.97*	50 ± 1.59	0.87 ± 0.15	38 ± 1.50*	60 ± 1.57*
Romifidine	Base line	112 ± 1.77	55 ± 1.67	1.65 ± 0.15	36 ± 2.16	65 ± 1.50
	15 min	206±1.59*	56 ± 1.47	1.67 ± 0.15	37 ± 1.47	89 ± 1.56*
	45 min	256±1.57*	54 ± 1.59	1.65 ± 0.18	36 ± 1.59	89 ± 1.56*
	75 min	216±1.58*	57 ± 1.58	1.68 ± 0.16	38 ± 1.52	95 ± 1.59*
	120 min	213±1.57*	51 ± 1.59	1.64 ± 0.15	38 ± 1.51	93 ± 1.56*
Detomidine + butorphanol	Base line	149 ± 1.57	48 ± 1.50	1.49 ± 0.57	36 ± 1.59	59 ± 1.55
	15 min	211±1.59*	50 ± 1.51	1.36 ± 0.56	26 ± 1.52*	55 ± 1.53
	45 min	230±1.55*	55 ± 1.56*	1.52 ± 1.55	33 ± 1.50	70 ± 1.54*
	75 min	200±1.50*	51 ± 1.57	1.48 ± 1.54	28 ± 1.55*	75 ± 1.58*
	120min	204±1.57*	51 ± 1.56	1.47 ± 1.53	26 ± 1.57*	75 ± 1.50*
Romifidine+ butorphanol	Base line	110 ± 1.37	57 ± 1.54	1.74 ± 0.15	32 ± 1.57	67 ± 1.50
	15 min	199±1.47*	44 ± 1.50*	1.78 ± 0.15	24 ± 1.77*	58 ± 1.54*
	45 min	230±1.67*	45 ± 1.55*	1.73 ± 0.15	28 ± 1.87	80 ± 1.52*
	75 min	269±1.59*	39 ± 1.56*	1.69 ± 0.150	32 ± 1.67	60 ± 1.57*
	120min	200±1.50*	43 ± 1.51*	1.74 ± 0.159	36 ± 1.55	83 ± 1.52*

* Significantly different to the value before injection (p<0.05)

No. of treated animals in each trial = 6

level was observed at 45 minutes after injection, followed by a non significant reduction until the end of experiment but still remaining above the baseline value. There was significant reduction in ALT activities at 15 minutes and then it was exhibited insignificant increasing at 45 minutes, after that it decreased significantly until 120 minutes (Table 4). Non significant changes in creatinine values were also observed. Romifidine-butorphanol injection was decreased significantly Hb value and lymphocytes counts and increased significantly the neutrophils. Both PCV% and Eosinophils were showed non significant changes while monocytes were increased significantly at 75 and 120 minutes after injection (Table 3). A significant increasing in glucose values and decreasing in urea levels were observed after romifidine-butorphanol injection, which continued until the end of observation period. No significant changes were observed for creatinine values. There was a significant reduction in ALT activities at 15 minutes followed by non significant changes until 120 minutes. There were significant changes in AST activities, which were varied between decreasing to increasing along the entire period of the experiment (Table 4).

DISCUSSION

In this investigation in Baladi goats, the intravenous combination of butorphanol with detomidine or romifidine was induced significant sedative and analgesic effects with the actual onset, duration and degree of both sedation and analgesia achieved compared with intravenous detomidine or romifidine alone [18,22,23). A significant difference in the duration of sedation (130.66 ± 8.52 minutes) and analgesia (125.00 ± 7.05 minutes) of the romifidine-butorphanol combination and the duration of sedation (120.33 ± 3.55 minutes) and analgesia (115.00 ± 7.05 minutes) of the detomidine-butorphanol combination were studied. However, the differences in the sedative and analgesic effects in the previous combinations are clinically relevant [24]. In the current investigation, all goats exhibited deep sedation and effective analgesia. Opioid and α_2-agonist agents are synergistic in terms of sedation and analgesia [25]. No excitatory reactions to auditory stimuli were observed in the goats post injection of α_2-agonist [26]. Watery salivation and tympany were noted [27, 28]. Salivation was found due to the goats' inability to swallow, not increased salivary secretion and to the position of the goats' heads, which allows saliva to flow out the mouth [9]. On the other hand, tympany results from activation of the receptors in the longitudinal muscles of the gastrointestinal tract, which lead to relaxation of these muscles, decreased spontaneous motility and finally the accumulation of gases in the rumen. Frequent urination was also observed in the goats, more so than in donkeys. This is due to inhibition of the antidiuretic hormone [29]. The results of this study clearly show that goats more sensitive to α_2-agonist. In horses the drugs are usually used in doses that enable the animal to remain standing although with marked ataxia. In goats these drugs may cause recumbency, unconsciousness and a state close to general anesthesia. Although all drugs used in the current investigation resulted in recumbency and induced a lack of motor coordination, the combination of romifidine and butorphanol caused longer-lasting ataxia (105.00 ± 1.39 minutes) in the goats [29]. Ataxia in horses is a common manifestation of sedation and it is therefore difficult to judge the quality of sedation without considering the degree of ataxia, especially after administration of α_2-agonist [30]. In the present investigation, there was a significant decrease (P<0.05) in PR with the intravenous administration of detomidine, romifidine and their combinations with butorphanol compared with the baseline values [31-33]. The decrease in PR was the strongest clinical reaction reported for the effects of the α_2-agonists [34-36]. Bradycardia is thought to be due to the increase in the vagal tone in response to depression and reflex baroreceptor stimulation in the carotid sinus is due in response to initial hypertension caused by administration of α_2-agonists [37]. In this study significantly decreased the RT of all treatment goats was observed. Non significant changes in RT were recorded in sheep and goat [28 and 38]. The reduction in RT is considered secondary to CNS depression and reduction in muscular activity [39]. All treated goats showed a significant decrease in RR, this reduction may be secondary to the CNS depression caused by α_2-agonist and the kappa opioid receptor agonist [40 and 41]. A significant decrease in Hb was observed after intravenous administration of the combination of butorphanol with either detomidine or romifidine. There was a significant decrease in PCV in romifidine treated goats, while the reduction was insignificant and transient in the detomidine, detomidine-butorphanol and romifidine-butorphanol groups [15, 23, 34]. In all groups, DLC% was exhibited slight fluctuations throughout all time intervals, which may be due to histamine released from the hypothalamic neurons. In this investigation lymphocytes

showed a significant decrease for romifidine-butorphanol combinations [23]. Serum analysis results revealed that AST and ALT activities were decreased significantly and then increased gradually in goats treated with intravenous butorphanol-detomidine or butorphanol-romifidine, this reduction may be induced by histamine through a mechanism that lowers the rate of hepatic damage by inhibition of production and/or release of inflammatory cytokines [42]. A significant increase in the glucose concentration was observed post injection of detomidine, detomidine-butorphanol, romifidine and romifidine-butorphanol [24, 23, 28]. Urea and creatinine were exhibited insignificant decreases and increases in all treated goats along the periods of observation [24]. These results may be due to alteration in renal function following vasodilatation, which caused by releasing of histamine and reduction in the adrenergic tone, resulting in decreased cardiac output, which affect renal function [43,44].

CONCLUSION

The present study confirmed that intravenous injection of 0.04 mg/kg body weight detomidine combined with 0.03 mg/kg body weight butorphanol or intravenous injection of 0.05 mg/kg body weight romifidine combined with 0.03 mg/kg body weight butorphanol showed a prolonged marked sedation and complete analgesia in Baladi goats than intravenous injection of detomidine or romifidine alone. The combination of butorphanol with detomidine or romifidine was induced bradycardia, which within acceptable value. The adverse effects on clinicophysiological and haematological values were mild, transient and within the physiological limits.

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