

SEDATIVE, ANALGESIC, HEMATOLOGICAL AND BIOCHEMICAL EFFECTS OF ROMIFIDINE IN CAMELS (CAMELUS DROMEDARIES).

H. M. MOHSEN*, M. A. MARZOK and SMM., ABUZEAD*****

Dept. Surgery, Anesthesiology and Radiology. Faculty of Vet. Med., Kafer-Elsheikh University.

Depart. Surgery, Anesthesiology and Radiology* and Depart. Physiology**, Faculty of Vet. Med., Suez Canal Univ.

Received: 22.2.2007.

Accepted: 4.3 2007.

SUMMARY

The present study was done on 12 clinically normal camels. The main objective was to evaluate the clinical usefulness, sedative, analgesic, hematological and biochemical effects of 3 dose rates of romifidine administered intravenously (IV) in camels. Camels were divided into 3 groups. Each group (n=4) was specified for one dose level of romifidine (40, 80 and 120 µg/kg body weight). Heart and respiratory rates, ruminal movements, muscle relaxation, response to auditory and tactile stimulations and degree of ataxia were recorded immediately (time 0) before administration of romifidine, 15, 30, 45, 60, 90, 120 and 180 minutes. The time of onset, degree and duration of sedation and analgesia were recorded for 3 hours after drug

administration. Blood samples were collected at the same times of the clinical observations for determination of hemoglobin (Hb %), packed cell volume (PCV %), RBCs and WBCs counts. Blood plasma was analyzed for blood glucose concentration. Blood serum was also analyzed for blood urea nitrogen and creatinine concentrations. The obtained results indicated significant decrease in heart rate, ruminal movement, head height and response to auditory and tactile stimuli. Meanwhile, significant increase in degree of ataxia, distance between the ear tips and blood glucose concentration were recorded after administration of romifidine. No significant changes in rectal temperature, respiratory rate. Hb %, PCV %, WBCs and RBCs counts, and

blood creatinine or blood urea nitrogen levels were recorded in all of the three tested doses. In conclusion, IV administration of romifidine seemed to be safe and effective sedative and analgesic agent for camels. Optimal sedation was achieved with IV doses of 80 µg/kg. While a dose of 120 µg/kg revealed profound sedation and analgesia.

INTRODUCTION

Despite the great advances in the field of sedatives and their uses in domestic animals, experience with their application on the camel have been still lacking until recent years (Fouad, 2000). Chlorpromazine hydrochloride, propionil promazine and acepromazine have been early evaluated as sedatives in camels (Said, 1972; Khamis et al., 1973 and Ali et al., 1989). In recent years sedation with alpha 2-adrenoceptor agonists (xylazine, detomidine, medetomidine & romifidine) has been found useful in the field of both veterinary and human anesthesiology (Hall et al., 2001). The principle physiological effects of the different alpha 2-adrenoceptor agonists are similar, in that they produce a retardation in heart rate, decrease in cardiac output and initial hypertension followed by prolonged hypotension (England and Clarke,

1996). These drugs have been used as sole agents to restraint of camels (Ali, 1988). If these agents are inadequate to complete involved surgical procedures, supplementation with local analgesic or induction with general anesthetic drugs have been used (white et al., 1986 and Fahmy et al., 1995). Xylazine was the initial alpha 2-adrenoceptor agonist which has been used for camel sedation (Denning, 1972). Xylazine in a dose of 0.25 mg/kg IM is adequate for many clinical uses in camels and seems to be superior to chlorpromazine and propionyl promazine (Khamis et al., 1973). Increasing the dose to 0.4 mg/kg intramuscular (IM) result in sternal recumbency within 11-15 minutes and still up to 1-2 hours (Custer et al., 1977 and Penshin et al., 1980). Detomidine has been also introduced for sedation in camel practice. Preliminary trials indicated that IM injection of detomidine (50 µg/kg) in camels revealed marked sedation and analgesia (Hall et al., 2001). Meanwhile, IV administration of detomidine (75 µg/kg) revealed profound sedation and analgesia (Elmaghraby and Alquda, 2005). Although, it was proved that alpha 2-adrenoceptor agonists exert a marked pressure increase in the mare uterus, it has not yet been established whether romifidine is safe for use in pregnant camels or other animal species (Schatzman et al., 1994). Atipamezole has been demonstrated to be effective in

reversal of both sedative/analgesic and physiologic changes in ruminants receiving alpha 2-adrenoceptor agonists (Raekallio et al., 1991 and Mohammad et al., 1995). In the llama, a related species, a combination of IV yohimbine and 4-amino-pyridine give rapid reversal of xylazine induced sedation (Reibold et al., 1989). Romifidine is an amino-imidazolidine derivative, selective and new alpha 2-adrenoceptor agonist drug (England et al., 1996). However, to the authors' knowledge, there is no report on the use of romifidine for sedation and analgesia in camels. The present study was therefore designed to evaluate the clinical usefulness, sedative, analgesic, hematological and biochemical effects of 3 dose rates of romifidine administrated IV in camels.

MATERIALS AND METHODS

Twelve adult one humped camels (9 males, 3 non-pregnant females) that were 4-13 years old with body weight ranged from 300-500kg were used along this study. All animals were considered healthy on the basis of physical examinations. Romifidine (*Sedavit*, 10 mg/ml, *Borehinger Ingelheim, vetmedica GmbH, Germany*) was administrated IV in three dose rates. Camels were allocated randomly into 3 groups with 4 camels/group. The experiments

were performed in a quiet roomy place with ambient lighting. At the beginning of each experiment, resting rectal temperature, ruminal movement, pulse and respiratory rates and complete blood picture were measured. Prior to the injection all animals were kept off food for 24 hours and water was withheld for 12 hours. Romifidine was injected IV at the dose levels of 40, 80 and 120 µg/kg respectively in all groups. All injections were given in a setting position then animals were left loose immediately after injections.

Evaluation of romifidine effects: Heart and respiratory rates, ruminal movements, muscle relaxation, response to auditory and tactile stimulations and degree of ataxia were recorded immediately (time 0) before administration of romifidine (to serve as control), 15, 30, 45, 60, 90, 120 and 180 minutes post injection. Two measures of muscle relaxation (the height of the lower lip from the floor and the distance between the ear tips) were taken. Response to auditory stimulation was scored by evaluating responses to banging on an empty metal bucket or metal bar close to the camels' head (0= non response; 10= marked rapid response to stimuli, as characterized by raising head and turning to face noise, or making evasive movements). Response to tactile stimulation was scored by evaluating responses to administration of focal pressure with a pen tip on the coronary band or

dorsal metatarsal area of the hind limb (0= no response; 10= brisk evasive response and retraction of the limb). Degree of ataxia was evaluated by walking the camel for a distance (0=unable to walk or move; 10= able to walk and step cleaning with all 4 feet). Sedation was assessed and graded to mild, moderate and deep. Central effects produced by the drugs rated the depth of sedation. The scale was: 1) no sedative effect; 2) reduced alertness with no other signs; 3) drowsiness and slight drop of the head and 4) marked drowsiness and recumbency. Drooping (ptosis) of the head, external conchae of the ear, lower lip and /or upper eyelid, prolapsing of the penis and frequency of urination were observed. Analgesia was detected and assessed by recording the response of the animal to needle pricks, pinching with artery forceps and electrical stimulation. Needle pricks and pinching with artery forceps were applied at the shoulder, flank area, perineum and dorsal metatarsal area of the hind limb. Electrical stimulation was applied through two electrodes placed, 3cm apart, on the clipped skin of fetlock of the right front leg and connected to a constant current shock generator (*IITC, Landing, USA*). Electrodes were kept in place by an adhesive wrap. During testing, a continuous DC current was gradually increased until a clean avoidance response (lifting the

leg) was apparent. At that moment the stimulus was stopped and the corresponding current (mA) recorded. The amplitude of the current to which response occurred was recorded and accordingly analgesia was graded from 0 to 3 as described in horses by Jöchle and Hamm (1986). The time of onset, degree and duration of sedation and analgesia were recorded for 3 hours after drug administration. Blood samples (5ml) were collected from the jugular vein at the same time of the clinical examinations for determination of Hb %, PCV %, RBCs and WBCs counts. Blood plasma was analyzed for blood glucose concentration. Blood serum was also analyzed for blood urea nitrogen and creatinine concentrations.

Statistical analysis of the data was performed using one-way ANOVA followed by pair wise comparison of probabilities (*Bonferroni correction*) according to Snedecor and Cochran (1980). Data were represented as means \pm standard deviations (SD). The difference was considered significant at $P \leq 0.05$.

RESULTS

Table 1 revealed that there were no significant differences among groups in regard to the weight or age of camels. Heart rate was decreased significantly from 15 through 120 minutes after IV administration of the three

doses of romifidine (table 1). Twenty four beats/ minute was the lowest rate recorded. Effects on respiratory rate varied during the period from induction of sedation till the recovery in the three tested doses. However, the changes in respiratory rates were not statistically significant (table 1). Changes in rectal temperature were also not statistically significant (table 1). Auscultation of the rumen showed a significant decrease in ruminal movement from 15 through 120 minutes after administration of 40 and 80 µg/kg doses and from 15 through 180 minutes after IV administration of 120 µg/kg dose of romifidine (table 1). One movement / 5 minutes was the lowest rate recorded. Head height was decreased significantly from 15 through 120 minutes after administration of 40 and 80 µg/kg doses and from 15 through 180 minutes after IV administration of 120 µg/kg dose of romifidine (table 1). Response to auditory stimulation was significantly decreased from 15 through 90 minutes after administration of 40 µg/kg dose and from 15 through 120 minutes after IV administration of 80 and 120 µg/kg doses of romifidine (table 1). Distance between the ear tips was significantly increased from 15 through 120 minutes after IV administration of the 3 doses of romifidine (table 1). The response to tactile stimulation was decreased significantly from 15 through 90 minutes after

administration of 40 and 80 µg/kg doses and from 15 through 120 minutes after IV administration of 120 µg/kg dose of romifidine (table 1). Degree of ataxia was increased significantly (i.e., ataxia score was decreased significantly) from 15 through 60 minutes after administration of 40 µg/kg dose, from 15 through 90 minutes after administration of 80 µg/kg dose and from 15 through 120 minutes after administration of 120 µg dose of romifidine (table 1). IV injections of romofidine induced apparent sedative effect within 2, 3 and 6 minutes at dose rates of 120, 80 and 40 µg/kg respectively. All animals remained calm and appeared to be unaware of their surroundings. Drooping (ptosis) of the lower lip, head, upper eyelid and external concha of the ear, deviation of the neck and hanging of the tongue out of the mouth were recorded (Fig. 1-4). Variable degrees of sedation were induced; the degree of sedation was more or less dose dependant and rated from mild to deep. Although all camels remained in a standing position after administration of romifidine in a dose of 40 or 80 µg/kg. Camels which received 120 µg/kg revealed sternal recumbency within 20 minutes (Fig. 5). The depth of sedation induced by 120 µg/kg dose (score 4) was greater than that induced by either 40 µg/kg (score 2) or 80 µg/kg (score 2&3) doses (table 2). The sedative

effect persisted for 38.42 ± 3.12 , 52.25 ± 4.59 and 66.75 ± 4.33 minutes after IV injection of romifidine at 40, 80 and 120 $\mu\text{g}/\text{kg}$ respectively.

The period of analgesia was shorter than the period of sedation (table 2). The analgesic effect persisted for 22.50 ± 7.83 , 33.75 ± 9.32 and 46.25 ± 4.33 minutes after IV injection of romifidine at 40, 80 and 120 $\mu\text{g}/\text{kg}$ respectively. IV administration of romifidine in a dose of 40 $\mu\text{g}/\text{kg}$ induced poor analgesic effect which ranged from 0 (no obvious analgesia) to grade 1 (mild analgesia). The analgesic effect of 80 $\mu\text{g}/\text{kg}$ induced moderate analgesic effect (grade 2), while the analgesic effect of 120 $\mu\text{g}/\text{kg}$ was excellent (grade 3) as indicated by lack of response to painful and electrical stimulations.

No adverse reactions were observed at administration site. Cardiac arrhythmias were detected in 4 camels after administration of the

3 doses of romifidine. Arrhythmias were first detected 15 minutes after administration of romifidine and presented for 15 to 20 minutes. Mild salivation and lacrimation were also detected. Protrusion of the penis was not observed in any animal. Frequent urination commencing about 60-90 minutes after administration of romifidine was observed along this study. All camels urinated more than once (range 2-5 times). Head edema following 120 $\mu\text{g}/\text{kg}$ doses was observed in 2 camels. IV administration of the three different doses of romifidine did not reveal significant changes in most of the hematological and biochemical values (Hb %, PCV %, WBCs and RBCs counts and blood creatinine or blood urea nitrogen levels). A significant hyperglycemia was observed 15 minutes after romifidine administration (table 3). The increased blood glucose was recorded till the time of recovery.

Table 1:- Changes in clinical parameters of camels given different doses of romifidine IV (Mean \pm SD)

| parameter | Dose | Time after administration (min) | | | | | | | |
|--|-------------|---------------------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|-----------------------|
| | | 0 | 15 | 30 | 45 | 60 | 90 | 120 | 180 |
| Heart rate (beats /min) | 40 μ g | 44.25 \pm 0.96 | 28.75 \pm 0.96* | 31.0 \pm 3.64* | 33.0 \pm 5.23* | 32.5 \pm 4.8* | 34.75 \pm 4.57* | 37.5 \pm 2.65* | 42.25 \pm 1.89 |
| | 80 μ g | 41.75 \pm 2.06 | 26.0 \pm 2.16* | 26.0 \pm 1.41* | 25.25 \pm 1.5* | 25.25 \pm 1.5* | 31.5 \pm 2.65* | 37.0 \pm 1.63* | 39.0 \pm 2.16 |
| | 120 μ g | 40.5 \pm 2.08 | 27.5 \pm 1.29* | 29.0 \pm 4.08* | 30.5 \pm 5.07* | 29.5 \pm 5.91* | 29.5 \pm 5.69* | 32.25 \pm 4.75* | 37.5 \pm 1.73 |
| Respiratory rate (breaths/min) | 40 μ g | 13.75 \pm 0.5 | 12.75 \pm 2.36 | 13.5 \pm 2.65 | 13.0 \pm 1.41 | 13.75 \pm 0.5 | 14.0 \pm 0.0 | 14.0 \pm 0.0 | 14.0 \pm 0.0 |
| | 80 μ g | 13.5 \pm 0.58 | 14.0 \pm 2.45 | 14.25 \pm 2.99 | 13.25 \pm 1.7 | 10.75 \pm 0.96 | 12.75 \pm 0.5 | 12.75 \pm 0.96 | 13.5 \pm 0.58 |
| | 120 μ g | 13.75 \pm 0.5 | 14.5 \pm 3.11 | 14.25 \pm 2.5 | 14 \pm 2.45 | 14 \pm 1.41 | 13.75 \pm 1.71 | 14 \pm 1.83 | 13 \pm 0.82 |
| temperature | 40 μ g | 37.52 \pm 0.12 | 37.67 \pm 0.09 | 37.72 \pm 0.17 | 37.72 \pm 0.12 | 37.7 \pm 0.14 | 37.7 \pm 0.08 | 37.67 \pm 0.09 | 37.65 \pm 0.1 |
| | 80 μ g | 37.77 \pm 0.09 | 37.9 \pm 0.08 | 37.92 \pm 0.15 | 37.9 \pm 0.14 | 37.7 \pm 0.11 | 37.6 \pm 0.14 | 37.55 \pm 0.17 | 37.57 \pm 0.29 |
| | 120 μ g | 37.72 \pm 0.17 | 37.67 \pm 0.35 | 37.52 \pm 0.35 | 37.57 \pm 0.4 | 37.45 \pm 0.17 | 37.52 \pm 0.15 | 37.47 \pm 0.31 | 37.42 \pm 0.47 |
| Ruminal movement | 40 μ g | 3.25 \pm 0.5 | 1.5 \pm 0.58* | 1.25 \pm 0.25* | 1.25 \pm 0.5* | 1.25 \pm 0.5* | 1.75 \pm 0.5* | 2 \pm 0.0* | 2.5 \pm 0.58 |
| | 80 μ g | 3.0 \pm 0.82 | 1.5 \pm 0.58* | 1.0 \pm 0.0* | 1.0 \pm 0.0* | 1.5 \pm 0.58* | 1.5 \pm 0.58* | 1.75 \pm 0.5* | 2.25 \pm 0.5 |
| | 120 μ g | 3 \pm 0.0 | 1.25 \pm 0.5* | 1.0 \pm 0.0* | 1.25 \pm 0.5* | 1.25 \pm 0.5* | 1.5 \pm 0.58* | 1.5 \pm 0.58* | 1.75 \pm 0.5* |
| Head height (cm) | 40 μ g | 171.0 \pm 2.83 | 62.75 \pm 5.97* | 71.5 \pm 9.47* | 77.5 \pm 8.1* | 81.75 \pm 6.38* | 89.0 \pm 6.38* | 110.0 \pm 4.08* | 163.25 \pm 5.68 |
| | 80 μ g | 170.0 \pm 5.72 | 60.25 \pm 6.75* | 52.0 \pm 2.16* | 62.5 \pm 2.08* | 70.5 \pm 1.73* | 78.0 \pm 3.56* | 89.25 \pm 4.35* | 161.5 \pm 4.51 |
| | 120 μ g | 173.2 \pm 4.65 | 61.25 \pm 4.92* | 51.5 \pm 2.89* | 60.75 \pm 2.06* | 66.0 \pm 3.37* | 75.0 \pm 5.1* | 88.25 \pm 2.87* | 141.0 \pm 11.58* |
| Distance between ear tips (cm) | 40 μ g | 22.75 \pm 1.5 | 28.0 \pm 1.63 | 28.5 \pm 1.00* | 27.0 \pm 1.41 | 26.75 \pm 1.89 | 26.0 \pm 1.41* | 25.25 \pm 0.96* | 24.25 \pm 0.96 |
| | 80 μ g | 21.75 \pm 1.71 | 27.75 \pm 1.71 | 27.75 \pm 1.26* | 27.25 \pm 1.5* | 26.5 \pm 1.29* | 26.25 \pm 1.71* | 25.5 \pm 1.00* | 24.0 \pm 0.82 |
| | 120 μ g | 23.0 \pm 0.82 | 28.25 \pm 2.06 | 28.25 \pm 1.71* | 28.0 \pm 1.41* | 28.25 \pm 1.26* | 27.25 \pm 1.26* | 27.0 \pm 1.41* | 24.75 \pm 1.26 |
| Response to auditory stimulation (0-5) | 40 μ g | 10.0 \pm 0.0 | 2.0 \pm 0.82* | 2.25 \pm 0.50* | 2.75 \pm 0.50* | 4.25 \pm 0.50* | 4.75 \pm 0.50* | 9.25 \pm 0.96 | 10.0 \pm 0.0 |
| | 80 μ g | 10.0 \pm 0.0 | 1.5 \pm 0.58* | 2.25 \pm 0.50* | 3.25 \pm 0.50* | 5.0 \pm 0.82* | 6.25 \pm 0.50* | 8.25 \pm 0.50* | 10.0 \pm 0.0 |
| | 120 μ g | 10.0 \pm 0.0 | 1.25 \pm 0.50* | 1.25 \pm 0.50* | 2.25 \pm 0.50* | 2.75 \pm 0.50 | 4.5 \pm 0.5* | 7.25 \pm 0.50* | 8.25 \pm 0.50 |
| Response to tactile stimulation (0-5) | 40 μ g | 10.0 \pm 0.0 | 3.0 \pm 0.82* | 2.75 \pm 0.50* | 3.5 \pm 0.58* | 3.75 \pm 0.50* | 5.5 \pm 0.58* | 10.0 \pm 0.0 | 10.0 \pm 0.0 |
| | 80 μ g | 10.0 \pm 0.0 | 2.25 \pm 0.50* | 2.75 \pm 0.96* | 3.75 \pm 1.50* | 5.5 \pm 1.29* | 7.0 \pm 0.82* | 9.5 \pm 0.58 | 10.0 \pm 0.0 |
| | 120 μ g | 10.0 \pm 0.0 | 2.5 \pm 1.29* | 2.25 \pm 0.50* | 2.0 \pm 1.41* | 2.5 \pm 0.58* | 5.0 \pm 0.82* | 6.25 \pm 0.50* | 9.5 \pm 0.58 |
| Degree of ataxia (0-5) | 40 μ g | 10.0 \pm 0.0 | 5.25 \pm 0.96* | 6.25 \pm 0.50* | 6.5 \pm 0.58* | 8.25 \pm 0.50* | 10.0 \pm 0.0 | 10.0 \pm 0.0 | 10.0 \pm 0.0 |
| | 80 μ g | 10.0 \pm 0.0 | 2.5 \pm 0.58* | 2.5 \pm 0.58 | 3.25 \pm 0.50* | 5.0 \pm 0.82* | 7.75 \pm 0.50* | 9.75 \pm 0.50 | 10.0 \pm 0.0 |
| | 120 μ g | 10.0 \pm 0.0 | 1.25 \pm 0.50* | 0.75 \pm 0.96* | 1.5 \pm 0.58* | 2.5 \pm 0.58* | 3.5 \pm 0.58* | 5.5 \pm 0.58* | 9.25 \pm 0.96 |

• Significantly ($p \leq 0.05$) different from baseline (0 min) value.

Table 2:- The effect of romifidine on the duration and grade of sedation and analgesia in camels (mean ± SD)

| Dose of romifidine | Sedation | | Analgesia | |
|--------------------|------------|----------------------------|------------|-------|
| | Duration | Grade | Duration | Grade |
| 40 µg/kg | 38.42±3.12 | Mild (score 2) | 22.50±7.83 | 0-1 |
| 80 µg/kg | 52.25±4.59 | Mild –Moderate (score 2-3) | 33.75±9.32 | 2 |
| 120 µg/kg | 66.75±5.14 | Deep (score 4) | 46.25±4.33 | 3 |

Table 3- Effect of romifidine on some hematological and biochemical parameters in camels (means± SD).

| Parameter | Dose | Time after administration (min) | | | | | |
|-----------------------|--------|---------------------------------|------------------|------------------|------------------|------------------|------------------|
| | | 0 | 15 | 30 | 60 | 120 | 180 |
| Glucose mmol/L | 40 µg | 5.05 ±0.69 | 5.81 ±0.51 | 6.08 ±0.56 | 7.63 ±0.57* | 7.83 ±0.52* | 7.76 ±0.89* |
| | 80 µg | 5.87 ±0.61 | 7.12 ±0.67* | 7.79 ±0.86* | 9.59 ±1.6* | 10.06 ±1.57* | 10.43 ±1.82* |
| | 120 µg | 5.8 ±1.25 | 8.5 ±1.32* | 8.8 ±1.91* | 9.46 ±2.02* | 10.09 ±1.96* | 10.65 ±1.81* |
| Creatinine mmol/L | 40 µg | 156.7 ±3.09 | 156.62 ±12.51 | 155.22 ±9.67 | 149.0 ±15.33 | 153.85 ±6.57 | 152.8 ±5.04 |
| | 80 µg | 158.77 ±7.8 | 167.22 ±16.62 | 157.12 ±11.36 | 158.07 ±13.58 | 156.05 ±11.58 | 156.45 ±9.52 |
| | 120 µg | 142.87 ±15.22 | 153.2 ±17.68 | 152.6 ±13.58 | 156.6 ±15.14 | 155.35 ±13.62 | 153.45 ±11.57 |
| Total protein gm/dl | 40 µg | 6.8 ±0.81 | 6.15 ±1.2 | 7.08 ±0.06 | 7.2 ±1.7 | 6.5 ±0.22 | 6.3 ±0.51 |
| | 80 µg | 6.44 ±0.22 | 6.77 ±1.2 | 5.8 ±0.36 | 6.5 ±0.18 | 6.6 ±0.50 | 6.8 ±0.55 |
| | 120 µg | 7.03 ±0.66 | 6.4 ±0.45 | 6.18 ±0.1 | 6.03 ±0.28 | 6.1 ±0.33 | 6.17 ±0.37 |
| RBC 10 ⁶ | 40 µg | 10.87 ±0.55 | 9.4 ±1.7 | 8.6 ±1.05 | 8.7 ±0.66 | 8.8 ±0.71 | 8.5 ±0.91 |
| | 80 µg | 6.91 ±0.27 | 8.4 ±1.71 | 7.16 ±0.66 | 7.5 ±0.66 | 7.02 ±0.77 | 6.9 ±0.44 |
| | 120 µg | 7.6 ±0.46 | 7.44 ±0.66 | 7.2 ±0.88 | 7.28 ±0.67 | 7.5 ±0.56 | 7.5 ±0.44 |
| Hb gm/dl | 40 µg | 11.1 ±0.66 | 10.95 ±0.88 | 9.2 ±1.7 | 8.9 ±0.71 | 8.8 ±0.82 | 9.1 ±0.66 |
| | 80 µg | 8.4 ±1.0 | 8.6 ±1.88 | 8.77 ±1.33 | 9.4 ±1.22 | 9.02 ±1.4 | 8.9 ±1.33 |
| | 120 µg | 10.3 ±0.87 | 10.1 ±0.95 | 9.6 ±0.88 | 9.2 ±0.8 | 9.4 ±0.55 | 10.0 ±0.77 |
| PCV % | 40 µg | 24.0 ±1.7 | 22.0 ±1.9 | 21.0 ±2.1 | 22.0 ±0.6 | 22.0 ±0.76 | 21.5 ±2.1 |
| | 80 µg | 23.0 ±0.6 | 24.0 ±0.99 | 22.0 ±1.6 | 22.5 ±1.2 | 22.0 ±0.88 | 21.0 ±1.3 |
| | 120 µg | 21.0 ±1.2 | 23.0 ±0.88 | 21.6 ±1.8 | 24.0 ±6.3 | 22.0 ±2.0 | 21.0 ±1.0 |
| WBC X 10 ³ | 40 µg | 13.0 ±3.9 | 11.5 ±3.4 | 15.2 ±4.8 | 15.0 ±2.66 | 14.8 ±5.6 | 14.0 ±5.1 |
| | 80 µg | 11.6 ±5.2 | 12.2 ±0.8 | 9.9 ±2.75 | 11.3 ±3.9 | 11.1 ±4.1 | 9.5 ±2.28 |
| | 120 µg | 11.2 ±0.39 | 9.2 ±0.55 | 10.1 ±3.1 | 10.5 ±5.4 | 9.1 ±2.2 | 8.9 ±1.67 |

*Significantly (p≤0.05) different from baseline (0 min) value.

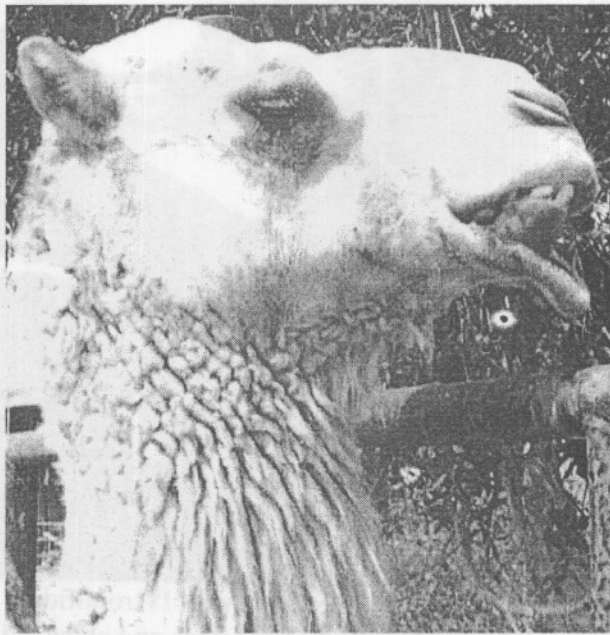


Fig. (1): The sedative effect of romifidine in a camel (drooping of the lower lip, upper eyelid and external concha of the ear).

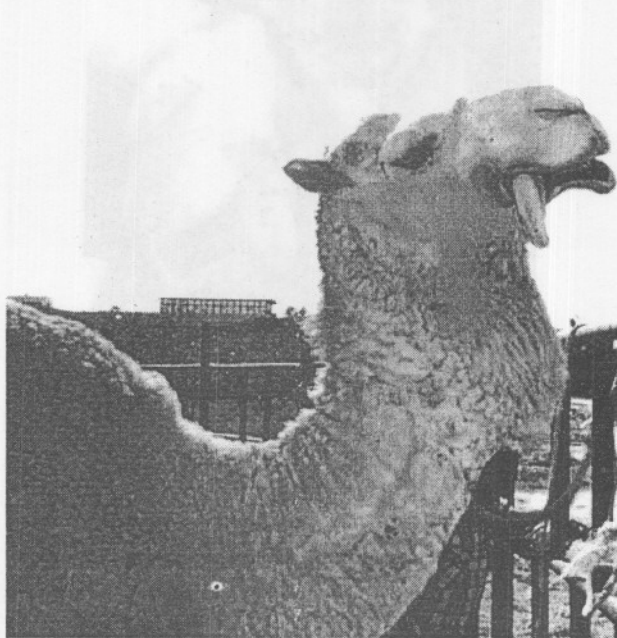


Fig. (2): The sedative effect of romifidine in a camel (hanging of the tongue outside the mouth).

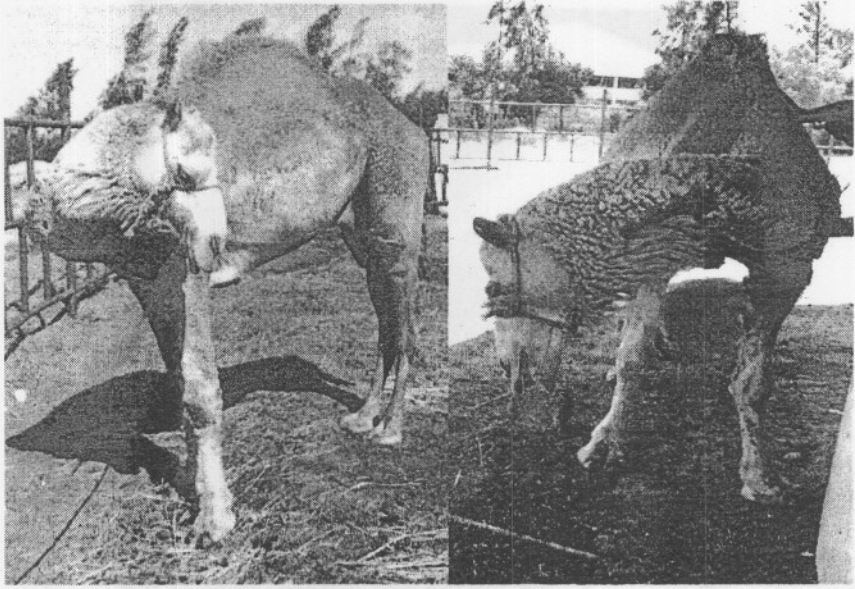


Fig. (3&4): Two camels after sedation with IV romifidine. Notice the drooped head, deviated neck and abducted limb.



Fig. (5): A camel in a sternal recumbency 30 minutes after IV administration of romifidine ($120 \mu\text{g}/\text{kg}$ b.wt.).

DISCUSSION

The need for knowledge of anesthetics and skills in their administration has a great value for veterinarians working in camel practice. The use of drugs to produce sedation as well as analgesia in camel clinical practice is mandatory either for some routine examinations or for many surgical interventions. Alpha 2-adrenoceptor agonists are frequently used in clinical veterinary medicine for calming animals, as well as for premedication because of their sedative, analgesic and muscle relaxant effects (Maze and Tranquilli, 1991). Xylazine and detomidine are used in camel practice (Denning, 1972; Bolbol et al., 1980 and White et al., 1987). While many clinicians still prefer IM route of administration, IV administration of alpha 2-adrenoceptor agonists gave the most reliable sedation and rapid onset of action. This might be due to the variability in the response which may be influenced in part by unpredictable drug absorption from the IM administration site, a finding which was supported by Short, 1992 and Hall et al., 2001. The pre-treatment (baseline) values for all measured variables were within normal limits for camel indicating that the camels were healthy and calm at the time of administration of the drug. IV administration of romifidine induced a significant decrease in heart rate

(England et al., 1992; Gasthuys et al., 1996; Amarpal et al., 2002 and Kinjavdekar et al., 2006). Bradycardia following administration of alpha 2- adrenoceptor agonists might be due to central stimulation that mediated through the vagus nerve (Hall et al., 2001). No significant effects on rectal temperature and respiratory rate of treated camels were observed after IV administration of the three doses of romifidine, a result which was in agreement with that reported by Kerr et al., 1996; Prado et al., 1999 and Selmi et al., 2004). The analgesic effect of romifidine in camels was nearly dose dependant, while the low dose (40 µg/kg) showed mild analgesic effect, the higher doses (80&120 µg/kg) revealed moderate to deep analgesic effect respectively. These results coincide with those of Celly et al., 1997 and Fierheller et al., 2004. A significant decrease in the ruminal movement of camels receiving romifidine was observed during this study. A similar inhibition of ruminal contractions induced by romifidine was observed in goats by Van Miert et al., 1994. Salivation was mild in the three tested dosages in this study. Similar finding was recorded by Fierheller et al., 2004 in cattle. Head height appeared to be an excellent indicator of the sedative effects of alpha 2-adrenoceptor agonists because it reflects muscle relaxation and awareness reduction. The reported significant decrease in

the auditory responses associated with romifidine, suggested that rapid and profound sedation was achieved following IV administration of romifidine. These results agree with those reported by Freeman and England 1999. In regard to the degree of ataxia, the results revealed that the high dose was associated with high degree of ataxia, a result that concurs with Short, 1992. The marked increase in urine production after administration of alpha 2-adrenoceptor agonists may be due to inhibition of antidiuretic hormone (ADH) release and hyperglycemia, a result which was in agreement with Hall et al., 2001. The absence of penis protrusion even in deeply sedated camels was consistent with the result observed after sedation of camels with xylazine (Khamis et al., 1973) and detomidine (El-Maghraby and Alqudah, 2005). This finding may be attributed to some anatomical features; where the preputial orifice of the dromedary is relatively narrow and surrounded by muscular tissue of the prepuce, which are directed backwards enabling the protrusion of the penis only in its erected state (Khamis et al., 1973 and El-Maghraby and Alqudah, 2005). The significant hyperglycemia seen following romifidine administration concurs with the result reported after camel sedation with

xylazine or detomidine (Penshin et al., 1986 and El-Maghraby and Alqudah, 2005). It may be attributed to an increase in adrenergic activity, decrease in the secretion and/or effects of insulin or increase in the secretion and/or effects of glucagons (Ali et al., 1989). Although, it was proved that alpha 2-adrenoceptor agonists exert a marked pressure increase in the mare uterus, it has not yet been established whether romifidine is safe for use in pregnant camels or other animal species (Schatzman et al., 1994). Further studies evaluating the use of romifidine in combination with other premedications, the cardiopulmonary, hemodynamic and its uterine effect in camels as well as the most effective drug to reverse the effects of romifidine in camels are clearly warranted. In conclusion, the present study demonstrated that IV administration of romifidine seemed to be safe and effective sedative and analgesic agent for camels. Optimal sedation was achieved with IV doses of 80 µg/kg. IV administration of romifidine at a dose rate of 120 µg/kg revealed profound sedation and analgesia. Furthermore, romifidine could be used as a good chemical restraint for a variety of diagnostic and surgical procedures (with local analgesia if necessary) in camels.

REFERENCES

- Ali, B.H. (1988): A survey of some drugs commonly used in the camel. *Veterinary Research Communications*, 12: 67-75.
- Ali, B.H.; El-Sanhouri, A.A. and Musa, B.E. (1989): Some clinical, hematological and biochemical effects of four tranquilizers in camels (*Camelus dromedarius*). *Revue Elev. Med.Vet. Pays Trop.*, 42 (1): 13-17.
- Amarpal; Kinjavdekar. P; Aithal, H.P.; Pawde, A.M. and Pratap. K. (2002): Analgesic, sedative and haemodynamic effects of spinally administered romifidine in female goats. *J Vet Med A Physiol Pathol Clin Med.*, 49(1):3-8.
- Bolbol, A.E.; Hassanein, A. and Ibrahim, H. (1980): Some studies in the camel after sedation with Rompun. *Vet. Med. Rev.*, 1: 55-60.
- Celly, C.S.; McDonell, W.N.; Young, S.S. and Black, W.D. (1997): The comparative hypoxaemic effect of four alpha 2-adrenoceptor agonists (xylazine, romifidine, detomidine and metomidine) in sheep. *J. Vet. Pharm. Ther.*, 20: 464-47
- Custer, R.; Kramer, L. and Kennedy, S. (1977): Hematologic effects of xylazine when used for restraint of Bactrian camels. *J. A. Vet. Med. Assoc.*, 171: 899-901.
- Denning, H.K. (1972): The use of Rompun in the dromedary in diagnostic splenectomy (infection with *trypanosoma evansi/surra*). *Vet. Med. Rev.*, 3/4: 239-242.
- El-Maghraby H.M. and Alqudah, K. (2005): Sedative and analgesic effects of detomidine in camels. *J. of Camel practice and Research*. 12: 41-45.
- England, G.C.; Andrews, F. and Hammond, R.A. (1996): Romifidine as a premedicant to propofol induction and infusion anaesthesia in the dog. *J. Small Anim Pract.*, 37(2):79-83.
- England, G.C. and Clarke, K.W. (1996): Alpha 2 adrenoceptor agonists in the horse a review. *Br Vet J.*, 152(6):641-57.
- England, G. C.; Clarke, K.W. and Goossens, L. (1992): A comparison of the sedative effects of three alpha 2-adrenoceptor agonists (romifidine, detomidine and xylazine) in the horse. *J Vet Pharmacol Ther.*, 15(2):194-201.
- Fahmy, L.S.; Farag, K.A.; Mostafa, M.B. and Hegaazy. A.A. (1995): Propofol anesthesia with xylazine and diazepam premedication in camels. *J. of Camel Practice & Resarch*: 111-113.
- Fierheller, E.E.; Caulkett, N.A. and Bailey, J.V. (2004): A romifidine and morphine combination for epidural analgesia of the flank in cattle. *Can Vet J.*, 45(11): 917-923.
- Fouad, K. A. (2000): Camel surgery and anesthesia. *Egypt J. Vet Sci.* 34: 1-10.
- Freeman, S.L. and England, G. C. (1999): Comparison of sedative effects of romifidine following intravenous, intramuscular, and sublingual administration to horses. *Am J Vet Res.*, 60 (8):954-959.
- Gathuys, F.; Martens, A. and Goossens, L. (1996): Quantitative and qualitative study of the diuretic effects of romifidine in the horse. *J.Vet. Anest.*, 23, 6-10.
- Hall, L.W.; Clark, K.W. and Trim, C.M. (2001): *Veterinary anesthesia*. 10th Ed. W. B. Saunders. PP 83-91.
- Jöchle, W. and Hamm, D. (1986): Sedation and analgesia with Domosedan in horses: Dose response studies on efficacy and duration. *Acta.Vet. Scand.* 82:68-84.
- Kerr C.L.; McDonell W. N. and Young S.S. (1996): A comparison of romifidine and xylazine when used with diazepam/ketamine for short duration

- anesthesia in the horse. *Can.Vet.J.*,37(10):601-9.
- Khamis, Y.; Fouad, K. and Sayed, A. (1973): Comparative studies on tranquilization and sedation in camelus dromedarius. *Veterinary Medical Review*, 4: 336-345.
- Kinjavdekar, P.; Aithal, H.P.; Amarpal; Pawde, A.M.; Pratap, K. and Singh, G.R. (2006): Potential effect of romifidine with lidocaine administration in goats. *Small Ruminant Research*, 64: 293-304.
- Maze, M. and Tranquilli, W. (1991): Alpha 2-adrenoceptor agonists: defining the role in clinical anesthesia. *Anesthesiology*, 74:581-601.
- Mohammad, F.K.; Zangana, I.K. and Abdul-Latif A.R. (1995): Reversal of medetomidine sedation in sheep by atipamezole and yohimbine. *Vet Hum Toxicol.*, 37(2):97-9.
- Penshin, P.K.; Nigam, J.M.; Singh, S.C. and Robinson, B.A. (1980): Evaluation of xylazine in camels. *J. Am. Vet. Med. Assoc.*, 177 (9): 875-878.
- Penshin, P.K.; Singh, A.p.; Singh, J.; Chawia, S.K. and Lakharu, J.C. (1986): Acid-base and blood gas changes following xylazine administration in buffalo and camel. *Indian J. of Animal Sc.*, 56 (2): 198-202.
- Prado, M.E.; Streeter, R.N.; Mandsager, R.E.; Shawley, R.V. and Claypool, P.L. (1999): Pharmacologic effects of epidural versus intramuscular administration of detomidine in cattle. *Am J Vet Res.*, 60 (10) : 1242 - 7.
- Raekallio, M.; Kivalo, M.; Jalanka, H. and Vainio, O. (1991): Medetomidine / ketamine sedation in calves and its reversal with atipamezole. *J Vet. Anesthe.*, 18 : 45-47.
- Reibold, T.W.; Kaneps, A.J. and Schmotzer, W.B. (1989): anesthesia in the llama. *Vet. Surg.*, 18: 400-4004.
- Said, A.H. (1972): clinical comparative studies on different tranquilizers in camel. *MVSc Thesis*. Cairo Univ.
- Schatzman U.; Jossfck, H.; Stauffer, J. and Goossens, L. (1994): Effects of alpha 2-adrenoceptor agonists on intrauterine pressure and sedation in horses: comparison between detomidine, romifidine and xylazine. *Zentralbl. Vet. Med. .A.*, 41 (7):523-9
- Selmi, A.L.; Barbudo-Selmi, G.R.; Mendes, G.M.; Figueiredo, J.P. and Lins, B. T. (2004): Sedative, analgesic and cardiorespiratory effects of romifidine in cats. *Vet Anaesth,Analg.*, 31(3) :195-206.
- Short, C. E. (1992): Alpha 2-adrenoceptor agents in animals: sedation, analgesia and anesthesia., 1st Ed. Veterinary practice publishing company, California.
- PP 23Snedecor, G.W. and Cochran, N.G. (1980): *Statistical methods*. The Iowa State University Press, 593.
- Van Miert, A. S.; Faghihi, S. M. and Van Duin, C.T. (1994): Food intake and rumen motility in dwarf goats. Effects of atipamezole on the inhibitory effects induced by detomidine, medetomidine and romifidine. *Vet Res Commun.* 18(6):457-69.
- White, R.J.; Bark, H. and Ball, S. (1986): Halothane anesthesia in dromedary camel. *Vet. Rec.*, 119: 615-617.
- White, R.J.; Ball, S. and Bark, H. (1987): Xylazine and ketamine anesthesia in the dromedary camel under field conditions. *Vet. Rec.*, 120 (5): 110/113

التأثير المهديء والمسكن لعقار الريموفيدين في الجمال

محسن محمد حسن* محمد عبد المنعم**، وسعيد أبو زيد***

قسمى الجراحة - كلية الطب البيطري - جامعة قناة السويس*، جامعة طنطا** وقسم الفسيولوجيا***
كلية الطب البيطري - جامعة قناة السويس.

أجريت هذه الدراسة لتقييم إستخدام مادة الريموفيدين في مجال التخدير في الجمال ذات السنم الواحد. حيث تم حقن ثلاث جرعات مختلفة من ذلك العقار (40 ، 80 ، 120 ميكروجرام/كيلو جرام من وزن الحيوان) في ثلاث مجموعات مختلفة من الجمال حيث تكونت كل مجموعة من ثلاث جمال. وتمت دراسة التأثير المهديء والمسكن وكذلك التغييرات في صورة الدم بصورة منتظمة لمدة 3 ساعات في تلك المجموعات. وقد لوحظ تأثر الجمال بعد فترة تراوحت من دقيقتين إلى ثلاثة دقائق بعد الحقن الوريدي للعقار وظهر ذلك بوضوح من خلال الهدوء الواضح للحيوان بالإضافة إلى بعض العلامات الأخرى مثل إرتخاء وتدلي الشفة السفلى والجفن الأسفل للعين والصوان الخارجي للأذن وترنح الحيوان بصور متفاوتة أدت إلى رقاد الجمال وعدم القدرة على الوقوف في بعض الأحيان (خصوصاً بالنسبة للجرعة الأعلى). وقد أمتدت فترة التهذئة إلى حوالي 38، 52، 66 دقيقة بالنسبة للجرعات الثلاثة على التوالي وتزامن التأثير المهديء مع تأثير تسكينى واضح للعقار وإن كان قد إمتد لفترة أقل إستمرت حوالي 22، 33، 46 دقيقة بالنسبة للجرعات الثلاثة على التوالي. ولقد إختلفت درجة التسكين باختلاف جرعة الريموفيدين وتناسبت معها تناسباً طردياً. ووجد أيضاً أن للعقار تأثير واضح على معدل ضربات القلب التي إنخفضت بصورة معنوية كذلك حركة الكرش وإرتفاع الرأس وإستجابة الأذن للمؤثرات الخارجية. بينما لوحظ إرتفاع ملحوظ في درجة الهزاع والمسافة بين نهاية الأذنين. وبإستثناء إرتفاع نسبة السكر بالدم فإنه لا توجد فروق ذات دلالة معنوية في تحليل صورة الدم على مستوى الجرعات الثلاثة المختبرة.

ولقد تبين أن جرعة 80 ميكوجرام/كيلو جرام نو فاعلية عالية في السيطرة على الجمال وفحصها بدون مضاعفات جانبية وتؤدي إلى مستوى عالي من التسكين يسمح بإجراء بعض التدخلات الجراحية.