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Clinical Use of Tramadol and Xylazine in Dromedary Camel Undergoing Soft Tissue Surgeries

[2]A.Y. Al-Taher, [1]M.K. Zabady, [1]A.I. Almubarak, [2]M. Ismail and [1]R.O. Ramadan
[1]Department of Clinical Studies,
[2]Department of Physiology, Biochemistry and Pharmacology,
College of Veterinary Medicine and Animal Resources,
Camel Research Centre, King Faisal University, Al-Hofouf, Saudi Arabia

Abstract: This study was conducted to evaluate the analgesic and sedative efficacy of the combination of tramadol-xylazine used in six dromedary camels underwent soft tissue surgeries and premidicated with Intravenous (IV) 0.2 mg kg^{-1} of xylazine. The combination was induced IV with 2.0 mg kg^{-1} of tramadol and 0.2 mg kg^{-1} of xylazine, IV top-up of the combination of the same original doses was injected whenever the analgesia was inadequate or when surgical stimulation provoked movement. A surgically satisfactory analgesia was achieved and maintained in all camels by this combination except in two camels that underwent perineal laceration and castration showing signs of distress and pain as the injection dose was insufficient even after a supplemental dose at the same original dose was administered. Mean time±SD from administration of the combination of tramadol-xylazine until end of operation was 39.5±10.1 min. This study concludes that the combination of tramadol-xyalzine was effective and safe to use in camels and suggests that combination can be improved upon by combining with local analgesic drug to achieve adequate depth of analgesia.

Key words: Camel, tramadol, xylazine, analgesia, anaesthesia, surgery

INTRODUCTION

Tramadol, a synthetic opioid is an analgesic with mixed opioid and nonopioid activities (Garrido *et al*., 2000). The nonopioid activity is achieved through indirect activation of postsynaptic alpha-2-adrenoreceptor, blocking impulses reaching the brain (Duthie, 1998). Tramadol has been used in veterinary anaesthesia as a pre-anaesthetic (Kongara *et al*., 2012) to improve the quality of anaesthetic induction and to improve the characteristic of recovery (Ajadi *et al*., 2009). The sedative and antinociception of tramadol were evaluated in camels (Al-Mubarak, 2013) where significant effects on sedation and nociceptive thresholds were observed. Xylazine is an alpha2-adrenoceptor agonist used commonly as sedative in veterinary anaesthesia (England and Clarke, 1996). It is considered the most common premedication used in camels (Al-Mubarak *et al*., 2008). It produces respiratory depression, bradycardia, initial hypertension followed by a prolonged hypotension and decreased cardiac output due to sympathetic blockade and vagal stimulation (Clarke and Hall, 1969; Maze and Tranquilli, 1991; Wagner *et al*., 1991). In camels, no studies have been reported on the combined use of tramadol and xylazine.

Therefore, the objective of this study was to evaluate the sedative and analgesic efficacy of this combination in camels undergoing soft tissue surgeries.

MATERIALS AND METHODS

Six dromedary camels of two breeds, 5 Majaheem and 1 Magateer, 4 females, 2 males were admitted in the Veterinary Teaching Hospital of the King Faisal University and were scheduled to undergo general soft tissue surgery. Mean age±SD of the animals was 5.3±3.9 years (range 3 months to 12 years) and their mean weight±SD was 473.3±273.6 kg (range 100-750 kg). Types of surgeries carried out were 2 ovarian cyst removal, 1 oesophageal obstruction, 1 perineal laceration, 1 rectovaginal fistula and 1 castration. Food but not water was with held for 48-72 h before surgery. Camels were restrained manually in sternal recumbency before an initial physical examination was performed. Xylazine (Rompun, Bayer, Turkey) as a single IV dose of 0.2 mg kg^{-1} was administered into the jugular vein. Camels were then positioned as required for surgery, the hair over the area of surgery was shaved and the skin was prepared for aseptic surgery. Approximately, 25 min after

Corresponding Author: A.Y. Al-Taher, Department of Clinical Studies, College of Veterinary Medicine and Animal Resources, Camel Research Centre, King Faisal University, Al-Hofouf, Saudi Arabia

pre-anaesthetic medication, a single dose combination of tramadol (Tramal, Grunenthal GmbH, Aachen, Germany) 2.0 and xylazine 0.2 mg kg^{-1} was administered IV. Baseline heart rate (manually by a stethoscope) and respiratory rate (counting thoracic movements) were assessed. These parameter values were further recorded at 5 min After Xylazine (AX) administration and at 5 min and then at every 10 min after Tramadol-Xylazine Administration (AXT) until the end of surgery. Surgery started 3-6 min after injection of the combination. Adequate level of sedation and analgesia was thought to be obtained when a camel shows no signs of resistance and when spontaneous movement or reflex responses to surgical interference were absent. The IV top-up of tramadol-xylazine of the same original doses was injected whenever the analgesia was inadequate or when surgical stimulation provoked movement. All data are listed as mean (±SD) unless otherwise indicated.

RESULTS AND DISCUSSION

Mean heart rate and respiratory rate measurements are presented in Table 1. Mean heart rate decreased after premedication with xylazine but returned to baseline after tramadol-xylazine administration and remained stable during operation. Mean respiratory rate did not differ as compared to baseline. Xylazine 0.2 mg kg^{-1} made an adequate pre-operative sedation and camel preparation. A surgically satisfactory analgesia was achieved and maintained in all camels by this combination, except in two camels (the perineal laceration and the castration) showing signs of distress and pain as the injection dose was insufficient even after a supplemental dose at the same original dose was administered. Mean time±SD from administration of the combination of tramadol-xylazine until end of operation was 39.5±10.1 min. Quality of recovery was evaluated as good in all patients as it was smooth and uneventful.

The increased knowledge of action of sedatives and analgesics drugs that are appropriate for camel practice is essential to decrease the risks in camel under going surgery. Combinations of drugs are often used in anaesthesia to make use of their individual characteristics and to minimize the dose of each drug. This requires an understanding of each drug and its actions in combination with other agents (Nunes *et al*., 2004).

Alpha-2 agonists may be combined with opioids to produce neurolepanalgesia that characterized by inattentiveness to the surrounding environment and profound analgesia (LeBlanc, 1991). Tramadol is both a weak opioid agonist with selectivity for the μ-receptor and a weak inhibitor of the reuptake of noradrenaline and serotonin. This dual mechanism of action may be attributed to the 2 enantiomers of racemic tramadol. The (+)-enantiomer has a higher affinity for the μ-receptor and is a more effective inhibitor of serotonin reuptake whereas the (−)-enantiomer is a more effective inhibitor of noradrenaline reuptake and increases its release by autoreceptor activation. Tramadol is extensively metabolised in the liver with the O-desmethyl (M1) metabolite of tramadol having a 200 fold higher affinity for opioid receptors than the parent drug (Scott and Perry, 2000). M1 is likely the principle reason for the analgesic effect produced by tramadol (Seo *et al*., 2011). In camels, the M1 was found to be the main metabolite following IV tramadol (Elghazali *et al*., 2008) which explain the significant effects on sedation and nociceptive thresholds observed in camels after tramadol administration in previous study (Al-Mubarak, 2013).

The tramadol dose of 2.0 mg kg^{-1} used in this study were based on previous studies on intravenously administered tramadol in healthy camel (Elghazali *et al*., 2008; Al-Mubarak, 2013) which is within recommended doses in other species that range from 1.5-3 mg kg^{-1} in dogs (Seddighi *et al*., 2009), 2.0-3.0 mg kg^{-1} in horses (Dhanjal *et al*., 2009) and 2.0-4.0 mg kg^{-1} in cats (Pypendop *et al*., 2009).

Heart rate decreased in this study following sedation with IV 0.2 mg kg^{-1} xylazine administration which is a typical effect of alpha-2 adrenergic agonists (Maze and Tranquilli, 1991; Wagner *et al*., 1991) due to sympathetic blockade and vagal stimulation. Mean heart rate returned to baseline after tramadol-xylazine administration and remained stable during operation. This is in agreement with previous results that showed tramadol is substantially haemodynamically stable (Duthie, 1998), although, transient haemodynamic effects characterized by a moderate increase in blood pressure have been recorded after IV administration in human (Muller *et al*., 1982). Tramadol causes less respiratory depression compared with morphine in human (Vickers *et al*., 1992).

Table 1: Mean values±SD of Heart Rate (HR) beats min^{-1} and respiratory rate (f_R) at the Baseline (BL) at 5 min after Xylazine Administration (5AX) at 5 min after Xylazine-Tramadol administration (5AXT) and 10-50 min after xylazine-tramadol administration

	Time (min)							
Variables	BL (n:6)	5AX (n:6)	5AXT (n:6)	10 (n:6)	20 (n:6)	30 (n:5)	40 (n:3)	50 (n:1)
HR	47.5±16.2	38.6±11.2	43.6±10.3	46.3±10.3	42.3±9.8	46.8±18.6	54.6±27.2	38
f_R	17.5±6.40	18.7±8.60	17.3±4.30	13.7±4.10	18.8±6.5	17.0±5.30	18.3±4.90	16

n: number of animals

However, mean respiratory rate in this study did not differ as compared to baseline except at 10 min after tramadol-xylazine administration in which may have been primarily caused by xylazine. It is not known whether this combination in this study is associated with cardiorespiratory depression or stimulation as arterial catheterization is problematical in this species due to their thick skin and muscle layers and so monitoring arterial blood gases and direct arterial blood pressure measurement was not carried out in this clinical study.

CONCLUSION

The quality of maintenance of surgical analgesia by this combination in this study was satisfactory for general soft tissue surgeries but inadequate for other soft tissue in regions that are rich in nerves (e.g., genital region) and exhibit sever pain during surgery. This research study was limited by the small number of cases but in conclusion it has shown that the combinations tramadol-xyalzine was effective and safe to use in camels and also suggests this combination can be improved upon by combining with local analgesic drug to achieve adequate depth of analgesia.

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