



RESEARCH ARTICLE

THE EFFICACY OF INTRANASAL ADMINISTRATION OF DEXMEDETOMIDINE, KETAMINE AND MORPHINE COMBINATION TO YOUNG DOGS

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ABSTRACT

The sedative effects of intranasal dexmedetomidine, ketamine and morphine combination were evaluated in young dogs. A combination of 0.1 mg/kg dexmedetomidine, ketamine 20 mg/kg and 0.4 mg/kg morphine was administered by inserting a lubricated catheter in intranasal. The sedation score was classified as 'moderate' from 2 to 10 minutes, 'light' from 10 to 30 minutes, the sedation level was insufficient from 30 to 45 minutes. The dogs were all awake at 45 minutes. Heart rate and rectal temperature did not change significantly from baseline at any time. Respiratory frequency decreased significantly ( $P < 0.05$ ) from baseline. Also SpO<sub>2</sub> progressively dropped 10- 15 minutes when O<sub>2</sub> supplementation was started, increasing significantly. PaCO<sub>2</sub> enhanced significantly ( $P < 0.05$ ) at 10, mins and PaO<sub>2</sub> lessening significantly ( $P < 0.05$ ) at 10, mins compared with baseline value. The intranasal dexmedetomidine-ketamine-morphine combinations has been successfully used for moderate sedation for 10 minutes in young dogs.

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INTRODUCTION

The studies have shown that transnasal route is an effective way to administer sedation and premedication to children (Henderson et al., 1998; Rey et al., 1991; Kendall et al., 2001). It is a easy non-invasive route and rapid onset of action comparable to that of IV administration because of the rich blood supply of the airway mucosa and bypassing the first pass hepatic metabolism. Also, this route is not painful and does not require trained personnel (Hadley et al., 2004). Intranasal administration may be an acceptable route of administration for bird (Vesal and Eskandari, 2006; Vesal and Zare, 2006; Moghadam et al., 2009; Mans et al., 2012), tortoise (Schnellbacher et al., 2012), dog (Eagleson, 2012), cat (Marjani, 2015) and rabbits (Robertson and Eberhart 1994). Limited information is available on dogs (Eagleson, 2012). Intranasal administration of midazolam gel was superior to both intranasal and rectal administration of midazolam solution with respect to peak plasma concentration and bioavailability (Eagleson, 2012). Dexmedetomidine is specific  $\alpha_2$  adrenoreceptor agonist that has both sedative and analgesic effects and reduction of anesthetic requirements together with increased hemodynamic.

The cardiovascular and respiratory depressant effects of dexmedetomidine have been studied in dogs by Murrell and Hellebrekers (2005). Dexmedetomidine can be effectively administered via the intranasal route in humans and animals (Yuen et al., 2008, Schnellbacher et al., 2012). Ketamine hydrochloride produces dissociative anaesthesia that is characterized by catatonic, amnesia and analgesia with or without actual loss of consciousness. Morphine, produce their pharmacological actions, including potent analgesia, as shown by its intranasal administration in humans (Kendall et al., 2001). But clinical trials that investigate the sedative effect of a mixture of intranasal dexmedetomidine, ketamine and morphine are absent in young dog. The aim of this study was to investigate the analgesic and sedative effect of intranasal dexmedetomidine, ketamine and morphine combinations in young dogs.

MATERIALS AND METHODS

Experiment was conducted in the Animal Hospital of Veterinary Faculty of the Firat University of Turkey in accordance with usual guidelines. Experiments were performed five young dogs (male), four to eight weeks of age and body weight of 2-5 kg. A combination of 0.1 mg/kg dexmedetomidine (Precedex 100µ/ml, Meditera, US), ketamine 20 mg/kg (1ml/100mg, Ketasol, Richter Pharma Ag, Austria)

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**Table 1. Effects of combination of Dexmedetomidine, Ketamine and morphine intranasal anesthesia on hematological and clinical parameters in dogs**

Time (mins)	0	5 mins	10 mins	15 mins	20 mins	25 mins	30 mins	35 mins	40 mins	45 mins
RT	38±0.6	38±0.4	38±0.5	38.8±0.8	38.6±0.6	38.5±0.5	38.4±05	38.3±06	38.1±02	38±0.5
HR	82±22	78±23	86±24	73±23	76±24	75±22	74±18	72±22	170±21	73±23
RR	300±8	28±12	25±21*	24±24*	20±18*	20±21*	22±22*	23±21*	24±23*	28±24*
SpO <sub>2</sub>	97± 5	93± 12	90±8*	87±7*	87±8*	92± 12	93± 14	94± 11	94± 8	95± 12
PaCO <sub>2</sub>	61±6			71±8*			66±5			63±4
PaO <sub>2</sub>	96±12			86±12*			92±13			94±11

Values are expressed as mean ± SD, n = 8; \*Values decreased significantly (P<0.05) from baseline.

and 0.4 mg/kg morphine (1ml/10mg, Morphine HCL, Galen, Turkey) was administered by inserting a lubricated catheter in intranasal. The level of sedation was assessed by recording the dog's position, the loss of the righting reflex, the palpebral reflex and reactions to other stimuli using a modified numeric rating scale (0–12) for rabbits (Raekallio *et al.*, 2002). This individual sedation score was assessed every 5 minutes by the same operator in all dogs and was classified as light (0–3), moderate (4–7) or deep (8–12). Analgesia was scored by the pedal withdrawal reflex (PWR) on a 0–2 scale as part of the sedation score. Rectal temperature (RT, °C), and heart (HR, beats/min), SPO<sub>2</sub> (%) and respiratory rates (RR, breaths/min) were recorded pre anesthesia and 5 minutes intervals. The respiratory rate was determined by direct observation of the thoracic movements. Vital parameters (heart rate, rectal temperature and SPO<sub>2</sub>(%)) were continuously monitored by a multiparametric monitor (Sino-Hero S80 VET China). The blood samples were taken at cephalic vein at 0,10, 20, 40 minutes period during sedation in EDTA injectors and later analyzed. The parameters assessed were venous blood gases (PaCO<sub>2</sub>, PaO<sub>2</sub>), by analysed a portable blood gas analyser (Edan I15 VET China).

Statistical analysis: The data for parametric or nonparametric observations analyzed using IBM SPSS 22 Statistics program. The data were presented as the mean ± SE. Significance was accepted at P<0.05.

## RESULTS

Normally distributed data are expressed as the mean \_ SD, whereas non-parametric data are reported as the median (range), as summarized in Table 1. The sedation score was classified as 'moderate' from 2 to 10 minutes, 'light' from 10 to 30 minutes, the sedation level was insufficient from 30 to 45 minutes. The dogs were all awake at 45 minutes. Heart rate and rectal temperature did not change significantly from baseline at any time. Respiratory frequency decreased significantly (P<0.05) from baseline. Also SpO<sub>2</sub> progressively dropped 10-15 minutes when O<sub>2</sub> supplementation was started, increasing significantly. PaCO<sub>2</sub> enhanced significantly (P<0.05) at 10, mins and PaO<sub>2</sub> lessening significantly (P<0.05) at 10, mins compared with baseline value.

## DISCUSSION

In the present study, we demonstrated that intranasal dexmedetomidine-ketamine-morphine combinations can provide sedation sufficient for completing routine clinical

examinations (radiological and physical ) in young dogs. Nasal catheterization is difficulty performed in dogs. The analgesic effect of intranasal dexmedetomidine-ketamine-morphine combinations in the present study was lower than reported in previous dog studies with midazolam gel. Also the sedation score was classified as moderate time to take short. Intranasal dexmedetomidine-ketamine-morphine combinations decreased the respiratory rate in dogs but had no significant effect on health rate and rectal temperature. In this study, respiratory frequency was severely reduced, although hypoxemia was lessened by O<sub>2</sub> supplementation. Significant changes in venous oxygen saturation (SpO<sub>2</sub>) and partial saturation (PaO<sub>2</sub>) have been observed 10-15 minutes in dog. The intranasal dexmedetomidine-ketamine-morphine combinations has been successfully used for moderate sedation in young dogs, as it avoids the discomfort associated with IV or IM injection.

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