ISSN: 0976-3031

Available Online at http://www.recentscientific.com

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 8, Issue, 7, pp. 18896-18898, July, 2017

International Journal of Recent Scientific Research

DOI: 10.24327/IJRSR

Research Article

CLINICO-PHYSIOLOGICAL EFFECTS OF ROMIFIDINE-KETAMINE COMBINATION IN DOG

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DOI: http://dx.doi.org/10.24327/ijrsr.2017.0807.0588

ARTICLE INFO

Article History:

Received 16th April, 2017
Received in revised form 25th May, 2017
Accepted 23rd June, 2017
Published online 28th July, 2017

Key Words:

Romifidine, Ketamine, Dog.

ABSTRACT

Ten clinically affected dogs of either sex and different age groups were divided into two groups consisting of five in each. Intramuscular injection of romifidine @ 30 µg/kg body weight and ketamine @ 5 mg/kg body weight was injected to group I and romifidine @ 40 µg/kg body weight along with ketamine @ 5 mg/kg body weight to group II. The induction time of 8.40 ± 0.24 minutes and 5.80 ± 0.37 minutes; duration of anaesthesia of 64.40 ± 0.81 minutes and 76.20 ± 0.96 minutes and recovery time of 86.40 ± 0.74 and 94.40 ± 0.67 minutes were recorded in group I and II respectively. Complete analgesia was present in group II. All the animals exhibited muscle relaxation, cessation of tail movement and salivation. Smooth induction and recovery were recorded in both the groups. In both groups heart rate, respiration rate, rectal temperature, tidal volume, minute volume and oxygen saturation decreased significantly ($p < 0.05$). Mean arterial pressure increased significantly ($p < 0.05$) in both the groups. Based on the observation, romifidine @ 40 µg/kg body weight and ketamine @ 5 mg/kg body weight could be recommended for surgical procedures. Romifidine @ 30 µg/kg body weight and ketamine @ 5mg/kg body weight is suggestive for minor surgical procedure.

INTRODUCTION

α-$_2$ adrenoceptor agonists have widely been used in veterinary medicine for their central effects of profound sedation, analgesia and muscle relaxation which can be easily reversed by use of its antagonists. Romifidine, a potent α-$_2$ adrenoceptor agonist, produces dose dependent analgesia (Figueiredo *et al.* 2005) and the antinociceptive effect is more pronounced than xylazine (Christovao *et al.* 2006). Romifidine causes bradycardia and apnoea (Freeman *et al.* 2002) and it is equally efficacious by intravenous, intramuscular or subcutaneous route. (England and Thompson, 1997). However, as per the available literature regarding the effects of romifidine in dogs indicates insufficient information, the present study was undertaken to study the clinico-physiological effects of romifidine-ketamine combination in dogs.

MATERIALS AND METHOD

Ten mongrel dogs of either sex weighting 10-12 kg were considered for the study. All the animals were randomly divided into two groups consisting 5 in each and prepared by withholding food for 12 hours and water for 6 hours prior to anaesthesia. Group I received romifidine @ 30 µg/kg body weight along with ketamine @ 5 mg/kg body weight intramuscularly. All the animals of group II received romifidine @ 40 µg/kg body weight and ketamine @ 5 mg/kg body weight intramuscularly. Following injection of anaesthetics, clinical parameters such as induction time, duration and depth of anaesthesia, recovery time, analgesia and degree of muscle relaxation were recorded in both the groups. Induction time was assessed by the time required from injection of anaesthesia to lie down. Duration of anaesthesia was considered as the time of onset of anaesthesia to the raising of the head. Depth of analgesia was ascertained by observing the cessation of eye reflex, movement of eye ball, jaw relaxation, protrusion of tongue, changing of respiratory pattern, salivation and giving incision for surgery. Recovery time was recorded from the induction time to the standing time. Analgesia was evaluated by pricking the paw with needle. Muscle relaxation was determined by protrusion of tongue and relaxation of jaw and limbs. Physiological parameters such as heart rate (beats/min), respiration rate (breaths/min), rectal temperature (ºC), tidal volume (L), minute volume (L/min), mean arterial pressure (mmHg), oxygen saturation (%) were recorded at 0, 5th, 15th, 30th, 45th, 60th and 90th minutes of post

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injection of anaesthetics. Heart rate was recorded by using stethoscope. Respiration rate was recorded by observing the up and down movement of abdomen for a minute. By inserting a clinical thermometer per rectum the rectal temperature was recorded. Mean arterial pressure was determined by using pressure cuff. Oxygen saturation was determined using pulse oxymeter. Tidal volume and minute volume were recorded using respirometer.

The data were analyzed by using SPSS 16.0 and GraphPad Prism 7.0.

RESULT AND DISCUSSION

In the dogs of group I receiving romifidine @ 30 µg/kg body weight along with ketamine @ 5 mg/kg body weight produced induction time of 8.40 ± 0.24 minutes, duration of anaesthesia of 64.40 ± 0.81 minutes and recovery time of 86.40 ± 0.74 minutes. Group II receiving romifidine @ 40 µg/kg body weight combined with ketamine @ 5 mg/kg boy weight the induction time reduced to 5.80 ± 0.37 minutes while the duration of anaesthesia and recovery time increased to 76.20 ± 0.96 minutes and 94.40 ± 0.67 minutes respectively. This shorter induction time might be due to the dose dependent effect in the degree and duration of sedation. This was in agreement with the findings of Figueiredo *et al.* (2005) following administration of two different doses of romifidine in horses. El-Margharaby *et al.* (2005) also reported dose dependent sedation of romifidine in donkeys.

Corneal, palpebral and paedal reflexes were present in all dogs of group I while absent in group II. Presence of palpebral reflexes following romifidine was also reported by Almubarak (2012) in camels. The dogs of all the groups were in lateral recumbency. It was due to romifidine produced analgesia and muscle relaxation. Findings of the present study was supported by the report of use of romifidine by Villamandos *et al.* (2006) and Redondo *et al.* (2000) in dogs. Cessation of tail movement was observed in both the groups. Similar findings were recorded by Aithal *et al.* (1996) using xylazine an another α_2-adrenoceptor agonist and ketamine combination in goats. Urination was recorded at the end of the study. This might be attributed to the inhibition of production and release of anti-diuretic hormone (ADH) (Cullen, 1996). This was in agreement with the finding of El-Maghraby *et al.* (2005) where he recorded urination after romifidine injection in donkeys.

Heart rate decreased significantly ($p<0.05$) from 79.20 ± 0.37 to 65.80 ± 0.37 beats/minute in group I and from 80.80 ± 0.37 to 61.80 ± 0.37 beats/minute in group II. The maximum reduction of heart rate was observed at 45 minutes of anaesthetic injection and gradually returned to the baseline. Bradycardia was more pronounced in group II which might be attributed to the higher dose of romifidine, as it is known to induce bradycardia attributed to increased parasympathetic tone in heart from the CNS. Significant ($p<0.05$) decrease in heart rate was also reported by Kerr *et al.* (1996) following romifidine injection in horse. This was in agreement with the finding of Moens and Fargotten (1990) following injection of xylazine or medetomidine, an another member of α-$_2$ adrenoceptor agonist group along with ketamine in dogs. Significant ($p<0.05$) decrease in respiration rate was recorded from 26.60 ± 0.92 to 17.40 ± 0.24 breaths/minute in group I and from 28.00 ± 0.31 to 14.80 ± 0.37 breaths/minute in group II. Respiratory depression might be due to the combined effects of anaesthetics in respiratory centre located in medulla oblongata of the brain (Figueiredo *et al.*, 2005). Maximum reduction of respiration rate was observed at 45 minutes post injection which was in accordance to the findings of Francisco *et al.* (2011) with the use of detomidine an another α_2 agonist and ketamine in calves. Rectal temperature decreased significantly ($p<0.05$) from 38.18 ± 0.14 to 37.59 ± 0.04 ^{0}C in group I and 38.50 ± 0.13 to 37.10 ± 0.05 ^{0}C in group II. The decrease in rectal temperature might be due to anaesthetic effects causing decrease in metabolic rate, muscle relaxation and depression of the thermoregulatory centre (Ponder and Clerke, 1980). The findings were in accordance with the report of Luna *et al.* (2000) after administration of romifidine in dogs. Initial increase in rectal temperature was observed at 5 minutes in all the animals which might be attributed to the centralisation of blood volume and peripheral vasoconstriction. Similarly, the initial rise was also reported by Freeman *et al.* (2002) following injection of romifidine in horses. Tidal volume decreased significantly ($p<0.05$) from 0.25 ± 0.03 to 0.17 ± 0.02 L in group I and 0.26 ± 0.05 to 0.16 ± 0.02 L in group II. Reduction of tidal volume might be attributed to the reduction in respiratory rate and increased CO_2 production (Tranquilli *et al.*, 2007). Luna *et al.* (2000) also recorded decreased tidal volume following administration of romifidine in combination with ketamine in dogs. Significant ($p<0.05$) decrease of minute volume was observed from 6.76 ± 0.37 to 3.23 ± 0.07 L/minute in group I and 7.48 ± 0.20 to 2.43 ± 0.07 L/minute in group II. This reduction might be due to the decreased respiration rate and tidal volume. Finding of the present study was in accordance with the report of Luna *et al* (2000) following administration of romifidine and ketamine in dogs. Significant decrease in minute volume following continuous infusion of dexmedetomidine in dogs was also reported by Peter *et al.* (2006). Significant ($p<0.05$) decrease in oxygen saturation was observed from 97.2 ± 0.00 to 94.40 ± 0.40 % in group I and 97.2 ± 0.00 to 93.80 ± 0.37 % in group II. Francisco *et al.* (2011) observed significant ($p<0.05$) decrease in oxygen saturation with the use of detomidine, an another α_2 agonist and ketamine in calves. MAP increased significantly ($p<0.05$) from 77.50 ± 1.04 to 89.75 ± 0.25 mmHg in group I and 78.25 ± 0.47 to 92.00 ± 0.40 mmHg in group II. This increase in MAP might be due to increased systemic vascular resistance related to the peripheral vasoconstriction (Langer, 1981). This was in agreement with the findings of Almubarak (2012) who used romifidine and ketamine in camels. Kilic (2004) also reported increased MAP after administration of medetomidine, an another α_2 agonist and ketamine in rabbits.

CONCLUSION

After the end of the study it could be concluded that romifidine @ 40 µg/kg body weight along with ketamine @ 5 mg/kg body weight produced better sedation, analgesia and muscle relaxation permitting surgical procedure. Therefore this combination can be suggested for clinical use. Romifidine @ 30 µg/kg b. wt. combined with ketamine @ 5 mg/kg b. wt. produced sedation and muscle relaxation with moderate analgesia is suggestive for minor surgical procedures in dogs.

ACKNOWLEDGEMENT

The authors are grateful to the Dean, Faculty of Veterinary Science, Khanapara, Guwahati for providing necessary facilities to carry out the research.

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How to cite this article:

Saikia A. *et al*.2017, Clinico-Physiological Effects of Romifidine-Ketamine Combination In Dog. *Int J Recent Sci Res.* 8(7), pp. 18896-18898. DOI: http://dx.doi.org/10.24327/ijrsr.2017.0807.0588

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