CLINICO-HEMATOLOGICAL STUDIES ON DOSE DEPENDANT MIDAZOLAM-KETAMINE ANAESTHESIA IN DOGS

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The onset of analgesia, duration of anesthesia and recovery time was determined in 6 healthy dogs of either sex in respect to dose dependency of midazolam in atropinized dogs, and midazolam following ketamine for induction of anaesthesia. Midazolam was administered in treatment Group-I @0.2mg/kg I/V ,in Group-II @ 0.3mg/kg I/V and in in Treatment Group-III @0.4mg/kg I/V. The onset of anaesthesia was 54.66±4.31, 34.16±4.37 and 26.66±1.31 seconds in treatment I, II and III where as the duration of anaesthesia was 34.58±1.79, 44.24±3.76 and 47.99±2.99 and recovery time was 146.83±5.32, 158.16±7.25 and 189.33±5.27 minutes respectively. The changes in rectal temperature, pulse and respiration were transient in nature. The changes in hematological parameters were also transient, however a highly significant increase was observed in neutrophil count at 12 to 24 hours and decrease in lymphocyte count from 3 to 96 hours in all the treatments.
Keywords: Dog, Ketamine, Midazolam

Introduction

Ketamine is widely accepted anaesthetic agent in many species including primates, dogs, cats and wild animals (Hall and Clarke, 1991). It is considered relatively safe as it causes minimal cardiovascular and respiratory depression and it stimulate cardiovascular function due to sympathomimetic effect (Wagner and Helleyer, 2000). Midazolam is a water soluble benzodiazepine derivative (Hall and Clarke, 1991). It shows rapid onset of action due to it's fast uptake into brain tissues. But the combination of ketamine and midazolam shows post anaesthetic muscle spasm in dogs and cats (Hellbreker *et al.*,1990 and Ajadi *et al.*,2008).

The present study was conducted to determine the dose dependant anaesthesia of ketamine – midazolam combination in dogs and to record the changes occurred in Clinical and haematological parameters.

Materials and Method

Six adult, clinically healthy mongrel dogs of either sex, weighing approximately 10 to 20 kg were selected for experiment. The body rectal temperature (°F), pulse and respiration rate per minute were simultaneously recorded for normal values during pre-experimental period. Four blood samples from each animal were collected during the pre-experimental period and analysed for normal values of haematological parameters.

Each of six animals in all three treatments received atropine sulphate @.05mg/kg I/M, 10 minutes prior to midazolam in different doses viz ; 0.2mg/kg, I/V, 0.3mg/kg I/V and 0.4mg/kg I/V in treatment group I ,II , and III respectively followed by ketamine HCl @ 20mg/kg I/V. The atropine and ketamine were kept on constant dose in all three treatments with variation in doses of midazolam.

Result and Discussion

The use of midazolam with different anaesthetic combination like ketamine in goats reported by Stegmann (1999). The result showed that there was adequate muscle relaxation and analgesia,similar observation were recorded by Cornick and Hartsfield (1992), Mutoh *et al.* (2002), Kojima *et al.* (2002) and Sano *et al.* (2003) with use of butorphanol-midazolam-glycopyrrolate as preanaesthetic to thiopentone anaesthesia in dogs. During recovery period, pedal reflex

and tongue were first to become conspicuous followed by reappearance of other body reflexes. The animal was able to stand on their feet without assistance. Onset of anaesthesia was noticed during completion of intravenous administration of ketamine in 54.66±4.31, 34.16±4.3 and 26.66±1.31 seconds in treatment I, II and III, respectively. This observation was found in accordance with the report of Corsen and Holocomb, (1978) and Ajadi *et al.* (2008). The midazolam-thiopentone combination produced smooth induction and good surgical anaesthesia in bovines (Cheema and Singh, 2002) and in cow calves (Bishnoi, 2001)

The duration of surgical anaesthesia was minimum in treatment I with mean value of 34.58± 1.79 followed by 44.24± 3.76 and 47.99±2.99 minutes in treatment II and III respectively. The high lipophilicity of midazolam, it's high metabolic clearance and rapid rate of elimination causes a short duration of activity (Reves *et al.*, 1985 and Greenblatt *et al.*,1983). The values of treatment III were significantly higher (P<.05) in comparision to treatment I and II. These findings supported the observation of Deppe *et al.* (1987) in cats, Bhaskar and Bai, 1990 in rats and Pandey *et al.* (1991) with diazepam-ketamine combination in dogs. The longer duration of anaesthesia in the present experiment could be due to potentiation of effect of ketamine by midazolam also suggested by Hall and Clarke, (1991).

Time for complete recovery from anaesthesia was minimum in treatment I with mean value of 146.83± 5.32 minutes followed by 158.16 ± 7.25 minutes in treatment II. In treatment III significant (P<0.05) increase with mean value of 189.33 ± 5.27 minutes were recorded. However Dundee and Wyant (1989) claimed midazolam to have less cumulative effect and rapid recovery which could probably be due to high lipid solubility, rapid distribution in peripheral tissues and faster metabolic biotransformation (John,1995). Clutton *et al.* (1997) reported quicker recovery in pigs following ketamine-midazolam anaesthesia.

Highly significant (P<0.01) increase in respiration rate was observed from 60-240 minutes and 75-120 minutes in treatment I and III, respectively. However, increase was nonsignificant in treatment II with maximum value of 54.80 ± 6.11 at 150 minutes. A drop of respiration was recorded in all three treatments at 15 minutes followed by its increase and this might be due to the depressant action of ketamine as suggested by Pandey *et al.*, (1991). The increase in respiration was also observed by Mottelib (1980) in buffalo calves. The drop is in accordance with the findings of Morel *et al.* (1980) and Hellyer *et al.*, (1991). Smith *et al.* (1991) also observed a significant decrease in respiratory rate following midazolam administration in pigs.

The pulse rate in all three groups showed highly significant (P<0.01) rise. A rise in pulse rate was observed from 15-20 minutes with maximum value of 164.70±8.48 and 168.00 ± 9.85 at 30 and 45 minutes in treatment I and II respectively. In treatment III the rise was observed between 15-180 minutes with maximum value of 165.71±10.10 at 60 minutes in comparision to their respective control values of 88.00±4.95, 88.50±2.02 and 86.50±3.81 in treatment I, II and III respectively. Similar findings were also mentioned by Jacobson *et al.* (1994). Bishnoi (2001) also reported similar changes in heart rate when midazolam and thiopentone sodium were administered in calves. Reves *et al.* (1985) reported significant increase in heart rate after administration of midazolam hcl in human beings. Jones *et al.* (1979) in dogs and Smith *et al.* (1991) in pigs.

A non significant decrease was recorded in rectal temperature in treatment II and III between 15 to 75 and 15 to 60 minutes respectively, while similar drop in treatment I was noticed from 90 to 240 minutes. Similar finding was reported by Luna *et al.* (1997)

and Bayen *et al.* (2002) in dogs and Bustamante and Valverde, (1997) in pigs. The decrease in rectal temperature could be due to the thermoregulatory depressant effect of ketamine which causes release of monamine from CNS as suggested by Bisen *et al*., (1994).

The value of TEC, TLC, Hb, PCV, eosinophil count and neutrophil count showed non significant variations and were transient. Decrease in haemoglobin concentration could be the combined effect of midazolam-ketamine on venous tone, pooling of blood in spleen, vasodilation and subsequently haemodilution during anaesthesia in dogs. However, a highly significant increase in neutrophil count at 12 to 24 hr interval in all the three treatments was observed. Maximum values were obtained at 24 hours in treatment I and II and 12 hours in treatment III, lymphocyte count showed highly significant decrease from 3 to 96 hours in treatment II and III and from 3 to 48 hours in treatment I, minimum value observed at 24 hours in all the treatment and this could be due to increased in plasma volume during anaesthesia on account of vasodilatation.

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