MIDAZOLAM WITH GLYCOPYRROLATE-XYLAZINE COMBINATION FOR PREMEDICATION IN KETAMINE ANAESTHESIA IN DOGS

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Abstract

The anaesthetic study was conducted in 12 female dogs of different breeds, subjected to elective surgical procedures (oophorectomies). They were randomly divided into two groups each consisting of six animals and were numbered serially from 1 to 6. Animals of group I were premedicated by intramuscular administration of glycopyrrolate (0.011mg/kg body weight) followed by xylazine (1.0 mg/kg body weight) at 15 minutes interval. In animals of Group II, ten minutes later midazolam (0.3 mg/kg body weight) was also administered intravenously. Fifteen minutes, after premedication in both the groups ketamine hydrochloride (10 mg/kg body weight) was administered intramuscularly for the induction and maintenance of general anaesthesia. In animals premedicated with midazolam, endotracheal intubation was easy and the degree of muscle relaxation during anaesthesia was good.The depth of anaesthesia achieved without midazolam premedication was found not satisfactory for major surgical procedures like laparotomy. But it was satisfactory in midazolam-premedicated animals. All the animals of both groups had an uneventful recovery, though the dogs showed varying degrees of dullness, which lasted for two to six hours.

Keywords: *Midazolam, Glycopyrrolate, Xxylazine, Ketamine, Anaesthesia, dogs*

In veterinary practice, injectable anaesthetic techniques are preferred due to the inherent peculiarities of animal patients, and the ease of administration of drugs. Commonly, drug combinations are being preferred to individual drugs, since it reduces the dose requirement and side effects. Among these, xylazine (α 2 agonist) and ketamine (a dissociative anaesthetic) are very popular anaesthetic combination for short duration surgical procedures. But untoward reactions like clonic head and limb movements followed by vocalization after painful stimuli had been reported during recovery period (Clark *et al.*, 1982). Intravenous administration of midazolam, with xylazine and ketamine induced a profound level of central nervous system depression and easy transition to unconsciousness with no struggling, vocalization or peddling (Tranquilly *et al.*, 1990). In the present study, evaluation of midazolam was carried out with glycopyrrolate-xylazine combination for premedication in ketamine anaesthesia in dogs.

Materials and Methods

The study was conducted in 12 female dogs of different breeds subjected to elective surgical procedures (oopherectomies) at the Department of Veterinary Surgery and Radiology of College of Veterinary and Animal Sciences, Mannuthy and the University

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Veterinary Hospital, Kokkalai and were divided into two groups *viz.*,Group I and Group II, each consisting of six animals.

All the dogs were clinically examined and were found apparently healthy. Preoperatively, water and food were withheld for 12 and 24 hours respectively. Animals of Group I were premedicated by intramuscular administration of glycopyrrolate (0.011mg/kg body weight) followed by xylazine (1.0 mg/kg body weight) at 15 minutes interval. In animals of Group II, 10 minutes later midazolam (0.3 mg/kg body weight) was also administered intravenously as a part of preanaesthetic medication. Fifteen minutes after premedication, in both the groups ketamine hydrochloride (10 mg/kg body weight) was administered intramuscularly for the induction and maintenance of general anaesthesia. Endotracheal intubation was carried out to keep the air way patent. During surgery five percent dextrose saline was administered intravenously to all the dogs.

The salient clinical signs exhibited by the dogs following the premedication, during induction, maintenance and recovery of anaesthesia were recorded. The physiological observations *viz.*, rectal temperature, pulse rate, rate of respiration, colour of visible mucous membrane, oxygen saturation (SpO_2), capillary refill time and blood coagulation time were recorded before the administration of pre anaesthetic combinations, immediately before, and at 30 and 90 minutes and at 24 hours after the administration of ketamine.

The induction time of anaesthesia was calculated as the time from the injection of ketamine to the disappearance of the pedal reflex and the duration of surgical anaesthesia as the time interval between the time of disappearance of pedal reflex and the time of return of pedal reflex. Muscle relaxation time was calculated as the time interval between the disappearance and the return of the tone of muscles of lower jaw. Depth of anaesthesia was evaluated during surgery by assessing the extent of analgesia, degree of muscle relaxation and unconsciousness, and graded as unsatisfactory, satisfactory, good or very good. The degree of muscle relaxation was rated as excellent (++++), good (+++), moderate (++) and poor (+), depending up on the resistance in opening the jaws manually and by the assessment of relaxation of the muscles of the abdomen during surgery. Recovery time was calculated as the time interval between the return of pedal reflex and the time when the animal could stand up and walk unassisted. All the data were statistically analysed.

Results and Discussion

The observations are presented in the table.The common clinical signs suggestive of sedation manifested by the dogs of both the groups following premedication with administration of glycopyrrolate and xylazine were winking of eyes, yawning, inco-ordination of movement, and assumption of sternal recumbency with head down posture. All the dogs in Group II were manually controlled in lateral recumbency for the intravenous administration of midazolam and there after lateral recumbency was maintained. The other symptoms noticed were vomiting, licking, urination and defecation. These symptoms in dogs following the administration of xylazine had been reported by Rajankutty (1996) and Varghese (2006). Xylazine induced vomiting had also been reported in dogs by Hall (1985). The possible reason for the vomiting can be attributed to the effect of xylazine. According to Moye *et al.* (1973), emetic action was considered advantageous as it empties the stomach thereby eliminating the possibility of aspiration during surgery and postoperatively.

Induction of anaesthesia was smooth in both the groups. The induction time of anaesthesia was found quicker in group II dogs (8.83 ± 0.40 min) than in group I (9.50 ± 0.72 min) due to the added sedative effect of midazolam. Similar findings were also reported by Hellyer *et al.* (1991) when midazolam was combined with ketamine. In Group I animals endotracheal intubation could be performed only with resistance, but it was easy in Group II in which midazolam was included for premedication. Hellyer *et al.* (1991) also reported rapid intubation as an added advantage of midazolam-ketamine combination in dogs, since it abolished the swallowing reflex.

The muscle relaxation time was more in Group II (49.83±1.85 min) than in Group I (41.20 ±2.14 min). The degree of muscle relaxation was poor in four animals and moderate in two animals in Group I and good in all dogs of Group II. Luna *et al.* (1992) had reported excellent muscle relaxation in horses following the administration of midazolam-xylazine combination.

The depth of anaesthesia was satisfactory in Group II, but was not satisfactory in all the animals of Group I. Hence to complete the surgical procedure, local infiltration anaesthesia at the laparotomy site using 2% lignocaine hydrochloride was also resorted to. From the study, it could be inferred that xylazine and ketamine combination at the dose rate of 1 mg/kg and 10 mg/kg respectively may not be always satisfactory for surgical procedures like laparotomy, but it could be achieved more satisfactorily in those animals premedicated with midazolam.

The duration of anaesthesia was prolonged in Group II (45.83 ± 1.54 min) than in Group I (36.70 ± 2.65 min). During recovery in a few of Group I animals, vocalization was noticed. The recovery time was found more in Group II were midazolam was included for premedication (80.00±5.17 min) than in Group II (71.70±4.01 min) may be due to its hypnotic action (Kanto *et al.*, 1982). All the animals had an uneventful recovery, though the dogs showed varying degree of dullness, which lasted for two to six hours and had normal food intake from the next day onwards.

There was marginal decrease in rectal temperature after premedication and during anaesthesia in both the groups. Decrease in rectal temperature during xylazine-ketamine anaesthesia (Sharma *et al.*, 1983; Mohan, 2006) and midazolam-xylazine anaesthesia

Table. Observations on physiological parameters before and after premedication,during anaesthesia and recovery, and at 24h. (Group I and II) (Mean ± SE) n=6

Parameters	Groups	Premedication		During anaesthesia (30min)	During recovery (90 min)	At 24 h
		Before	After			
Rectal Temperature (°C)	I	38.92± 0.15	38.92± 0.14	[a]38.79 ± 0.21	38.45± 0.18*	38.71±0.21
	II	39.10±0.07	38.99±0.04*	[a]38.91±0.15	38.75±0.13	38.94±0.08
Pulse Rate (per min)	I	100.67±6.86	106.67±15.76	[a]95.00±1.69	92.33±1.89	90.50±2.42
	II	91.17±4.12	83.17±2.86	[b]87.17±2.07	90.00±2.62	86.50±3.24*
Respiration Rate (per min)	I	33.67±4.63	24.50±2.35*	26.67±5.56	23.83±2.26	23.83±2.20*
	II	24.67±6.70	17.33±2.55	19.17±4.06	23.50±6.82	33.0±5.79
Oxygen Saturation (SpO2)(per cent)	I	92.0±2.05	[a]94.0±1.61*	[b]94.67±0.42	[b]95.17±0.70	93.67±0.42
	II	82.33±3.48	[a]94.33±0.42*	[a]97.17±0.87*	[a]98.33±0.21*	95.0±1.37 *
Blood Coagulation Time (min)	I	3.52 ±0.13	3.78 ±0.20	3.92 ±0.08*	3.78 ± 0.13	3.75 ±0.11
	II	3.85 ±0.11	3.92 ±0.11*	4.17 ±0.10*	4.22 ± 0.11*	4.18 ±0.07*
Capillary Refill Time (in sec)	I	2.00±0.23	1.50±0.26	1.50±0.22	1.50±0.22	1.83±0.22
	II	1.50 ±0.23	1.33±0.22	1.83±0.21	1.50 ±0.17	1.66 ±0.22
Systolic Blood Pressure (mm Hg)	I	130.67±3.03	158.00± 4.73	213.17±5.17	154.83±4.60	132.33±4.89
	II	139.83±2.21	159.67±2.01	181.83±6.36	168.17±2.47	140.83±2.79
Diastolic Blood Pressure (mm Hg)	I	78.33±2.95	100.17±2.11	152.33±3.10	102.17±2.71	79.33±2.52
	II	84.14±2.03	104.50±1.64	148.50±1.80	103.33±1.64	84.17±2.29
Mean Blood Pressure (mm Hg)	I	99.83±4.50	118.67±3.24	173.00±2.98	123.00±2.69	100.50±4.33
	II	105.00±2.16	125.67±2.20	167.83±2.27	124.33±1.89	103.17±1.84

(P<0.05) Significant at 5 per cent level.

** Row means compared to the mean value before premedication*

** Column means with alphabetic superscripts in common (a, b, c, d) is not statistically significant.*

in dogs (Koc *et al.*, 2002) had been reported. The decrease in body temperature during anaesthesia can be attributed to the depressant effect of the drugs on the central nervous system. Peripheral vasodilatation also may be a contributing factor in midazolam premedication (Ramaswamy *et al.*, 1991).Koc *et al.* (2002) opined that the decrease in body temperature during xylazine-midazolam anaesthesia could be due to peripheral vasodilatation, decrease of basal metabolic rate and muscle tone and depression of thermoregulatory mechanism.

There was decrease in pulse rate after premedication, during anaesthesia and recovery in all the groups though there was a mild increase after premedication in Group I. But in Group II, such an increase was not observed probably due to the sedative effect of midazolam. A decreased heart rate followed by normal value during recovery in xylazine-midazolam anaesthesia (Koc *et al.*, 2002) had been reported.

There was decrease in respiration rate following premedication in both the groups. Decrease in respiration rate following the administration of xylazine (Peshin *et al.*, 1980), midazolam (Bishnoi and Saini, 2005a), ketamine (Haskins *et al.*, 1985), xylazine-ketamine (Haskin *et al.*, 1986) and xylazine-midazolam (Koc *et al.*, 2002) had been reported in dogs.

The colour of the visible mucous membrane was pale roseate in all the animals throughout the period of observation, indicating the stability of peripheral circulation. There was significant ($P<0.05$) increase in S_PO_2 level after premedication in Group I and II.

The capillary refill time was seen decreased after premedication in Group I (1.50±0.26) and Group II (1.33±0.22). During anaesthesia it was increased in Group II (1.83±0.21) where midazolam was included for premedication. This increased capillary refill time noticed may be due to the peripheral vasodilatation effect and the loss of muscle tone produced by midazolam (Koc *et al.*, 2002). There was an increase in coagulation time after premedication and during anaesthesia in both the groups.

There was significant increase in systolic blood pressure in Group I (158.00± 4.73) and after premedication, during anaesthesia and recovery whereas in Group II, where midazolam was included, there was significant increase during anaesthesia (181.83±6.36). Melvin *et al.* (1982) and Shenoy *et al.* (2002) also observed significant decrease in systolic pressure following the administration of midazolam. There was increase in diastolic pressure after premedication in Group I (100.17±2.11) while it was (104.50±1.64) in Group II, but during anaesthesia it showed a significant increase in both the groups. There was significant increase in mean blood pressure after premedication and during anaesthesia with a decreasing trend during recovery in all the groups.

From the present study, it could be concluded that, midazolam with glycopyrrolate-xylazine combination as preanaesthetic medication produced adequate sedation in dogs. This preanaesthetic combination in ketamine anaesthesia permitted easy endotracheal intubation, resulted in good muscle relaxation and satisfactory depth and duration of anaesthesia and smooth recovery for surgical procedures of short duration.

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