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Comparative study on the use of diazepam-ketamine and midazolam-ketamine as induction agents for butorphanol-acepromazine-glycopyrrolate as premedicant and propofol as maintenance in dogs

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Abstract
The present study was carried out on twelve dogs to study the clinical efficacy of two anesthetic protocols in which Butorphanol, Acepromazine and Glycopyrrolate (BAG) is used as preanesthetic agent. In the dogs of group I, anaesthesia was induced by Diazepam and Ketamine hydrochloride and in group II with Midazolam and Ketamine. Following induction, anaesthesia was maintained with Propofol. The anaesthetic effects like induction, duration and recovery time were recorded. In conclusion BAG proved to be an effective premedicant combination. BAG provided excellent analgesic, sedative and antisialogauge effects during surgical procedures. Midazolam and Ketamine combination acted as a superior induction agent to the combination of Diazepam-Ketamine. Recovery was rapid, smooth and uneventful in Diazepam-Ketamine induction and Propofol maintenance in comparison to Midazolam-Ketamine induction and Propofol maintenance.

Keywords: BAG, diazepam, midazolam, ketamine and propofol

Introduction
The appropriate selection of premedicant drugs can significantly contribute to perioperative analgesia, intraoperative cardiovascular stability and quality of recovery (Duke-Novakovski *et al*., 2016) [4]. Proper use of preanaesthetic medication (tranquilizers, sedatives, analgesics etc.) is imperative to produce the optimal desired effect with minimal side effects (Muir and Hubbell, 2012) [8]. Use of a combination of anaesthetic agents with different mechanisms of action, offers the benefit of using lower doses of individual agents that produce sufficient anaesthesia, while reducing the possibility of risks associated with over dosage (Ibrahim, 2017) [7] thereby rendering it safe. Several induction agents have been used in veterinary anaesthesia. However, Diazepam-Ketamine (Al-Redah, 2011; Ferreira *et al*., 2015; Yohannes *et al*., 2018) [2, 5, 14] and Midazolam-Ketamine (Al-Redah, 2011; Abdel-Hady *et al*., 2017) [1, 2] are some of induction agents employed in canine practice.Very scanty information and limited reports on Diazepam-Ketamine and Midazolam-Ketamine as induction agents for Butorphanol- Acepromazine-Glycopyrrolate (BAG) as premedicant and Propofol as maintenance agent in dogs. Therefore, the present clinical study conducted on these drugs.

Materials and Methods
The present study was carried out on twelve dogs aged between 4 months to 10 years presented for various surgical operations.

Design of study
The twelve dogs were randomly divided into two groups (group I and group II) comprising of six dogs in each group. All the dogs were uniformly premedicated with Butorphanol, Acepromazine and Glycopyrrolate (BAG) at dose rate of 0.2, 0.04 and 0.01 mg/kg body weight respectively as a combination in one syringe administered intramuscularly. After, fifteen minutes the dogs were anaesthetized and maintained under anaesthesia as follows:
In group I, anaesthesia was induced by slow I/V injection of Diazepam at the rate of 0.28 mg/kg and Ketamine hydrochloride at the rate of 5 mg/kg body weight over a period of 60-90 seconds whereas in group II, fifteen minutes after premedication, anaesthesia was similarly induced with slow I/V injection of Midazolam at the rate of 0.28 mg/kg and Ketamine at the

rate of 5 mg/kg and Ketamine at the rate of 5 mg/kg body weight over a period of 60-90 seconds (I/V). Following induction of anaesthesia in both the groups of dogs, anaesthesia was maintained with I/V administration of Propofol at the rate of 0.5-2.0 mg/kg body weight. Incremental doses of Propofol were administered "to effect" whenever required during the surgical procedure through the intravenous life line. (Table.1. & Fig 1.)

Table1: Design of the clinical study

S. No	Group	Number of dogs	Age (Years/Months)	Sex	Body Wt (kg)	Breed	ET size (mm)	Surgeries Performed	Anaesthetic protocol
1	I	6	2.6 yrs	M	30	Labrador	8.5	Aural haematoma	Premedication- BAG Induction- D-K Maintenance-Propofol
			8 yrs	M	30	Labrador	7.5	Bone plating	
			9.6 yrs	M	29	German Shepherd	8.5	Perineal hernia	
			8 yrs	F	25	Doberman	9	Digit amputation	
			3 yrs	F	30	German Shepherd	8.5	Vaginal hyperplasia	
			6.5 yrs	F	20	German Shepherd	6.5	Ovariohysterectomy	
2	II	6	10 yrs	M	20	Non descript	6.5	Perineal hernia	Premedication-BAG Induction-M-K Maintenance-Propofol
			10 yrs	M	10	Non descript	5.5	Castration	
			4 month	M	10	Non descript	5.5	Bone plating	
			10 yrs	F	30	German Shepherd	8.5	Mammary tumor	
			1.3 yrs	F	8.8	Pomerarian	5.5	Ovariohysterectomy	
			5 yrs	M	39	Great Dane	8	Aural haematoma	

BAG: Butorphanol-Acepromazine-Glycopyrrolate; D-K: Diazepam-Ketamine; M-K: Midazolam-Ketamine

Fig 1: Drugs used in the present study: Butorphanol, Acepromazine, Glycopyrrolate, Diazepam, Midazolam, Ketamine and Propofol.

Results

BAG produced sedation within 4 to 18 minutes with mean sedation time of 12.25±1.29 minutes. The sedation score ranged from 3 to 4 in all dogs. BAG provided moderate (slight resistance) to profound (resistance none) sedation. Among the 12 dogs, sedation was adjudged to be moderate in 10 dogs (83.33%) and profound in 2 dogs (16.67%).

In group I, the time of induction ranged from 55 seconds to 71 seconds, with a mean induction time of 62.33±1.29 seconds. In group II, the time of induction ranged from 25 seconds to 43 seconds, with a mean induction time of 31.67±1.67 seconds. The induction time in the dogs of group I was significantly higher when compared to group II (Table 2). Induction was found to be good in four dogs and fair in two dogs of group I whereas induction was good in all the dogs of group II induced with midazolam- ketamine.

Table 2: The induction time in the dogs of group I was significantly higher when compared to group II

	Group- I (n=6)	Group-II (n=6)
Induction Time* (In seconds)	62.33^{a}±1.29 (Range 55-71 seconds)	31.67^{b}±1.67 (Range 25-43 seconds)

*-Significant ($p \leq 0.05$) - Means with different superscripts differ significantly.

The data revealed that the maintenance period was significantly higher in group II. The results of the data are presented in table 3.

Table 3: The data revealed that the maintenance period was significantly higher in group II

	Group- I	Group-II
Duration of Surgical Anaesthesia* (In Minutes)	45.22^{a}±1.68 (Range 38-50 Minutes)	61.19^{b}±1.40 (Range 55-65 Minutes)

*-Significant ($p \leq 0.05$) - Means with different superscripts differ significantly.

In group I recovery time was found to be shorter (128.83±2.43 minutes) when compared to the recovery time of (205.00±5.97 minutes) resulting from group II (Table 4). Recovery was found to be gradual, smooth, quiet, rapid and comfortable in group I, whereas recovery was gradual, slow, moderate and restless in group II.

Table 4: Recovery was found to be gradual, smooth, quiet, rapid and comfortable in group I

	Group- I	Group-II
Recovery Time* (Minutes)	128.83^{a}±2.43 (Range 120-135 Minutes)	205.00^{b}±5.97 (Range 186-223 Minutes)

*-Significant ($p \leq 0.05$) - Means with different superscripts differ significantly.

Discussion

The results indicated that the preanaesthetic preparation were satisfactory, since no untoward effects were noticed in any animal. BAG provided moderate (slight resistance) to profound (resistance none) sedation, Pottie *et al*. (2008) [9]. The present results were akin with results of Pramodh and Mohindroo (2010) [10] and Ranpariya *et al*. (2013) [11] with BAG protocol. Singh *et al*. (2013) [12] also reported mild to profound sedation after BAG administration in dogs.

The midazolam-ketamine combination produced significantly shorter induction time when compared to diazepam-ketamine anesthesia combination. Similar observation was made by Hellyer *et al*. (1991) [6]. The quality of induction was adjudged to be fair to good with diazepam-ketamine induction and these results were similar to observations of White *et al*. (2001) [13]. Hellyer *et al*. (1991) [6] and Ranpariya *et al*. (2013) [11] also stated that good, smooth and satisfactory induction was observed after ketamine-midazolam administration. Ferreira *et al*. (2015) [5] also reported that diazepam-ketamine produced good quality of induction as indicated by calm transition and no paddling following their studies.

The propofol as the maintenance agent in our present study produced satisfactory results. This observation was in accordance with the report of Caines *et al*. (2014) [3].

Recovery was found to be gradual, smooth, quiet, rapid and comfortable in group I, whereas recovery was gradual, slow, moderate and restless in group II, Pottie *et al*. (2008) [9]. The diazepam-ketamine combination produced better recovery from anesthesia in comparision midazolam-ketamine combination. Similar observations were reported by Hellyer *et al*. (1991) [6]. Smooth recovery seen in all the dogs premedicated with BAG. Pramodh and Mohindroo (2010) [10] and Ranpariya *et al*. (2013) [11] also made similar observations.

Conclusion

Use of BAG fifteen minutes prior to induction proved to be an effective premedicant combination. BAG subsided adverse effects of each premedicants when used combinedly and provided excellent analgesic, sedative and antisialogauge effects. Induction of anaesthesia was found to be superior with when Ketamine injected along with Midazolam in comparision to Diazepam combination. Both the anaesthetic protocols tested in the present study provided satisfactory deep surgical anaesthesia in dogs of two groups but recovery was rapid, smooth and uneventful in Diazepam-Ketamine induction and with Propofol maintenance.

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