# SAFETY AND EFFICACY OF BUTORPHANOL-ACEPROMAZINE-GLYCOPYRROLATE AS PREMEDICANT COMBINATION TO MIDAZOLAM-KETAMINE INDUCTION AND ISOFLURANE MAINTENANCE IN CANINE ORTHOPAEDIC SURGERY

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## ABSTRACT

The objective of this study was to evaluate anaesthetic efficacy and safety of BAG (Butorphanol, Acepromazine and Glycopyrrolate) as premedicant to midazolam-ketamine induction and isoflurane maintenance in clinical canine orthopaedic cases. The clinical study was carried out in 18 cases. Dogs were premedicated with intramuscular injection of butorphanol, acepromazine and glycopyrrolate @ 0.2, 0.04 and 0.01 mg/kg b.wt. respectively, mixed in a single syringe. Induction was performed using midazolam – ketamine @ 5mg/kg b.wt. and 0.28 mg/kg b.wt., respectively administered intravenously. Anaesthesia was maintained with isoflurane. The preanaesthetic combination provided moderate to profound sedation. Induction was smooth and satisfactory in all the dogs with ketamine-midazolam and stable maintenance with isoflurane during orthopaedic procedures, viz., intramedullary pinning, limb amputation, setting Ilizarov circular external fixator and type II external fixator. BAG as preanaesthetic to ketamine-midazolam induction and isoflurane maintenance proved safe and effective in orthopaedic surgery in dogs.

**KEY WORDS:** Canine orthopaedic, BAG (Butorphanol-Acepromazine-Glycopyrrolate), Premedicant, Midazolam-ketamine induction, Isoflurane maintenance.

## INTRODUCTION

Introduction of new orthopaedic techniques demand a new and specific anaesthesia, pain management and rehabilitation protocol. Promotion of multidisciplinary approach to orthopaedic patients optimize outcome and minimize the cost. The aim of this study was therefore to evaluate anaesthetic efficacy and safety of a newer combination- BAG (Butorphanol, Acepromazine and Glycopyrrolate) as premedicant to midazolam-ketamine induction and isoflurane maintenance in clinical canine orthopaedic surgery.

## MATERIALS AND METHODS

The study was conducted on eighteen dogs of different breeds and sex, aged between 3 months to 12 years. All the animals were kept off feed for 24 hours (12 hours for pups) and off water for 12 hours prior to anaesthesia. Preanaesthetic evaluation was performed by observing general status, history, physical examination and laboratory profile. On the basis of preanaesthetic evaluation, the dogs were selected for surgery. The general status of animals was evaluated by recording rectal temperature, heart and respiratory rates, mucous membrane color and capillary refill time. All the animals were premedicated with butorphanol-acepromazine-glycopyrrolate (BAG) @ 0.2, 0.04 and 0.01 mg/kg b.wt. as a mixture in a single syringe administered intramuscularly. After 15 minutes, induction was performed using intravenous injection of midazolam – ketamine @ 5 mg/kg b.wt. and 0.28 mg/kg b.wt, respectively. Tracheal intubation was performed after restraining the dog in sternal recumbency with suitable sized endotracheal tube under the guidance of laryngoscope. Maintenance of anaesthesia was done with isoflurane using anaesthetic machine with ventilator (Model 2800C, Mallard Medical Inc).

Physiological parameters, viz., rectal temperature, pulse rate, respiratory rate and mean SpO2 were measured during anaesthesia at 5, 15, 25, 35, 45 and 60 minutes with the help of multipara monitor. Haematological parameters, viz., haemoglobin (Hb), packed cell volume (PCV), total leukocyte count (TLC), total erythrocyte count (TEC), differential leukocyte count (DLC), and biochemical parameters, viz., glucose, total protein, serum creatinine, blood urea nitrogen (BUN) and alkaline phosphatase were estimated from serum at 0 min and 15 min after premedication and 30 min after induction.

Clinical parameters assessed were quality of sedation, induction and recovery, duration of anaesthesia (from onset of analgesia until animal started to recover), induction time (loss of response to pin prick), intubation time (time from induction to successful intubation), sitting time (end of anaesthesia to resumption of sternal recumbency), standing time (from end of anaesthesia till animal stood unassisted), complete recovery time (from end of anesthesia until animal resumed feeding or drinking) and complications, if any. The data was analyzed statistically.

## RESULTS AND DISCUSSION

The purpose of this trial was to assess anaesthetic safety and efficacy of anaesthetic protocol in orthopaedic cases under clinical setting. BAG provided moderate to profound sedation with mean onset at 13.00 ± 0.48 min. Acepromazine provides profound (Roon *et al.,* 2007) to moderate (Posner, 2007) sedation via antidopaminergic effects. Butorphanol produces mild sedation in dogs, when injected IM at 0.5 mg/kg b.wt. (Pircio *et al.,* 1976) as premedicant however, accompanied with vomiting (Dyson, 2002). Induction with ketamine-midazolam administered intravenously over a period of 60-90 seconds was found adequate. Induction was judged on the basis of palpebral reflex, jaw tone and pedal reflex. Tracheal intubation guided by laryngoscope was easy and prompt as reported earlier (Hellyer *et al.,* 1991 and Kavechiya, 2010). Majority of inductions (16 of 18) was of good quality. Among 18 dogs studied, 2 (11.11%) showed apnea. The time for induction

**Table 1:** Changes in physiological responses following general anaesthesia in canine orthopaedic patients (Mean ± SE; n=18)

| Time period | Rectal temperature (°F) | Pulse rate (per minute) | Respiratory rate (per minute) | $SpO_2$ (per cent) |
|---|---|---|---|---|
| **Base value** | 102.66±0.15$^{a}$ | 151.43±10.37 | 30.28±2.68$^{a}$ | 96.57±1.38 |
| **AP** | 101.86±0.19$^{ab}$ | 153.43±12.46 | 34.28±3.80$^{a}$ | 95.14±2.58 |
| **0 min.** | 101.20±0.20$^{bc}$ | 176.00±11.07 | 19.71±2.52$^{b}$ | 96.57±0.89 |
| **5 min.** | 100.63±0.36$^{bcd}$ | 164.14±9.21 | 20.57±2.93$^{b}$ | 96.14±0.74 |
| **10 min.** | 100.27±0.41$^{cd}$ | 156.86±9.47 | 16.71±2.43$^{b}$ | 96.28±1.02 |
| **15 min.** | 100.30±0.37$^{cd}$ | 157.00±6.42 | 15.57±2.94$^{b}$ | 95.86±1.32 |
| **25 min.** | 100.17±0.52$^{cd}$ | 154.86±5.68 | 13.28±2.26$^{b}$ | 97.86±0.51 |
| **35 min.** | 99.68±0.68$^{cd}$ | 149.43±4.77 | 13.86±2.55$^{b}$ | 97.71±0.56 |
| **45 min.** | 99.60±0.75$^{d}$ | 157.00±4.50 | 12.50±0.96$^{b}$ | 97.00±0.68 |
| **60 min.** | 99.10±0.83$^{d}$ | 153.50±4.57 | 13.83±1.56$^{b}$ | 96.67±1.05 |

* *AP = After preanaesthesia, 0 min. = induction of general anaesthesia.*

* *Means bearing common superscript within the column do not differ significantly (P>0.05).*

was 30.17 ± 0.00 seconds. Induction is reported to be smooth and free from excitement with ketamine-midazolam in dogs (Hellyer *et al.,* 1991).

The average values of pulse rate, SpO2, respiratory rate and rectal temperature recorded before preanaesthesia (base value), 15 min. after preanaesthesia (AP), and at 0 (induction), 5, 10, 15, 30, 45 and 90 minute during anaesthesia are presented in Table 1. There was a gradual reduction in the mean rectal temperature from base value till 60 minute after induction. The rate of reduction in rectal temperature was significant at 0, 10 and 45 minutes of anaesthesia. The decrease in rectal temperature during general anaesthesia is attributed to peripheral vasodilatation, inhibition of skeletal muscle movement, reduction in metabolic rate and depression of the thermoregulatory centers (Jadon and Kumar, 1994).

Pulse rate increased up to 0 minutes of induction followed by decrease in values till the end of operation. However, the changes were gradual and non-significant. Significant increase in heart rate has been documented after ketamine-midazolam induction (Butola and Singh, 2003) and also during isoflurane anaesthesia (Mutoh *et al.,* 1997) in dogs. The increase in the heart rate in isoflurane anaesthesia is probably due to decreased arterial blood pressure induced by the baroreflex (Mutoh *et al.,*1997) or sympathetic stimulation by increased PaCO2 (Steffy and Howland, 1996).

With the induction of general anaesthesia (0 minute), there was a sudden and significant ($P \leq 0.05$) decrease in respiratory rate, however, it remained within normal limit throughout the 60 minutes of anaesthetic period. There was non-significant fluctuation in the oxygen saturation during entire period of anaesthesia and the values were within normal range (Table 1). A slight elevation in the SpO2 observed immediately after induction might be due to administration of oxygen along with inhalant agent.

The haemoglobin concentration decreased non-significantly (Table 2) from base value up to 30 minutes of anaesthesia. During general anaesthesia vasodilation causes increased rate of haemodilution that affects the haemoglobin concentration (Bhatia *et al.,* 1979). Decrease in haemoglobin concentration might also be due to pooling of red blood cells in the spleen during anaesthesia, as has been demonstrated after barbiturate administration in dogs, goats, sheep and cattle (O'Brein and Heath, 1968).

**Table 2: Changes in haematological parameters following general anaesthesia in canine orthopaedic patients (Mean ± SE; n=18)**

| Haematological parameters | Time periods | | |
|---|---|---|---|
| | Base value | 0 min. | 30 min. |
| Haemoglobin (g/dL) | 11.43± 2.17 | 10.03± 1.78 | 8.48± 1.37 |
| Packed cell volume (%) | 33.21±6.00 | 27.83±4.96 | 27.41±3.44 |
| Total erythrocytic count (x $10^{6/}$µL) | 5.17±0.81 | 4.33±0.70 | 4.31±0.45 |
| Total leucocyte count (x $10^{3}$/µL) | 21.19 ± 3.01 | 22.33± 5.02 | 15.96± 2.51 |
| Lymphocyte (%) | 11.17± 2.80 | 7.75± 3.05 | 9.67± 3.36 |
| Neutrophil (%) | 79.72± 3.94 | 84.80± 2.36 | 81.43± 3.86 |
| Monocyte (%) | 5.25± 0.83 | 4.85± 1.19 | 6.45± 0.89 |
| Eosinophil (%) | 3.08± 1.10 | 2.13± 0.56 | 1.89± 0.60 |

The packed cell volume also decreased non-significantly (Table 2) that reached minimal level at 30 minutes after induction. The fall in PCV is thought to be due to splenic sequestration of redblood cells (Usenik and Cronkite, 1965). Likewise total erythrocyte count also started falling down after administration of pre-anaesthetic (Table 2). The TEC changes could be due to sequestration of blood cells in spleen and lungs during anaesthesia (Lumb and Jones, 1996). After a non significant rise in total leucocyte count at the time of induction it decreased non significantly at 30 minute of anaesthesia.

The decrease in TLC during anaesthesia (Table 2) may be attributed to adrenocortical stimulation and subsequent effect of glucocorticoids on circulating neutrophils and lymphocytes (Schalm, 1965; Oyama *et al.,* 1970). Differential leucocyte count revealed non-significant change in values of neutrophils and lymphocytes, of which neutrophil per cent increased, whereas lymphocytes per cent decreased. The changes in the number of eosinophils, basophils and monocytes were negligible.

The mean levels of BUN, TP, creatinine and AKP in serum remained unaltered (Table 3) throughout anaesthesia, whereas there was gradual and significant ($P \leq 0.05$) increase in glucose levels from base value with peak at 30 min after induction. The stress associated with anaesthesia is believed to stimulate the hypothalamus and pituitary in turn responds by increasing secretion of ACTH that stimulate production of glucocorticoids contributing for hyperglycaemia (Dikshit and Prasad, 1971).

**Table 3: Changes in blood serum biochemical constituents following general anaesthesia in canine orthopaedic patients (Mean ± SE; n=18).**

| Serum biochemical parameters | Time periods | | |
|---|---|---|---|
| | Base value | 0 min | 30 min |
| AKP (IU/L) | 117.94 ± 1.60 | 117.38 ± 1.53 | 120.73 ± 0.65 |
| Glucose (mg/dL) | 72.38 ± 0.75[a] | 79.33 ± 0.68[b] | 82.00 ± 0.36[b] |
| Total protein (g/dL) | 6.78 ± 0.34 | 6.22 ± 0.25 | 6.11 ± 0.14 |
| BUN (mg/dL) | 15.12 ± 0.68 | 15.23 ± 0.21 | 15.68 ± 0.29 |
| Creatinine(mg/dL) | 0.60 ± 0.031 | 0.62 ± 0.030 | 0.64 ± 0.027 |

* *Means bearing common superscript within the row do not differ significantly (P>0.05).*

The quiet, rapid and complete recovery from anaesthesia is of prime importance. Time required to attain recovery was 10.00 ± 2.64 minutes, and the mean time to resume food or water was 150.66 ± 17.31 min in the present study.

Based on the observations, it is concluded that the use of butorphanol-acepromazine-glycopyrrolate 15 minutes prior to induction of general anaesthesia is an effective premedicant combination in canine orthopaedic cases. This combination neutralized the side effects of individual agents and provided excellent analgesic, sedative and anti-sialogogue. Induction with ketamine-midazolam

proved optimum in clinical orthopaedic cases. Recovery was fast, uneventful and free of any excitement.

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