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Research Article

HAEMATO-BIOCHEMICAL PROFILE IN GLYCOPYRROLATE PREMEDICATED DOGS MAINTAINED WITH ISOFLURANE ANAESTHESIA WITH INDUCTION OF PROPOFOL, KETOFOL AND ETOMIDATE

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ABSTRACT

This was a randomized blinded clinical study conducted to compare the effects of propofol, ketofol and etomidate on haematological parameters in glycopyrrolate premedicated dogs maintained with isoflurane. The 18 male mongrels bred dogs came for castration were randomly divided into three groups *viz.*, group P, KP & E, comprising six animals in each group. All the animals of the three groups were premedicated with glycopyrrolate @ 0.01 mg/kg IM, 10 minutes before induction. Propofol @ 6 mg/kg IV, ketofol @ 4 mg/kg and etomidate @ 3 mg/kg was administered as induction agent in group P, KP and E, respectively. Maintenance of anaesthesia was carried out by using isoflurane in all three groups. This was followed by castration in all dogs and assessment of parameters. Hemato-biochemical parameters were evaluated at (baseline) 0 min and thereafter 5, 15, 30, and 60 minutes after induction. There was no significant difference in Hb, PCV, TLC, monocyte, lymphocyte and granulocyte among the three groups throughout the observation period but TEC showed a significant ($p<0.05$) decrease in group E from 15 min onwards as compared to group P and KP. Similarly, in all three groups, serum glucose showed a significant increase at the end of anaesthesia. ALT, AST, BUN showed non-significant changes in all three groups. GGT and creatinine showed a significant difference in both P and KP groups but not in group E. Therefore, it can be concluded that the entire anaesthetic drug can be used as an anaesthetic protocol for surgical intervention in the dog but etomidate will be a better option in case of ill patients.

Keywords: Dog, Etomidate, Haemato-biochemical, Isoflurane, Ketofol, Propofol

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The surgical intervention of small animals are most often done under general anaesthesia due to the types of procedures typically performed, the small size of the patient, their suitability to general anaesthesia, and the greater degree of control. A balanced anaesthesia protocol can be used whereby different drugs with different effects are used and hence that a high dose of just one drug can be avoided. The intravenous anaesthetic agent used for induction and maintenance of anaesthesia in animals is propofol, ketamine (Lin *et al.*, 1997) and etomidate (Perk *et al.*, 2002). Ketamine and propofol are two completely different sedatives which mitigate each other's deficits due to their opposing physiological effects (Green *et al.*, 2011). In ketofol, propofol provides rapid and smooth induction, maintenance of anaesthesia and recovery from anaesthesia and ketamine provides analgesic effects (Wamaitha *et al.*, 2019). The association of ketamine and propofol may reduce unwanted adverse effects of both drugs since these drugs act on different extremes - excitation and depression, respectively (Mair *et al.*, 2009). Etomidate is rapidly hydrolyzed in the liver and excreted in the urine. Etomidate induced minimal changes in cardiopulmonary function in hypovolaemic dogs (Pascoe *et al.*, 1992). Therefore, the study was initiated to compare the efficacy of propofol, ketofol and etomidate on haematological parameters in glycopyrrolate premedicated dogs maintained under isoflurane.

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MATERIALS AND METHODS

The study was carried out on eighteen male dogs that were brought to the Teaching Veterinary Clinical Complex (TVCC), College of Veterinary Sciences and Animal Husbandry, Central Agricultural University, Selesih, Aizawl for castration. All the animals were randomly divided into three equal groups *viz.*, Group-P, Group-KP and Group-E with six animals in each group. Food was withheld for approximately 12 h before premedication, and all dogs were found healthy based on a clinical examination before each experimental session. Induction and maintenance of anaesthesia were achieved in the three groups as follows.

S.No.	Groups (n=6)	Pre-anaesthetics dose & route	Anaesthetic Induction & route	Anaesthetic maintenance up to 60 minutes
1	P	Glycopyrrolate @ 0.01 mg/ kg IM	Propofol @ 6 mg/kg IV	2-4% Isoflurane
2	KP	-do-	Ketofol @ 4 mg /kg (each drug 2 mg/kg) IV	-do-
3	E	-do-	Etomidate @ 3 mg/kg, IV	-do-

The doses of propofol, ketofol and etomidate were chosen based on the results from a previous study.

For evaluation of anaesthetic efficacy of propofol, ketofol and etomidate on haematological parameters, 5 ml blood was collected from cephalic or saphenous veins, in EDTA vials and clot activator vials before premedication at 0 minutes (baseline), thereafter 5, 15, 30 and 60 minutes after induction and during maintenance of anaesthesia. The haematological parameters *viz.*, haemoglobin (Hb), packed cell volume (PCV), total erythrocytic count (TEC), total leukocyte count (TLC), monocyte count (M), Lymphocyte count (L) and granulocyte count (G) were estimated with the help of automated haematology cell counter (MS4e, France) and biochemical parameters *viz.*, blood glucose, alanine amino transferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT), blood urea nitrogen (BUN) and creatinine were estimated by Evolution 201 UV-visible Spectrophotometer with the help of commercial kits.

All the data were statistically analysed by SPSS version 20 where a two-way Analysis of variance (ANOVA) was used for quantitative parameters and the significant values in the ANOVA were further tested through the Duncan multiple range test. Results are presented as mean±SD and differences were considered significant when $P < 0.05$.

RESULTS AND DISCUSSION

Effect of anaesthetic protocol on haematological parameters: The analysis of blood parameters is one of the most valuable methods available for modern diagnostics (Anver Celik, 2004) and can provide important information about the internal environment of the organism (Kristan *et al.*, 2012). Haematological and biochemical profiles are frequently used for the evaluation of the effect of anaesthetics (Kristan *et al.*, 2012).

The study showed that there was no significant difference in Hb, PCV, TLC, monocyte, lymphocyte and granulocyte among the three groups throughout the observation period but TEC showed a significant ($p<0.05$) decrease in group E from 15 min onwards as compared to group P and KP (Fig. 1) and non-significantly the Hb level was decreased from 5 min onwards after induction as compared to the before premedication (Fig. 1A). A similar trend of observation in regards to haematology also observed by Bayan *et al.* (2002) with propofol anaesthesia, Sharma *et al.* (2017) with ketofol and Perk *et al.* (2002) in a study of Etomidate/Alfentanil anaesthesia in dogs. The decrease in Hb and PCV value in the present study might be due to the splenic pooling of erythrocytes that occur with most of the anaesthetics or due to haemodilution in response to fluid therapy during anaesthetic protocol (Thejasree *et al.*, 2018).

The PCV level of all the three groups showed a non-significant decrease from 5 min to 15 mins and thereafter rnon-significantly increased towards the baseline in all three groups throughout the observation period (Fig. 1B). Similar observation also recorded in the case of TEC and TLC (Fig. 1C & D). The decrease in TLC might be due to an increase in plasma volume during anaesthesia on account of vasodilatation resulting in vascular pooling (Steffy *et al.*, 1976). Splenic sequestration during anaesthesia might be the cause of a decrease in TLC within the groups.

There was a non-significant difference observed in different leucocyte count at different time intervals within all three groups. There was no significant difference observed among the three groups at different time intervals regarding monocyte and lymphocyte count but the levels were in decreasing trend (Fig. 1E & F) whereas granulocyte count showed non-significant increasing trend in groups throughout the observation period after the induction of anaesthesia (Fig. 1G). The rise in granulocyte count and decrease in lymphocyte count might be due to adrenocortical stimulation and the subsequent effect of glucocorticoids on circulating neutrophils and lymphocytes (Sengar *et al.*, 2020).

Effect of anaesthetic protocol on biochemical parameters: The anaesthetic effect of propofol, ketofol and etomidate on biochemical parameters showed a significant ($P \leq 0.05$) and ($P \leq 0.01$) increased in glucose level throughout the observation period (Fig. 2A). Among the groups, glucose value was significantly ($p < 0.05$) increased in group P and group KP at 30 and 60 min time intervals as compared to group E. A similar increase in blood glucose was also reported by Bayan *et al.* (2002) with propofol, Njoku (2015) with ketofol and Perk *et al.* (2002) with etomidate/alfentanil anaesthesia in dogs. The increases in blood glucose concentrations found in the present study reflected the response of anaesthetised dogs to metabolic stress. Increases in plasma glucose are mediated by the release of catecholamines, presumably in response to the hypoxia caused by the cessation of respiration in anaesthetised dogs.

Enzyme activity in blood plasma can be a stress indicator. There was no significant difference observed in the case of ALT and AST among the groups at a different level, but non-significantly increased throughout the observation period. A significant change in the activity of the mentioned enzymes indicates tissue damage, which may be stress-induced (Svoboda, 2001). The GGT level in group P and KP were significantly ($P \leq 0.05$ & $P \leq 0.01$,

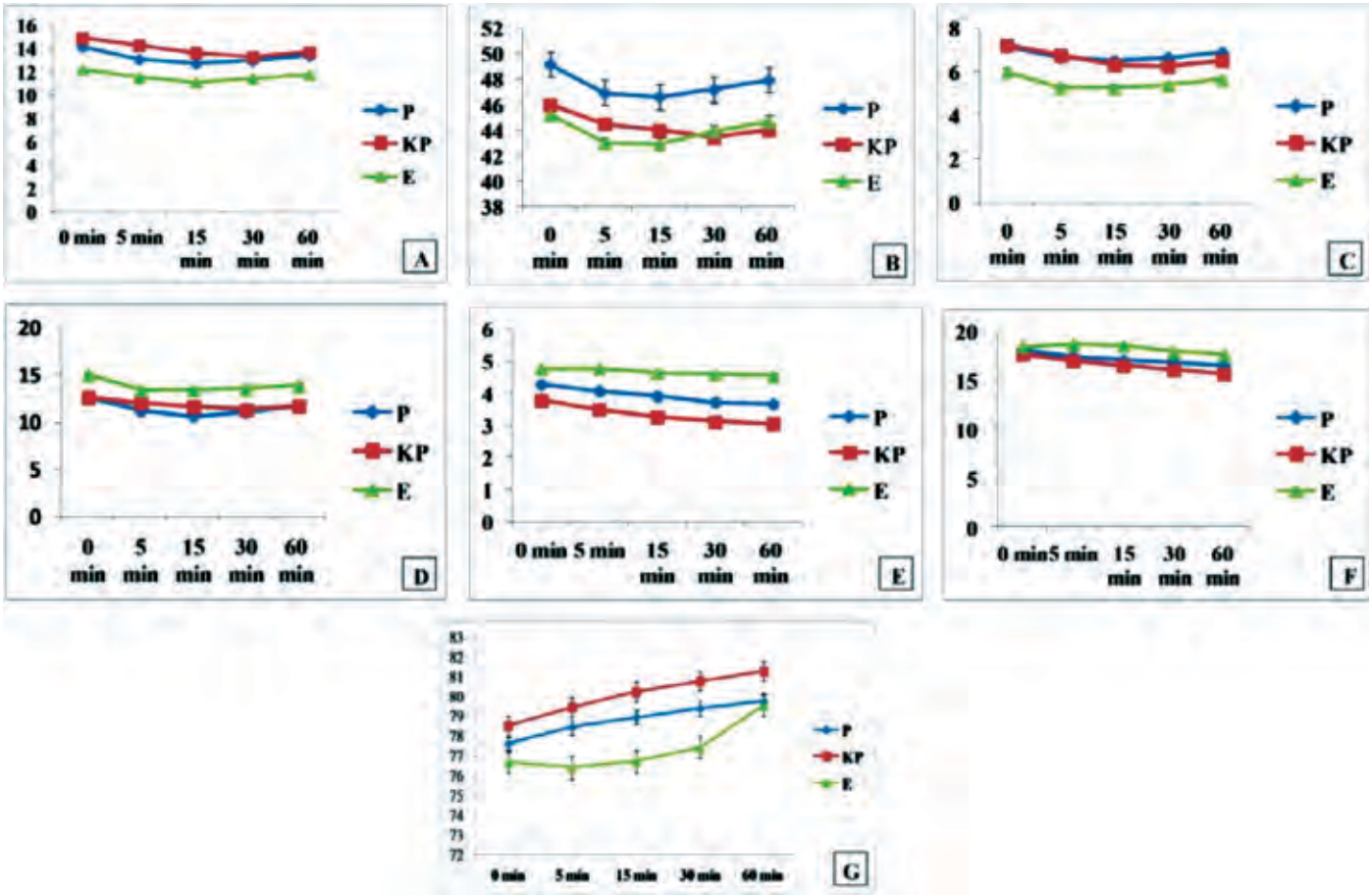

Fig. 1. Effect of anaesthetic protocol *viz.*, propofol, ketofol and etomidate on haematological parameters. **(A)** Haemoglobin; **(B)** Packed cell volume; **(C)** Total erythrocyte count; **(D)** Total leucocyte count; **(E)** Monocyte count; **(F)** Lymphocyte count; **(G)** Granulocyte count

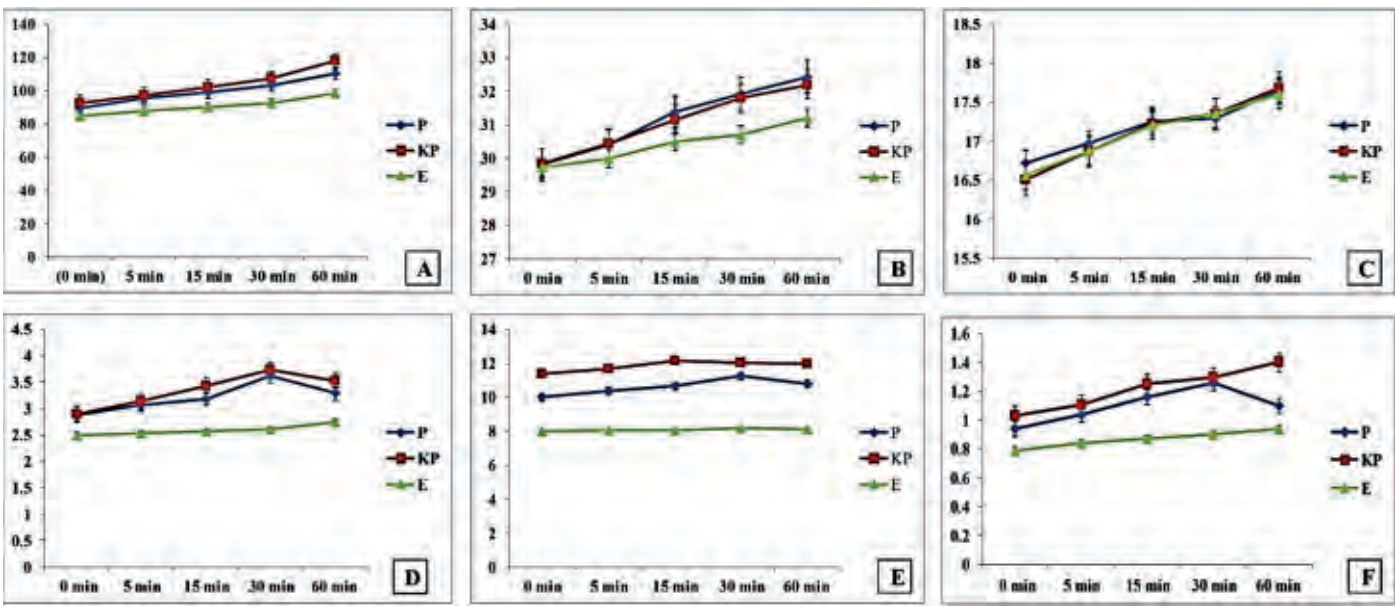

Fig. 2. Effect of anaesthetic protocol *viz.*, propofol, ketofol and etomidate on biochemical parameters. **(A)** Glucose; **(B)** ALT; **(C)** AST; **(D)** GGT; **(E)** BUN; **(F)** Creatinine

respectively) increased however in group E, non-significant increase at a different time interval (Fig. 2B, C, D). Changes in GGT levels might be due to the strong anaesthetic effect of propofol and ketofol. Creatinine values recorded at baseline and all other time intervals for all the three groups showed significant variations in group E compared to group P and KP but were within the normal range. It might be due to the use of different induction agents in different groups and random selection of animals in groups or might be both.

The BUN level non-significantly increased up to 30 min in group P, KP and E but towards the end part of the observation; it declined towards the baseline (Fig. 2E). The creatinine level was significantly ($P \leq 0.01$) increased throughout the observation period in group P, whereas the level was significantly ($P \leq 0.01$) increased up to 30 min then turn to baseline level at 60 min in group KP. But, in group E, non-significant ($P \geq 0.05$) increase of creatinine observed throughout the study period (Fig. 2F). The significant increase in creatinine value in both group P and group KP might be due to the temporary inhibitory effects of anaesthetic drugs on the renal blood flow leading to a decrease in glomerular filtration.

Critical analysis revealed that there was no significant variance on haemato-biochemical parameters among the propofol, ketofol and etomidate groups, but the etomidate group showed better results in comparison to the other groups in terms of haematology and biochemical parameters. There was no variation of haemato-biochemical parameters among the time intervals in etomidate group. Therefore, etomidate anaesthesia can be used in the case of an ill patient.

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