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Haemato- biochemical Changes Following Administration of Propofol in Combination with Buprenorphine in Atropinized Dogs

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ABSTRACT

The aim of study to find out the effect on haematological and biochemical parameters following administration of propofol alone and in-combinaiton with buprenorphine. Propofol was given to effect in group I (control), whereas buprenorphine @ 0.015 mg/kg b.wt. was given as preanaesthetic before propofol "to effect" in dogs of group II .Atropine sulphate was injected I/M @ 0.04 mg/kg b.wt. 20 minutes prior to each treatment in both the groups.Hb, PCV and TEC showed a significant fall ($P<0.05$) at initial intervals of observation as compared to base line whereas, other haematological parameters were non-significantly variables at different intervals of observation in both the groups.A non significant alteration in the level of total serum protein, alkaline phosphatase activity, serum creatinine and blood urea nitrogen could be recorded at different observation periods either within the group or among the groups. There was significant increase in serum glucose level at 1hr in both treatment groups followed by a progressive decrease in its value which reached to pretreatment value within 24hrs. There was significant increase ($P<0.05$) in AST value at 1hr in group Iwhereas in group II, it could be recorded at hr 1 and 2 of observation.A significant elevation ($P<0.05$) in ALT value could be recorded in both groups of animals at hr1 and 2 of observation as compared to their respective baseline value.It is concluded that propofol alone and in combination with buprenorphine produced no deleterious effect on the vital organs, hence can be used safely in dogs.

Keywords: Biochemical changes, haematological changes, buprenorphine, dogs, propofol

General anesthesia is usually induced with a combination of drugs. In Addition to the hypnotic agent, such as propofol, opioids are often used due to their synergistic hypnotic and analgesic properties. Propofol is a unique non-barbiturate, non-steroid, short-acting general intravenous anaesthetic agent (Hofmeister *et al.* 2008).

Pharmacodynamically, the interaction between propofol and the opioids is generally found to be synergistic (Vuyk, 1997). Buprenorphine is a partial μ opioid agonist and a strong kappa antagonist. It has high affinity for the μ receptors, with slow dissociation resulting in a long duration of action. At higher doses, it begins to behave more like an antagonist, limiting the maximal analgesic effect. Thus, it has a very wide margin of safety (Sporer, 2004). It is about 25 times more potent than morphine and has a low level of physical dependence. As parenteral analgesic, buprenorphine has been administrated by the epidural, intra-articular, intramuscular, intravenous, and subarachnoid routes as well as by continuous subcutaneous infusion. Most opioids require redosing at every 4-6 hours. Buprenorphine provides analgesia for up to 6 to 8 hours after administration. Therefore, it has an advantage over other short acting opoids. Because of its longer analgesic action compared to other opiates, buprenorphine can be used before and during surgery to provide post operative analgesia. The present paper deals with the changes of haemato - biochemical parameters following administration of propofol alone and in – combination with buprenorphine.

MATERIALS AND METHODS

The study was conducted in 10 dogs, randomly divided in to two groups with five dogs in each group. Propofol was given to effect in group I (control), where as Buprinorphine @ 0.015mg/kgbwt was given as preanaesthetic before propofol "to effect" in dogs of group II. Atropine sulphate was injected I/M @ 0.04 mg/kg b.wt. 20 minutes prior to each treatment. Propofol 'to effect" was administered intravenously in each animal of both groups, after administration of anaesthetic agents to produce general anaesthesia till the loss of pedal reflex which served as a guide for the development of surgical anaesthesia.

Following administration of propofol, haematological changes viz.heamoglobin(Hb) (gm/dl), total erythrocyte count (TEC). ($\times 10^6$ /µl of blood), total leucocyte count (TLC). ($x10^3$ µl of blood), differential leucocyte count (DLC). (%), packed cell volume (PCV). (%), blood platelets ($\times 10^5$ mm^3) were carried out at the time intervals of 5, 10, 20, 30 and 60 minutes of propofol administration.

For harvesting blood serum, 4-5 ml of blood was collected before and at time intervals of 1 hr, 2 hr, 4 hr. and finally at 24 hr in a clean and dry test tube without anticoagulant by dry glass syringe through siliconized catheter placed in radial vein or recurrent tarsal vein. The blood was allowed to clot within the test tube in a standing position for nearly 30 minutes and then centrifuged it for 20 minutes at 3500 rpm. The supernatant serum was collected in a clean dry test tube by rubber bulb pipette. The separated serum was used for estimation of serum protein (Biuret method), alkaline phosphatase (Tris carbonate buffer method), serum creatinine (Jaffe's method), serum urea nitrogen (GLD – urease method), ALT (IFCC method), AST (IFCC method) and GGT (IFCC method) were carried out by Auto analyzer (Erba Mannheim Chem-5 plus V2) using Erba diagnostic kit.

The data obtained were statistically analyzed by analysis of variance (ANOVA) as per method described by Snedecor and Cochran (1994). The level of significance was set to be 0.05.

RESULTS AND DISCUSSION

Haemoglobin value exhibited significant fall at 5 min in group I and at 10 min. of observation in group II after propofol administration. PCV showed a significant fall

Table 1: Mean ± S.E. value of Haemoglobin (gm/dl), PCV (%), TEC($\times 10^6$ µl)of different groups at different time intervals of observation

Parameters	Groups	Period of observation (in minutes)					
		0	5	10	20	30	60
Haemoglobin	I	10.72 ±0.28a	9.35 ±0.23b	10.70 ±0.12 a	10.50 ±0.18a	10.75 ±0.26 a	11.00 ±0.19a
	II	10.96 ±0.15a	9.74 ±0.39ab	9.18 ±0.73 b	10.66 ±0.36ab	11.16 ±0.71 a	11.40 ±0.58a
Packed cell volume	I	33.56 ±0.29a	30.22 ±0.24b	29.42 ±0.48b	33.90 ±0.64a	34.18 ±0.96a	34.14 ±0.56a
	II	33.97 0.46a	29.95 ±1.05b	29.37 ±0.38b	32.55 ±1.02ab	34.18 ±1.74a	34.94 ±1.37a
Total erythrocyte count	I	6.58 ±0.15a	6.05 ±0.18ab	6.10 ±0.13b	6.09 ±0.28a	6.21 ±0.24a	6.48 ±0.15a
	II	6.74 ±0.27a	6.09 ±0.26ab	5.88 ±0.23b	6.79 ±0.27a	6.80 ±0.25a	6.78 ±0.29a

Values did not differ significantly between the groups (P>0.05)

Values with different superscripts in a row (small letters) differed significantly (P<0.05).

Table 2: Mean ± S.E. value of glucose (mg/dl), GGT (IU/L), AST (IU/L) and ALT ((IU/L)) of different groups at different time intervals of observation

Parameters	Groups	Period of observation (hours)				
		0	1	2	4	24
Glucose	I	77.00 ± .79[a]	81.00 ± 1.67[b]	75.80 ± 1.51[ab]	78.00 ± .80[ab]	78.00 ± 0.94[ab]
	II	78.46 ± 1.79[a]	82.46 ± 1.67[b]	77.26 ± 1.51[ab]	79.46 ± 0.80[ab]	79.46 ± 0.94[ab]
GGT	I	3.80 ±0.73	4.20 ±0.58	4.60 ±0.24	4.00 ±0.32	4.40 ±0.24
	II	4.00 ±0.84	4.80 ±0.58	4.60 ±0.24	4.60 ±0.24	4.00 ±0.32
AST	I	34.52 ± 0.35[a]	36.54 ± 0.20[b]	35.78 ± 0.33[b]	34.58 ± 0.30 [a]	34.60 ± 0.44[a]
	II	33.94 ± 0.28[a]	35.96 ± 0.19[b]	36.04 ± 0.33[b]	33.74 ± 0.37 [a]	33.68 ± 0.12[a]
ALT	I	41.80 ± 0.30[a]	42.94 ± 0.20[b]	42.06 ± 0.42[ab]	41.46 ± 0.28[a]	41.5 ± 0.34[a]
	II	41.86 ± 0.30[a]	42.98 ± 0.22[b]	42.44 ± 0.35[b]	41.66 ± 0.43[a]	41.52 ± 0.35[a]

Values did not differ significantly (P>0.05) among the groups.

Values with different superscripts in a row (small letters) differed significantly (P0.05).

(P<0.05) at 5 min. of observation in both the groups, whereas, TEC exhibited significant fall at 10 min of observation in both the groups. However, the values of Hb, PCV and TEC afterwards at different intervals of observation showed increasing trends and returned near to the base line value (Table 1). Fall in Hb, PCV and TEC after propofol in dogs has also been reported by various workers (Gill et al. 1996; Venugopal *et al.* 2002; Suresha *et al.* 2012). Decrease in these values might be due to splenic dilation resulting in splenic sequestration of R.B.C. In contrast to present finding, Soordaya (2001) reported an increase in Hb on induction with propofol in dogs. The values of tolal leucocyte counts, platelets, differential leucocyte counts (neutrophil, eosinophil, lymphocyte and monocyte) recorded at different intervals were transient and non- significantly variables in both the groups. These findings were in agreement with Chandrashekharappa (2009) using propofol and pentazocine lactate in dog.

A non-significant variation of platelets in present study was in accordance with the findings of Dardoni *et al.* (2004) in human following administration of propofol or fentanyl or propofol –fentanyl –sevoflurane.

The total serum protein level and alkaline phophatase activity did not show any significant variation (P>0.05) at any interval of time either within or among the groups. However, the elevation in alkaline phosphatase value could be observed during the initial phase of anaesthesia. The non significant alteration in total serum protein might also attributed to splenic pooling of erythrocytes which caused overloading of water in blood. The present finding corroborates with the finding of Apaydin *et al.* (2006) using propofol and diazepam combination in dog. The alkaline phosphatase of normal adult appears to be mainly derived from liver with a small variable intestinal component. The non significant alteration in alkaline phosphatase might be

due to temporary effect of drugs on liver metabolism.

The values of creatinine and serum urea nitrogen were transiently and non – significantly increased (P>0.05) at initial intervals after administration of agents. However, the values returned towards the base value by end of observation. The finding of this study was similar to Kim-Jiwan *et al.* (1999), Chandrashekharappa *et al.* (2009) in dog. The non significant alteration in creatinine and blood urea nitrogen value might be due to increased level of anti diuretic hormone (ADH) along with decreased glomerular filtration as emphasized by Lobetti and Lambrechts (2000) and Suresha *et al*. (2012) during anaestheic procedure in dogs.

A transient but significant increase in glucose level was observed at 1 hr post induction in both the groups. The maximum increase in blood glucose level was noticed at 1 hr which tended to reach near the base value at 24 hr post induction in both the groups (Table 2). This corroborates with the finding with propofol (Bayan *et al.* 2002), buprenorphine (Gupta, 2010) and meperidine – diazepam (Kumar *et al*. 1989) in dogs. Rise in glucose level may be due to activation of the sympathoadrenal system releasing adrenaline which in turn mobilized glycogen from liver during anaesthesia. Clark (1968) and Allison *et al*. (1969) have suggested that the stress with anaesthesia leads to alteration in endocrine secretion of insulin antagonists such as growth hormone and cortisol causing temporary diabetic state. In the present study the increased serum glucose level might be attributed to decreased membrane transport of glucose, decreased glucose utilization, impaired insulin activity or increased concentration of adrenocortical hormones.

GGT value did not show a significant variation in both the groups which is anaccordance with Apaydin *et al.* (2006).

ALT and AST showed a significant increase (P<0.05) in both the groups during 1 hr to 2 hrs post induction of propofol which gradually approached to preinjection value within 24 hrs of induction (Table 2). Increase in AST level has been reported in clinical trials assessing buprenorphine for addiction treatment (Petry *et al*. 2000). Propofol is rapidly cleared by hepatic and perhaps, extrahepatic metabolism. It is mainly metabolized by glucoronide conjugation in liver (Kanto and Gepts, 1989). Buprenorphine is highly bound to plasma protein (96%) primarily to α and β globulin fractions. Buprenorphine is demethylated by cytochrome P450. Both buprenorphine and nor-buprenorphine are excreted via glucoronide conjugation in liver (Johnson *et al*. 2005).Propofol along with buprenorphine are metabolized mainly in liver. So, the transient increase in ALT and AST level might be due to hepatic metabolism of these drugs which returned back to the normal physiological level indicating no undesirable effect on liver.

CONCLUSION

It is concluded that propofol alone and in combination with buprenorphine produced no deleterious effect on the vital organs, hence can be used safely in dogs.

REFERENCES

Allison, S.P., Tomlin, P.J. and Chamberlain, M.J. 1969. Some effects of anaesthesia and surgery on carbohydrate metabolism. *Br. J. Anaesth*., **41:** 588.

Apaydin, N., Kibar, M. and Uyanik, F. 2006. The effects of propofol and thiopental sodium anaesthesia on serum enzyme activity in dogs. *Indian Vet. J.,* **83**: 624-626.

Bayan, H., Sarma, K.K. and Chakravarty, P. 2002. Biochemical and haematological changes during propofol anaesthesia in canine. *Indian J. Vet. Surg.*, **23**: 95-96.

Chandrashekharappa, M. and Ananda, K.J. 2009. Evaluation of anesthetic combinations of propofol with pentazocine lactate and chloramphenicol in dogs. *Indian Vet. J*., **86:** 577-579.

Clarke, R.S.J. 1968. The influence of anaesthesia with thiopentone and propandid on the blood sugar level. *Br. J. Anaesth*., pp. 40-46.

Dordoni, P.L., Frassanito, L., Bruno, M.F., Proietti, R., de Cristofaro, R., Ciabattoni G., Ardito, G., Crocchiolo, R., Landolfi, R. and Rocca, B. 2004. In vivo and in vitro effects of different anaesthetics on platelet function**.** *Br. J. Haematol.,* **125**(1): 79-82.

Gill, J.R., Rodriguez, J.F., Ezquerra, L.J., Vives, M.A., Jimenez, J. and Uson, J.M. 1996. Development of anaesthesia and changes in the blood parameters in dogs medicated with propofol. *Medicina-Veterinaria,* **13**(4): 242-246.

Gupta, A.N. 2010. Evaluation of medetomidine and dexmedetomidine with propofol for total intravenous anaesthesia and tramadol and fentanyl for analgesic management of canine orthopaedic patients. M.V.Sc. thesis submitted to deemed university IVRI, Izatnagar.

Hofmeister, E.H., Williams, C.O., Braun, C. and Moore, P.A. 2008. Propofol versus thiopental: effects on peri-induction

intraocular pressures in normal dogs. *Vet. Anaesth. Analg.*, **35:** 275-281.

Johnson, R.E., Fudala, P.J. and Payne, R. 2005. Buprenorphine: Consideration for pain management. *J. Pain Symptom Manage*, **29**: 297-326.

Kanto, J. and Gepts, E. 1989. Pharmacokinetic implications for the clinical use of propofol. *Clin. Pharmacokinetic*, **17**: 308-326.

Kim-Jiwan., Inho-Jang., Kim, J.W. and Jang, I.H. 1999. The effects of xylazine premedication on propofolanaesthesia in the dog. *Korean J. Vet. Cli. Med.*, **16**(1): 86-94.

Kumar, N. Kumar, A. and Singh, B. 1989. Haematological and biochemical effects of a combination of meperidine and diazepam in dogs. *Indian J. Vet. Surg.*, **10**(2): 120-123.

Lobetti, R. and Lambrechts, R. 2000. Effects of general anaesthesia and surgery on renal function of healthy dogs. *Am. J. Vet. Res.*, **61**(2): 121-124.

Petry N.M., Bickel, W.K., Piasecki, D., Marsh, L.A. and Badger, G.J. 2000. Elevated liver enzyme levels in opioid – dependent patients with hepatitis treated with buprenorphine. *Am. J. Addict.*, **9**: 265-269.

Snedecor, G.W. and Cochran, W.G. 1994. Statistical Methods. 8th Edn., Oxfords and IBH Publishing Co., New York, p. 59.

Sooryada, S. 2001. Clinical Evaluation of xylazine – propofol anaesthesia in dogs M.V.Sc. Thesis submitted to Kerala Agricultural University, Mannuthy, Thrissur.

Sporer, K.A. 2004. Buprenorphine: a primer for emergency physicians. *Ann. Emerg. Med.*, **435**: 580-584.

Suresha, L., Ranganath, B.N., Vasanth, M.S. and Ranganath, L. 2012. Haemato-biochemical studies on triflupromazine HCL anddiazepam premedication for propofol anaesthesia in dogs. *Vet. World*, **5**(11): 672-675.

Venugopal, A., chandrasekhar, E.L. and Haragopal, V. 2002. Effects of propofol-ketamine anaesthesia with or without premedication in dogs. *Indian J. Vet. Surg.*, **23**(2): 106-107.

Vuyk, J. 1997. Pharmacokinetic and pharmacodynamic interaction between opioids and propofol. *J. Clin. Anaesth.*, **9**(6 suppl.): 23S-26S.