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Alternations on haemato-biochemical profiles following administration of atropine-buprenorphine-propofol anaesthesia in goats

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Abstract
The study was conducted to evaluate the alternations on haemato-biochemical profiles following administration of atropine-buprenorphine-propofol anaesthesia in six healthy non-descript goats of either sex weighing between 20-25 kg by administrating atropine sulphate @ 0.04 mg/kg I/M followed by buprenorphine @ 10 mg/kg I/M and 10 min. later induction of anaesthesia with propofol @ 5mg/kg I/V. Hb, PCV and TLC showed non-significant decrease at 60 min. however, the following values showed increasing trends at different time intervals of observation and returned to near base value by 6 hrs. There was significant (P<0.05) increase in neutrophils with significant (P<0.05) decrease in lymphocyte values. Serum glucose showed significant (P<0.05) elevation at 60 min. after atropine-buprenorphine-propofol administration whereas non-significant increase in serum urea nitrogen, serum creatinine, AST and ALT were observed at different time intervals. However, these changes were within normal physiological limits. Therefore, it can be concluded that atropine-buprenorphine-propofol combination does not produce any deleterious effect on vital organs and changes remain within physiological limits, thus can be safely used in goats.

Keywords: Atropine, buprenorphine, goats, haemato-biochemical, propofol

Introduction
Goat is a multi-purpose animal which provide meat, milk, hide, fibre and manure. It has been described as a poor man's cow (or mini-cow) because of its immense contribution to the poor man's economy. It not only provides nutritious and easily digestible milk to their children but is also regular source of additional income for poor, landless or marginal farmers. Anaesthesia is an indispensable prerequisite for most surgical interventions both in humans and animals. General anaesthesia is usually induced with combination of two or more drugs. Atropine sulphate is obtained from plant *Atropa belladonna* which is used as preanaesthetic to prevent salivary, bronchial, tracheal and gastric secretions and to inhibit the bradycardiac effects of vagal stimulation. Propofol (2, 6-di-isopropylphenol) is a unique non-barbiturate, non-steroid, short acting general intravenous anaesthetic agent (Hofmeister *et al*., 2008) [5]. Therefore, it is widely used in the clinical setting as an induction agent and to maintain short periods of unconsciousness. Rapid recovery and reduced side effects make it the drug of choice, especially for ambulatory surgical interventions. Propofol should be combined with analgesic drugs as it is devoid of any substantial analgesic effects. In addition to the hypnotic agent, such as propofol, opioids are often used due to their synergistic hypnotic and analgesic properties (Anandmay *et al*., 2016) [2]. Pharmacodynamically, the interaction between propofol and opioids is generally found to be synergistic (Vuyk, 1997) [19]. Buprenorphine is a derivative of morphine alkaloid the bane having partial agonist activity at μ opioid receptor and antagonist activity at kappa opioid receptor with a long duration of action. It is about 25 times more potent than morphine and has a low level of physical dependence. Buprenorphine provides analgesia for up to 6 to 8 hours after administration. Due to its excellent analgesic properties buprenorphine is a drug that finds broad clinical applications for cats, dogs, exotic species and laboratory animals. It provides analgesia for the management of pre-operative/ post –operative pain as well as other painful injuries (Roughan and Flecknell, 2002) [14]. Due to the fact that the elimination is mainly hepatic as it is metabolized in the liver and excreted through bile, there is no risk of accumulation in patients with renal failure.

There is very little information in the literature on the use of buprenorphine with propofol anaesthesia in goats, therefore, the present study was undertaken to evaluate the alternations on haemato-biochemical parameters following administration of atropine-buprenorphine-propofol anaesthesia in goats.

Materials and Methods

The present study was conducted in six healthy non-descript goats of either sex weighing between 20-25 kg using atropine sulphate @ 0.04 mg/kg I/M followed by buprenorphine @ 10 mg/kg I/M and 10 min. later induction of anaesthesia with propofol (5mg/kg I/V). For estimation of haematological profiles *viz*., hemoglobin (Hb), packed cell volume (PCV), total leucocyte count (TLC) and differential leucocyte count (DLC) after administration of propofol, the blood was collected from jugular vein in a clean sterile glass vial containing ethylene diamine tetra acetic acid 1 mg/ml from goats before premedication (0 min.) and 30, 60, 120 minutes and 6 hrs. After induction of anaesthesia. For blood serum, 4-5 ml of venous blood was collected without anticoagulant in sterilized dry test tube and allowed to clot at room temperature. After two hours, serum was separated with the help of pasture pipette and the following biochemical profiles *viz*., serum glucose (mg/dl), serum urea nitrogen (mg/dl), creatinine (mg/dl) aspartate aminotransferase (AST) (U/L) and alanine aminotransferase (ALT) (U/L) were estimated at 0 min., and 30, 60, 120 minutes and 6 hrs interval post anaesthesia. The mean and standard error of recorded values were calculated and one way analysis of variance (ANONA) was used to compare the means at different intervals as per the standard procedure outlined by Snedecor and Cochran (1994).

Results and Discussion

Hematological profiles

The Mean± S.E values on haematological profiles following administration of atropine-buprenorphine-propofol anaesthesia in goats at various time intervals are shown in Table 1. In the present study, hemoglobin (Hb) showed non-significant decrease at 60 min (8.5±0.27 gm. %) as compared to base value (10.70±0.44 gm. %). A non-significant decrease was also recorded in PCV at 60 min (from 33.33±0.42 to 31.00±0.42%). TLC showed non-significant decrease at 60 min (from 33.58±0.23 to 31.16±1.49 $x10^3$cu. mm^{-1}). However, the values of Hb, PCV and TLC afterwards showed increasing trends at different time intervals of observation and returned to near base value by 6 hrs. The decrease in these values might be due to spleenic dilation resulting in spleenic sequestration of blood cells during anaesthesia or due to increase in plasma volume during anaesthesia on account of vasodilatation resulting in vascular pooling. Neutrophils count showed a significant (P<0.05) increase from 34.33±1.76 to 44.73±0.70% up to 60 minutes whereas, lymphocyte count decreased significantly (P<0.05) from 65.16±0.51 to 60.16±0.30% up to 60 minutes and these values returned to near base values at 6 hrs of study period. There was a corresponding neutrophil in response to lymphocytopenia. This rise in neutrophils count and decrease in lymphocyte count might be attributed to the adrenocortical stimulation and subsequent effect of glucocorticoids on circulating neutrophils and lymphocytes (Soliman *et al*., 1965) [17]. This increase in neutrophils count might be associated with systemic stress associated with endogenous release of corticosteroids after administration of an aesthetics (Benjamin, 1985) [3]. The eosinophil's increase was non-significant in animals following administration of atropine-buprenorphine-propofol, from 2.06± 0.16 to 2.33± 0.21 at 120 minutes and monocytes showed a non-significant decrease at 60 min (from 2.25±0.33 to 1.72±0.21%) after administration of atrophine-buprenorphine-propofol anaesthesia. Thereafter, these values gradually returned to base value. Pathak *et al*. (2012) [12] recorded reduction in Hb and PCV values but the changes were non-significant after intraspinally administration of buprenorphine at lumbosacral space in buffalo calves. Fall in Hb, PCV and TLC after propofol has also been reported by Kelawala *et al*. (1991) [8] in goats and Singh *et al*. (2014) [15] in buffalo calve. Anandmay *et al*. (2016) [2] reported significant fall (P<0.05) in Hb, PCV and TEC at initial intervals of observation as compared to baseline whereas, TLC and DLC (neutrophils, eosinophil, lymphocyte and monocyte) varied non-significantly up to 24 hours of observation following administration of propofol in combination with buprenorphine in atropinized dog.

Table 1: Mean± S.E. value of haematological profiles following administration of atropine-buprenorphine-propofol in goats at various time intervals

Haematological Profiles	0 min.	30 min.	60 min.	120 min.	6 hr.
Hemoglobin (gm. %)	10.70±0.44	9.0±0.40	8.5±0.27	9.4±0.23	10.2±0.11
Packed Cell Volume (%)	33.33±0.42	32.16±0.30	31.00±0.42	31.96±0.76	32.00±0.30
Total Leucocytes Count (x 10^3cumm^{-1})	33.58±0.23	32.67±0.49	31.16±1.49	32.77±1.03	33.25±0.30
Neutrophils (%)	34.33±1.76	37.66±1.85	44.73*±0.70	35.66±1.11	34.06±0.30
Lymphocyte (%)	65.16±0.51	63.83±1.07	60.16*±0.30	64.10±0.44	65.00±0.44
Eosinophil (%)	2.06±0.16	2.18±0.47	2.26±0.55	2.33±0.21	2.03±0.49
Monocyte (%)	2.26±0.33	1.90±0.40	1.72±0.40	1.96±0.40	2.12±0.47

* P<0.05 = Significant at 5% level when compared to base value

Biochemical Profiles

The Mean± S.E. values on biochemical profiles following administration of atropine-buprenorphine-propofol anaesthesia at various time intervals in goats are shown in Table 2. There was significant (P<0.05) elevation of serum glucose (from 80.54±2.61 to 89.96±2.79 mg/dl) following administration of atropine-buprenorphine-propofol anaesthesia. The maximum increase in serum glucose level was noticed at 120 min. which later on decreased and returned to normalcy gradually within 6 hrs. This corroborates with the findings of Amanda *et al.* (2016) [2] with propofol-buprenorphine in atropinized dogs. Similarly, Kumar *et al.* (2010) [9] also reported hyperglycemia after administration of propofol premeditated with *cannabis indica* (Bhang) extract in dogs whereas, Pathak *et al*. (2012) [12] reported non-significant variation in plasma glucose concentration after intraspinal administration of buprenorphine in buffalo calves. 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. However, since hyperglycaemia produced was transient in nature and within the normal physiological limit. Further the rise in glucose level may be due to activation of the sympathoadrenal system releasing adrenaline which in turn mobilized glycogen from liver during anaesthesia. Allison *et al.*, (1969) [1] have suggested that the stress with anaesthesia and surgery may lead to alteration in endocrine secretion of insulin antagonists such as growth hormone. Cortisol and catecholamine causing temporary diabetic state by gluconeogenesis and glycogenolysis as well as decrease in peripheral use of glucose (Desborough, 2000) [4]. The values of serum urea nitrogen and serum creatinine showed non-significant transient increase at 60 minutes following administration of atropine-buprenorphine-propofol anaesthesia and these values tend to return towards the base level by end of observation. Similar observations were reported by Anandmay *et al.* (2016) [2] with propofol-buprenorphine in atropinized dogs. The non-significant alternation in creatinine and blood urea nitrogen values might be due to increased level of antidiuretic hormone (ADH) alongwith decreased glomerular filtration as emphasized by Lobetti and Lambrechts (2000) [10] and Suresha *et al*., (2012) [18] during anaesthetic procedure in dogs. Pathak *et al*. (2012) [12] reported slight variation in BUN could be due to minimal action of buprenorphine on renal blood flow and kidney excretory function following spinal analgesia in buffalo calves. Effect on plasma creatinine levels was negligible which suggested least deleterious effect of buprenorphine after its intraspinal administration at lumbosacral space in buffalo calves. AST showed very marginal increase after administration of buprenorphine-propofol anaesthesia which gradually approached to preadministration level within 6 hrs in all the animals. Increase in AST level has been reported in clinical trials assessing buprenorphine for addiction treatment (Petry *et al.* 2000) [13]. A significant increase in AST was noticed in buffalo calves after administration of medetomodine-pentazocine- propofol anaesthesia (Mandagiri *et al*., 2015) [11] which remained within the physiological limit. It corroborates with the findings of Anandmay *et al.* (2016) [2] following administration buprenorphine-propofol in dogs. There was non-significant increase in ALT up to 60 min (from 23.27±1.93 to 25.20±0.88 U/L respectively) with a gradual decrease up to 6 hrs. in the present study. Propofol is rapidly cleared by hepatic and perhaps, extra hepatic metabolism. It is mainly metabolized by glucoronide conjugation in liver (Kanto and Gepts, 1989) [7]. Buprenorphine gets highly bound to plasma proteins (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) [6]. Propofol along with buprenorphine are metabolized mainly in liver. So, the transient increase in ALT and AST levels might be due to hepatic metabolism of these drugs which returned back to the normal physiological levels indicating no undesirable effect on liver. There were transient changes in all the haemato-biochemical profiles but within physiological limits. From the present study, it could be concluded that atropine-buprenorphine-propofol an aesthetic combination can safely be used in goats.

Table 2: Mean± S.E. value of biochemical profiles following administration of atropine-buprenorphine-propofol in goats at various time intervals

Biochemical Profiles	0 min.	30 min.	60 min.	120 min.	6 hr
Glucose (mg/dl)	80.54±2.61	85.30**±0.87	88.20**±2.63	89.96**±2.79	83.04±5.02
Serum Urea Nitrogen (mg/dl)	24.67±0.33	25.93±0.64	26.80±0.54	25.80±0.54	24.93±0.43
Serum Creatinine (mg/dl)	0.93±0.03	1.08±0.08	1.11±0.03	1.04.±0.03	1.00±0.04
AST (U/L)	74.60±2.35	75.30±2.09	75.26±1.79	75.40±1.82	75.18±1.58
ALT(U/L)	22.17±1.93	24.34±0.95	25.20±0.88	24.22±0.89	24.00±0.81

* $P<0.05$ = Significant at 5% level when compared to base value
** $P<0.01$ = Significant at 1% level when compared to base value

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