Effect on Haematological and Biochemical Profiles Following Administration of Ketamine Alone and in Combination with Dexmedetomidine or Butorphanol in Atropinized Dogs

Krishna Kumar Verma*, S. K. Tiwari, Rukmani Dewangan and Raju Sharda

Department of Veterinary Surgery and Radiology, College of Veterinary Science and A.H. Anjora Durg (C.G), India

*Corresponding author

A B S T R A C T

The present study was conducted on 18 healthy dogs of either sex weighing between 10-20 kg to evaluate the effects on various haematological and biochemical profile using ketamine alone and in combination with dexmedetomidine or butorphanol in atropinized dogs. The experimental work was divided into three groups K (ketamine), DK (dexmedetomidine-ketamine) and BK (butorphanol-ketamine). Atropine sulphate @ 0.04 mg/ kg intramuscularly was administered 15 minutes prior to treatment in all the groups of animals. Haematological studies revealed non-significant changes in haemoglobin, Packed cell volume, Total erythrocyte count, Total leucocyte count and Differential leucocyte count at various time intervals after different treatments in group K, DK and BK. Serum glucose showed a significant (P<0.01) increase in all the groups initially which returned to base values by 24 hrs. Other biochemical parameters like serum total protein, serum urea nitrogen, creatinine and serum enzyme viz. AST and ALT values showed non-significant changes at various time intervals in all the three groups but was within normal physiological range. There were transient changes in haemato-biochemical profiles which were compensated and returned towards normalcy by 24 hrs in all the three groups. It was concluded that ketamine in combination with dexmedetomidine or butorphanol can be safely used as general anaesthetic in compromised and clinically healthy dogs.

K e y w o r d s
Atropine, Butorphanol, Dexmedetomidine, Dog, Ketamine

Introduction

Perfect anaesthesia is mandatory for successful surgery to achieve immobilization, relaxation and unconsciousness. Inspite of new analgesic and anaesthetic drugs, none of the agent fulfils the qualities of an ideal analgesic and anaesthetic agent. Therefore, combination of sedatives and anaesthetic agents has been widely used in animal practice. Today is an era of balanced anaesthesia where two or more drugs are combined to achieve optimum hypnosis, analgesia and muscle relaxation. Atropine, the most important of the alkaloids obtained from Atropa belladonna is used in premedication as an anticholinergic and to antagonize the unwanted muscarinic effects of anticholinesterases. Alpha-2 adrenoceptor agonists are frequently used as pre-
anaesthetics in veterinary practice. Dexmedetomidine is a potent and highly selective alpha 2 adrenoceptor agonist with sympatholytic, sedative, amnestic and analgesic properties (Carollo et al., 2008) which makes it for use in various anaesthetic regimes. Opioids are the most commonly used analgesics to supplement anaesthesia due to their efficacy, rapid onset of action and safety. Butorphanol is a parenteral synthetic opioid agonist-antagonist analgesic of the nalorphane-cyclozocine class. Its chemical structure is similar to morphine. Butorphanol is a potent analgesic agent with a favourable side effect profile (Gross et al., 1990). Ketamine is a congener of phencyclidine, non-barbiturate, non-narcotic agent and chemically designed as (2-(O-chlorophenyl)-2-methylaminocyclohexanone). When administered parenterally produces catalepsy of short duration and shows apneustic breathing pattern which is characterized by prolonged inspiratory duration and relatively short expiratory time. However, ketamine does not provide adequate muscle relaxation and analgesia. Ketamine also provides cardiovascular stability when given in dexmedetomidine preanaesthetized dogs. Since only little information was available, therefore present paper deals with alterations of haematological and biochemical profiles following administration of ketamine alone and in combination with dexmedetomidine or butorphanol in atropinized dog.

**Materials and Methods**

Eighteen healthy dogs of either sex weighing between 10 to 20 kg body weights were randomly divided into three groups viz., group K, group DK and group BK, comprising of 6 animals in each. All dogs were dewormed with Praziquelplus (Albendazole 300mg with Praziquental 25 mg) Tab. @ 1 Tab. / 10 kg body weight orally fifteen days before the start of trials. The animals were fasted for overnight and the drinking water was withheld for 4 hours before the administration of anaesthesia. The animals were kept under uniform feeding and managemental practices throughout the experiment. The animals of all the groups were premedicated with atropine sulphate @ 0.04 mg/ kg intramuscularly 15 minutes prior to treatment. In group K were kept control where ketamine HCl alone was administered @ 5 mg/kg by slow intravenous injection. In groups DK and BK, where dexmedetomidine @ 10 µg/kg i/m and butorphanol @ 0.2 mg/kg i/m was administered, 10 minute later followed by ketamine HCl @ 5 mg/kg by slow intravenous injection respectively.

The haematological profile estimated were haemoglobin, packed cell volume, total erythrocyte count, total leucocyte count, differential leucocyte count for which 1.5 ml blood was collected from the cephalic vein of each animal in vacutainer containing ethylene diamine tetra acetic acid 1 mg/ml before premedication (0) and at 30, 60, 120, 180 minutes, 6 hour and 24 hour after induction of anaesthesia. These parameters were estimated by standard procedures using auto haematology analyzer (Mindray, BC-2800 Vet). Five ml of venous blood was collected without anticoagulant in vacutainer and allowed to clot at room temperature. After two hours, serum was separated with the help of pasture pipette and the following biochemical parameters were estimated at 0 min., and 30, 60, 120 180 minutes 6 hrs and 24 hrs interval post anaesthesia. The biochemical profile which includes are serum glucose (mg/dl), serum total proteins (mg/dl), serum urea nitrogen (mg/dl), creatinine (mg/dl) aspartate aminotransferase (AST) (U/L) and alanine aminotransferase (ALT) (U/L). These parameters were estimated with the help of standard procedures using semi-automated analyzer (Bayer semi-automatic analyzer -RA-50 chemistry).
The data was analyzed as per the standard procedure outlined by Snedecor and Cochran (1994). The mean and standard error of the recorded values were calculated and data were analyzed using Analysis of Variance (ANOVA).

Results and Discussion

Haematological profiles

The effects on haematological profiles after administration of ketamine alone and in combination with dexmedetomidine and butorphanol in atropinized dogs at various time intervals (Mean±S. E.) are shown in Table 1. There was a gradual and non-significant increase in haemoglobin level in all the three groups and the values returned to near preadministration level up to 24 hrs. In group K, there was a non-significant increase (from 15.02±0.36 to 15.12±0.30 g %) in the haemoglobin up to 120 min. Where ketamine alone was administered. In group DK, a non-significant increase was noted at 60 min (from 13.47±0.60 to 14.10±0.59 g %) after administration of dexmedetomidine-ketamine. However, the values fluctuated to near normalcy in other intervals. In group BK, a non-significant increase (from 13.77 ±0.63 to 13.88 ±0.62 g %) was reported at 60 min. after administration of butorphanol-ketamine which fluctuated to near normalcy at rest of the time intervals. Therefore, subsequently decreased and approached to near preadministration level by 24 hrs.

Packed-cell-volume (%) at various time intervals in all the three groups remained near the baseline and no significant difference from the baseline value was found at any interval of time. In the animals of group K, PCV values remained near the baseline and no significant difference from the baseline value was found at any interval of time. In the animals of group DK, PCV followed the same pattern as in group K. PCV values stayed above the baseline but the values at different time intervals did not differ significantly from the baseline values. In the animals of group BK, PCV values fluctuated just near the baseline throughout the period of observation without significant changes at different intervals. In the present study, decreased Hb and PCV have been observed in all the groups due to stressful condition of anaesthesia as research was carried out during summer season. In contrast to present study, Rafee, 2013 have reported reduced Hb and PCV values following administration of dexmedetomidine-pentazocine-midazolam in dogs. This might be due to pooling of circulatory blood cells in the spleen or other reservoirs secondary to decreased sympathetic activity may explain the decrease in Hb, PCV and TEC (Wagner and Hitchcliff, 1991). Similar findings are also reported by Sika (2013) following use of xylazine with butorphanol in dogs anaesthetized with ketamine.

A non-significant increase in total erythrocyte count (TEC) was noticed at various time intervals and the values fluctuated between 6.43±0.23 to 6.51±0.22 X 10^6 cu. mm^-1, 6.95±0.09 to 7.20±0.03 X 10^6 cu. mm^-1 and 6.92±0.03 to 6.95±0.02 X 10^6 cu. mm^-1 at various time interval in group K, DK and BK respectively. Thereafter, the values attained near normal levels. These transient changes in TEC might be attributed to stress of anaesthesia (Jain, 1986) and might be also due to dilatation of spleen, resulting in splenic sequestration of erythrocyte under the influence of different anaesthetics.

These findings are in agreement with the observation of Bisen et al., (1994) after ketamine administration in dogs. Umar and Adam (2013) reported significant decrease in Hb, PCV and RBC produced by ketamine-dexmedetomidine anaesthesia in dogs. In group K, a non-significant decrease in TLC values
from $11.73 \pm 0.50$ to $11.63 \pm 0.49 \times 10^3 \text{cu.mm}^{-1}$ was observed up to 120 min post anaesthesia, thereafter it increased non-significantly to return near base values by 24hrs. In group DK, a non-significant decrease from $12.02 \pm 0.34$ to $11.70 \pm 0.34 \times 10^3 \text{cu.mm}^{-1}$ was observed at 60 min post anaesthesia. Thereafter, TLC increased non-significantly up to 24 hr to return to preadministered level. In group BK, no significant difference from the baseline value was found at any interval of time and values remained near the baseline. The decrease in TLC during ketamine anaesthesia in all the groups might be due to increase in plasma volume during anaesthesia on account of vasodilatation resulting in vascular pooling (Steffy et al., 1976). Carrol et al., (1997) reported that total and differential leukocyte counts might be altered by stress events, and corticosteroid induced changes. This might indicate that the doses of alpha-2 adrenergic agonists (xylazine) and ketamine used in the present study were not sufficient to control stress completely. Umar and Wakil (2013) reported a decrease in total WBC with corresponding increase in leukocytic differentials in a study involving goats using ketamine and medetomidine.

In the present study, there was a corresponding lymphocytosis in response to neutropenia in all the groups. A transient decrease in neutrophil and corresponding increase in lymphocyte was observed in all the three groups post anaesthesia. In group K, neutrophils count showed a non-significant decrease (from $69.02 \pm 0.14$ to $68.27 \pm 0.12$ %) after administration of ketamine alone up to 120 min post anaesthesia. Thereafter, it increased to near normalcy by 24 hrs. In group DK and BK, neutrophils count showed a non-significant decrease from $70.93 \pm 0.44$ to $70.12 \pm 0.35$ % and $70.72 \pm 0.32$ to $70.18 \pm 0.29$ % at 60 min. post anaesthesia respectively. Thereafter it fluctuated to near normalcy up to 24 hrs. In group K, a non-significant increase in lymphocyte count from $23.30 \pm 0.28$ to $23.73 \pm 0.14$ % was observed up to 120 min. post anaesthesia. Thereafter, the values returned to near normalcy by 24 hrs. In group DK and BK, a non-significant increase from base value $21.90 \pm 0.38$ to $22.55 \pm 0.12$ % and $21.72 \pm 0.33$ to $22.35 \pm 0.20$ % was observed up to 60 min. post anaesthesia respectively. Thereafter values returned to near base value up to 24 hrs. The decrease in neutrophils and corresponding increase in lymphocytes might be due to stimulation of lymph nodes caused by stress. Similar to present study, Amarpal et al., (1998) had also reported a decreased neutrophil count after administration of alpha-2 agonists in dogs. Chacko (2003) also observed a decrease in neutrophils and increase in lymphocytes after epidural use of fentanyl citrate in dogs. Whereas Sika (2013) has reported that there was an increase in neutrophil count along with concurrent lymphocytopenia after administration of xylazine-butorphanol combination in dogs anaesthetized with ketamine.

There were non-significant changes in monocyte and eosinophil counts after various treatments in all the three groups of animals. There was a non-significant increase in eosinophil values in all three groups at 120 min. post anaesthesia. The value ranged between $3.28 \pm 0.31$ to $3.74 \pm 0.16$ in group K, between $3.40 \pm 0.10$ to $3.73 \pm 0.11$ in group DK and between $3.55 \pm 0.09$ to $3.78 \pm 0.06$ in group BK. However the values returned to normalcy by 24 hrs in all the three groups. Eosinophils showed a non-significant increase in all the groups of animals after drug administration. This possibly might be attributed to the adrenocortical stimulation and subsequent effect of glucocorticoids (Soliman et al., 1965). Similar observations were also made after administration of ketamine and detomidine in goats (Dilip Kumar, 1993) and detomidine in cattle and sheep (Koichev et al., 1988).
Table 1 Mean±S. E. value of haematological profiles following administration of ketamine alone and in combination with dexmedetomidine or butorphanol in atropinized dogs at various time intervals

| Parameters                          | Groups | 0              | 30  | 60  | 120 | 180 | 6 hrs | 24 hrs     |
|-------------------------------------|--------|----------------|-----|-----|-----|-----|------|-----------|
| Haemoglobin (gm %)                  | K      | 15.02±0.36     | 15.05±0.32 | 15.03±0.27 | 15.12±0.30 | 15.05±0.28 | 14.77±0.29 | 14.90±0.27 |
|                                    | DK     | 13.47±0.60     | 13.88±0.57 | 14.10±0.59 | 13.90±0.60 | 13.88±0.66 | 13.67±0.62 | 13.40±0.61 |
|                                    | BK     | 13.77±0.66     | 13.83±0.63 | 13.88±0.62 | 13.82±0.67 | 13.80±0.64 | 13.75±0.66 | 13.73±0.62 |
| Packed Cell Volume (%)             | K      | 49.93±0.56     | 49.95±0.52 | 49.97±0.51 | 50.00±0.48 | 49.88±0.46 | 49.80±0.48 | 49.77±0.47 |
|                                    | DK     | 48.00±0.67     | 48.13±0.71 | 48.35±0.48 | 48.57±0.43 | 48.48±0.65 | 48.43±0.66 | 48.37±0.67 |
|                                    | BK     | 48.07±0.35     | 48.18±0.35 | 48.40±0.35 | 48.30±0.37 | 48.27±0.33 | 48.20±0.35 | 48.17±0.34 |
| Total Erythrocyte Count (x 10⁶cumm⁻¹) | K     | 6.43±0.23      | 6.49±0.22  | 6.50±0.22  | 6.51±0.22  | 6.50±0.23  | 6.45±0.22  | 6.43±0.24  |
|                                    | DK     | 6.95±0.09      | 7.00±0.07  | 7.20±0.03  | 7.09±0.04  | 6.99±0.05  | 6.98±0.05  | 6.97±0.06  |
|                                    | BK     | 6.92±0.03      | 6.93±0.04  | 6.95±0.06  | 6.90±0.03  | 6.88±0.06  | 6.85±0.06  | 6.89±0.06  |
| Total Leucocytes Count (x 10³cumm⁻¹) | K     | 11.73±0.50     | 11.72±0.47 | 11.65±0.46 | 11.63±0.49 | 11.67±0.49 | 11.69±0.50 | 11.70±0.47 |
|                                    | DK     | 12.02±0.34     | 12.05±0.33 | 11.82±0.33 | 11.70±0.34 | 11.75±0.33 | 11.83±0.31 | 11.88±0.30 |
|                                    | BK     | 12.14±0.39     | 12.07±0.40 | 12.02±0.42 | 12.03±0.40 | 12.05±0.38 | 12.06±0.39 | 12.07±0.42 |
| Neutrophils (%)                    | K      | 69.02±0.14     | 68.73±0.32 | 68.37±0.10 | 68.27±0.12 | 68.43±0.12 | 68.52±0.13 | 68.83±0.10 |
|                                    | DK     | 70.93±0.44     | 70.30±0.18 | 70.12±0.35 | 70.25±0.30 | 70.33±0.29 | 70.52±0.73 | 70.82±0.22 |
|                                    | BK     | 70.72±0.32     | 70.48±0.70 | 70.18±0.29 | 70.28±0.08 | 70.32±0.26 | 70.40±0.24 | 70.45±0.19 |
| Lymphocyte (%)                     | K      | 23.30±0.28     | 23.33±0.20 | 23.67±0.18 | 23.73±0.14 | 23.47±0.19 | 23.40±0.22 | 23.35±0.15 |
|                                    | DK     | 21.90±0.38     | 22.27±0.55 | 22.55±0.12 | 22.27±0.38 | 22.20±0.29 | 22.18±0.19 | 21.72±0.12 |
|                                    | BK     | 21.72±0.33     | 22.20±0.50 | 22.35±0.20 | 22.33±0.18 | 22.25±0.17 | 22.02±0.15 | 21.61±0.12 |
| Eosinophil (%)                     | K      | 3.28±0.31      | 3.55±0.15  | 3.72±0.07  | 3.74±0.16  | 3.67±0.12  | 3.70±0.04  | 3.25±0.19  |
|                                    | DK     | 3.40±0.10      | 3.60±0.11  | 3.70±0.09  | 3.73±0.11  | 3.52±0.14  | 3.42±0.11  | 3.38±0.12  |
|                                    | BK     | 3.55±0.09      | 3.68±0.10  | 3.73±0.05  | 3.78±0.06  | 3.73±0.06  | 3.73±0.10  | 3.53±0.11  |
| Monocyte (%)                       | K      | 3.43±0.16      | 3.40±0.29  | 3.38±0.14  | 3.25±0.16  | 3.30±0.09  | 3.34±0.12  | 3.50±0.25  |
|                                    | DK     | 3.94±0.12      | 3.92±0.09  | 3.90±0.09  | 3.87±0.18  | 3.82±0.08  | 3.77±0.09  | 3.73±0.11  |
|                                    | BK     | 3.97±0.06      | 3.83±0.10  | 3.78±0.16  | 3.70±0.09  | 3.77±0.06  | 3.82±0.09  | 3.85±0.06  |
Table 2 Mean±S. E. value of Biochemical profiles following administration of ketamine alone and in combination of dexmedetomidine or butorphanol in atropinized dogs at various time intervals (Mean±S. E.)

| Parameters                           | Groups | 0          | 30        | 60        | 120       | 180       | 6 hrs      | 24 hrs      |
|--------------------------------------|--------|------------|-----------|-----------|-----------|-----------|------------|-------------|
|                                      |        |            |           |           |           |           |            |             |
| Serum Glucose (mg/dl)                | K      | 88.80±4.80 | 91.58±4.53| 95.30**±3.58| 92.23**±5.88| 89.20±3.80| 89.98±2.91| 88.47±1.98  |
|                                      | DK     | 89.65±3.82 | 90.47±2.92| 94.55**±2.42| 105.42**±3.12| 99.55**±2.87| 90.95±3.15| 89.40±2.02  |
|                                      | BK     | 89.03±3.50 | 93.48**±2.62| 94.90**±4.28| 98.83**±2.98| 89.27±2.06| 89.05±1.56| 88.80±1.83  |
| Serum Total Protein (g/dl)           | K      | 6.47±0.05  | 6.40±0.10  | 6.37±0.07  | 6.33±0.08  | 6.32±0.09  | 6.27±0.11  | 6.28±0.11   |
|                                      | DK     | 6.12±0.15  | 6.05±0.87  | 6.02±0.05  | 5.99±0.09  | 5.98±0.14  | 5.99±0.12  | 6.02±0.08   |
|                                      | BK     | 5.92±0.05  | 5.91±0.06  | 5.90±0.04  | 5.88±0.07  | 5.89±0.52  | 5.89±0.05  | 5.88±0.08   |
| Serum Urea Nitrogen (mg/dl)          | K      | 21.48±0.24 | 21.50±0.43 | 21.88±0.40 | 21.90±0.24 | 21.88±0.49 | 21.65±0.42 | 21.43±0.42  |
|                                      | DK     | 20.50±0.08 | 20.52±0.03 | 20.60±0.21 | 20.78±0.11 | 20.22±0.20 | 20.68±0.19 | 20.50±0.17  |
|                                      | BK     | 20.08±0.10 | 19.98±0.07 | 19.90±0.21 | 19.88±0.05 | 19.91±0.15 | 19.94±0.07 | 20.02±0.06  |
| Serum Creatinine (mg/dl)             | K      | 0.88±0.25  | 0.89±0.12  | 0.90±0.18  | 0.95±0.31  | 0.91±0.20  | 0.90±0.58  | 0.89±0.40   |
|                                      | DK     | 0.95±0.15  | 0.96±0.20  | 0.98±0.14  | 0.99±0.25  | 1.13±0.13  | 1.03±0.18  | 0.99±0.11   |
|                                      | BK     | 0.98±0.04  | 1.02±0.15  | 1.03±0.42  | 1.04±0.05  | 1.02±0.39  | 1.01±0.05  | 0.99±0.03   |
| ALT (U/L)                            | K      | 27.50±0.43 | 28.32±0.62 | 28.83±0.60 | 28.08±0.37 | 27.93±0.42 | 27.83±0.60 | 27.52±0.58  |
|                                      | DK     | 27.67±0.42 | 28.17±0.31 | 28.99±0.26 | 29.33±0.73 | 28.43±0.56 | 28.17±0.60 | 27.47±0.49  |
|                                      | BK     | 19.67±0.80 | 20.00±0.73 | 20.05±0.49 | 20.17±0.65 | 20.07±0.40 | 19.83±0.33 | 19.62±0.52  |
| AST (U/L)                            | K      | 33.50±0.43 | 33.65±0.22 | 33.83±0.48 | 33.53±0.49 | 33.42±0.43 | 33.48±0.56 | 33.48±0.76  |
|                                      | DK     | 31.33±0.33 | 31.50±0.34 | 32.82±0.37 | 31.83±0.60 | 31.70±0.48 | 31.52±0.40 | 31.39±0.45  |
|                                      | BK     | 30.34±0.33 | 30.53±0.45 | 30.80±0.40 | 30.70±0.43 | 30.52±0.49 | 30.46±0.33 | 30.28±0.17  |

**P<0.01 = Significant at 1% level when compared to base value
There was a non-significant decrease in monocyte value up to 120 mins. In all the three groups. The value decreased from 3.43±0.29 to 3.25±0.16 %, 3.94±0.12 to 3.87±0.18 % and 3.97±0.06 to 3.70±0.09 % in group K, DK and BK respectively. However the values returned to normalcy by 24 hrs in all the three groups. This non-significant decrease/ increase might be attributed to the adrenocortical stimulation and subsequent effect of glucocorticoids (Soliman et al., 1965). The transient decrease in monocyte at initial intervals might be attributed to stress due to anaesthesia.

**Biochemical profiles**

The effects on biochemical profiles after administration of ketamine alone and in combination with dexmedetomidine and butorphanol in atropinized dogs at various time intervals (Mean±S. E.) are shown in Table 2. There was significant increase in serum glucose level with peak at 60, 120 and 120 min. post anaesthesia in group K, DK and BK respectively. In group K, significant (P<0.01) increase in serum glucose from 88.80 ±4.80 to 95.30±3.58 mg/dl was recorded with the highest value at 60 min. In group DK, a highly significant (P<0.01) increase in serum glucose level from 89.65±3.82 to 105.42±3.12 mg/dl was recorded at 120 min. This was followed by gradual decrease in serum glucose level to baseline. In group BK, a highly significant (P<0.01) increase in serum glucose from 89.03±3.50 to 98.83±2.98 mg/dl was recorded at 120 min after administration of butorphanol-ketamine anaesthesia. Thereafter, the values decreased and returned to normalcy by 24 hrs, in all the three groups. 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. Ketamine has been reported to cause sympathetic stimulation leading to release of catecholamines and increased glucose concentration in plasma. Similar findings were found by Camkerten et al., (2013) and and Sharma et al., (2014). Sharif and Abouazra (2009) have suggested that the under stressful condition especially during anaesthesia leads to alteration in endocrine secretion of insulin antagonists such as growth hormone and cortisol causing temporary diabetic state. Administration of an alpha-2 agonist activates alpha-2 receptors on pancreatic beta cells and inhibits the release of insulin (Ambrisko and Hikasa, 2002). 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. Increased glucose levels in this study might have been due to the decreased insulin release by the inhibitory effects of dexmedetomidine (Restitutti et al., 2012).

A non-significant and transient decrease in the level of serum total protein was observed in all the groups. In group K, a non-significant decrease from 6.47±0.05 to 6.33±0.08 g/dl at 120 minute while in group DK, a non-significant decrease from 6.12±0.15 to 5.98±0.14 g/dl was recorded at 180 min. post anaesthesia, however the values returned to normalcy in 24 hrs in both the groups. In group BK, total protein values fluctuated near base value during observation period without any significant changes. This non-significant decrease in total proteins might be due to the increased levels of glucocorticoids, increased adrenal activity and increased protein turnover resulting in decreased plasma protein and albumin. Decrease in insulin levels might modify the general metabolism and impair protein synthesis (Schumann, 1990). The decrease in total protein level may be due to haemodilution. Similar findings have been observed after administration of ketamine
with alpha-2 agonist in dogs by Umar and Adam (2013). The non-significant alteration in total serum protein in all the groups might be due to splenic pooling of erythrocytes which caused overloading of water in blood.

A non-significant increase in serum urea nitrogen and creatinine was observed in group K and DK whereas in group BK, there was non-significant decrease. Serum urea nitrogen non significantly increases from 21.48±0.24 to 21.90±0.24 and 20.50±0.08 to 21.22±0.22 mg/dl at 120 and 180 minute post anaesthesia in group K and DK respectively, while in group BK, a non-significant decrease was recorded up to 60 minute post anaesthesia, afterwards the value returned towards normalcy up to 24 hrs in all the groups. Similarly, Rafee (2013) has observed a non-significant increase in BUN values following administration of dexmedetomidine-butorphanol/pentazocine as preanaesthetic followed by induction with midazolam and maintenance with ketamine in dogs. The increased hepatic urea production from amino acid degradation could also account for the observed increase in blood urea values during the maximum depth of anaesthesia. The increase in urea nitrogen values might be attributed to the temporary inhibitory effects of anaesthetic drugs on the renal blood flow, which in turn might have caused a rise in plasma urea nitrogen level as suggested by Kinjavdekar et al., (2000). A non-significant increase in blood urea nitrogen has been reported following use of medetomidine along with butorphanol in dogs (Ahmad, 2010). Whereas, Surbhi et al., (2010) reported that urea values decreases following administration of butorphanol with xylazine, medetomidine and dexmedetomidine administration in canine undergoing orthopaedic surgery.

Serum creatinine level in group K and DK showed non-significant increase upto 120 and 180 min. post anaesthesia respectively while in group BK, a non-significant increase was recorded upto 120 min. which returned to the base values by 24 hrs in all the three groups after various treatments. A non-significant increase in serum urea nitrogen and creatinine may be due to temporary inhibitory effects of drugs on renal blood flow and consequent decrease in glomerular filtration rate, resulting in the rise in their level. Ketamine alone causes non-significant increase in creatinine and serum urea nitrogen. A non-significant increase in creatinine values have been reported following medetomidine-ketamine anaesthesia in dogs (Chonde et al., 2004). In the present study, it is difficult to assess the possible renal damage, because all the values were within the normal physiological limits.

A non-significant increase in the values of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) was observed in animals of group K and DK while in group BK, the values of alanine amino transferase and aspartate aminotransferase fluctuated near base value during the study period without any significant changes. In group K and DK, ALT non-significantly increases from 27.50±0.43 to 28.83±0.60 U/L and 27.50±0.43 to 29.33±0.60 U/L at 60 and 120 min. while AST also non-significantly increases from 33.50±0.43 to 33.83±0.48 U/L and 30.33±0.34 to 32.82±0.37 U/L at 60 min. post anaesthesia respectively. Both AST and ALT values returned near normalcy level by 24 hr in all the groups. ALT is the liver specific enzyme in dogs and the pathology involving the hepatic parenchyma allows the leakage of large amount of this enzyme in the blood. The transient increase in ALT and AST level might be associated with increased cell membrane permeability in response to haemodynamic changes induced by anaesthetic agents as result of oxidative transformation of these drugs in the liver.
during the process of elimination. Metabolism of ketamine occurred in the liver in most of the species including humans, horses and dogs (Kaka et al., 1979). Pathak (1997) also observed increase in AST values up to 60 mins during xylazine-ketamine anaesthesia in dogs. Sharma et al., (2014) recorded non-significant increase in ALT levels of dogs, which were administered with dexmedetomidine. In the present study, the transient change in ALT and AST values might be due to hepatic metabolism of these drugs was within the normal physiological range are indicative of no deleterious effects on liver and the possibility of pathological changes could not be ruled out. Similarly, Camkerten et al., (2013) found no significant alterations in various haematological and biochemical parameters with xylazine and ketamine combination and reported values in normal range at different time intervals.

On the basis of result of the present study, it is concluded that transient changes in haematobiochemical profiles were compensated within 24 hrs and have no deleterious effect on vital organs and changes remained within normal physiological limit. Therefore, ketamine in combination with dexmedetomidine or butorphanol can be safely used as general anaesthetic in compromised and clinically healthy dogs.

References

Ahmad, R. A. 2010. Studies on sedative, analgesic and anaesthetics effects of dexmedetomidine and its combination with midazolam, fentanyl and ketamine in dogs. M.V.Sc. Thesis submitted to Deemed University, Indian Veterinary Research Institute, Izatnagar (U.P.)
Amarpal, Aithal, H. P., Pratap, K. and Singh, G. R. 1998. Neuroleptanalgesia with medetomidine and pentazocine in goats. Indian Vet. J. 75: 150–154.
Ambrisko, T. D. and Hikasa, Y. 2002. Neurohormonal and metabolic effect of medetomidine compared with xylazine in Beagle dogs. Can. J. Vet. Res. 64: 42-49
Bisen, S. S., Pandey, S. K., Sharma, I.J., Chandrapuria, V.P. and Bhargava, M.K. 1994. Biochemical and haematological effects of certain analgesic premedicants with ketamine hydrochloride in dogs. Indian J. Anim. Sci. 64(6):613-615
Camkerten, I., Sindak, N., Ozkurt, G., Ipek, H., Biricik, H. S. and Sahin, T. 2013. Effect of ketamine-xylazine anesthesia on some haematological and serum biochemical values of Bozova Greyhounds. Veterinary faculty Dergisi Harran University, 2(1): 27-31.
Carollo, D. S., Nossaman, B. D. and Ramadhyani, U. 2008. Dexmedetomidine: A review of clinical applications. Curr. Opin. Anaesthesiol. 21: 457-461
Carrol, G. L., Hartsfield, S. M. and Hambleton, R. 1997. Anaesthetic effects of tiletamine-zolazepam, alone or in combination with butorphanol, in goats. JAVMA, 211: 593-597.
Chacko, B. 2003. Epidural effects of fentanyl citrate alone, along with local analgesic and its reversal in dogs. M.V.Sc. Thesis, JNKVV, Jabalpur (M.P.)
Chonde, M. S., Tiwari, S. K., Shinkar, D. S. and Sharda, R. 2004. Cardiopulmonary effects of medetomidine and diazepam in ketamine anaesthetized dogs. Indian Vet. Med. J. 28(2):188-190.
Dilip Kumar, D. (1993). Studies on detomidine hydrochloride as a preanaesthetic to ketamine anaesthesia in goats. M.V.Sc. Thesis Deemed University, IVRI, Izatnagar, (U.P.)
Gross, M. E., Tranquili, W. J. and Thurmon, J. C.1990.Haemodynamic effects of IV midazolam-xylazine-butorphanol in dogs. Veterinary Surgery. 19: 173-180
Jain, N.C. 1986. Haematological Techniques. In: Schalm’s Veterinary Haematology. 4th Ed. Lea and Febiger, Philadelphia. pp. 20-86
Kaka, J. S., Klavano, P. A. and Hayton, W. L. 1979. Pharmacokinetics of ketamine in horses. Am. J. Vet. Res., 40: 978-981.
Kinjavdekar, P., Singh, G. R., Amarpal, Aithal, H. P., Pawde, A. M. 2000. Physiologic and biochemical effects of subarachnoidally
administered xylazine and medetomidine in goats. Small Rum. Res. 38:217-228.

Koichev, K., Golemanov, D., Houbenov, H. and Aminokov, B. 1988. Experimental study on the effect of “Domesedan” in sheep and cattle. J. Assoc. Vet. Anaesthesist, 15: 114.

Pathak, J. C. 1997. Experimental studies on the efficacy of xylazine hydrochloride with and without dissociative anaesthetic in dogs. M.V.Sc. thesis submitted to JNKVV, Jabalpur (M.P.).

Rafee, M. A. 2013. Evaluation of midazolam and ketamine anaesthesia for ovariohysterectomy in dexmedetomidine with or without butorphanol/pentazocine premedicated dogs. M.V.Sc. Thesis submitted to Deemed University, Indian Veterinary Research Institute, Izatnagar, (U.P.).

Restittuti, F., Raekallio, M., Vainionpaa, M., Kuusela, E. and Vainio, O. 2012. Plasma glucose, insulin, free fatty acids, lactate and cortisol concentrations in dexmedetomidine-sedated dogs with or without MK-467: A peripheral alpha 2 adrenoceptor antagonist. Vet. J. 193: 481-485

Schumann, D. 1990. Post-operative hyperglycaemia. Clinical benefits of insulin therapy. Heart Lung. 19(20): 165-173.

Sharif, S. I. and Abouazra, H. A. 2009. Effect of intravenous ketamine administration on blood glucose levels in conscious rabbits. Am. J. Pharma. and Toxico., 4(2): 38-45.

Sharma, R., Kumar, A., Kumar, A., Sharma, S. K., Sharma, A. and Tiwari, N. 2014. Comparison of xylazine and dexmedetomidine as premedicant for general anaesthesia in dog. Indian J. Anim. Sci. 84: 8-12

Sika, P. K. 2013. Evaluation of butorphanol along with xylazine or dexmedetomidine as preanaesthetic to ketamine or propofol anaesthesia in canine patients. M.V.Sc. Thesis submitted to OUAT, Bhubaneswar, India.

Snedicor, G. W. and Cochran, W. G. 1994. Statistical Methods, 8th Edition, Oxfords and IBH Publishing Co., New York, 59.

Soliman, M. K., Amrousii, S. E. and Khamis, M. Y. 1965. The influence of tranquilizers and barbiturates anaesthesia on the blood picture and electrolytes of dogs. Vet. Rec. 77: 1256

Steffy, E. P., Gillespie, J. R., Berry, J. D., Eger, E. I. and Schalm, O. W. 1976. Effects of halothane and halothane- nitrous oxide on haematocrit and plasma protein concentration in dog and monkey. American Journal of Veterinary Research 37: 959-962

Surbhi, Kinjavdekar, P., Amarpal, Aithal, H. P., Pawde, A. M., Pathak, M. C. and Borena, B. M. 2010. Physiological and biochemical effects of medetomidine-butorphanol-propofol anaesthesia in dogs undergoing orthopaedic surgery. Indian J Vet Surg. 31(2): 101-104.

Umar, M. A. and Adam, M. K. 2013. Effects of combination of ketamine-medetomidine anaesthesia on haematology and some serum chemistry parameters in dogs. J. Home. 34: 808-813

Umar, M. A. and Wakil, Y. 2013. Effects of the combination of ketamine and medetomidine anaesthesia on haematological parameters in sahel goats. Sok J Vet Sci, 11: 66-69.

Wagner, A. E. and Hitchcliff, K. W. 1991. Cardiovascular effects of xylazine and detomidine in horses. Am. J Vet Res. 52: 651-657.

How to cite this article:

Krishna Kumar Verma, S. K. Tiwari, Rukmani Dewangan and Raju Sharda. 2018. Effect on Haematological and Biochemical Profiles Following Administration of Ketamine Alone and in Combination with Dexmedetomidine or Butorphanol in Atropinized Dogs. Int.J.Curr.Microbiol.App.Sci. 7(06): 2568-2577. doi: https://doi.org/10.20546/ijcmas.2018.706.303