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Original Research

Evaluation of intravenous Acepromazine-Butorphanol-Propofol anaesthesia on Canine serum biochemistry

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ABSTRACT

In order to increase accuracy and ensure safety during surgical procedures, anaesthesia is a necessary precondition for most diagnostic and surgical procedures in humans and animals. This study was designed to determine the changes in serum biochemical parameters following Acepromazine-Butorphanol-Propofol (ABP-combination) and propofol alone (PRO alone) anaesthesia in dogs. Ten (10) apparently healthy dogs with mean age of 1.59±0.77 years and a mean body weight of 15.5±1.96 kg were obtained from live dog market in Maiduguri, North-eastern Nigeria. The dogs were divided randomly into two groups, ABP-combination and PRO-alone groups. Following premedication with Acepromazine at 0.02mg/kg and Butorphanol at 0.05mg/kg iv., 4mg/kg Propofol was used to induce total intravenous anaesthesia (TIVA) after five minutes of premedication in ABP-combination group, while PRO-alone at 6mg/kg was used to induce anaesthesia without premedication in PRO-alone group. Creatinine (sCr), Alanine aminotransferase (ALT) and Blood urea nitrogen (BUN) were determined using standard laboratory procedures. The ALT, sCr and BUN showed no difference ($p>0.05$) within the group but were significantly ($p<0.05$) different between the groups. The levels of Alanine aminotransferase in both ABP and PRO treatments showed significant difference ($p<0.05$) at 10minutes, 1hour, 6hrs and 24hours. Significant difference ($p<0.05$) was observed in sCr levels between the two treatments, at 10minutes, 1hour and 6hours respectively. Blood urea nitrogen in both treatments differed ($p<0.05$) significantly at 6hours and 24hours post anaesthesia. The results of this study showed that ABP-combination following TIVA provides transient non-significant ($p>0.05$) effect on serum biochemical parameters. Therefore, the combination of ABP can be used during surgical procedures in dog.

Keywords: Acepromazine, anaesthesia, Butorphanol, dogs, Propofol, serum biochemistry.

INTRODUCTION

Controlled, reversible unconsciousness, analgesia, and muscle relaxation are the hallmarks of anaesthesia (Thurmon & Short, 2007). Improving surgical accuracy is an essential precondition for the majority of medical and diagnostic procedures in humans and animals (De Moor *et al*, 2010, Elks, 2014,).

Over time, intravenous anaesthesia has gained popularity and acceptance in veterinary practice as a more acceptable method of achieving ideal surgical anaesthesia in comparison with inhalational anaesthesia, which necessitates the use of multiple facilities for the delivery of volatile anaesthetic agents and the potential hazard to the patient during administration (Umar *et al*., 2006; Yamashita *et al*., 2007; Umar *et al.,* 2007; Dantino *et al*., 2022). Combining analgesic, muscle relaxant, and sedative drugs — properties that are rarely offered by a single anaesthetic drug- is the usual goal of the anaesthetic agent combining technique in order to achieve balanced anaesthesia (Waelbers *et al*., 2009; Morton and Hall 2012; Umar *et al*., 2007). During general anaesthesia, the combination of anaesthetic drugs is typically administered in a dosage that maximizes the desired or major effects while minimizing the negative effects. This allows the beneficial effects of each anaesthetic agent to be utilized to achieve an appropriate depth of surgical anaesthesia while causing predictable and minimal effects on the organs involved in drug metabolism and excretion (Thurmon & Short, 2007; Gapsiso *et al.,* 2023).

To attain balanced anaesthesia, total intravenous anaesthesia (TIVA) should be used in conjunction with other drug

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combinations and techniques that are appropriate for the ever-evolving demands of advanced diagnostic and therapeutic modalities (Waelbers *et al*. 2009; Bajwa *et al.* 2010). Propofol (2,6-diisopropylphenol) is an intravenous phenolic compound that is non-barbiturate. It induces anaesthesia smoothly and quickly, resulting in a brief period of unconsciousness followed by a swift and uneventful recovery (Hall *et al.,* 2001; Umar *et al*., 2006). One phenothiazine tranquillizer that is frequently used for premedication and mild sedation is acepromazine, a phenothiazine that does not produce analgesia but facilitates the induction of anaesthesia at clinically prescribed doses (Hall *et al*., (2001). On the other hand, butorphanol is a synthetic agonist–antagonist opioid analgesic of the morphine type that is frequently used as a supplement for balanced general anaesthesia and for the treatment of moderate–to-severe pain (Elks, 2014).

In order to provide balanced anaesthesia in dogs and to evaluate acepromazine, butorphanol and propofol's effects on drug metabolism and excretion organs, in addition to paucity of information regarding ABP drug combinations and Propofol-alone (PRO) for anaesthesia in dogs in the study area, necessitated the choice of the drugs for TIVA. The purpose of the study was to assess how the ABP combination affected the serum biochemical markers creatinine, blood urea nitrogen, and alanine aminotransferase in dogs.

METHODOLOGY

EXPERIMENTAL ANIMALS AND MANAGEMENT

All procedures performed in this experimental study were in accordance to the guidelines of the animal care and use committee of the University of Maiduguri (ethical approval number: FVM/UM/AUEC/19/002). Ten (10) apparently healthy dogs comprising six males and four female of good clinical condition and having mean body weights of 15.5 ± 1.96 kg and age 1.59 ± 0.77 years old were used. The dogs were kept at the kennels and fed corn food and rice once daily and clean water was provided *ad libitum.* Following a two-week period of acclimatization, they were randomized into two treatment groups, the Acepromazine-Butorphanol-Propofol (ABP) combination group and the Propofol (PRO) alone group.

Three drugs Acepromazine, (Neurotranq® 10mg/ml Virbac, RSA Pty. Ltd. South Africa), Butorphanol (Dolorex® 10mg/ml Intervet SA Pty. Ltd. South Africa) and Propofol® 1% Frensenius Kabi SA Pty. Ltd. South Africa) were used in two treatment groups: ABP-combination and PRO-alone groups for the anaesthesia to which the dogs were assigned.

Animals assigned to ABP group were premedicated with acepromazine (0.02mg/kg iv) and butorphanol (0.05mg/kg iv). Using insulin syringes, the calculated doses of the two medications for premedication were taken from separate vials and combined into a single 5 ml syringe. Water for injection was then added to the mixture to make up to 1 ml before the mixture was administered intravenously (iv) through a 22G × 0.9 DEN-V i.v. cannula (Polybond India Pvt Ltd. Maharashtra India) inserted into the cephalic vein, 27.0±1.0 seconds after, the induction of anaesthesia with propofol (4 mg/kg) iv followed. In both groups, 2ml of blood was collected before premedication and during the anaesthesia at 10minutes interval and at 1hr, 6hrs and 24hrs post-anaesthesia, thereafter sera samples were harvested. The dogs assigned to propofol-alone group were not premedicated but anaesthesia was induced with 6mg/kg of propofol intravenously through cephalic vein.

MEASUREMENT OF SERUM BIOCHEMICAL PARAMETERS

Alanine aminotransferase, creatinine and blood urea nitrogen were measured in the sera samples collected. The blood samples were collected before the commencement of the treatments for baseline values and later collected at 10 minutes intervals during anaesthesia and then 1 hour, 6 hours and 24 hours after the anaesthesia. The blood samples were gently dispensed into well labelled plain vacutainer tubes and allowed to clot for 2 hours at room temperature thereafter centrifuged 1200xG for 5 minutes. The sera were thereafter harvested into micro-vial (1ml) tubes and stored at -20^{o}C before analysis. Alanine-aminotransferase (ALT) was determined using the method of Schmidt and Schmidt (1963) and the concentration of ALT in the serum was calculated from a standard table (Randox Laboratory Ltd. U.K.). Serum Creatinine (sCr) was determined using Randox Laboratory kits and procedures (Natelson *et al.,* 1951). The Blood Urea Nitrogen (BUN) was determined by diacetyl method of Natelson *et al.,* (1951) using Randox Laboratory Kits and procedures.

STATISTICAL ANALYSIS

The data were presented as mean ± SD. One Way Repeated Measure Analysis of variance (ANOVA) was used to analyse data within group while student T-Test was used to analyse data between the groups. Analyses were considered significant at $p < 0.05$.

RESULTS

The duration of anaesthesia for ABP-combination was 30.0±5.8 minutes while that of PRO-alone was 13.6±4.8 minutes, therefore, no values were obtained for PRO at 20 minutes and 30 minutes due to shorter duration of anaesthesia.

The baseline value for ABP-combination was 49.6±14.5µ/L. There was a non-significant ($p > 0.05$) decrease in ALT level from 10 minutes to 1 hour following the treatment in ABP-combination. The level rose insignificantly ($p > 0.05$) at 6

hours and at 24 hours above the baseline (Fig 1). The changes in the ALT levels did not differ significantly ($p > 0.05$) from the baseline. The baseline ALT value for PRO-alone was 57.4±39.2 µ/L and there were no significant ($p > 0.05$) changes in ALT values during the sampling time from the baseline. Comparing the results on the effects of the two treatments on ALT showed significant ($p < 0.05$) difference between ABP-combination and PRO-alone at 10 minutes during anaesthesia, 1 hour, 6hours and 24 hours post anaesthesia. ABP-combination showed increase from its baseline while PRO-alone showed decrease from its baseline (Figure I).

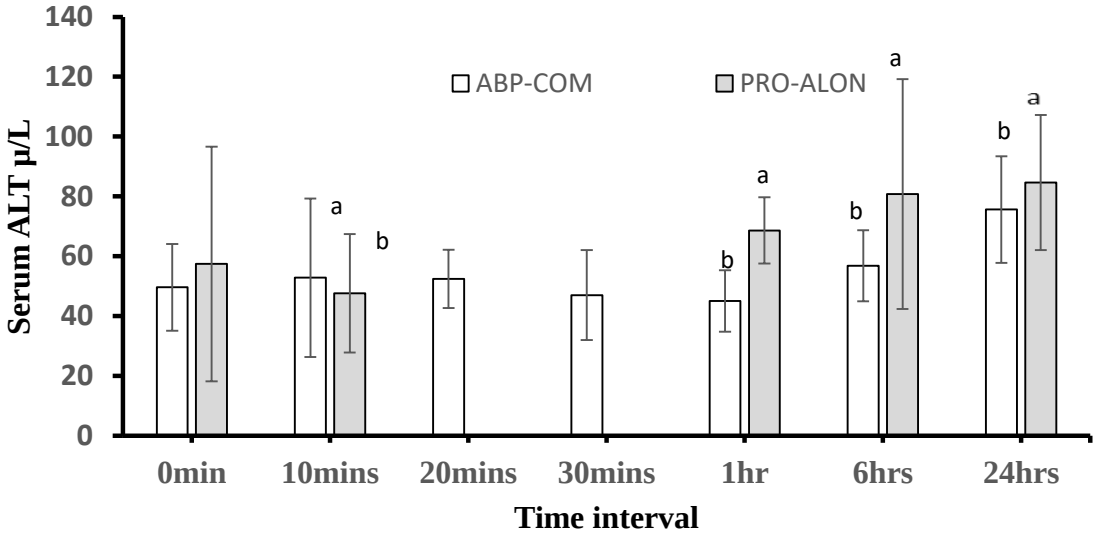

Fig. 1. Effect of ABP-Combination and PRO-Alone on Alanine aminotransferase (ALT) in dogs. Values with different alphabet for a Time interval are significantly different ($p<0.05$)

The serum creatinine (sCr**)** baseline value obtained from the study for ABP-combination was 83.6 ± 30.1 mmol/L. There was slight increase in sCr levels at 10 minute and 20 minutes respectively from baseline. There was decrease in sCr level observed at 30 minutes, 1 hour and 6 hours respectively. The sCr level increased to a peak in 24 hours, which was higher than the baseline value. The changes in sCr levels recorded at various sampling times within the ABP-combination group did not differ significantly ($p > 0.05$) from the baseline. The baseline value of sCr for PRO-alone was 101.4 ± 13.7 mmol/L. There was decrease sCr level at 10 minutes, and the sCr level rose at 1 hour, followed by dropped at 6 hours and later increased at 24 hours. No values for PRO-alone at 20 minutes and 30 minutes during anaesthesia due to shorter duration of anaesthesia with PRO-alone. All the sCr values for PRO-alone recorded did not differ significantly ($p>0.05$) from the baseline (Fig 2). The two treatments recorded increased sCr values above their baseline values at 24 hours post anaesthesia which did not differ significantly ($p > 0.05$) between them (Figure II.).

The baseline value of Blood urea nitrogen BUN for ABP-combination was 3.9 ± 1.3 µmol/L). There was non-significant ($p > 0.05$) decrease in BUN levels at 10 minutes, 20 minutes and 30 minutes followed by non-significant ($p > 0.05$) rise in the BUN level at 1 hour, 6 hour and 24 hours post anaesthesia. The fluctuation in the BUN level did not differ significantly ($p > 0.05$) from the baseline (Fig 3). The baseline value of BUN for PRO-alone treatment was 4.4 ± 1.6 µmol/L. The BUN level dropped non-significantly ($p > 0.05$) at 10 minutes and 1 hour, rose at 6 hours'and dropped again at 24 hours. Comparing the effects of ABP-combination with PRO-alone on BUN showed significant ($p < 0.05$) difference in BUN values at 6 hours and 24 hours (Fig 3.).

DISCUSSION

The values for ALT within the groups did not differ significantly ($p > 0.05$) but the effect of the two groups when compared, vary significantly ($p < 0.05$) with time. This finding agreed with the report of Anandmay, *et al*., (2012), who reported that a variable and consistent non-significant ($p > 0.05$) increase in ALT, which were within the physiological limits, could be noticed at different intervals in dogs.. The findings of this study varied with the findings of Dewangan *et al*., (2016) who reported a significant ($p < 0.01$) variation in serum ALT values between groups following xylazine and propofol anaesthesia in dogs. Shabir *et al*. (2014) also reported a significant ($p < 0.05$) difference

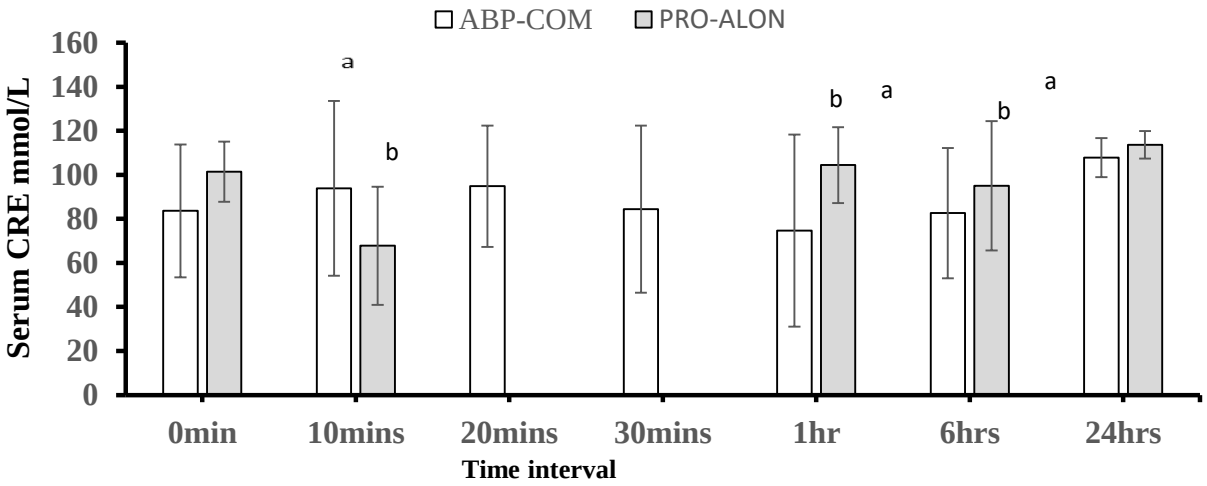

Figure II. Effect of ABP-Combination and PRO-Alone on Creatinine (sCr**) in dogs**
Values with different alphabet for a Time interval are significantly different ($p<0.05$)

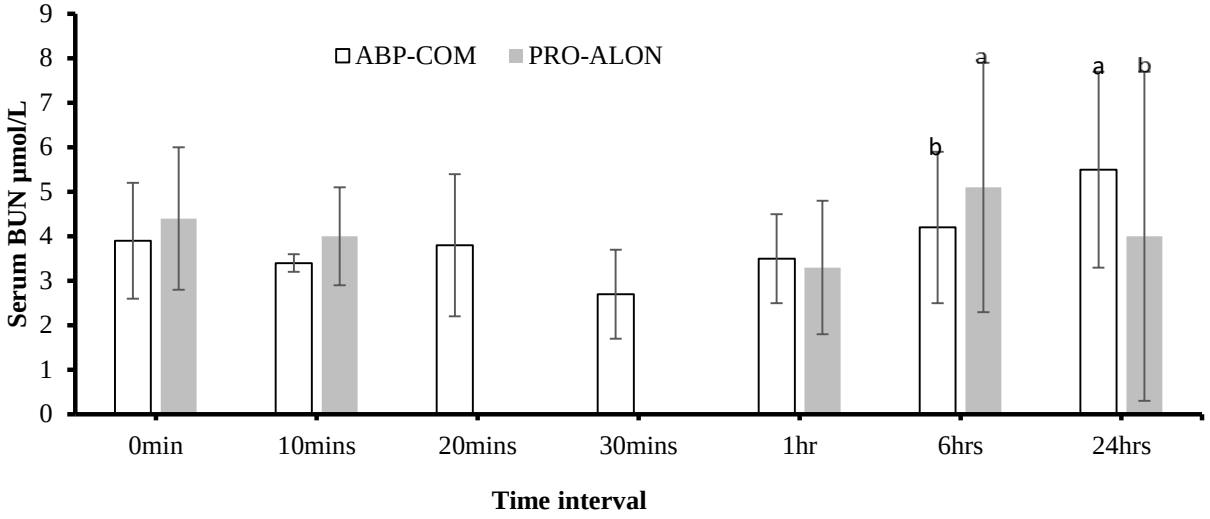

Figure III. Effect of ABP-Combination and PRO-Alone on Blood Urea Nitrogen (BUN) in dogs.
Values with different alphabet for a Time interval are significantly different ($p<0.05$)

in ALT levels following propofol bolus induction in humans. The transient non-significant increase in ALT level recorded in this study could be attributed to the hepato-tolerance activities of acepromazine present in the combination which help prevent any possible hepatic injury or metabolism of the drug by the liver (Cattai *et al*., 20018). Because of the antisympathetic and antiarrhythmic properties and dopamine inhibition activity of acepromazine, the drug help stabilize drug metabolic activities of liver by inducing vagally-bradicardia followed by systemic vasodilatation thereby slows down excessive flow of blood to the liver, which in turn reduces hepato-toxicity (Turi & Williams, 2011). The findings of this study differ with the findings of Anandmay *et al*., (2012), who reported a significant ($p < 0.05$) increase in ALT level at 1 and 2 hours post induction of propofol which later return to the baseline within 24 hours after the induction. In the present study, both treatments recorded non-significant ($p > 0.05$) increase in ALT values above baseline values 24 hours post anaesthesia. The transient increase in ALT values in ABP-combination group could be due to hepatic metabolism of acepromazine and butorphanol which returned back to normal physiological level indicating no undesirable effect (Anandmay *et al*., (2016).

The non-significant ($p > 0.05$) variations in sCr levels recorded with ABP-combination in this study could be attributed to the increased level of antidiuretic hormone (ADH) along with decreased glomerular filtration activity during anaesthesia procedure in dogs (Suresha *et al*., 2012). ABP-combination recorded initial non-significant ($p > 0.05$) increase in creatinine while PRO-alone recorded non-

significant ($p > 0.05$) decrease in creatinine value from baseline after induction of anaesthesia. The variation in sCr values recorded between the two treatments could be attributed to the metabolism, bioavailability and half-life of the acepromazine (6 to 8 hours) and butorphanol (3 to 4 hours) in dogs which is longer than propofol (40minutes) as reported by Morton, (1998); Hammond & Nickelson (2008); Maddison *et al*., (2008); Hall *et al* (2001).

The non-significant ($p > 0.05$) variation in BUN values recorded post anaesthesia between the two treatments could be due to the longer half-life of acepromazine (6 to 8 hours) and butorphanol (3 to 4 hours) which is longer than propofol (40minutes) alone in dogs (Morton, 1998; Hammond and Nickelson 2008; Maddison *et al*., 2008; Hall *et al* 2001). The non-significant ($p > 0.05$) changes in BUN values recorded during anaesthesia in this study shows non-nepro-toxicity of the anaesthestic agent which are usually observed following drug metabolism and the half-life of the anaesthetics (acepromazine has 6 to 8 hours, butorphanol has 3 to 4 hours while Propofol has about 40minutes in dogs) which vary (Bougherara & Bouaziz 2014). Acepromazine causes vasodilatation which increases blood flow to the kidneys while butorphanol often increases left ventricular end-diastolic pressure and an increased systemic arterial pressure brings about increase blood flow to the kidneys thereby reducing any deleterious injury to the kidneys (Hall *et al*., 2001). This could be the reason for the non-significant ($p > 0.05$) changes in the BUN level recorded in this study.

CONCLUSION

Both ABP combination and PRO-alone recorded transient non-significant effects on the liver and kidney during and after anaesthesia which indicates their suitability for use in dogs. The non-significant fluctuation in the ALT, sCr and BUN within the groups during after anaesthesia, shows that the ABP combination and PRO-alone doses used did not cause any deleterious effect or changes in the serum biochemical parameters. Nevertheless, the significant changes recorded between the groups were as a result of differences in doses of the propofol in the two groups and the inclusion of acepromazine and butorphanol in ABP combination. At the doses used in this study, ABP combination and propofol-alone are safe and can be used in dogs. Further clinical and surgical trials are recommended to determine quality of anaesthesia in other species of animals.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest

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