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# EVALUATION OF HAEMATOBIOCHEMICAL AND CARDIOPULMONARY PARAMETERS IN GOATS UNDERGOING ORTHOPEDIC SURGERY USING TOTAL INTRAVENOUS ANAESTHESIA

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## ABSTRACT

This research was done to identify the usefulness of clinico-physiological and haematobiochemical effects of total intravenous anaesthesia affected by combination of diazepam-propofol-ketamine with constant rate of infusion in goats undergoing orthopedic surgery (bone plating). Five goats having metatarsal and metacarpal fracture were included in the study. The animals were sedated with diazepam @ 0.25 mg/kg inducted with ketamine and propofol at the dose rate of 2.0 mg/kg each and maintained with diazepam, ketamine and propofol at the dose rate of 0.02 mg/kg/hr, 2.40 mg/kg/hr and 0.96 mg/kg/hr, respectively after using volumetric syringe driving pump. The clinico-physiological and haematobiochemical parameters of above said animals were recorded at 0 min before sedation (baseline), 1, 5, 10, 15, 20, 30, 60 and 120 minutes after induction of anaesthesia (Indoor Surgery Clinic, Department of Veterinary Surgery, University of Veterinary and Animal Sciences Lahore, Pakistan). A score of (1.00±0.00) for the anesthetic parameters was observed, indicating a smooth induction, good muscular relaxation, and easy recovery at various time intervals following therapy compared to baseline before induction: the heart rate, respiration rate, rectal temperature, blood pressure, and oxygen haemoglobin saturation were substantially different ($p<0.05$). Throughout the observation period, there were non-significant differences in the packed cell volume, haemoglobin concentration, leukocyte, granulocyte, lymphocyte, and monocyte counts ($p>0.05$). At various points during the observation period: the levels of serum glucose, alanine aminotransferase, aspartate aminotransferase, and cortisol varied considerably ($p>0.05$) in comparison to 0 minutes (the baseline) prior to the induction of anesthesia. It was determined that goats underwent complete intravenous anaesthesia caused by a mixture of diazepam, propofol, and ketamine.

**Key Words:** Anaesthesia, small ruminants, constant rate infusion, bone platting



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## INTRODUCTION

Anaesthesia is considered as a vital prerequisite for both humans and animals for the majority of surgical procedures (Muhammad *et al*., 2009). It is thought to offer reversible cataplexy, analgesia, muscle relaxation, immobility with little adiverse effects, smooth and quick psychomotor recovery, and protective reflex (Bajwa *et al.,* 2010 and Hemming, 2010).

As no medicine can give all the components of general anaesthesia, hence, balanced anaesthesia is required to make it possible. In balanced anaesthesia technique two or more anaesthetic drugs are used in combination to attain the targeted components of general anaesthesia while inducing the minimum negative effects of each drug on cardiopulmonary function (Mama, 2000, Chamanvali *et al., 2022).* Total intravenous anaesthesia (TIVA) which is very uncommon in goats is now more widely accepted as inhalant anaesthetic agents when used as general anaesthesia. Additional benefits of TIVA include: steady intra-operative administration, easy induction, and reduced workplace pollution (Dzikiti, 2013). To avoid the danger of regurgitation and tympany during general anaesthesia administration, at the moment it can be safely used on ruminants with a rapid induction and rapid recovery as a result of propofol utilization in combination with other anaesthetic drugs (Bodh *et al*, 2013; Sharma *et al*, 2010). Because of their quick onset, anticonvulsant characteristics, and low deleterious effects on the cardiovascular system, benzodiazepines were favoured in production animals (Carroll and Hartsfield 1996; Olkkola and Ahonen, 2008). Propofol administration via constant rate infusion or multiple bolus infusion has been recognized as the most effective

method for inducing and maintaining general anaesthesia (Malik *et al.* 2011). Propofol when given in bollus followed by constant infusion gave sheep and goats a tolerable level of anesthesia (Zama *et al.* 2003; Khan, 2006; Hall *et al.* 2001; Prassinos *et al.* 2005). Propofol has been demonstrated to be an excellent anaesthetic agent to induce and keep maintaining general anaesthesia in a variety of species, whether used alone or in conjunction with other induction agents (Caines *et al*. 2014; Dahi *et al.* 2015; Meierhenrich *et al.* 2010; Mattos *et al*. 2013). Ketamine was found to be a good option for continuous intravenous infusion, but it was noted to be more cumulative than propofol (Nikitas *et al*., 2005; Hodgkinson and Dawson, 2007). By first administering a bolus infusion of ketamine and then a constant rate infusion, anaesthesia was induced and maintained more successfully (Malik *et al.,* 2011). In addition to providing excellent analgesia, ketamine stimulates the heart (Muir *et al.,* 2000; Hall *et al.,* 2001). Multiple bolus and constant rate infusion strategies were chosen as the preferred methods for inducing and maintaining anaesthesia. Recently, typical bolus approach has been used to administer intravenous anaesthetic drugs which might not only result in high animal mortality but also present a significant obstacle for surgeons. However, by adopting the constant rate infusion approach and the notion of TIVA, this issue can be overwhelmed more successfully. The whole intravenous anaesthesia regimen and its administration by constant rate infusion in animals have only been the topic of a few researches worldwide. Consequently, anaesthesia of the small ruminant is difficult and yet a pipe dream that can be safely realized by taking into account of current development in modern medications. Therefore, the goal of the current experiment was to evaluate the effectiveness of diazepam, propofol and ketamine given to fractured goats undergoing orthopaedic intervention in conjunction with constant rate infusion.

## MATERIALS AND METHODS

The study was conducted according to the guidelines approved by the ethical review committee University of Veterinary and Animal Sciences Lahore, Pakistan Vide Letter NO. DR/27 dated January 10, 2019. Five female goats with metatarsal and metacarpal fractures that were 8 to 12 months old and weighed an average of 24 to 30 kg were brought to outdoor Surgery Clinic of the University of Veterinary and Animal Sciences, Lahore for this research. The acquisition was made such that their fracture was ascertained using radiographs. Twelve hours were passed between the last meal and the experiment. However, animals were given free access to water (Adetunji *et al.,* 2002). Animals were weighed on an electronic scale thirty minutes before surgical intervention. The propofol induction doses were calculated based on earlier research (Prassinos *et al.,* 2005; Zonca *et al.,* 2012). The left side of the neck was clipped around the jugular furrow as access to the jugular veins. Methylated spirit was used to cleanse the skin, and 18G intravenous catheters were inserted for blood collection and anaesthesia delivery (Adetunji *et al.,* 2002; Correia *et al.,* 1996). After sedation with diazepam @ 0.25 mg / kg (Domosedan injection, Orion Corporation, Finland) anaesthesia was given in combination of propofol and ketamine @ 2 mg/kg body weight each (Fresofol 1 % injection, Fresenius Kabi, Austria). Once the goats were recumbent, a volumetric syringe-driving pump and a constant rate infusion of (diazepam @ 0.02 mg/kg/hr + ketamine @ 2.40 mg/kg/hr and propofol 0.96 mg/kg/hr) were used to maintain the anaesthesia for two hours. Anesthetized goats were then placed on right lateral recumbency. Reduction of fracture was made by internal fixation of bone plating. For aseptic surgery; preparation of operative site was done with antiseptic solution and a drap was applied on the limb. On the lateral aspect of the fractured limb, a skin incision was given starting distally from the proximal joint up to and above the distil joint for the exposure of fracture site. Reduction of the fracture was done and bone holding clamp was used to hold the bone. Fractures were of metacarpal and metatarsal bones and were immobilized by using bone plates. The fractures were oblique in nature. For the reduction of fracture; suitable dynamic compression plates were applied on dorso-lateral aspect of fracture. On both the cortices of the fractured, bones holes were tapped with drilling for the fixation of screws. Suturing of subcutaneous tissue was done with catgut number 2 using simple continuous suture pattern. Monofilament silk number 2 as a suture material was used on skin by using simple interrupted suture.

The evaluation of anaesthesia was done by using the following parameters:

**Parameters evaluated**

**Sedation Quality:** Fifteen minutes after pre-anesthetic treatment, behavioural changes were seen to assess sedation (Kalhoro *et al.,* 2000; Shah, 2008) and were classified as following:

1 (no sedation) all reflexes present, and animal alert
2 (mild sedation) minute reductions of reflexes and dullness
3 (moderate sedation) weak reflexes, calm behaviour and partial closure of eyelids
4 (deep sedation) well defined weak reflexes, recumbent state and closed eyelids

**Quality of analgesia:** The reaction of the animals was observed to a deep pin prick fifteen minutes after the pre-anesthetic administration to determine the degree of analgesia. It was then classified as following (Kalhoro *et al.,* 2000; Shah, 2008)

1 used to show a strong response to a pinprick and not to provide any analgesia
2 used for displaying weak response to pin prick but providing mild analgesia
3 used for displaying occasional response to pin prick but providing moderate analgesia
4 used for displaying no response to pin prick but providing excellent analgesia

**Anesthetic parameters:** Parameters of anaesthesia: like quality of induction, quality of muscle relaxation and quality of recovery were evaluated after post induction of anaesthesia at the interval of 5 minutes throughout the procedure by using score card by Ghurashi *et al.*, (2009) Table 1.

**Table 1: Anaesthetic parameter score card**

| Score | Quality | Characteristic |
|---|---|---|
| **Induction quality score** | | |
| 1 | Smooth | Steady falling down with no limb rigidity and padding |
| 2 | Fair | Steady falling down with no limb rigidity and mild padding |
| 3 | Rough | Gradual falling with sturdy limbs rigidity and vigorous padding |
| **Analgesia quality score** | | |
| 1 | Excellent | No response |
| 2 | Fair | Minor response, with minor fasciculation of muscle |
| 3 | Poor | Vigorous response, with moderate to severe fasciculation of muscle |
| **Muscle relaxation quality score** | | |
| 1 | Excellent | Completely relaxed limbs, abdomen, neck and jaw muscles |
| 2 | Good | Moderate relaxation of limbs, abdomen and neck muscles |
| 3 | Poor | Completely rigid limbs, abdomen, neck and jaw muscles |
| **Recovery quality score** | | |
| 1 | Smooth | Animal stand in first effort without assistance and slight ataxia |
| 2 | Fair | Required two or three efforts to stand without assistance |
| 3 | Poor | Calm behaviour but animal required assistance to stand |
| 4 | Very poor | Excitement signs in the course of recovery |

**Clinico-physiological parameters:** The clinic-physiological parameters were monitored starting at 0 minutes prior to sedation (baseline) after that; following anaesthetic induction at every 1, 5, 10, 15, 20, 30, 100 and 120 minutes, and thereafter until complete recovery. Oxygen haemoglobin saturation, heart rate, respiratory rate, partial pressure of oxygen, partial pressure of carbon dioxide,: systolic, diastolic and mean arterial blood pressure (SAP, DAP, MAP) and rectal temperature were measured before treatment, at 0 minutes (baseline), 1 minutes after induction, and then at intervals of every 10 minutes throughout the maintenance of anaesthesia, Rectal temperature (°F) was recorded using a digital thermometer, and the heart rate (beats/min) and respiration rate (breaths/min) were both measured using stethoscopes. Each goat's left forelimb was wrapped with a pediatric noninvasive blood pressure (NIBP) monitor to measure mean arterial, systolic and diastolic pressure. To test the haemoglobin oxygen saturation, the pulse oxy-meter was also wrapped around the tongue. A 20-gauge catheter was placed in the left auricular artery for the collection of arterial blood samples in to 2mL heparinized syringes. A blood gas analyzer was used to measure the partial pressures of oxygen and carbon dioxide.

**Haematobiochemical parameters:** Five mL of blood samples were collected in plain tubes with 23-G needle through jugular vein. Serum was harvested after centrifugation and stored at -20°C. After this, both blood and serum samples were brought to University Diagnostic Laboratory (UDL, UVAS) for haematological (exigo, EOS-Vet, Sweden) and biochemical evaluation (Biosystem, BTS 350, Spain). The packed cell volume (%), haemoglobin (g/dl), total erythrocyte count ($10^{12}$/l) and total leukocyte count ($10^{9}$/l) were evaluated at 0 min before sedation (baseline), 1 min after anesthetic induction and then at 5, 10, 15, 20, 30, 60, and 120 minutes by using automatic haematology analyzer. At the same times, a biochemical analyzer was used to check the levels of blood urea nitrogen, total plasma protein, cortisol, aspartate aminotransferase, alanine phosphatase, glucose, and creatinine. By extracting 0.5 mL of plasma in 5 mL of diethyl ether, the ether phase was evaporated and then dissolved in 0.5 mL of assay buffer, and the cortisol level was in an aliquot. Finally, the enzyme-immunoassay method was used to measure the cortisol level.

**Statistical Analysis:** One-way analysis of variance (ANOVA) was used to analyze the data in the SAS 9.1 version of statistical analysis software at ($p<0.05$). Significant means were compared through Duncan's Multiple Range Test (DMRT) at different intervals of time.

# RESULTS

## Anesthetic Parameters

**Analgesia Induction, sedation, muscle relaxation and recovery score:** The mean value of analgesia score was found (1.00±0.00) indicating excellent. The mean value of induction score was found (1.00±0.00) indicating smooth induction. The mean value of muscle relaxation score was found (1.00±0.00) indicating excellent muscle relaxation. The mean value of recovery score was found (1.00±0.00) indicating smooth recovery.

**Evaluation of clinico-physiological parameters:** The respiratory rate, heart rate, oxygen haemoglobin saturation, blood pressure and rectal temperature differed ($p<0.05$) at different time intervals after treatment compared to base line before induction as shown in Table 2. The heart rate showed decreasing trend at 60 min compared with base line at 0 min and increasing trend at 120 min. The results showed decreasing trend of respiratory rate at 120 min with peak decrease at 30 min compared with a base line at 0 min during anesthesia. The results also showed slightly decreasing tendency of rectal temperature but values were remain in normal range (39.1±0.09 to 38.3±0.03°C) at 120 min.

Systolic arterial pressure varied considerably ($p<0.05$) from baseline at 0 min before induction at various points after therapy. Systolic arterial pressure increased throughout the course of 120 min, according to the results. When compared to the baseline diastolic arterial pressure of 0 min prior to induction, the diastolic arterial pressure varied ($p>0.05$) throughout time following treatment. 0 min before induction, the mean arterial pressure varied ($p>0.05$) at various time points following treatment. The partial pressure of oxygen differed ($p<0.05$) at different time intervals after treatment compared to zero minutes (base line) before induction.

The results showed decreasing trend of partial pressure of oxygen. Following treatment, the partial pressure of carbon dioxide varied ($p< 0.05$) when compared to the baseline value of 0 min before induction. The results also showed increasing trend of partial pressure of carbon dioxide**.** The oxygen haemoglobin saturation differed ($p<0.05$) at different time intervals after treatment compared to 0 min (base line) before induction. The analysis showed decreasing trend of oxygen haemoglobin saturation**.**

**Table 2. values Mean (±SE) of respiratory rate (breaths/min), heart rate (beats/min), diastolic, systolic and mean arterial pressure (mm Hg), rectal temperature (°C), partial pressure of oxygen (PaO2%), oxygen haemoglobin saturation (SpO2%) and carbon dioxide (PaCO2%) after administration of diazepam, propofol and ketamine using total intravenous anesthesia during bone plating in goats.**

| Variables | Time (Min) | | | | | | | | P-Values |
|---|---|---|---|---|---|---|---|---|---|
| | 0 Min | 5 Min | 10 Min | 15 Min | 30 Min | 45 min | 60 min | 120 min | |
| HR | 61.6±0.55 | 57.0±0.40 | 58.4±0.51 | 55.4±0.24 | 54.4±0.24 | 53.2±0.20 | 54.2±0.20 | 62.8±0.20 | 0.003 |
| RR | 15.0±0.00 | 14.4±0.40 | 14.4±0.40 | 13.6±0.40 | 13.2±0.20 | 13.0±0.31 | 13.8±0.20 | 14.4±0.24 | 0.012 |
| Temp | 39.1±0.09 | 39.1±0.03 | 39.0±0.04 | 38.8±0.05 | 38.6±0.24 | 38.5±0.07 | 38.3±0.10 | 38.3±0.03 | 0.016 |
| MAP | 91.1±0.83 | 84.6±0.67 | 86.6±1.43 | 86.7±1.63 | 85.3±1.87 | 84.5±1.97 | 84.9±2.51 | 84.5±2.34 | 0.218 |
| DAP | 73.2±1.88 | 71.2±1.88 | 74.8±1.82 | 73.2±1.88 | 77.0±1.41 | 71.6±1.69 | 72.8±1.85 | 73.8±2.15 | 0.351 |
| SAP | 112.4±2.06 | 111.0±1.87 | 113.6±2.24 | 112.4±2.06 | 112.2±1.88 | 114.4±2.06 | 112.4±2.06 | 113.4±2.06 | 0.000 |
| PaO2 | 81.8±0.52 | 78.4±0.22 | 76.5±0.51 | 75.9±0.74 | 76.2±0.86 | 75.6±0.90 | 74.9±0.84 | 74.8±0.78 | 0.008 |
| PaCO2 | 33.5±0.33 | 40.9±1.61 | 43.7±2.39 | 47.1±3.06 | 48.2±3.02 | 50.4±3.43 | 51.1±3.76 | 52.1±3.54 | 0.060 |
| SpO2 | 90.6±0.47 | 87.9±0.84 | 87.2±0.90 | 87.2±0.98 | 88.5±1.14 | 86.0±1.24 | 85.6±1.10 | 85.4±1.28 | 0.070 |

P values ≤ 0.05 in column indicated significant effect of combined total intera-venous anesthesia (TIVA) on different physical parameters during surgical intervention in goats

**Haematobiochemical parameters:** The findings revealed that leukocyte, granulocyte, lymphocyte, monocyte, red blood cell counts, packed cell volume and haemoglobin concentration variations over the observation period were not statistically significant as shown in the result (Table 3).

The results showed that the serum glucose level, alanine aminotransferase, aspartate aminotransferase and cortisol varied ($p>0.05$) over the observation period compared to 0 min (base line) before induction of anesthesia as shown in figures (1-4). The results also showed that blood urea nitrogen and creatinine value differed ($p>0.05$) at different time intervals during observation period compared to 0 min before induction of anesthesia (Table 3).

**Table 3. values Mean (±SE) of haemoglobin (g/dL), packed cell volume (%), glucose (mg/dL), total leukocyte count ($10^{12}$/l), total erythrocyte count($10^{12}$/l), alanine aminotransferase (U/L), cortisol level (ng/mL), aspartate aminotransferase (U/L), creatinine (mg/dL) and blood urea nitrogen(mg/dL) after administration of diazepam, propofol and ketamine as TIV anesthesia.**

| Variable | Time (Min) | | | | | | P-value |
|---|---|---|---|---|---|---|---|
| | 0 Min | 10 Min | 20 Min | 30 Min | 60 Min | 120 Min | |
| WBC | 53.1±0.45 | 50.1±0.47 | 50.1±0.40 | 51.3±0.44 | 51.5±0.51 | 52.3±0.44 | 0.528 |
| GRAN | 14.5±0.37 | 13.2±0.56 | 12.8±0.50 | 13.2±0.48 | 12.4±0.52 | 13.3±0.47 | 0.621 |
| LYM | 32.0±0.42 | 34.3±1.06 | 36.1±1.15 | 32.7±0.35 | 32.5±0.48 | 33.3±0.57 | 0.624 |
| MONO | 4.2±0.03 | 4.5±0.11 | 4.1±0.22 | 4.4±0.11 | 4.5±0.05 | 4.0±0.16 | 0.446 |
| RBC | 11.1±0.08 | 11.4±0.06 | 11.2±0.07 | 11.0±0.05 | 11.2±0.03 | 11.0±0.04 | 0.099 |
| HB | 9.3±0.08 | 8.5±0.11 | 9.3±0.03 | 9.2±0.02 | 9.2±0.02 | 8.8±0.05 | 0.507 |
| PCV | 20.3±0.09 | 19.8±0.09 | 20.5±0.05 | 20.5±0.09 | 20.5±0.05 | 20.4±0.05 | 0.413 |
| GLUC | 63.4±0.87 | 68.9±1.04 | 84.8±1.17 | 81.1±1.00 | 66.2±1.09 | 58.5±0.53 | 0.000 |
| BUN | 15.8±0.36 | 16.3±0.27 | 16.0±0.37 | 16.4±0.14 | 16.5±0.12 | 16.6±0.19 | 0.208 |
| CRE | 1.5±0.06 | 1.5±0.01 | 1.5±0.01 | 1.5±0.01 | 1.5±0.01 | 1.4±0.03 | 0.210 |
| ALT | 12.2±0.35 | 12.3±0.29 | 12.8±0.48 | 13.1±0.21 | 12.9±0.33 | 12.6±0.20 | 0.042 |
| AST | 21.3±0.24 | 21.2±0.07 | 21.0±0.08 | 21.5±0.20 | 21.8±0.29 | 21.8±0.24 | 0.028 |
| CORT | 15.1±0.07 | 20.5±0.19 | 28.6±0.27 | 33.9±0.24 | 38.4±0.38 | 38.1±0.37 | 0.000 |

P values ≤ 0.05 in column indicated significant effect of combined total intera-venous anesthesia (TIVA) on different blood parameters during surgical intervention in goats

## DISCUSSION

The goal of the current investigation was to determine how well goats pre-medicated with diazepam responded to a combination of propofol and ketamine administered intravenously during the reduction of a metacarpal or metatarsal fracture. Maintenance of general intravenous anesthesia with a synergism of ketamine and propofol resulted into deep sedation and excellent analgesia. Deep sedation and profound analgesia kept consistent for 120 minutes maintenance period of entire surgical procedure. Profound sedation is resulted into the synergistic sedative effects of diazepam, propofol, and ketamine. Although synergistic mechanism of action is not clear but synergistic interaction of propofol and ketamine has also been explained in previous study (Arora, 2008). The combination of diazepam, propofol and ketamine resulted in excellent analgesia and deep sedation (Loh and Dalen, 2007; Arora, 2008). The mixture of anesthetics or sedatives enhanced the analgesic and sedative effect of individual drug (Rauser and Lexmaulova, 2002). Maintenance of total intravenous anesthesia with a combination of diazepam-propofol and ketamine produced a relatively smooth and rapid induction, good muscle relaxation, and better recovery (Ragab *et al*., 2022). Smooth induction is due to the combined effects of ketamine and propofol which have been also reported in some earlier studies (Matthews *et al.*, 1993; Amin and Najim, 2011). Smooth recovery may be because of a non-cumulative effect of propofol as revealed in some other studies (Doherty and Greene, 2002; Dzikiti *et al.*, 2009). The synergistic interaction between diazepam, propofol, and ketamine can be attributed towards easy induction and smooth muscular relaxation. Moreover, it also produces smoothly and problem-free recovery after surgical intervention in fractured goats. Goats that were kept under anaesthesia using a propofol-ketamine combination were recovered in well health state. Propofol and ketamine infusions are said to produce satisfying anaesthesia with a rapid onset, and quick recovery (Zonca *et al.*, 2012; Asif *et al*., 2022). Based on cardiovascular results; maintaining general intravenous anaesthetic with a propofol and ketamine combination, had no effect on cardiovascular function and kept it more stable than other groups. This is because administration of many medications in combination results into lesser adverse effects than administering each separately. This is perhaps potential negative effects are primarily dose-dependent when administered in combination. The dosage of each drug can be decreased with just minor negative effects. The circulatory inhibitory properties of ketamine and propofol are responsible for the drop in heart rate. In this study, non-significant reduction in heart rate is attributable to the addition of propofol which likely counteracted the bradycardic action of detomidine to a larger extent when combined with ketamine. Similar findings were also reported in calves by Pawde, (2000) who reported that the combination of propofol-daizepam-ketamine caused trivial decrease in heart rate. However, our findings contradict with other study reported in donkeys (Ali, 2013) which explained that midazolam-ketamine in combination significantly lowered heart rate. When diazepam, propofol, and ketamine are used to maintain general intravenous anaesthesia, the reductions in

systolic, diastolic, and mean arterial pressure are comparatively less. This is mainly because when these anaesthsia used in combination, the dose of each treatment can be lowered which ultimately leading to minimal side effects. In addition to this, potential side effects of anaesthesia are also typically dose-dependent. Secondly, higher cardiovascular stability may be the result of the administration of propofol and ketamine together which had minimal adverse effects on arterial blood pressure. Blood pressure dropping after propofol infusion (Muir and Gadawski, 2002; Leite *et al.,* 2008; Dzikiti *et al.,* 2010; Sooryadas *et al.,* 2011; Clarke *et al.,* 2014) and hike after ketamine infusion were also resulted in earlier study (Ilkiw *et al.,* 1992). More stable lung function is maintained when diazepam, propofol, and ketamine are used together. This is because side effects are frequently dose-dependent and may be reduced when three medications are delivered simultaneously resulting into fewer side effects. This is partly due to ketamine's bronchodilator properties which reduce propofol's overall respiratory depressive effects and maintain more stable lung function. A typical side effect of propofol has been reported as suppression of respiratory rate (Wiese *et al.,* 2010). The medications' direct depressive effects on the brain in general and on the thermoregulatory area of the hypothalamus in particular are likely to be decreased in body temperature. The lowered rectal temperature was the result of lesser muscular activity or a lower basal metabolic rate during anaesthesia. Another typical side effect of propofol has been hypothermia (Bodh *et al.,* 2013). diazepam, propofol, and ketamine were used to maintain general intravenous anaesthesia along with declines in haemoglobin oxygen saturation ($SpO_2$) and partial pressure of oxygen ($PaO_2$). As documented in prior investigations, the vasoconstriction or respiratory depressive activity of propofol may have contributed to this decline (Mair *et al.,* 2009; Suarez *et al.,* 2012; Maney *et al.,* 2013). When used in combination, the dose of each drug can be decreased to reduce adverse effects because the potential side effects of the pharmaceuticals are dose-dependent. Additionally, a substantially lesser increase in the partial pressure of carbon dioxide was produced by this diazepam-propofol-ketamine combination ($PaCO_2$). No respiratory arrest and better oxygen saturation were found with the combination of diazepam, propofol and ketamine. Therefore, it may be accepted in cases where decreased respiratory and cardiovascular function. These outcomes are consistent with the results reported by Guzel *et al.,* (2006) who revealed that diazepam-propofol combination showed no respiratory arrest but improved oxygen saturation than propofol-diazepam alone. The partial pressure of carbon dioxide in horses increased significantly as a result of general intravenous anaesthesia maintained with ketamine, medetomidine, and propofol, according to Umar *et al.,* (2006) who published these results. The negligible changes in haematological markers are a result of the antagonistic haemodynamic effects of ketamine and propofol, which ultimately have negligible adverse effects. Propofol and ketamine both have adversative haemodynamic effects according to certain earlier investigations (Sakai *et al.,* 1999; Furuya *et al.,* 2001; Srivastava *et al.,* 2006; Aouad *et al.,* 2008; Arora, 2008; Mair *et al.,* 2009). The fact that the combination of several medications in term of anaesthesia had a fewer adverse effects which is perhaps main cause of the minimal alterations in haematological parameters.

The non-significant drop in haemoglobin content, packed cell volume, and total erythrocyte count is evidence that red blood cells have been sequestered in spleen (Kinjavdekar *et al.* 2010; Al-Redah, 2011). Both anaesthetic and surgical stress have been seen to cause minor alterations in haematological parameters, although these changes were only temporary and of no clinical significance. Similar outcomes were observed by (Kelawala *et al.,* 1991; Yakubu *et al.,* 2020) whom mentioned a non-significant decrease in haemoglobin concentration, total erythrocyte count and packed cell volume in goats was shown when propofol, ketamine, and daizepam were combined. Similar to the findings, a substantial increase in total leukocyte count was seen by (Sharma *et al.,* 2010; Ismail *et al.,* 2010). The fact that the combination of different medicines had less side effects may account for the minimal increases in blood glucose, cortisol, alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, and creatinine levels that were reported. The hyperglycemic effects of ketamine and propofol are what caused the blood glucose level to rise from its initial amount (Sharif and Abouazra, 2009; Saha *et al.,* 2005). It is reported that surgery-related stress is the cause of the elevated blood glucose level in some studies (Njoku, 2015; Udegbunam *et al.,* 2012). This is because tissue injury from rumenotomy may cause pain mediators to be activated. The release of stress hormones by the autonomic and central nervous systems as a result of the activation of pain mediators delayed the metabolism utilization, and production of glucose or lipid breakdown which in turn raised blood glucose levels as that mentioned by Singh *et al., (*2003). The adrenergic inhibiting the release of insulin from pancreatic beta cells or promotion of glucagon release is the cause of the elevated glucose level. This is because throughout the length of the anaesthesia and bone plating, there was a drop in metabolic rate, minimal muscle movement, and minimal glucose utilization. Same interpretations were also noted in ruminants (Okwudili *et al.,* 2014; Tandia, 2010). These results in agreement with Ismail *et al.,* (2010) who described that the combination of ketamine, xylazine and diazepam caused a considerable rise in blood sugar in goats. The combination of diazepam, propofol, and ketamine used to maintain complete intravenous anaesthesia caused relatively little increase in

alanine aminotransferase and aspartate aminotransferase. This occurs as a result of the fact that combining different medications produced less fatal effects than either single drug. The elevation of liver enzymes may result into a mild liver depression which probably might be due to the medicines' toxic effects on hepatic blood flow. These observations are consistent with the results of Ismail *et al*., (2010) who mentioned an elevation in alanine aminotransferase and aspartate aminotransferase levels in goats and sheep when xylazine, ketamine, and diazepam were administered in combination.

Maintaining total intravenous anaesthesia by utilizing a combination of diazepam, propofol, and ketamine resulted into a relatively marginal rise in blood urea nitrogen along with least influence on creatinine level. This modest rise in blood urea nitrogen concentration may be caused by a reduction in renal blood flow which leads to minor kidney depression and an accumulation of nitrogenous compounds in the blood. Earlier investigations also revealed similar results (Montane *et al.,* 2003, Montane *et al.,* 2008; Baishya, 2010; Rina *et al.,* 2018). Total intravenous anaesthetic maintained using a mixture of ketamine, propofol, and diazepam caused reduced stress according to the cortisol response. A rise in cortisol was seen due to substantial surgical stress during bone plating which is due to stimulated nociceptive receptors. Moreover, it triggered the release of adrenocorticotropic hormone which in turn boosted the adrenal cortex's ability to secrete cortisol as reported by Martín *et al., (*2001). However, the administration of propofol-ketamine combination successfully reduced the anxious reaction to surgical stimulation. Strong analgesia is produced when diazepam and ketamine are combined, and this lowers the degree of cortisol release. The use of propofol fentanyl anaesthesia also helped to lessen the stress response caused by superficial soft tissue surgery. (Schöffmann *et al.,* 2009).

**Conclusion:** In conclusion, it was established that total intravenous anaesthesia in goats as a result of diazepam, propofol, and ketamine in combination produced sufficient anaesthesia with minor transient alterations in clinic-physiological and haemato-biochemical parameters.

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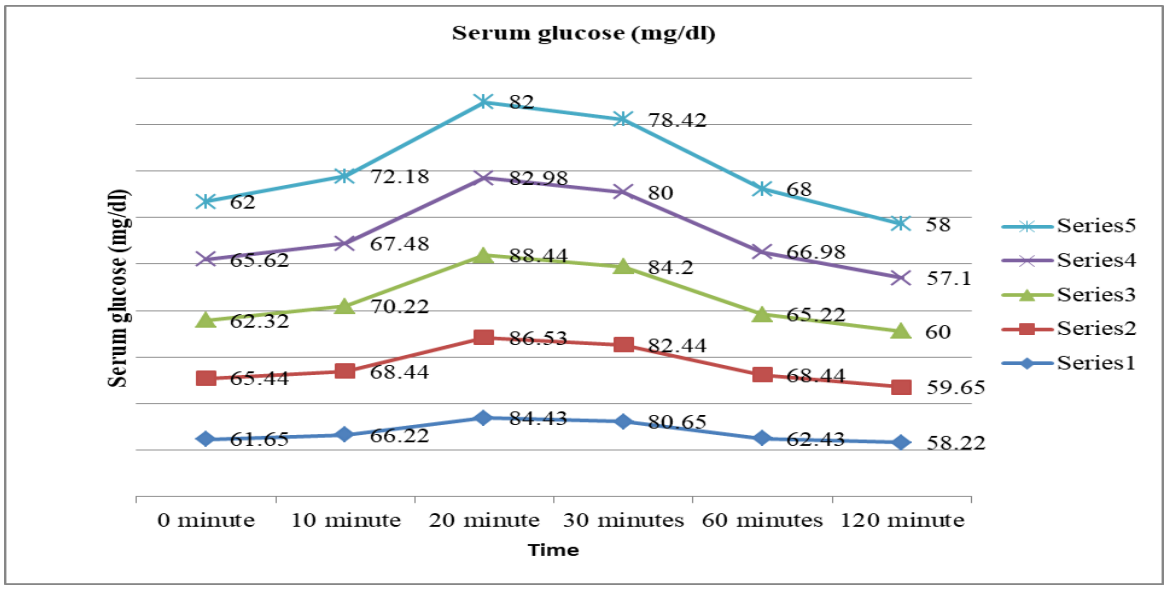


**Figure 1 shows significant increase in Aspartate aminotransferase (U/L) among different time intervals**

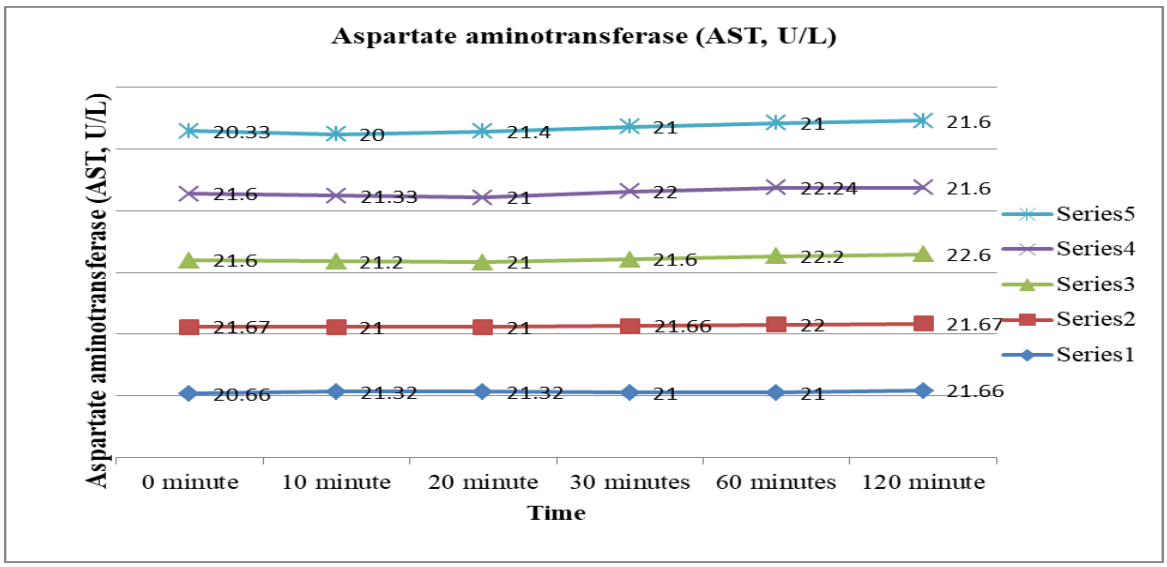


**Figure 2 shows significant increase in Aspartate aminotransferase (U/L) among different time intervals**

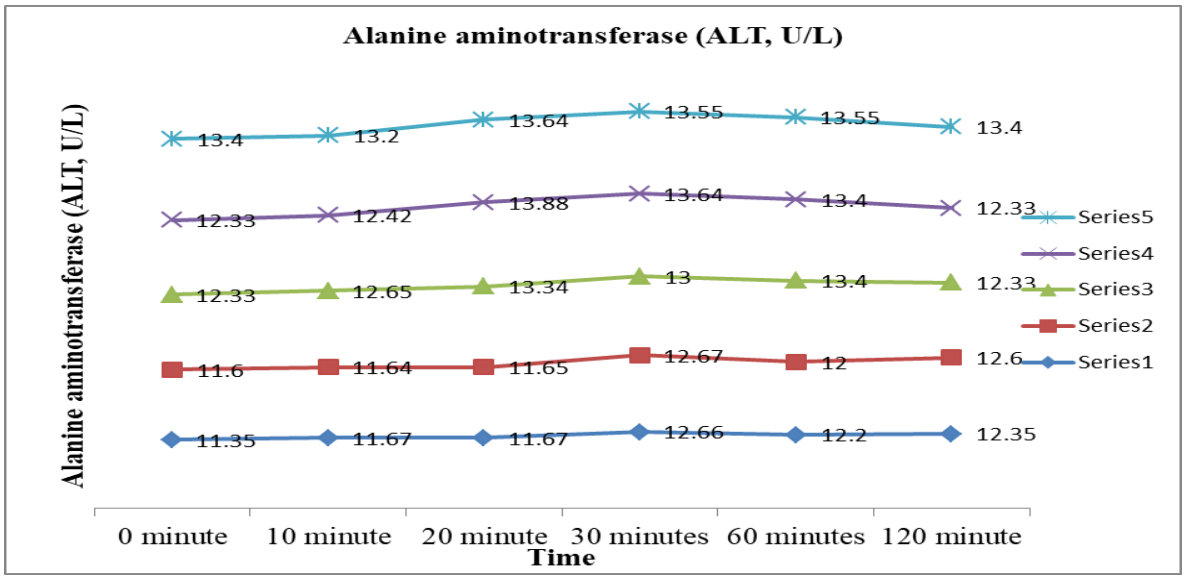


**Figure 3 shows significant increase in Alanine aminotransferase (U/L) among different time intervals**

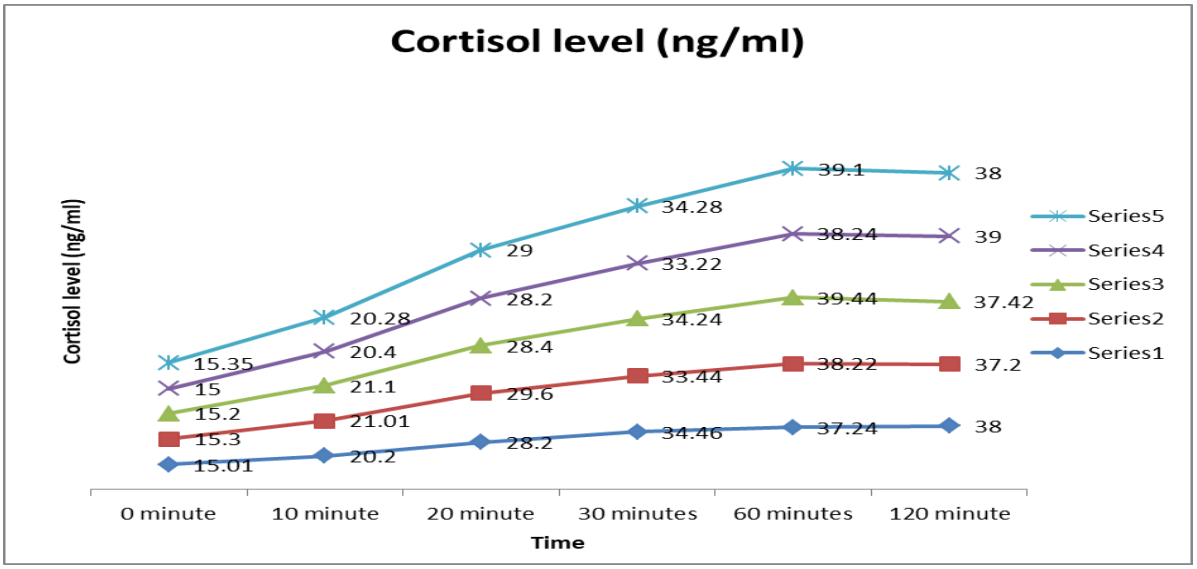


**Figure 4 shows significant increase in Cortisol level (ng/mL) among different time intervals**