Propofol exhibit shorter recovery time than thiopentone infusion in Small East African goats

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SUMMARY

Goat as ruminants are not good subjects for general anaesthesia complicated by their anatomical structures, effects associated with general anaesthetic administration and recovery periods. The present study aimed to evaluate two anaesthetic agents known to have short induction and recovery period as suitable for total intravenous anaesthesia. A total of fourteen goats of 14.7kg mean weight and randomly divided into two groups of seven animals each were used in the study. One group received induction dose of 6mg/kg of 1% propofol and the second group received 12mg/kg dose of 2.5% thiopentone respectively. Anaesthesia was maintained by continuous infusion for 30 minutes using a CRI pump where a double dose of induction for propofol group and same induction dose for thiopentone group added in 100mls of normal saline were used. Results indicated a similar induction time for propofol and thiopentone ($p>0.05$); both drugs had depressive effect on respiration. Thiopentone showed a considerable tachycardia and rectal temperature increase unlike propofol which maintained the pre-injection values of these parameters. The time to return to consciousness was significantly shorter for propofol compared to thiopentone ($p<0.05$). In addition, propofol showed superior quality of anaesthesia compared to thiopentone. The study recommends the use of propofol for induction and maintenance of anaesthesia for short procedures requiring general anaesthesia in goat.

Keywords: *Intravenous, Anaesthesia, Thiopentone, Propofol, Small East African Goat.*

INTRODUCTION

Total intravenous anaesthesia (TIVA) is a method of inducing and maintaining general anaesthesia exclusively by intravenously administered drugs, without simultaneous administration of any inhalation agent (Sear, 1991; Anderson and Houghton, 2019; Flacknell *et al.*, 2015). TIVA can be given by simple intravenous bolus or variable rate continuous infusion (Flacknell *et al.*, 2015). Thiopentone, ketamine, propofol and a combination of these drugs with α_2 adrenergic receptor agonist, opiates or skeletal muscle relaxants had been employed for TIVA in different species (Sear, 1991; Anderson and Houghton, 2019; Flacknell *et al.*, 2015, Riebold *et al*, 1978).

However, ruminants like goats are not good subjects for general anaesthesia due to the danger of regurgitation and inhalation of ingesta compared to other domesticated animals. Proper pre anaesthesia preparation of the animal is known to minimize the complications associated with general anaesthesia. Practices such as restriction of feeds and water intake for a predetermined time interval, proper protection of the airway to prevent rumen contents entering the tracheal through passive regurgitation coupled with periodical decompression of the rumen are mandatory pre- and intra-operative safety measures or procedures.

Despite of these precautions, some surgical procedures, practice setting and locations may compel surgeons to use some anaesthetic protocol solely utilizing injectable anaesthetics and thus the need for TIVA (Sear, 1991).

The triple drip "consisting of 50mg xylazine, 1-2gm ketamine instilled to one liter of 5% guaifenesin" is common infusion ingredient for TIVA in a ruminant which is usually given to effect (Seddighi and Doherty, 2016). Other infusions protocols using ketamine, propofol, fentanyl, midazolam, lidocaine and their combinations have been shown to induce adequate anaesthesia or minimize MAC for inhalant anaesthetics when employed as part of balanced anaesthesia in goat (Riebold *et al*, 1978; Vieitez *et al*, 2017). However, the overall selection of anaesthesia protocol to use is largely predetermined by the drug availability and the practice setting.

In Tanzania, food animal practice and surgery are conducted at farm level or in the field where facilities for inhalant anaesthetic administration does not exist. The anaesthetic protocols available for a practitioner are those that employ local or regional analgesia with or without some form of restraints or antipsychotic agents. It was therefore important to evaluate some anaesthetics that are readily available as alternative to local and regional analgesia protocols in Small East African Goats in Tanzania. The present study thus compared propofol and thiopentone for total intravenous anaesthesia in goats for short duration anaesthesia with two specific objectives namely (i) to compare the induction and recovery time and (ii) to compare the cardio-pulmonary dynamics for thiopentone and propofol throughout anaesthesia.

MATERIAL AND METHODS

The study was permitted by Sokoine University of Agriculture and conducted in accordance with the approved research protocol. A total of 14 healthy adult Small East African goats with a mean weight of 14.7kg were used in this study. At the farm, animals were allowed to graze freely and no additional supplementary feeds were provided. All animals were dewormed three months before commencement of the study. During the evening, animals were housed in the raised, corrugated and slatted stall that allowed dung and urine to drop down.

A cross sectional design was employed, the 14 study animals were randomly divided into two groups of seven animals each where each group had four males and three female goats respectively. As a general rule, a day prior to anaesthesia, animals were confined in the stall and provided only water at night proceeding to administration of anaesthesia as precautions to minimize complications associated with general anaesthesia.

On the day of experiment, pre-anaesthetic cardiopulmonary parameters (Respiration Rate, Heart Rate and, Rectal Temperature) were determined and recorded. This was followed by shaving the area around the jugular vein, cleaned and then the jugular vein was located and cannulated using a 20G intravenous catheter and held in place using adhesive tapes. Animals in the first group received intravenous induction dose of 6mg/kg of 1% propofol (Dzikiti *et al*., 2010., Reid *et al*., 1993) while the second group received 12mg/kg of 2.5% thiopentone (recommended dose range from 5.5mg/kg to 22mg/kg) as pointed out by EMEA (2001).

The maintenance of general anaesthesia for propofol group used double of the dose calculated for induction while the thiopentone group used same amount of dose calculated previously for induction and each added into 100mls of normal saline for infusion. Immediately after successful induction, the animal was connected to an infusion machine (Master Flex, USA) set to deliver at the rate of 0.2mg/kg/min propofol and thiopentone respectively to maintain anaesthesia for the duration of thirty minutes.

Following the connection of the infusion pump cardiopulmonary parameters were noted and recorded at an interval of 5 minutes for the duration of 30 minutes. Pin pricking, eyeball and tongue retraction were used to determine the levels of anesthesia and awake signs.

After 30 minutes of anaesthetic infusion, the machine was switched off and recording started including induction time,

time to first limb movement, time to stand and time to regaining movement (ambulation). The nature of recovery was observed and recorded in all tested animals. Similarly, the values recorded for pre-, intra- and post- anaesthesia cardio-pulmonary parameters were recorded.

Data analysis

Data were analyzed using Wilcoxon's Rank Sum Test as described by Sykes et al. (1981). Pre-anaesthesia and subsequent readings for the two drugs were compared. P-value less than 0.05 was considered to be significant.

RESULTS

Anaesthesia induction, anaesthesia depth and arousal

The induction time, time to first limb movements, standing and regaining motion or ambulation is indicated in **Table 1**. The two drugs showed no differences on induction time but in all other parameters, propofol treated group appeared to return to normal mentation or vigilance and ambulation significantly much faster.

Ocular signs observed for animal injected with propofol exhibited a rostro-ventral rotation of the eyeball; while thiopentone treated goats had their eyeball centrally fixed. Animals injected with propofol showed non response to toe pin pricks while those under thiopentone responded.

Table 1. Parameters associated with induction and arousal time in Small East African Goats

S.N.	Recorded Parameter	Propofol (n=7)	Thiopentone (n=7)	
1	Induction Time (Seconds)	37.86±11.13	35.71±10.97	0.144 (P>0.05)
2	Time to first limb movements (Minutes)	1.36±0.85	7.29±2.81	0.0005 (P<0.05)
3	Time to Standing (Minutes)	4.36±2.17	23.29±11.48	0.002 (P<0.05)
4	Time to regain ambulation (Minutes)	6.71±2.43	35.57±17.45	0.003 (P<0.05)

Induction time: The duration from injection of anaesthetic induction drug to the time the animal becomes unconsciousness. Time to first limb movement-: The duration from when anaesthetic infusion was stopped to the time when the animal showed the first signs of limb movement. Time to stand: The duration from when anaesthetic infusion was stopped to the time when the animal was able to stand up but not moving.

Time to regain movement or ambulation: The time from when anaesthetic infusion was stopped to the time the animal started to move around.

Respiration rates

The two drugs showed a declining trend of respiration rate. The decline was relatively smoother in Propofol than thiopentone treated animals which showed spiking and declining trend. None of the two groups showed a return normal respiration rates at the end of 30minutes observation time (Figure 1A).

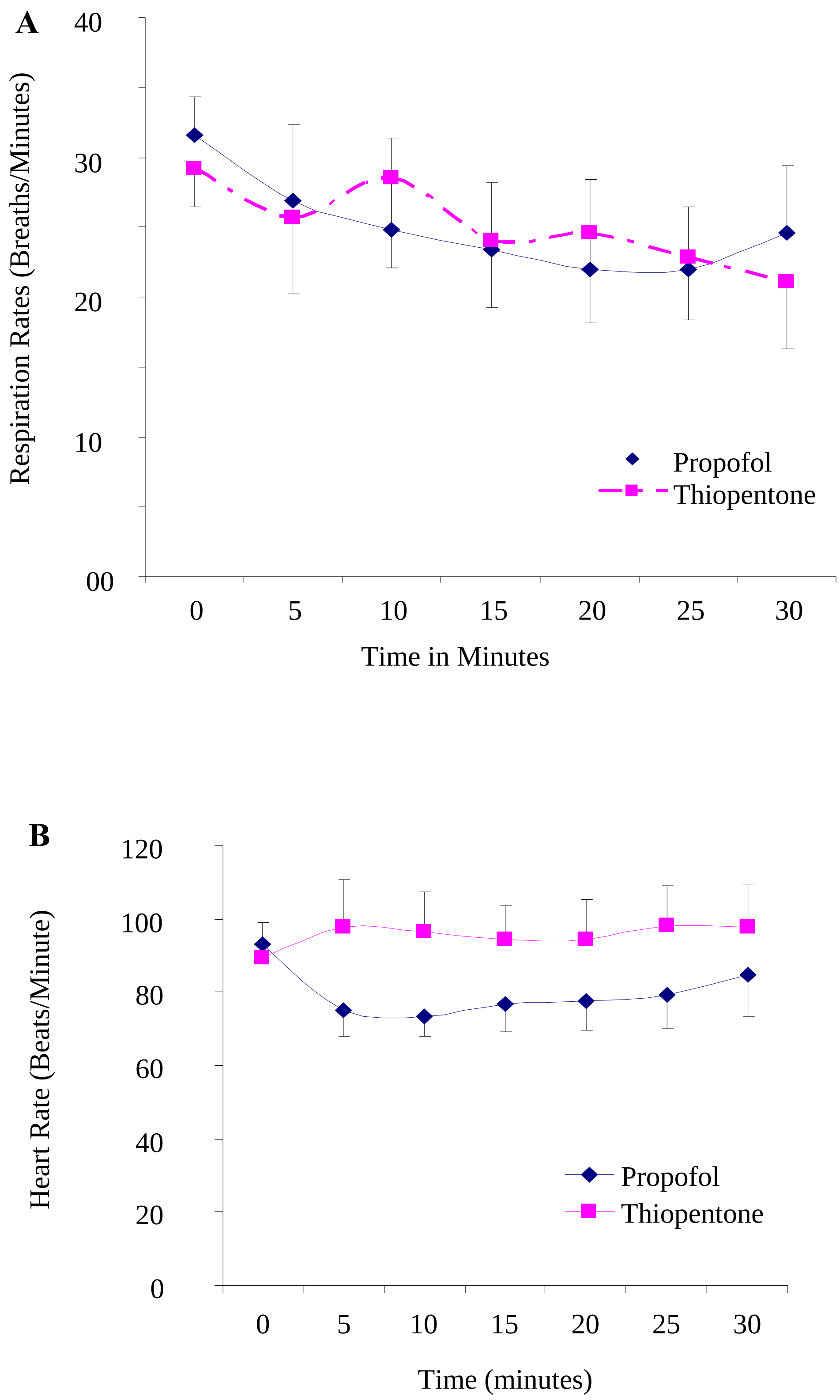

Figure 1A: Relatively linear respiration rate in goats infused with propofol compared to thiopentone (n=7, per group). **B**. Slightly increased heart rates for goat infused with thiopentone as compared to propofol (n= 7, per group)

Heart Rates

Propofol showed immediate decline within the first five minutes and then slowly and gradually increased but did not attain the pre injection heart rate while thiopentone showed immediate increase for the first five minutes and thereafter increased at a decreasing rate but did not attain the pre injection heart rate value (Figure 1B).

Rectal Temperature

The two drugs, propofol and thiopentone showed a reduction of the mean rectal temperature throughout the observation time.

The rectal temperature values continued to decrease for the first 5 minutes and thereafter followed by a non-significant increase throughout with values not attaining the pre injection rectal temperature records.

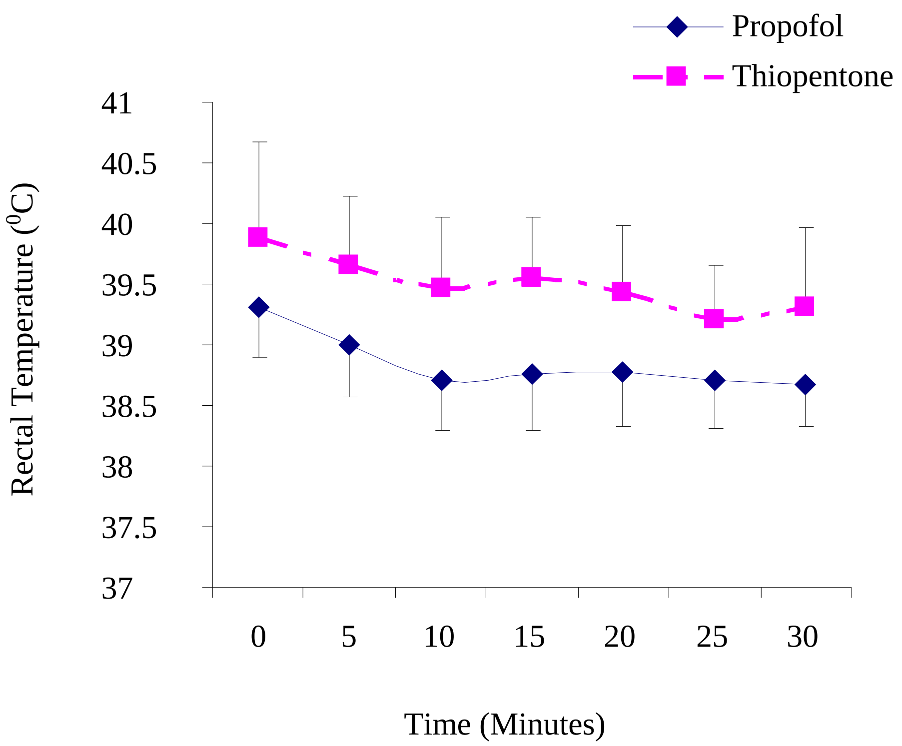

Figure 2: Overall gradual decrease in rectal temperature values after propofol and thiopentone infusion in Small East African goats (n=7, per group).

DISCUSSION

The rapid induction without excitatory effects was observed for propofol and thiopentone signifying the two drugs to attain a high tissue concentration immediately after initial injection to brain circulation and consequently attained high brain tissue saturation that contributed to rapid onset of anaesthesia. This effect is somewhat owed to anatomical predisposition where the brain is among the highly perfused organs (Dice, Sack and Wessing, 1987), the lipophilic nature of anaesthetic agents (Hall and Clark, 1991) and having approximately similar therapeutic index; 3.4 versus 3.91 for propofol and thiopentone respectively (Sear, 1991).

However, the recovery time appeared to differ between the two drugs with propofol treated group showed quicker return to limb movements, standing and regaining motion or ambulation than thiopentone.

These observations are related to the pharmacodynamics and pharmacokinetic nature of propofol and thiopentone. Both drugs are highly lipophilic, and thus tends to be bound in fatty tissues; differently however, propofol gets degraded more quickly to inactive metabolite, the glucoronide and the corresponding quinol-glucoronide and sulphates (Mether *et al.*, 1989., Lange *et al.*, 1990) while thiopentone degradation give rise to active metabolites-pentobarbitone which through redistribution, augments the already existent anaesthesia and consequently lead to delayed recovery (Sear, 1991).

Propofol and thiopentone are known to lack analgesia inducing properties (Kastiner, 2015). In this study, the animals treated with propofol showed a rostro-ventral rotation of the eyeball and lack of response to pin pricks while those under thiopentone had their eyeball centrally fixed and, exhibited reflex withdrawal of their limb upon stirring with noxious stimuli. Animals given propofol subjectively graded to have attained surgical anaesthesia stage three planes I, while those under thiopentone placed under stage 2 of anaesthesia.

The lack of analgesia and reflex response to pain stimuli is a feature for all barbiturate (Hall and Clarke, 1991); surgical anaesthesia can be achieved by increasing plasma concentration and thus subjecting patients to increased likelihood of developing undesirable barbiturate effects.

On the contrary, the rapid metabolism and redistribution property of propofol provide a wide anaesthetic concentration window to enable propofol infusion to effect more practical (Sear, 1991) in a manner similar to inhalant anaesthetic administration. In practice, a balanced anaesthesia involving premedication with potent analgesics or supplementations with inhalant anaesthetics or analgesic infusions will enable surgery to be accomplished at a relatively lower dose of propofol or thiopentone.

In the present study, the duration of anaesthesia for propofol and thiopentone was approximately 30 and 60 minutes respectively. It shows therefore that, for any short duration anaesthesia, propofol protocol can suffice while those procedures that last for at least one hour, thiopentone can be used. However, the final decision on which drugs to use lies on the surgeon preference, drug availability and drug cost.

Generally, the physiological normal parameters for respiration and heart rates and rectal temperatures in goat varies and are provided in ranges of 15-40 breaths per minute, 70-110 beats per minute and 38.5^{o}C-39.5^{o}C respectively in that order (Smith, 1996). On the other hand, propofol and thiopentone are known for their cardio-pulmonary and basal metabolism depression effects (Hall and Clarke, 1991; Seddighi *et al*, 2016). The observed fluctuations on respiration and heart rates and on rectal temperatures were therefore attributed by the actions of these drugs on different organ systems and, possibly the extent and duration being modified by the drug adsorption, redistribution and metabolism.

The depression of respiration and heart rates and rectal temperatures on propofol treated animals is attributed by the increased arterial blood carbon dioxide level and suppression of respiratory, myocardial and temperature regulation centres (Hall and Clarke,1991). On the other hand, rapid injection of thiopentone is associated with fall in blood pressure which tends to return to normal values, but often with persistent tachycardia, that can manifest by persistent increase of heart rates (Figure 1B). Thiopentone also appear to have direct effect on myocardium and has been associated with sporadic incidences of arrhythmias which in normal cases do not culminate to fibrillation (Hall and Clarke, 1991).

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CONFLICT OF INTEREST

Authors have no conflict of interest on the issues presented in this article

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