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Comparative Evaluation of Thiopental Sodium and Ketamine Hydrochloride in the Maintenance of General Anaesthesia during Exploratory Laparotomy in Nigerian Indigenous Dogs

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ABSTRACT

This study was conducted to evaluate the effects of thiopental sodium and ketamine hydrochloride on rectal temperature, pulse and respiratory rates, anaesthetic duration/recovery time in dogs during the maintenance of general anaesthesia post-induction with thiopental sodium. Ten apparently healthy male and female dogs, aged 12-30 months, weighing 7-14 kg were divided into two groups of 5 dogs each. Atropine (0.02 mg/kg) and chlorpromazine (4 mg/kg) were used for premedication. Thiopental sodium (20 mg/kg) was used for induction and maintenance in group A while dogs in group B were given thiopental sodium (20 mg/kg) for induction and ketamine hydrochloride (20 mg/kg) for maintenance. Duration of anaesthesia to recovery time, and vital parameters were monitored and recorded accordingly. Results revealed group A had significantly (p<0.001) prolonged duration of anaesthesia to recovery time (400 minutes) when compared to group B (200 minutes). Significant decrease was however observed in rectal temperature of group A at 50 minutes (p< 0.05), 60-90 minutes (p<0.01) and100-110 minutes (p<0.001) when compared to group B. Similarly, the respiratory rates of dogs in group A showed significant decrease at 50 minutes (p< 0.01), 60-110 minutes (p< 0.001) when compared to group B. There was no significant (p> 0.05) effect in the pulse rates of either group. It was concluded that a relative shorter recovery time, stability in rectal temperature, pulse and respiratory rates in the group maintained with ketamine hydrochloride were observed when compared to the group induced and maintained with thiopental sodium.

Key Words: Anaesthesia; Ketamine HCl; Recovery time; Temperature; Thiopental sodium

INTRODUCTION

The conduct of general anaesthesia has come a long way since the first anaesthetic delivered by Morton using ether in 1846 at Massachusetts General Hospital. Major strides in airway management and the discovery of new drugs have enabled delivery of what is today known as “balanced anaesthesia”. Loss of consciousness, analgesia, and muscle relaxation are the three main components of a balanced anaesthesia (Weiser *et al.,* 2016). General anaesthesia is defined as a state of controlled loss of consciousness using one or more anaesthetic agents. These agents can be broadly divided into parenteral or inhalational based on the mode of administration (Weiser *et al.,* 2016).

According to history, surgery was said to be horribly painful and the development of anaesthesia allows the performance of surgical operations without pains. This is one of the greatest achievements in human and veterinary medicine. No single drug is capable of producing balanced anaesthesia; this has further encouraged the use of adjunct to anaesthesia with the use of premedication, muscle relaxants, maintenance anaesthetic agents and analgesics (Aliu, 2007)

Over the years different researches have been conducted on different anaesthetic agents so as to maximize and explore the safest means of anaesthetic protocol and agents to use. On this note much works have been done on the dissociative effects of ketamine, a phencyclidine, which produces intense analgesia through N-methyl-D-aspartate (NMDA) receptor antagonism and inhibition of μ-, δ-, and κ-opioid receptors. Ketamine anaesthesia preserves respiration and airway patency and may decrease the incidence of postoperative nausea and vomiting through its opioid sparing effect (Aronsohn *et al.,* 2019). Recent literature highlights renewed interest in ketamine for acute pain management, particularly in patients at risk for adverse events related to opioid administration (Potter and Choudhuri, 2014).

The principles of enhanced recovery have challenged anaesthesiologists to develop evidence-based strategies for

safe, effective pain control without side effects that prolong recovery and return to preoperative functional status. Anaesthetic techniques that promote rapid sustained awakening, early ambulation and control of postoperative pain without sedation, respiratory depression, or nausea and vomiting are needed. (Aronsohn *et al.,* 2019).

Sodium thiopental, also known as Sodium Pentothal (a trademark of Abbott Laboratories), thiopental, thiopentone, or Trapanal (also a trademark), or Fatal-Plus in veterinary euthanasia contexts, is a rapid-onset ultra-short-acting barbiturate general anaesthetic. Sodium thiopental is not used to maintain anaesthesia in surgical procedures because of its short half-life and through infusion, it displays zero-order elimination, causing an elongation in recovery time of the patient, (Morgan and Curran, 2006). This research was designed to evaluate the effects of thiopental sodium and ketamine hydrochloride in the maintenance of thiopental sodium-induced general anesthesia in Nigerian indigenous dogs.

MATERIALS AND METHODS

Ethical Approval

Ethical approval was obtained from the Ahmadu Bello University Committee on Animal Use and Care (ABUCAUC) with the approval number ABUCAUC/2018/077.

Experimental Animals

Ten (10) apparently healthy Nigerian indigenous dog breeds of either sex (six males and four females) aged between 12 months to 30 months and weighed 7 kg to 14 kg were used in the study. The animals were housed in the kennel of the Small Animal Clinic of the Veterinary Teaching Hospital, Ahmadu Bello University, Zaria. They were adequately fed with food and water *ad libitum*, and also allowed to acclimatize for two weeks before commencement of the study. Blood and faecal samples were taken from each animal for laboratory analysis in Protozoology, Helminthology and Clinical Pathology Laboratories. The kennels were washed cleaned and disinfected with Izal Germicide® (Saponated cresol). Ivermectin was administered subcutaneously to each of the dogs for management and control of ectoparasites.

Experimental Procedures

The dogs were divided into two groups (A and B) of five animals each (n = 5). Group A were those administered 20 mg/kg thiopental sodium intravenously (induction) + 20 mg/kg thiopental sodium intravenously (maintenance) while group B were administered 20 mg/kg thiopental sodium intravenously (induction) + 20 mg/kg ketamine HCl intramuscularly (maintenance).

Phase I: Pre anaesthesia Phase

All dogs were premedicated with atropine sulphate at a dose of 0.02 mg/kg and chlorpromazine at 4mg/kg administered intravenously through the cephalic vein.

Phase II: Induction Phase

Induction was achieved with thiopental sodium at dose of 20 mg/kg. This was followed by monitoring of anaesthetic reflexes to ascertain the attainment of surgical plane of anaesthesia.

Phase III: Maintenance Phase

The maintenance dose

Seventy-five percent (75%) of the total calculated doses of the anaesthetics (thiopental sodium and Ketamine Hydrochloride) were used for maintenance of anaesthesia at dose rate of 20 mg/kg. The maintenance doses were divided into three fractions (i,e 25% of the calculated total dose) and administered at intervals of time.

Intervals of administration of anaesthetic maintenance doses

The first maintenance doses were administered 10 minutes post induction followed by 30 minutes intervals in both cases.

Last duration of administration of anaesthetic maintenance doses

The last fraction of the maintenance dose was administered at 70 minutes post in duction in both groups.

Route of administration of anaesthetic maintenance doses

Group A were administered thiopental sodium for maintenance of anaesthesia intravenously while group B received ketamine hydrochloride intramuscularly.

The duration of anaesthesia to recovery, rectal temperature, pulse rate and respiratory rate were monitored and recorded.

Data Analysis

Data were expressed as a mean ± Standard Error of Mean (SEM) and presented in graphs. Student t-test was used for the analysis. Graph Pad Prism version 5.0 for windows from Graph Pad Prism Software (San Diego, California, USA) was used. Values of $p<0.05$ were considered as statistically significant.

RESULTS

Rectal Temperature (°C)

Significant decrease was observed in the rectal temperature of group A at 50 minutes ($p< 0.05$), 60-90 minutes ($p< 0.01$) and 100-110 minutes ($p< 0.001$) when compared to group B. (Figure 1).

Pulse Rate (beats/minutes)

There was no significant difference ($p> 0.05$) on the pulse rates of dogs induced and maintained with thiopental sodium and also, the group induced with thiopental sodium and maintained with ketamine HCl even though, an increase in the pulse rates were observed in all the groups (Figure 2).

Respiratory rate (cycles/minutes)

The respiratory rates of dogs in group one showed significant decrease at 50 minutes ($p< 0.01$), 60-110 minutes ($p< 0.001$) when compared to group two. (Figure 3).

Duration of Recovery Time

Significantly longer ($p<0.001$) duration of recovery from anaesthesia was observed in the group that was induced and maintained with thiopental sodium when compared to the group induced with thiopental sodium and maintained with ketamine HCl (Figure 4).

DISCUSSION

This research was conducted to compare the effects of thiopental sodium and ketamine hydrochloride in maintenance of anaesthesia post-induction with thiopental sodium. The duration of anaesthesia to recovery and the physiological parameters for all surgical patients for both groups were monitored and changes in the respiratory rate, pulse rate and rectal temperature observed and recorded accordingly.

Significant decreases in rectal temperature were observed in the groups induced and maintained with thiopental sodium compared to the groups treated with ketamine HCl.

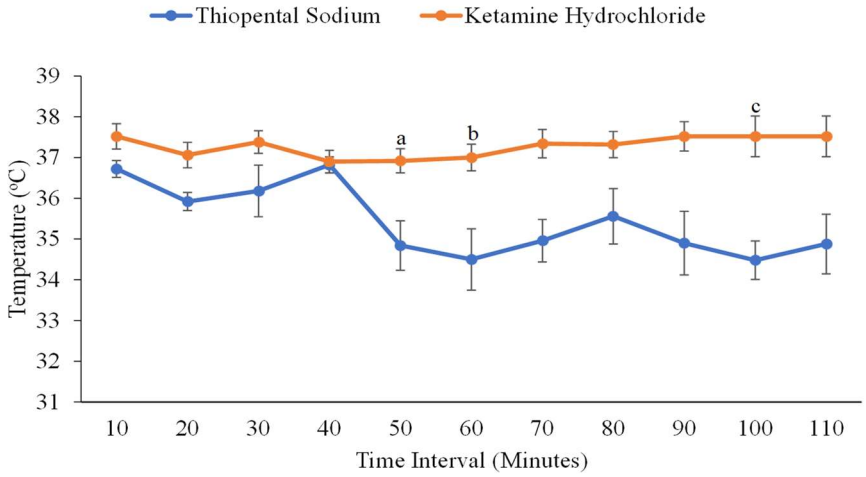

Figure 1: Comparative mean rectal temperature (°C). Values are expressed as mean ± SEM (n=5), $^{a}p < 0.05$; $^{b}p < 0.01$; $^{c}p < 0.001$.

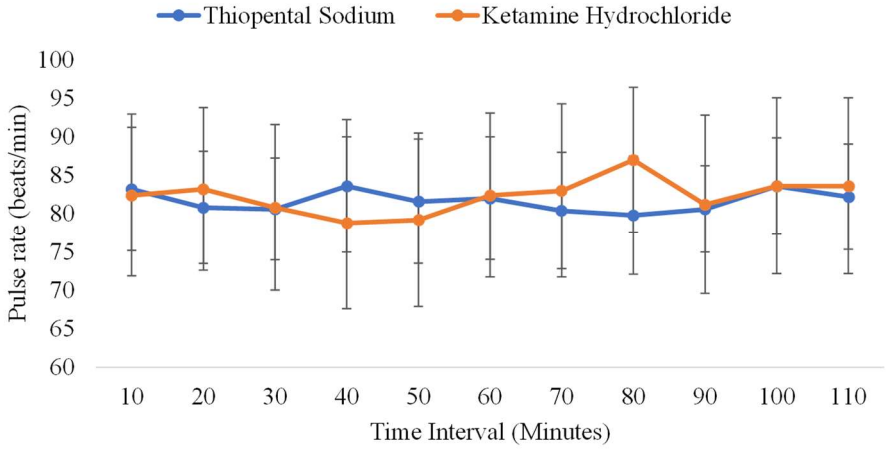

Figure 2: Comparative mean pulse rate (beats/min). Values are expressed as mean ± SEM (n=5), $p > 0.05$.

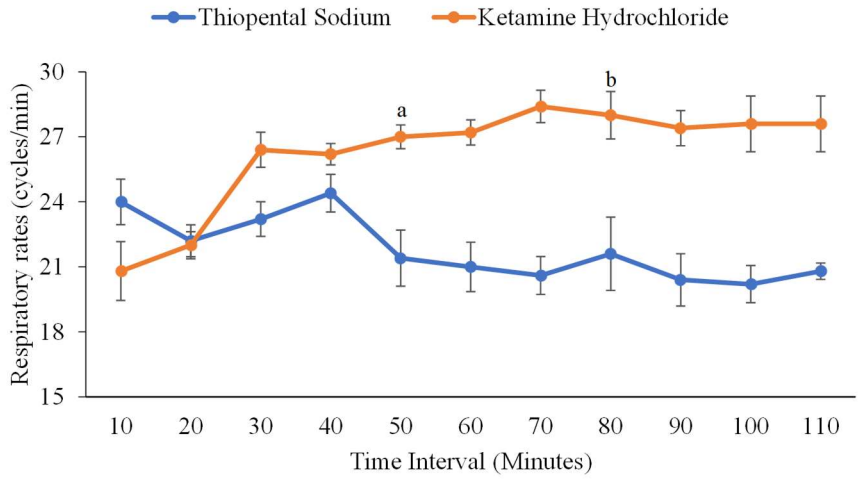

Figure 3: Comparative mean respiratory rates (cycles/min). Values are expressed as mean ± SEM (n=5), $^{a}p < 0.01$; $^{b}p < 0.001$.

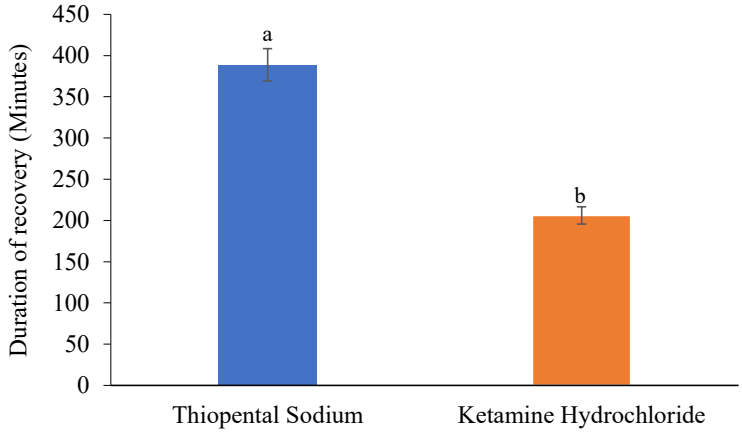

Figure 4: Duration of recovery time. Values are expressed as mean ± SEM (n=5), $p < 0.001$.

This finding is in conformity with the previous work done by Pundits (2008). The progressive decrease in the rectal temperature was due to the ability of thiopental sodium to stimulate the release of histamine causing vasodilatation with consequent hypothermia. Also, according to Thurmon *et al.* (1996), the significant decrease of body temperature might be due to direct depressant effect of thiopental on the central nervous system and consecutively thermoregulatory center in the hypothalamus.

Significant decreases in patient's respiratory rates were observed in the group induced and maintained with thiopental sodium compared to the group maintained with ketamine HCl. This finding agrees with the work done by Pundits (2008) who discovered the occurrence of respiratory depression and apnoea after thiopental administration. Similarly, earlier studies have shown that thiopentone injection caused pulmonary depression (Gaudy *et al.,* 1983; Huang *et al.,* 1997; Gargiulo *et al.,* 2012).

There was no significant effect between the groups maintained with ketamine HCl and thiopental sodium on the pulse rates even though, increases in heart rates were observed in all the groups. The increase in the pulse rates observed in the thiopental sodium groups have been reported by other researchers e.g., Emami *et al.* (2006) who observed increase in heart rates following thiopentone anaesthesia in donkeys. Udegbunam and Udegbunam (2014) reported same in rabbits. Intravenous injection of thiopentone leads to venous dilation and peripheral pooling of blood (Reilly, 1994) as well as decrease in mean arterial pressure (MAP), decrease cardiac output and increase in heart rate (Huang *et al.,* 1997). Other reasons for increase in heart rate include; baroreflex response to reduction in MAP (Aun *et al.,* 1993), sympathetic nerve stimulation post thiopentone injection (McGrath and Mackenzie, 1977) and cardio stimulation caused by hypercarbia (Huang *et al.,* 1997).

The increase in the heart rate observed in the groups treated with ketamine was also reported by Pundits (2008). He asserted that all the effect is related to sympathetic stimulation, with increased circulating concentrations of catecholamine, resulting in peripheral vasoconstriction and direct cardiac stimulation.

In the present research, the groups that were induced and maintained with thiopental sodium showed a significantly prolonged duration of recovery from anaesthesia compared to the group maintained with ketamine HCl. This finding is in-line with the work done by Morgan and Curran (1981). Thiopental sodium is said to have a short half-life and its infusion at repeated doses at interval of time leads to the display of zero-order elimination with consequent prolongation in recovery time of the patient. Following intravenous https://en.m.wikipedia.org/wiki/Injection_(medicine)injection, the drug rapidly reaches the brain and causes unconsciousness within 30-45 seconds. At 60 seconds, the drug attains a peak concentration of about 60% of the total dose in the brain. Thereafter, the drug distributes to the rest of the body, and in about 5-10 minutes the concentration is low enough in the brain that consciousness returns, Sodium thiopental would have to be given in large amounts to maintain an anaesthetic plane, because of its non-analgesic effects. Sodium thiopental repeated administration leads to a display of zero-order elimination pharmacokinetic (Morgan and Curran1981). Also observed, the patients treated with ketamine showed evidence of analgesia by none response to pain compared to the thiopental groups. This effect of ketamine is probably due to its ability to produce intense analgesia through NMDA receptor antagonism and inhibition of μ-, δ-, and κ-opioid receptors as reported by Aronsohn *et al.* (2019).

Overall, the precise recovery period, relative stability in the rectal temperature, pulse and respiratory rates in group treated with ketamine hydrochloride indicates that the agent is excellent in maintenance of anaesthesia post induction with thiopental sodium. Domino and Warner (2010), asserts that, ketamine serves as a good field anaesthetic because it provides quick effects and doesn't cause hypotension or respiratory depression as observed in this study. Pundit's studies (2008) reported that, ketamine produces probably unique cardiovascular effects, with an increase in mean arterial blood pressure, heart rate, and pulmonary arterial and central venous pressures. All these effects are related to sympathetic stimulation, with increased circulating concentrations of catecholamine, resulting in peripheral vasoconstriction and direct cardiac stimulation. Therefore, the drug is a valuable agent for hypotensive or hypovolemic patients.

In conclusion, the study showed the achievement of smooth maintenance of anaesthesia in the groups administered ketamine HCl when compared to the group that was induced and maintained with thiopental sodium alone. Furthermore, thiopental sodium depressed the vital parameters, with prolonged recovery time following repeated administration. Ketamine hydrochloride on the other hand, did not depress the vital parameters with analgesic effect and shorter recovery time suggesting effectiveness of ketamine in maintenance of anaesthesia post induction with thiopental sodium in Nigerian Indigenous dogs.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

Authors Contribution

EGE, MAS designed the study; EGM supervised the research and edited the manuscript; DS helped supervised the research. MAS performed the experiment with help from STM and AAB; FK, STM and AAB contributed to the analysis and interpretation of the results; MAS, DS and FK drafted the manuscript. All authors contributed to the discussion of the result, read and agreed to the published version of the manuscript.

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