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Original Research Article

Influence of Two Kinds of Anaesthetic Agents on Urea and Creatinine Levels in Male Wistar Rats

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Abstract: ***Background*:** The use of anaesthetics, local or general, is common in hospital setting for surgical interventions. Anaesthetic agents are capable of producing changes on the renal physiology and affecting important biochemical aspects like blood urea and creatinine. It is important to study these effects as they are helpful in determining the safety of such drugs on laboratory animals which can be translated in clinical trials in future research. This experiment was done to determine the effects of ketamine and lidocaine on the level of urea and creatinine in the serum of male Wistar rats. ***Methodology*:** A total of 35 adult male Wistar rats were used for this study and they were randomly classified into 5 groups, after one week acclimatization period. These groups included the control group, a lidocaine-treated group without adrenaline, a lidocaine treated group with adrenaline, a ketamine-treated group and a group treated with a combination of ketamine and lidocaine. The anaesthetic agents were administered, at a standard dose, intraperitoneally, and blood samples were obtained after exposure. Biochemical assays to determine serum urea and creatinine were done through the use of standard methods. One way ANOVA analysis with special emphasis on any significant differences among groups was conducted on data. ***Results and Discussion*:** It is established in this study that anaesthetic drugs especially the ketamine group has the capacity to increase urea and creatinine levels of rats. This shows that ketamine anaesthetic drug has the capacity to cause kidney disorders. In view of the above, it is recommended that patient undergoing surgeries under ketamine anaesthetics should do so with caution. Pre-operative systemic review should be encouraged. ***Conclusion*:** Ketamine and lidocaine greatly affect the level of serum urea and creatinine in male Wistar rats and their combined application had the most significant effects. These findings emphasise the importance of the choice of anaesthetic agents and how they are dosed during an experiment to reduce possible impairments to the kidney.

Keywords: Anaesthetic Agents, Serum Urea, Creatinine, Male Adult Wistar Rats.

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1. INTRODUCTION

Anaesthesia is essential for successful surgical interventions to achieve immobilization and unconsciousness (Costa, 2020). Ketamine is a type of anaesthesia that stimulates cardiovascular function causing increase heart rate and blood pressure (Costa, 2020). The use of ketamine as sole anaesthetic has been used to achieve sedation analgesic and comfort while in operating table (Costa, 2020). Lidocaine, firstly synthesized by Soredish Chemist Iofgren has been used extensively for pain management (Costa, 2020). Post administration complications have been recorded in both lidocaine and ketamine anaesthesia and such complications include kidney dysfunction, hemolysis and ionic imbalance (Brown, 2014).

Excessive levels of lidocaine can cause changes in the ionic composition and protein plasma with haemopoletic collapse these changes are attributable to ionic imbalance. The net effect is normally a modest kidney dysfunction when recommendation doses are exceeded. Clementine *et al.,* (2012) reported increase in sodium, calcium, sodium, creatinine and urea with ketamine and Lidocaine use in goats while Destina *et al.,* (2013) reported decrease in sodium concentration, urea and creatinine with ketamine in human subjects when combined with other anaesthetics, these parameters were not altered.

Little or no work has been reported on serum creatinine and urea levels changes attributed to anaesthesia; hence this study is stepping in to fill this literature gap.

2. METHODOLOGY

2.1: Ethical Approval

This study was performed with animals treated in accordance with guide for the care and use of laboratory animals after securing ethical statement approval from the Research Ethics Committee (REC) of the Faculty of Basic Medical Sciences (FBMS), Rivers State University with REC approval number: RSU/FBMS/REC/23/160.

2.2: Experimental Animals

Thirty five (35) Wistar rats were acquired for the purpose of this study. The rats were housed in a well-ventilated room with adequate light source and temperature. The animals were fed adequately and allowed for acclimatization for one week before commencement of the experiment.

2.3: Drugs

The experimental rats were treated with 5mg/kg of ketamine according to Yohanne *et al.,* (2018) who used same doses of ketamine in his study while 2% of lignocaine at 2mg/kg according to Yakubu *et al.,* (2020) were administered to the experimental rats.

2.4: Experimental Design

Thirty five (35) male Wistar rats were divided into five (5) groups of six (6) rats each.

Group 1: This is the control group. The rats in this group were administered with 1ml of diluted distilled water orally for 2 days.

Group 2: Male Wistar rats in this group received 2mg/kg of plain lignocaine (lidocaine without adrenaline) for 2 days.

Group 3: Male Wistar rats in this group received 2mg/kg of lidocaine with adrenaline for 2 days.

Group 4: Male Wistar rats in this group received 5mg/kg of ketamine every day for 2 days.

Group 5: Male Wistar rata in this group received 5mg/kg of ketamine and 2mg/kg of lidocaine combined together everyday for 2days.

2.5: Collection of Blood samples from Experimental Rats

At the end of treatment with drugs, the rats were sacrificed and blood samples collected by cardiac punctures into various sample bottles for haematological, hemostatic, haemorheological and biochemical investigations using appropriate techniques.

2.6: Estimation of Serum Biochemical Profile

Blood samples were collected and serum separated via centrifugation at 3000rpm for 15 minutes and serum estimated using fully automated serum analyser (Microlab Biochemistry Germany) for determination of serum electrolytes, urea and creatinine.

2.7: Statistical Analysis

Values for the results are pressed as meant SEM. The statistical analyses were done using the one way analysis of variance (ANOVA). Computer softwares, Microsoft excel 2013 edition and SPSS 23.0 windows were used. Differences between mean were considered at $p<0.05$.

3. RESULTS

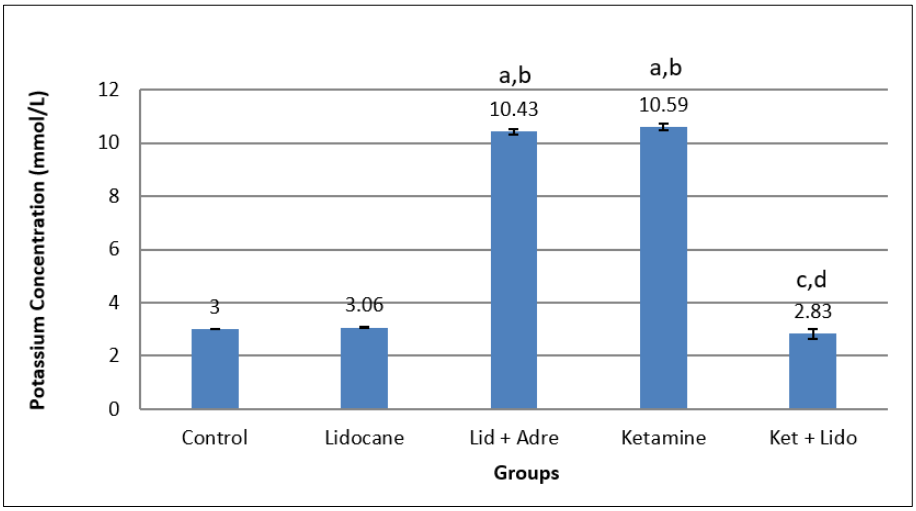

Figure 1: Comparing potassium concentrations in all the experimental groups. Results presented as mean ± SEM. a, b, c, and d = versus control, lidocaine, Lid plus adre, and ketamine groups respectively at p<0.05

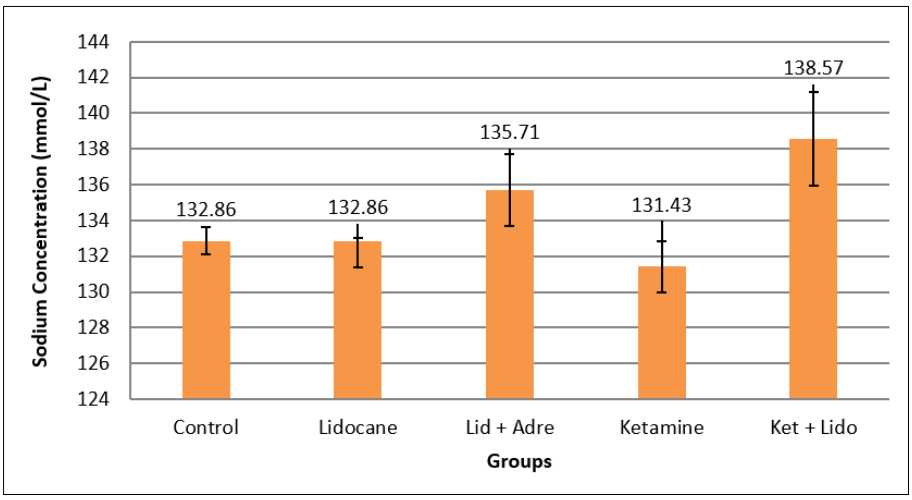

Figure 2: Comparing sodium concentrations in all the experimental groups. Results presented as mean ± SEM

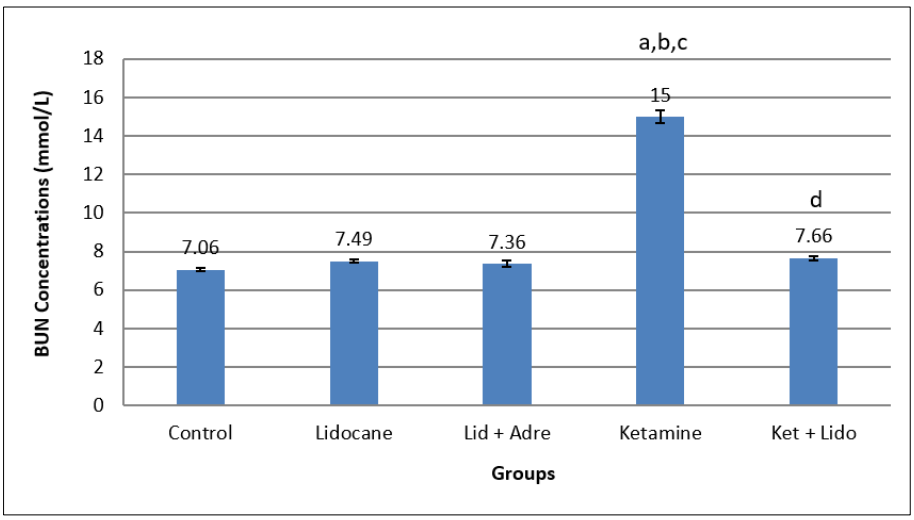

Figure 3: Comparing blood urea nitrogen levels in all the experimental groups. Results presented as mean ± SEM. a, b, c, and d = versus control, lidocaine, Lid plus adre, and ketamine groups respectively at p<0.05

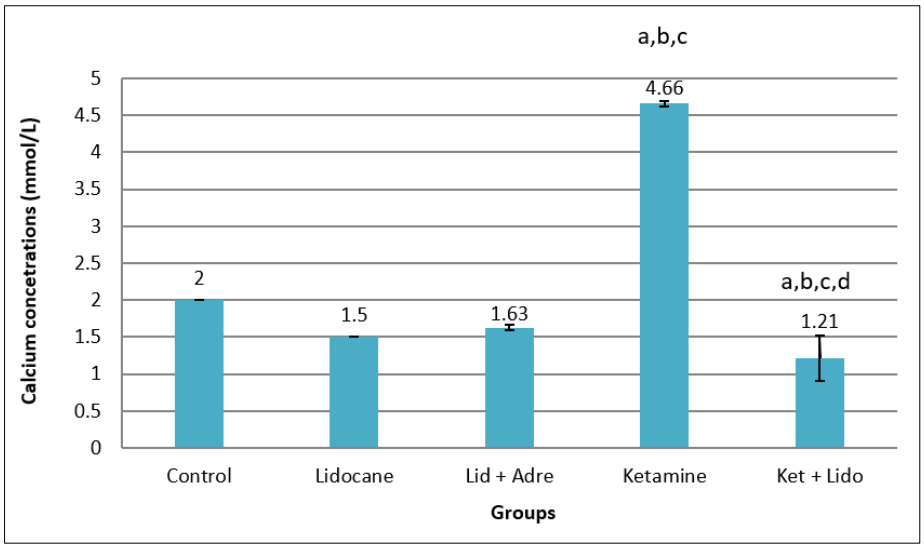

Figure 4: Comparing calcium concentrations in all the experimental groups. Results presented as mean ± SEM. a, b, c, and d = versus control, lidocaine, Lid plus adre, and ketamine groups respectively at p<0.05

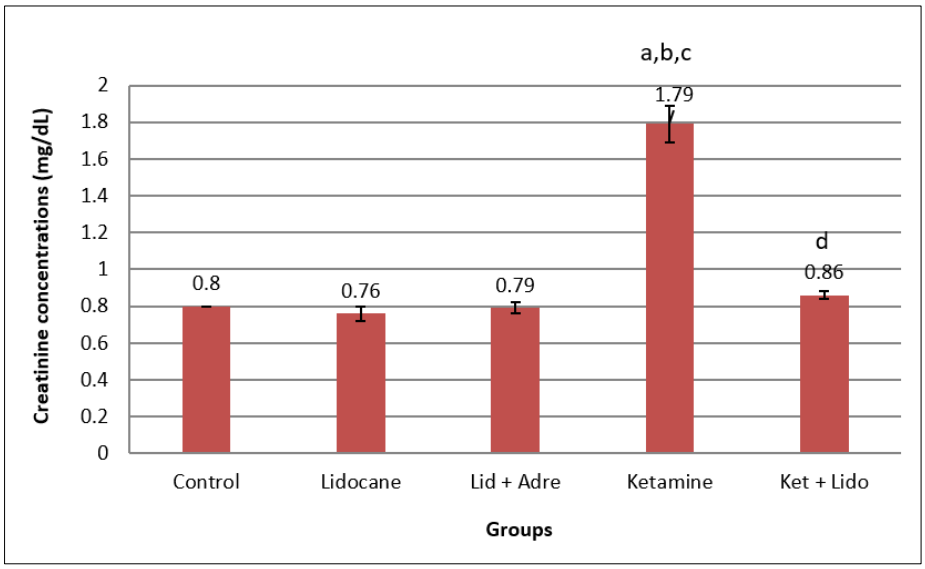

Figure 5: Comparing creatinine levels in all the experimental groups. Results presented as mean ± SEM.a, b, c, and d = versus control, lidocaine

4. DISCUSSION

Impact of anaesthetics drugs was evaluated in male wistar rats after acclimatization in animal house at faculty of Basic medical sciences.

Both low and high creatinine has been observed to be related to risk of clinical and subclinical health challenges. High creatinine level is associated with kidney failure. The high creatinine levels instigated by ketamine anaesthetic agent are a major factor that can cause kidney disorders.

According to different studies, high creatinine level are indicates of induced renal malfunction and a useful tool to reflect the malfunction caused by ketamine anaesthesia. This present study has demonstrated that ketamine anaesthetic agent has the capacity to increase creatinine levels of users which is an inductor to kidney malfunction and disorder. This finding is consistent and in consonance with the reports of Clementina *et al.,* (2012) who reported increase in urea and creatinine following ketamine and Lidocaine use in goats.in order twist, the reports of reported Destina *et al.,* (2013) which reported decrease in urea and creatinine in human subjects contradicts the findings of the present study.

5. CONCLUSION

It is concluded as follows:

1. General anaesthetic agent made up ketamine has the capacity to increase creatinine levels of users and can predispose them to kidney disorder.
2. When ketamine anaesthesia is used in combination with lidocaine anaesthesia, it can counteract the negative effect of ketamine.

6. RECOMMENDATION

1. The use of ketamine anaesthetic agents on already established patient with kidney disease should be discouraged.
2. The use of ketamine in combination with lignocaine should be encouraged.
3. Surgeons should be proactive and ensure thorough review of systems before the use of ketamine anaesthetic agents.

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