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Original Research Article

Effect of Combined Anaesthetic Agents on Serum Electrolytes and Plasma Proteins in Male Wistar Rats

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Abstract: ***Background*:** Anaesthetic agents are gaining popularity in the world of diagnostic and surgical procedures, but little is known about their combined biochemical action. This paper compared the impacts of ketamine and lidocaine given alone and in combination with each other on serum electrolytes and plasma proteins in male Wistar rats. ***Methodology*:** 35 male Wistar rats randomized to five groups (n=6): control, lidocaine, lidocaine with adrenaline, ketamine, and ketamine with lidocaine. The samples of blood were taken out at the end of the experimental period by cardiac puncture. Automated biochemical methods were done to determine serum electrolytes (sodium, potassium, chloride, calcium), plasma proteins (total protein, albumin, globulin, fibrinogen). The data were presented in the form of mean ± SEM and compared by a one-way ANOVA with p=0.05. ***Results*:** Lidocaine adrenaline and ketamine had a significant impact on serum potassium levels in comparison with the control group, making it prone to hyperkalemia. Ketamine too raised serum calcium, total and globulin and fibrinogen levels significantly but albumin was not altered significantly. The level of Na+ and Cl were found to have small, non significant differences among the groups. ***Discussion*:** The observed case of hyperkalemia after administration of ketamine and lidocaine combined with adrenaline indicates the disruption of the ion transportation process on the membrane, and causes the concern of cardiovascular issues, particularly in patients with an underlying electrolyte disturbance, or with medications that inhibit the ion transport. The rise in the levels of calcium and globulin after the exposure of ketamine also points to the possible metabolic and inflammatory regulation. ***Conclusion*:** Ketamine and lidocaine combined and administered separately produce a significant change in serum potassium, calcium, and plasma protein. The use of these agents should hence be cautious especially among those individuals who are inclined to hyperkalemia or cardiovascular diseases.

Keywords: Ketamine, Ludocaine, Serum Electrolytes, Plasma Proteins, Male Wistar Rats.

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INTRODUCTION

Anaesthetics prevents the feeling of pain by inhibiting nerves from transmitting signals to the brain (Cividjian *et al.,* 2017). Scientists don't know exactly how all types of anaesthetics work but they do know that anaesthetics block pain by altering neuro-transmitters release that can cause signal transmission (Excitation) or signal blockage (inhibitory) (Mahalaxmi & Rao, 2025). It also alters the activities of ion channel proteins which passes through nerve cell membrane to transmit signal (Zhou & Guan, 2022). Both general and local anaesthetics work in a manner to prevent ion passage thereby blocking signal transmission (Lirk *et al.*, 2018).

The risks of complications during or after anaesthesia are often difficult to separate from those of the procedure for which the anaesthesia is being given, but there are related to three factors: The health of the individual, the complexity and stress of procedure itself as well as the anaesthtic technique (Cusack & Buggy, 2020).

Major perioperative risks can include death, heart attack, pulmonary embolism, kidney failure, local anaesthetic toxicity, hyperthermia and hypertension. According to Readman *et al.,* (2017), varied concentration of anaesthetics and responses towards different anaesthetics greatly varies from species to species. Clementina *et al.,* (2012) reported increase in sodium, calcium, urea with ketamine use in goats.

Sarenac *et al.,* (2023) carried out research on effect of different anaesthetics on biochemical parameters and reported increase in serum sodium, total protein, fibrinogen, decrease in albumin, increase in serum calcium level with lidocaine use.

METHODOLOGY

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 Research Ethics Committee (REC) of the Faculty of Basic Medical Sciences (FBMS), Rivers State University with REC approval number: RSU/FBMS/REC/23/160.

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.

Drugs

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

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 1mg/kg of plain lignocaine (lidocaine without adrenaline) for 2 days.
Group 3: Male Wistar rats in this group received 1mg/kg of lidocaine with adrenaline for 2 days.
Group 4: Male Wistar rats in this group received 0.5mg/kg of ketamine every day for 2 days.
Group 5: Male Wistar rats in this group received 0.5mg/kg of ketamine and 1mg/kg of lidocaine combined together everyday for 2days.

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 biochemical investigations using appropriate techniques.

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.

Statistical Analysis

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

RESULTS

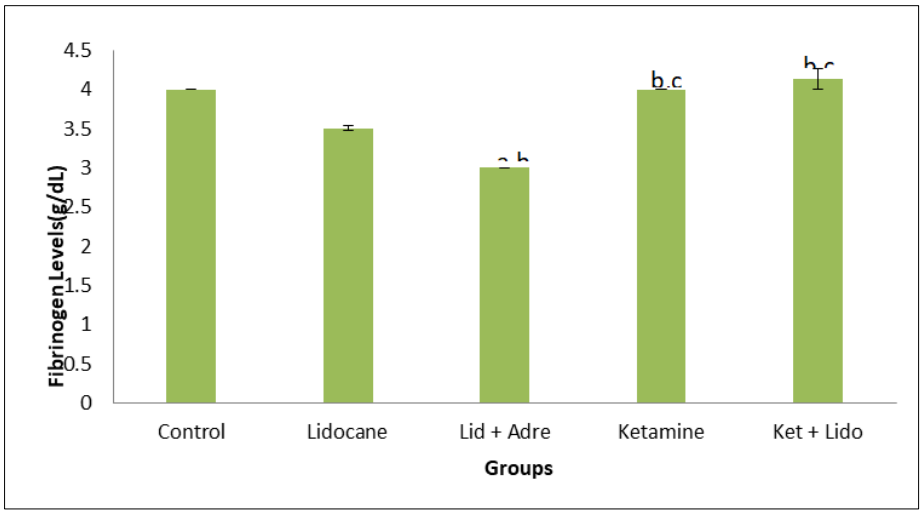

Figure 1: Comparing fibrinogen levels in all the experimental groups. Results presented as mean ± SEM. a, b, c, and d = versus control, lidocane, Lid plus adre, and ketamine groups respectively at p<0.05

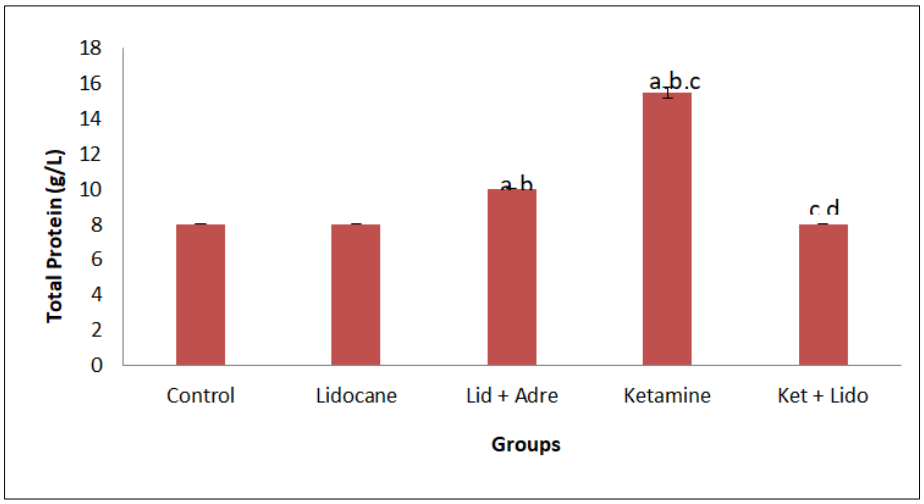

Figure 2: Comparing total protein concentration in all the experimental groups. Results presented as mean ± SEM. a, b, c, and d = versus control, lidocane, Lid plus adre, and ketamine groups respectively at p<0.05

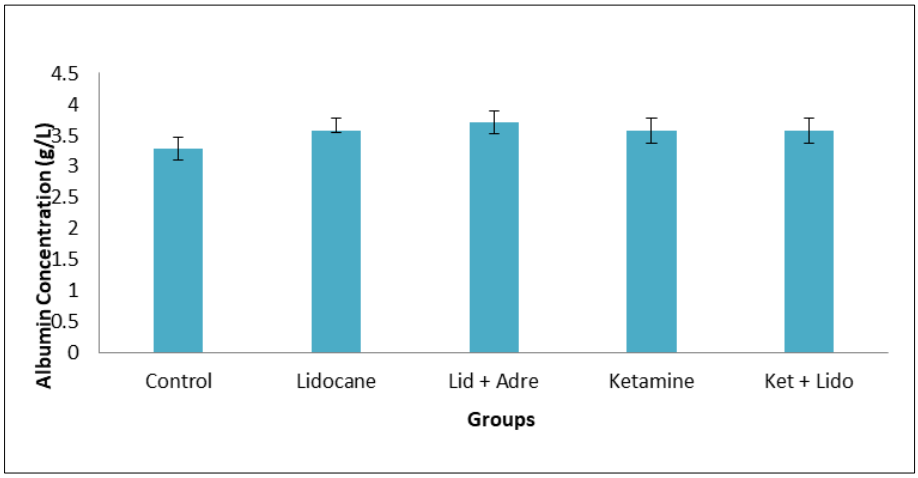

Figure 3: Comparing albumin concentrations in all the experimental groups. Results presented as mean ± SEM.

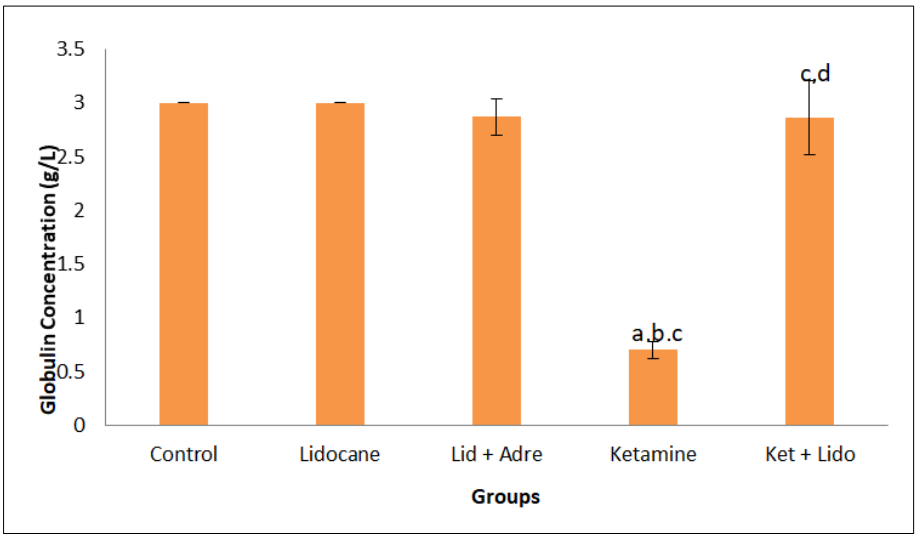

Figure 4: Comparing globulin in all the experimental groups. Results presented as mean ± SEM. a, b, c, and d = versus control, lidocane, Lid plus adre, and ketamine groups respectively at p<0.05

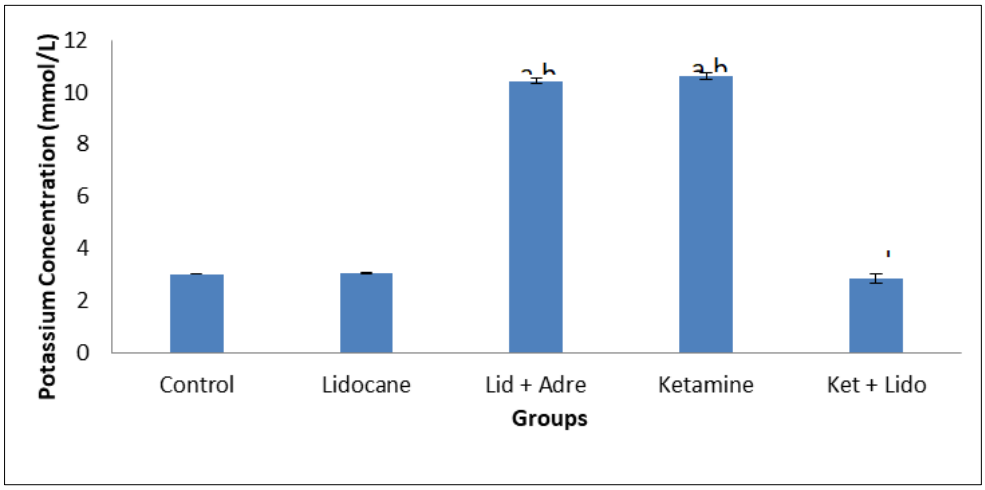

Figure 5: Comparing potassium concentrations in all the experimental groups. Results presented as mean ± SEM. a, b, c, and d = versus control, lidocane, Lid plus adre, and ketamine groups respectively at p<0.05

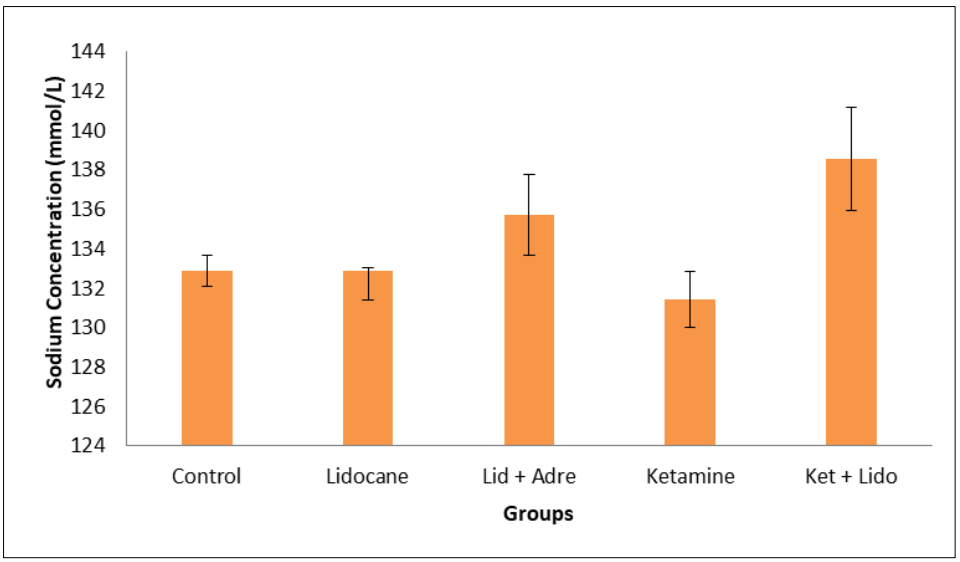

Figure 6: Comparing sodium concentrations in all the experimental groups. Results presented as mean ± SEM.

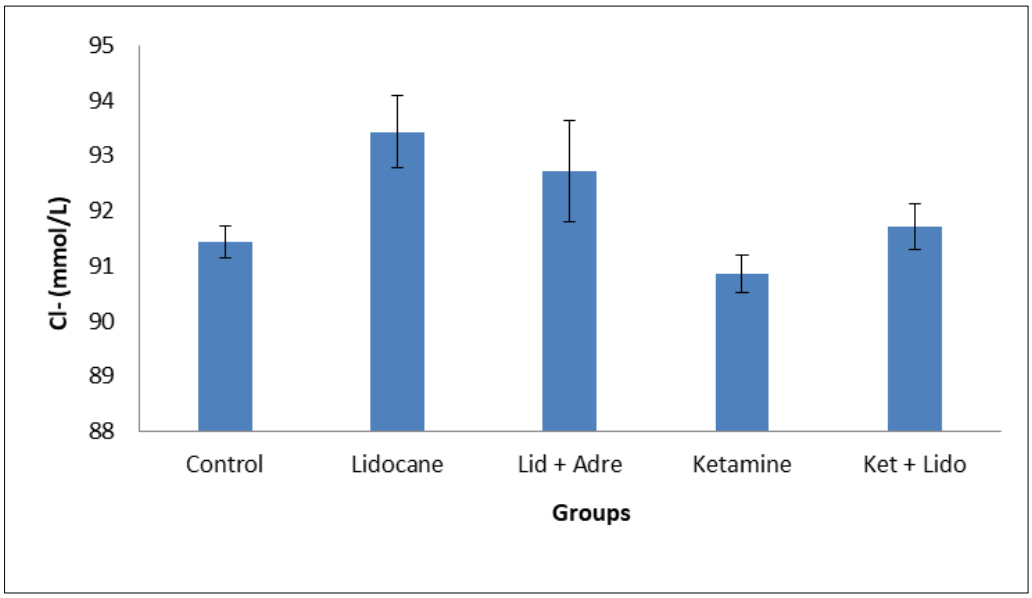

Figure 7: Comparing chloride levels in all the experimental groups. Results presented as mean ± SEM.

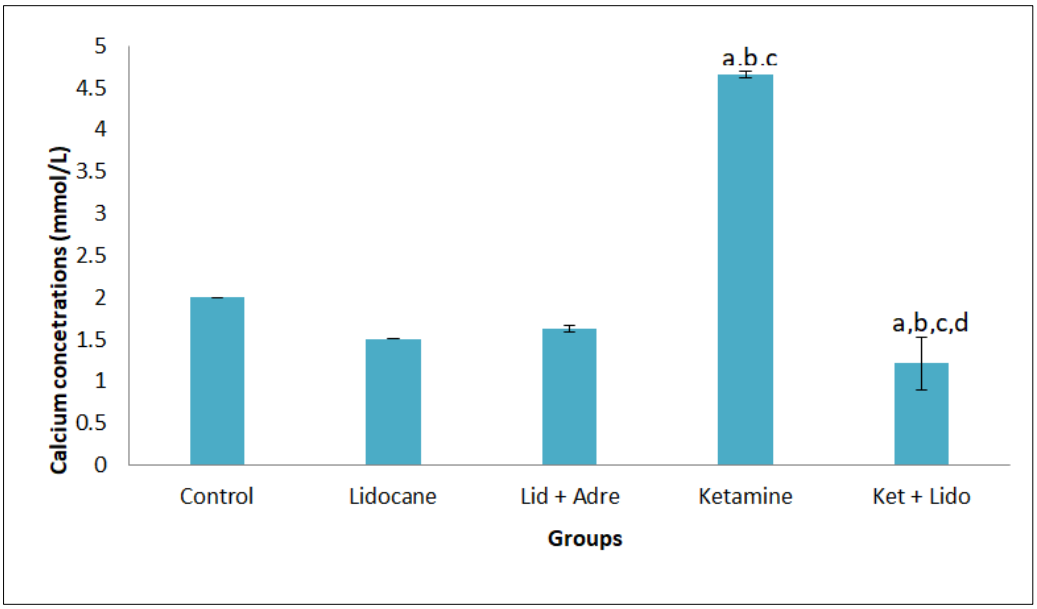

Figure 8: Comparing calcium concentrations in all the experimental groups. Results presented as mean ± SEM. a, b, c, and d = versus control, lidocane, Lid plus adre, and ketamine groups respectively at $p<0.05$

DISCUSSION

The relationship between two anaesthetic agents on serum electrolytes and plasma proteins of male Wistar rats were evaluated randomly.

It was observed that both lidocaine containing adrenaline and ketamine significantly increased serum potassium concentration suggesting that prolonged use of anaesthetic drugs could lead to hyperkalemia. Thus continuous use of anaesthetic agents as beneficial as it is, should be use in caution including avoiding the excessive intake of food with high potassium content including fruits and vegetables.

Also, since ketamine and lidocaine containing adrenaline can increase potassium, it could be dangerous or fatal for patients taking other drugs that also may increase potassium such as heparin, aldosterone antagonists, non-steroidal anti-inflammatory drugs (NSAIDS), potassium sparing diuretics, angiotensin converting enzyme (ACE) inhibitors.

Anaesthetic use without caution could be detrimental on health in patient with already established history of increased potassium and as such, organs like heart, kidney, intestines are at risk of damage. The reports of this study is in consonance with the reports of

some investigators who reported increase in potassium with anaethetic use.

It was also observed that ketamine anaesthetic agent significantly increases calcium concentration, this reports contradicts reports of some investigators in literatures who reported decrease in calcium concentration with anaesthetic use. Hatcher (2017) reported a significant reduction of serum calcium concentration with anaesthetic use.

It was also observed that ketamine anaesthetic agents increases total protein and globulin and this report is in consonance with the reports of Sarenac *et al.,* (2023) who reported increase in total protein and serum calcium concentration with lidocane.

CONCLUSION

The following conclusion was drawn from this study:

i. Anaesthetic agents have shown potentials to alter serum electrolytes of users
ii. Anaesthetic agents especially ketamine does not alter albumin levels but increases total protein instigating the elevation of globulin, this may increase the risk of cardiovascular disorder in users
iii. Anaesthetic agent's increases potassium concentration and can predispose users to hyperkalemia
iv. Anaesthetic agent's increases calcium concentration of users

RECOMMENDATION

i. Use of anaesthetic in patient with high potassium should be done with caution
ii. Patient undergoing surgical interventions requiring administration of katemine should be properly evaluated or reviewed before surgery
iii. Patients with already established history of ACE inhibitors, heparin, NSAID use, should use anaesthetic drugs with caution
iv. Surgeons and anaesthetists are advised to use ketamine anaesthetic drugs with caution in patient with history of excessive intake of food, fruits, leaves rich in potassium.

Conflict of Interests: The authors declare no competing interest.

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