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Original Research Article

Aggregability and Deformability of Red Blood Cell (RBC) of Male Wistar Rats Treated with Ketamine and Lidocaine Anaesthetic Drugs

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Abstract: ***Background*:** Red blood cell (RBC) aggregability and deformability are determining factor of blood viscosity, microcirculatory flow, and oxygenation of tissues. These hemorheological properties can be modified by different pharmacological agents such as anesthetics. This study explored the impact of two widely used anesthetic drugs, ketamine and lidocaine, on aggregability and deformability of the RBCs in male Wistar rats. ***Methodology***: The male Wistar rats (N= 35) were subdivided into five groups of six each. Group 1 was a control which was subjected to distilled water. Group 2 got 2 mg/kg lidocaine (plain), Group 3 got 2mg/kg lidocaine with adrenaline, Group 4 experienced 5mg/kg ketamine and Group 5 had a combination of 5mg/kg ketamine with 2mg/kg lidocaine. The treatments were done on two days. At the termination of treatment rats were sacrificed and blood samples were taken through cardiac puncture. The deformability of the RBCs was determined through diffraction ektacytometry and automated rheoscopy, and the aggregability indices were determined through rheoscopes based on light transmission at rest. Analysis of data was done through ANOVA where the significance was $p < 0.05$. ***Results and Discussion*:** The results indicated that there were no significant changes in RBC aggregability and deformability of all treatment groups against the controls. The ketamine alone or the combination of ketamine and lidocaine had no effect on the erythrocyte rheological behaviour. These findings are in line with the past studies that have shown that these anesthetics have insignificant effects on blood viscosity, hematocrit or plasma rheology. ***Conclusion*:** Ketamine and lidocaine do not negatively impact on RBC aggregability and deformability of male Wistar rats. Their application seems to be hemorheologically secure with no threat of causing the blood viscosity and microcirculatory flow disruption.

Keywords: RBC Aggregability and Deformability, Ketamine, Lidocaine, Male Wistar Rats.

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INTRODUCTION

Red cell deformability depends on several factors and it is an important determinant of blood viscosity (Abkarian & Viallat, 2015). At low shear rates, rigid red blood cells are less likely to aggregate than deformable red blood cells (Kim *et al.,* 2015). Therefore, loss of RBC deformability at very low shear rate results in a decrease in blood viscosity.

Red blood cell deformability is also a key determined of blood flow in microcirculation. Indeed, any decrease of RBC deformability may affect low resistance, tissue perfusion and oxygenation (Fischer, 2019).

Red blood cell aggregation is a reversible formation of three-dimensional stacks of red blood cell, called rouleaux which takes at low shear rates (Flormann, 2017; Melepattu, 2025). Red blood cell aggregation depends on both plasma and cellular factors (Rampling, 2019). Fibrinogen is the most physiologically relevant macromolecule that promotes red blood cell aggregation (Fischer 2019). Other molecules such as thrombospondin and von willebrand factor also play a role (Nader *et al.,* 2018; Baskurt, O. K., & Meiselman).

The impact of red blood cell aggregation on blood flow, tissues perfusion and vascular resistance is complex and depends on the vascular areas where RBC aggregates are flowing (Nader *et al.,* 2018). Red blood cell aggregates usually form in low shear rate areas such as in veins or in bifurcations (Kaliviotis *et al.,* 2017). Increased RBC aggregation is also known to cause a dramatic increase in blood viscosity in these zones (Nader *et al.,* 2018; Alexy *et al.,* 2022).

The use of anesthetics drugs is prevalent in both clinical and experimental environments but the resulting impacts on blood rheology remain an area of interest. Ketamine is a dissociative general anesthetic that is characterized by a rapid onset and analgesic effect (Natoli, 2021), whereas lidocaine is a reversible nerve blocker that is a widely used local anesthetic, commonly used alone or together with adrenaline (Prabhakar *et al.,* 2015). The degree to which these agents affect RBC deformability and aggregation is yet to be determined despite their prevalent use. It is important to understand these effects since changes in erythrocyte mechanics may impact on hemodynamic stability with the use of these anesthetic agents.

The study thus examines the effect of ketamine and lidocaine, used individually and in combination, on RBC aggregability and deformability in male Wistar rats. The evaluation of these hemorheological parameters provided by this study will aid in understanding whether these anesthetic agents have the potential to change the microcirculatory performance or the viscosity of blood when they are used in clinical practice.

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 his 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 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 every day 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 evaluation of aggregability and deformability indices investigations using appropriate techniques.

Estimation of Red Blood Cell Deformability

Diffraction ektacytometer and automated rheoscope were used to measure the mean deformability value for the total red blood cell population investigated and the deformation distribution index of individual cells respectively. Deformation assays of a whole single cell was possible by means of optical tweezers.

Estimation of Erythrocyte Aggregability

The rate and final extent of red blood cell aggregation was measured by means of rheoscopes (increase in light transmission during stasis).

Statistical Analysis

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

RESULTS

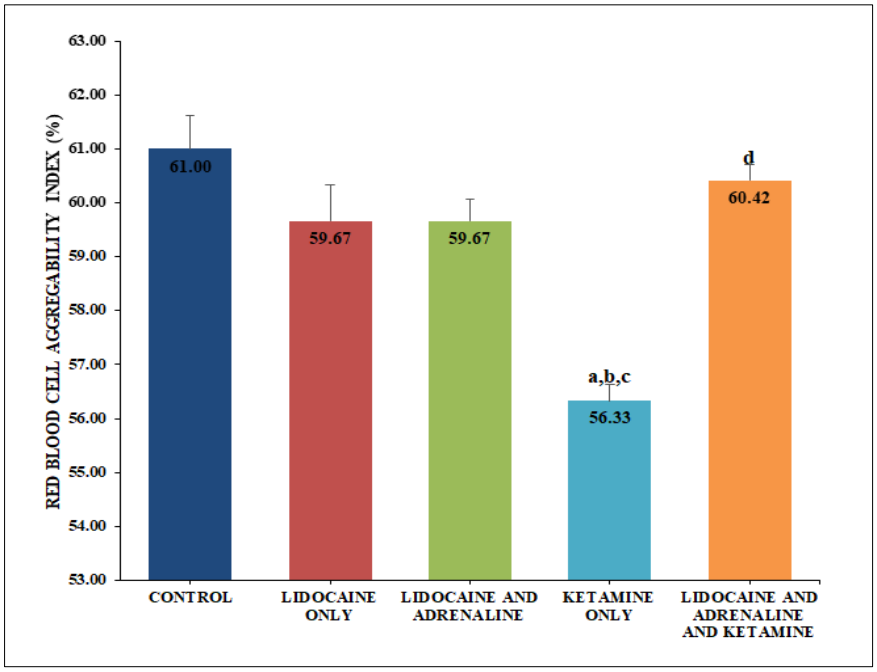

Fig. 1: Comparing the red blood aggregability index of the experimental groups. Results presented as mean ± SEM
a,b,c and d = versus control, lidocaine, lid + adr, ketamine and lid + lid + adr + ketamine groups respectively at $p<0.05$.

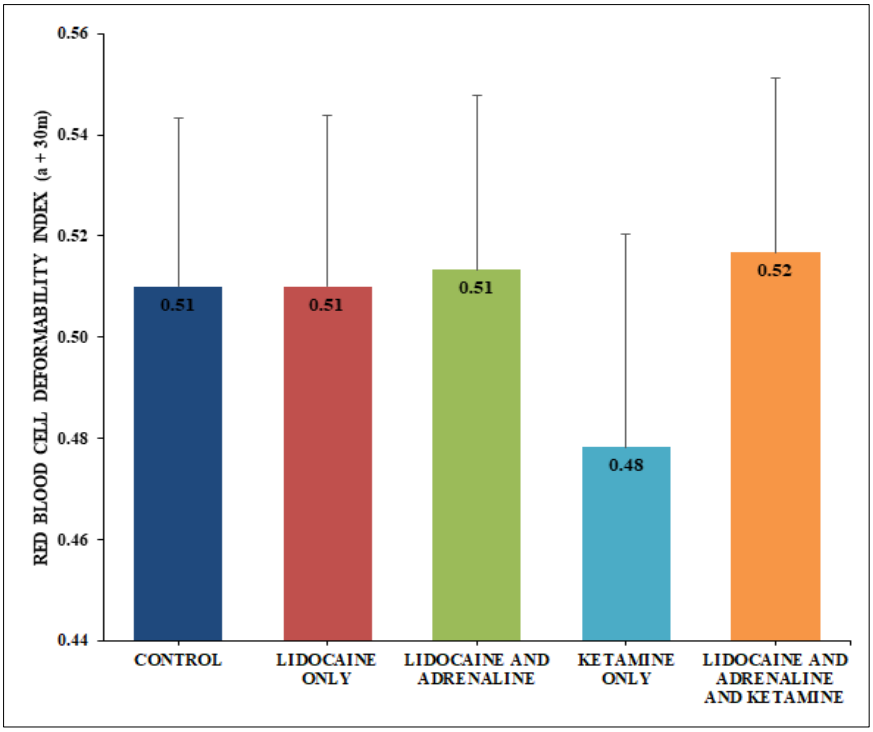

Fig. 2: Comparing the red blood cell deformability index of the experimental groups. Results presented as mean ± SEM

DISCUSSION

This study evaluated the relationship that exists between anesthetic agents on aggregability and deformability of red blood cells in male Wistar routs. These structures demonstrated that aggregability and deformability parameters were not altered. This conform with the findings of some reporters who reported that ketamine does not have the capacity to alter aggregability index, deformability index, hematocrit, blood and plasma viscosity of goats treated with ketamine and lidocaine. Since red blood cell deformability is a key determinant of blood flow in micro circulation, increasing vascular resistant at high viscosities, this study demonstrate that this key determinant is not altered aligning the RBC with the direction of flow studies have recently shown that RBC cellular properties can also modulate a cell's intrinsic tendency to aggregate termed RBC aggregability.

Studies have shown that plasma protein and other micro molecules are responsible for the formation of RBC aggregates.

Fibrinogen is the most physiologically relevant macro molecule that promotes RBC aggregation. The non-significant change on RBC on aggregability index on male Wistar rats treated with anesthetic agents and increase in fibrinogen contradicts the report of some investigators who asserted that fibrinogen is a relevant macro molecule that promotes red blood cell aggregation.

The finding of this study aligns with the reports of some investigation with the report of some investigators who depicted that ketamine anesthetic agents treated on male Wistar rats does not cause significant change in blood viscosities (Mostafa, 2018).

CONCLUSION

This study concluded that anesthetic agents, both local or general anesthesia, does not have the capacity to cause deformation of red blood cell. They also do not have the tendency of forming RBC aggregates, neither do they alter blood viscosity.

Recommendations

The following recommendations are drawn from this study:

1. Use of ketamine and lidocaine anesthetic agents are safe.
2. Use of anesthetic agents in individuals with high level of fibrinogen are encouraged.
3. Use of anesthetic agents in patient with hypertension is safe
4. Use of anesthetic agents does not have the tendency to increase blood viscosity hence does not predispose users to hypertension.

Conflicts of Interest: The authors declare no competing interest.

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