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Blood Rheology as an Indicator of Microcirculatory Changes in Experimental Preterm Labor

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Abstract

Preterm labor is a multifactorial process involving endocrine, inflammatory, vascular, and uterine mechanisms. Changes in blood rheology may influence microvascular perfusion and therefore provide additional information about circulatory alterations associated with premature delivery. To investigate selected hemorheological characteristics in experimental models of preterm labor induced by mifepristone and oxytocin. Forty pregnant rats were divided into three groups: control (n=20), mifepristone-induced preterm labor (n=10), and oxytocin-induced preterm labor (n=10). Erythrocyte aggregation, erythrocyte deformability, plasma viscosity, and whole blood viscosity were assessed after delivery. Selected conventional coagulation parameters were also measured. Both experimental models were associated with increased erythrocyte aggregation and reduced erythrocyte deformability. The aggregation index increased from 49.8±3.5% in controls to 67.4±4.2% in the mifepristone group and 58.9±3.8% in the oxytocin group ($p<0.001$). Whole blood viscosity increased from 4.15±0.25 mPa·s in controls to 5.35±0.32 mPa·s and 4.85±0.30 mPa·s in the mifepristone and oxytocin groups, respectively ($p<0.001$).

Plasma viscosity also increased, whereas routine coagulation parameters showed comparatively limited changes. Experimental preterm labor was accompanied by measurable changes in blood rheology. Increased erythrocyte aggregation, impaired erythrocyte deformability, and elevated whole blood viscosity may indicate altered blood-flow conditions at the microcirculatory level.

KEYWORDS: preterm labor; hemorheology; erythrocyte aggregation; erythrocyte deformability; blood viscosity; microcirculation.

Introduction

Preterm birth remains an important obstetric and public health problem worldwide. Its frequency and clinical consequences have been extensively documented, while its mechanisms are recognized as heterogeneous rather than attributable to a single pathological pathway [1-4]. Premature activation of uterine activity may occur in association with hormonal changes, inflammation, placental dysfunction, cervical remodeling, and disturbances of maternal-fetal vascular adaptation [3,4]. The rheological characteristics of blood are important determinants of tissue perfusion. Blood viscosity depends on plasma viscosity, hematocrit, erythrocyte deformability, and erythrocyte aggregation. These parameters can substantially influence resistance to blood flow, particularly within the microcirculation [5,6]. Increased erythrocyte aggregation and reduced deformability may impair the passage of red blood cells through small vessels and alter local blood-flow conditions [7-10].

Microcirculatory disturbances are relevant to pregnancy because placental and uterine tissues require adequate vascular adaptation throughout gestation. Alterations in placental vascular function and oxidative stress have been discussed in relation to several pregnancy complications [11]. From a biomechanical perspective, therefore, evaluation of blood rheology may provide information that is not fully reflected by conventional coagulation tests. The present study focused on changes in erythrocyte aggregation, erythrocyte deformability, plasma viscosity, and whole blood viscosity in two experimental models of preterm labor. The objective was to determine whether these parameters demonstrate measurable alterations during experimentally induced premature delivery.

Materials and Methods

Experimental design

The study included 40 pregnant outbred white rats (370-415 gr). Animals were divided into three groups: Control group: n=20; Mifepristone-induced preterm labor: n=10; Oxytocin-induced preterm labor: n=10. The control animals were evaluated at gestational days 21-22, whereas experimental preterm labor was induced at gestational day 20. Blood samples were collected after delivery for hemorheological and coagulation analysis.

Hemorheological assessment

The following parameters were evaluated: erythrocyte aggregation index; erythrocyte deformability index; plasma viscosity; whole blood viscosity. These parameters were selected because erythrocyte aggregation and deformability are important determinants of blood-flow behavior, particularly in the microcirculation [5-10].

Coagulation assessment

Prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen concentration, D-dimer concentration, and platelet count were also determined. We used Counter C1 (Germany). Quantitative results are presented as mean ± standard deviation (SD). Differences were considered statistically significant at $p<0.05$.

Results

The most pronounced differences between the groups concerned the hemorheological parameters. The erythrocyte aggregation index was 49.8±3.5% in the control group, compared with 67.4±4.2% in the mifepristone group and 58.9±3.8% in the oxytocin group ($p<0.001$). Thus, erythrocyte aggregation was increased in both experimental groups, with a greater change observed following mifepristone administration. The erythrocyte deformability index decreased from 0.92± 0.04 in controls to 0.78±0.05 in the mifepristone group and 0.80±0.04 in the oxytocin group ($p<0.001$). Plasma viscosity increased from 1.24±0.05 mPa·s in controls to 1.39±0.07 mPa·s and 1.35±0.06 mPa·s in the mifepristone and oxytocin groups, respectively ($p<0.01$). A similar pattern was observed for whole blood viscosity. The control value was 4.15±0.25 mPa·s, increasing to 5.35±0.32 mPa·s in the mifepristone group and 4.85±0.30 mPa·s in the

oxytocin group (p<0.001). The conventional coagulation profile demonstrated less pronounced changes. PT and aPTT did not differ significantly between groups. Fibrinogen increased from 2.85±0.24 in controls to 3.18±0.31 and 3.05±0.28, while D-dimer increased from 0.42±0.07 to 0.56±0.09 and 0.51±0.08, respectively (p<0.05). Platelet counts did not differ significantly. You can see Fig. 1 and Fig. 2.

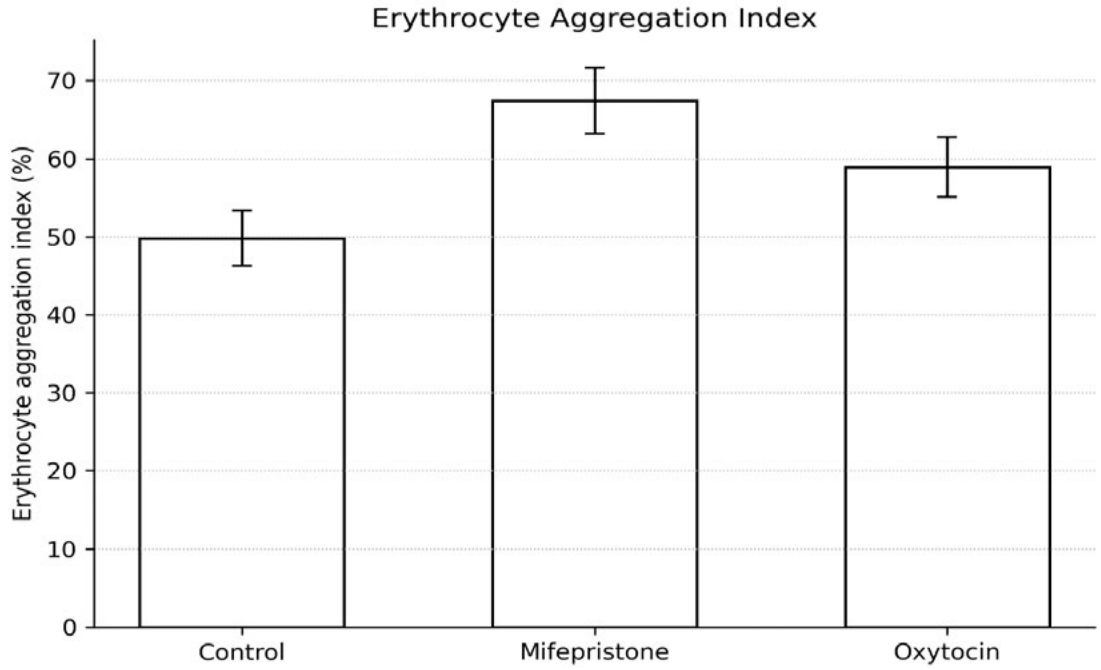


Fig.1. Erythrocy te aggregation index in control, mifepristone, and oxytocin groups. Data are presented as mean±SD.

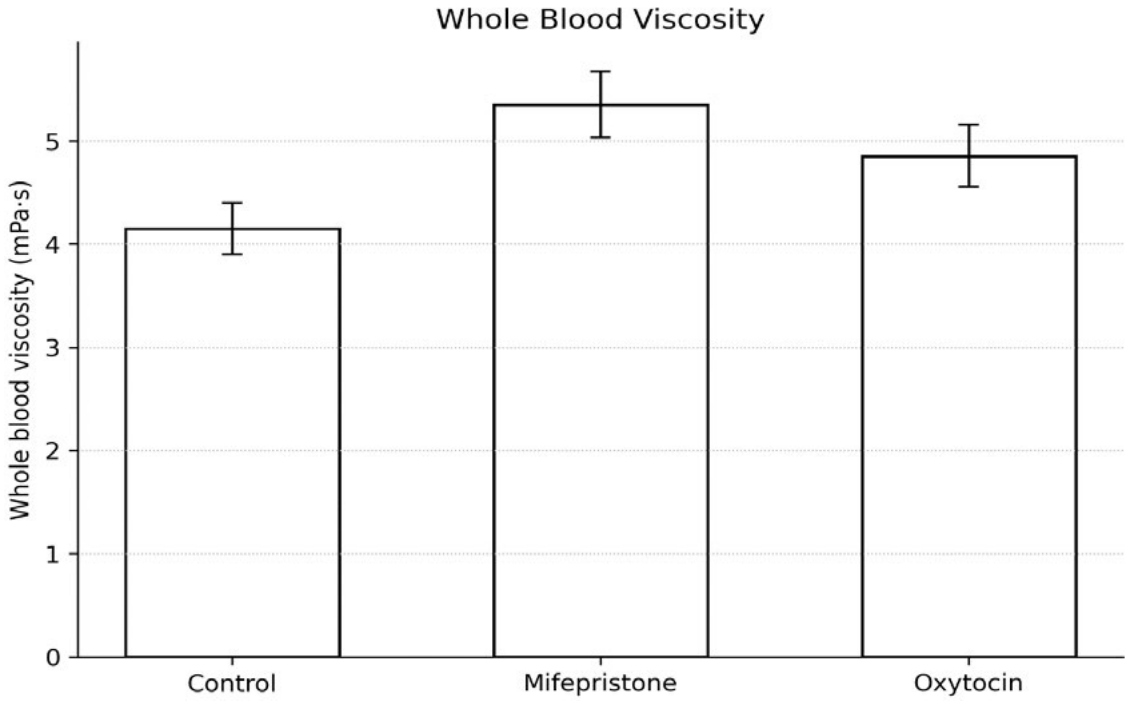


Fig. 2. Whole blood viscosity in control, mifepristone, and oxytocin groups. Data are presented as mean±SD.

Discussion

The present findings demonstrate a coordinated change in several hemorheological characteristics during experimentally induced preterm labor. The increase in erythrocyte aggregation occurred together with a reduction in deformability, suggesting a structural and biophysical shift toward less favorable blood-flow properties [5-10,15-20]. Both parameters are recognized as crucial determinants of whole blood viscosity, vascular wall shear stress, and overall microvascular resistance [5-10,15,17].

The elevation in whole blood viscosity provides additional evidence of altered blood-flow behavior under shear force. Blood viscosity is not a static property; it dynamically changes according to cellular mechanical traits, plasma protein levels (especially fibrinogen), and flow dynamics, playing a particularly vital role in maintaining capillary tissue perfusion in small microvessels [5,6,15,16]. Under low shear rates, increased erythrocyte aggregation promotes the formation of reversible cellular networks and large "rouleaux" clusters [7-10,12,15]. Concurrently, reduced cellular deformability severely impairs the ability of red blood cells to reconfigure and bend when entering and navigating narrow microvascular channels [7-10,17-20].

In the present experiment, the observed changes were noticeably more pronounced in the mifepristone-treated group regarding erythrocyte aggregation and whole blood viscosity. This difference likely reflects the distinct pharmacological and molecular pathways through which different experimental interventions trigger premature myometrial contractions [18]. Mifepristone, as a competitive progesterone receptor antagonist, blocks progesterone-mediated uterine quiescence, triggers a cascade of extracellular matrix breakdown, and promotes local inflammatory alterations in microvascular beds [4,14,18,24]. However, the current study was not specifically designed to isolate the exact cellular signal transduction pathways responsible for this difference.

The relatively modest changes in conventional coagulation parameters – such as prothrombin time (PT), activated partial thromboplastin time (aPTT), and total platelet count – compared with the hemorheological parameters are also noteworthy. Plasma fibrinogen and D-dimer levels were elevated in both experimental groups, signaling an underlying alteration in the procoagulant and fibrinolytic profiles [16]. Nevertheless, the significantly more dominant changes in erythrocyte aggregation, membrane deformability, and whole blood viscosity strongly suggest that evaluating blood rheology provides valuable complementary diagnostic insights beyond traditional coagulation panels.

From a microcirculatory and hemodynamics perspective, these findings hold substantial clinical and physiological relevance. Red blood cell aggregation and deformability govern hydraulic flow resistance, cell-free layer dynamics, and transcapillary oxygen exchange in terminal vascular networks [5-10,15-20]. Previous hemorheological

and uteroplacental research has consistently shown that adverse shifts in erythrocyte biomechanics directly correlate with microvascular perfusion deficits, endothelial stress, disturbances in microvascular blood flow, and tissue hypoxia [8-10,18-21].

These findings should, however, be interpreted within the context of inherent animal model limitations:

1. The number of animals / sample size was relatively small.
2. Inflammatory mediators and cytokines, oxidative stress markers, endothelial function indexes, and placental histopathology were not simultaneously quantified [11].

Therefore, the present results establish a strong physiological association between experimental preterm labor and systemic hemorheological dysregulation, rather than proving a single causal mechanism [1-4].

Conclusion

Experimental preterm labor is associated with profound alterations in systemic hemorheological properties. Significant increases in erythrocyte aggregation, reductions in red cell deformability, and elevations in both plasma and whole blood viscosity were characteristic of both experimental models. Notably, the changes in red cell aggregation and whole blood viscosity were most pronounced in the mifepristone group. These findings strongly support the application of hemorheological profiling as a complementary biomarker tool for investigating microcirculatory, blood-flow, and placental perfusion abnormalities associated with preterm labor [5-10,13,15-20, 22,23].

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Conflicts of interest. The authors have no conflict of interest to declare.

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