

0271-5198(94)00041-7

PROCEEDINGS - PART VI

FIRST INTERNATIONAL AND EIGHTH EUROPEAN

CONFERENCE ON CLINICAL HEMORHEOLOGY

Vienna, Austria, 5-8 July 1993

SYMPOSIUM: FREE SESSION - GYNECOLOGY AND NEONATOLOGY

MODIFICATIONS OF ERYTHROCYTE AGGREGATION DURING LABOR AND DELIVERY

J.F. BRUN, P. BOULOT (*), O. ROUSSEAU (*),
A. EL BOUHMADI (*), F. LAFFARGUE (*) J.L. VIALA (*), A. ORSETTI.
Service d'Exploration Physiologique des Hormones et des Métabolismes
(Professeur A. Orsetti), Hôpital Lapeyronie, 34059 Montpellier-cédex, France;
Laboratoire de Physiologie II, Institut de Biologie, Faculté de Médecine,
Montpellier, France; (*) Service de Gynécologie et Obstétrique de Montpellier,
13 Avenue du Professeur Grasset, 34050 Montpellier.

(Accepted by Guest Editor O. Linderkamp)

ABSTRACT

Pregnancy is associated with erythrocyte hyperaggregation which acutely returns to baseline during delivery, while a transient hyperviscosity syndrome induced by uterine contractions can be observed. We aimed at analyzing more precisely the modifications of erythrocyte aggregation during labor. 71 uterine contractions in 30 pregnant women (19-45 yr, mean 27.2 + 9) were studied, with RBC aggregation (SEFAM erythroaggregometer) measured before, during and after the contraction. Aggregation indices at 10 and 60 sec progressively increased throuhout labor (p<0.01). Partial and total dissociation thresholds progressively decrease during labor with a nadir (-10%) at delivery (p<0.01). The aggregation time is transiently shortened (p<0.01) during labor. Although previous measurements with the Myrenne aggregometer showed only during labor a return to nonpregnant values, this analysis by laser backscattering indicates that the stressful events which occur during uterine contractions increase the tendency of RBCs to form aggregates, although they disaggregate more easily.

Key words: labor, erythrocyte aggregation, hemorheology

INTRODUCTION

During pregnancy, blood rheology is markedly modified (1-5). One of the most important hemorheologic changes during this period is an increase in erythrocyte aggregation (6-7). This parameter acutely returns to baseline during delivery (2). However, delivery is not only marked by the return of blood rheology to non-pregnant values. There is also a transient hyperviscosity syndrome which seems to result mostly from uterine contractions (8). Therefore, the modifications of a complex biological phenomenon such as RBC aggregation might be less simple than a return to baseline values. It could be hypothesized that some parameters of RBC interactions are also influenced by the stressful events which occur during delivery. Since laser backscattering offers a more precise analysis of RBC aggregation than the light transmission method (9-10) we investigated the modifications of erythrocyte aggregation at the end of pregnancy with this technique.

MATERIAL AND METHODS

patients.

30 pregnant women (19-45 yr, mean 27.2 ± 9) were studied. Labor occurred spontaneously at 37-42 wk gestation. RBC aggregation was measured before, during and after each contraction. A total number of 71 uterine contractions was studied: 24 before 4 cm dilatation, 26 after 4 cm dilatation, 21 during delivery. No medication (e.g. analgesia) was given.

instrumentation

Blood was drawn on vacutainer tubes, from a catheter set in the antecubital vein. The anticoagulant was EDTA (0.18% EDTA K₃). Hematocrit was adjusted to 40% ± 0.5 % by removal or adjustment of plasma. RBC aggregation was measured with the SEFAM aggregometer which is based upon the experiments of Mills (13-14) on cell disaggregation behavior in shear flow. This device measures the changes in backscattered light which are observed when sheared RBC suspensions are abruptly brought to a full stop. The decrease in the optical signal reflects the formation of RBC aggregates (11). Some parameters are derived from the curve of light intensity as a function of time. The aggregation time is the reciprocal of the initial slope (calculated between 0.5 and 2 sec after the shear has stopped). The aggregation index at 10 sec is a measurement of the extent of erythrocyte aggregation and is the relative surface area above the curve calculated over the first 10 seconds. This device measures also disaggregation thresholds, by submitting blood to a succession of shear rates from 600 s⁻¹ to 7 s⁻¹. The total disaggregation threshold is the shear rate below which the backscattered light intensity starts to decrease, indicating that the shear stress applied to aggregates is no longer sufficient for allowing complete dispersion of RBC aggregates. The partial disaggregation shear rate is defined as the shear rate corresponding to the intersection point of the two asymptotes drawn from the extremes (maximum and minimum shear rate). Statistical analysis was performed by one way analysis of variance (ANOVA).

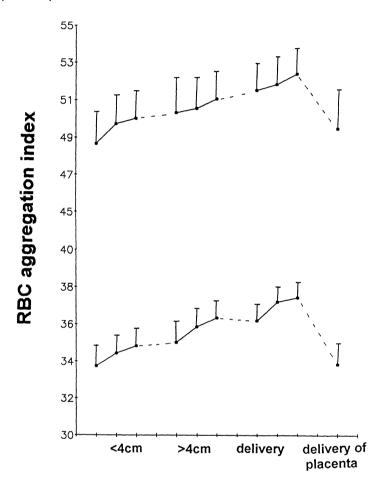
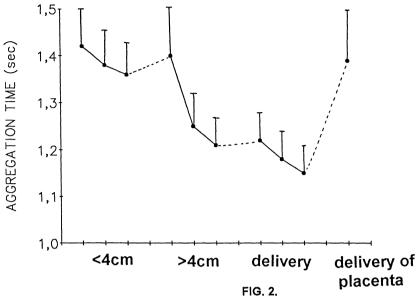


FIG.1

Evolution of RBC aggregation indices (see text) during uterine contractions at different moments of labor and delivery. Upper line: index at 60 s; lower line: index at 10 s. The increase is significant during each uterine contraction (ANOVA p<0.01) as well as during the whole process of labor (ANOVA p<0.01).

RESULTS

Fig. 1 shows that aggregation indices at 10 and 60 sec progressively increased throghout labor (p<0.01) and return after delivery to the value observed at the beginning of labor. Fig. 2 shows that the aggregation time is transiently shortened (p<0.01) during labor. Fig 3 shows that the partial dissociation



Changes in RBC aggregation time during labor. This parameter decreases during uterine contractions (ANOVA p<0.01) and exhibits a general decrease throghout labor (ANOVA p<0.01).



Changes in RBC partial disaggregation threshold during labor. This parameter decreases during uterine contractions (ANOVA p<0.01) and exhibits a general decrease throghout labor (ANOVA p<0.01).

thresholds progressively decrease during labor with a nadir (-10%) at delivery (p<0.01).

DISCUSSION

Our preceding studies on blood rheology during labor used another technique for measuring RBC aggregation: the light transmission method, derived from the works of H. Schmid-Schönbein (15) and widely used among hemorheologists (Myrenne aggregometer). We observed two points: RBC aggregation, which is high during pregnancy, decreases during delivery and returns to non-pregnant values; this decrease occurs gradually, during each uterine contraction. (8-9). We postulated that this decrease was due to the physiological decrease in fibrinogenemia during labor (16).

The picture when RBC aggregation is measured by laser backscattering is quite different. The decrease in RBC aggregation threshold indicates that RBCs become more easily dissociable, consistent with our previous observations. However, we find also some modifications reflecting increased aggregation: shorter aggregation time, higher aggregation index at 10 and 60 sec.

Thus, beside the return to the flow condition of a non-pregnant organism, some aspects of RBC aggregation reflect the transient hyperviscosity syndrome we previously described during labor (8-9).

The physiological relevance of these complex hemorheologic modifications during labor and delivery remains unclear. Some of the rheologic changes, resulting in transient hyperviscosity, may decrease blood flow in order to reduce blood loss during this highly hemorragic period. However, our understanding of the influence of RBC aggregation on blood flow at the different levels of circulation remains uncomplete and no clear interpretation can be given. By contrast, a reduction of the disaggregation threshold is probably beneficial for O₂ delivery, since studies in peripheral obliterative arterial diseases (in diabetic subjects) showed a negative correlation between this threshold and transcutaneous O₂ pressure (17). The causal mechanism of these rheologic modifications, which are probably due to metabolic and hormonal changes during labor, remain also to be studied.

REFERENCES

- 1. GAEHTGENS P, SCHICKENDANTZ S. Rheologic properties of maternal and neonatal blood. <u>Bibl Anat 13</u>, 107-108, 1975
- 2. FOLEY ME, ISHERWOOD DM, McNICOL GP. Viscosity, haematocrit, fibrinogen and plasma proteins in maternal and cord blood. Br J Obstet Gynaecol 85, 500-504, 1978.

- 3. FOLEY ME, COLLINS R, McDONALD D. Whole blood viscosity in umbilical cord blood, adult pregnant and non-pregnant blood: the influence of plasma factors. Clinical Hemorheology 3, 285, 1983.
- 4. BUCHAN PC. Evaluation and modification of whole blood filtration in the measurement of erythrocyte deformability in pregnancy and the newborn. J. Hematol 45, 97-105, 1980.
- 5. THORBURN J., DRUMMOND M.M, WHIGHAM K.A., LOWE G.D.O., FORBES C.D., PRENTICE C.R.M., WHITFIELD C.R. Blood viscosity and haemostatic factors in late pregnancy, preeclampsia and fetal growth retardation. Br J Obstet Gynaecol 89, 117-122, 1982.
- 6. HUISMAN A, AARNOUDSE JG, KRANS M, HUISJES HJ, FIDLER V, ZIJLSTRA WG. Red cell aggregation during normal pregnancy. Br J Haematol 68, 121-124, 1988
- 7. OZANNE P, LINDERKAMP O, MILLER FC, MEISELMAN HJ. Erythrocyte aggregation during normal pregnancy. <u>Am J Obstet Gynecol 147</u>, 576-583, 1983.
- 8. BRUN J.F., BOULOT P., FONS C., HEDON M.N., VIALA J.L., ORSETTI A.. Paramètres hémorhéologiques pendant l'accouchement normal et la contraction utérine. Rev Franç Gynécol Obstet 86, 148-153, 1991.
- 9. BRUN J.F., BOULOT P., HEDON M.N., VIALA J.L., ORSETTI A. Modifications Physiologiques de la Rhéologie Sanguine au Cours de la Grossesse Normale et de l'Accouchement. Resultats Préliminaires. <u>Artères et Veines 8</u>, 552-557, 1989.
- PIGNON B., MULLER S., JOLLY D., SIADAT M., PETITFRERE E., VESSEL B., DONNER M., POTRON G., STOLTZ J.F., 1988. Validation d'une méthode d'approche de l'agrégation érythrocytaire par rétrodiffusion laser. In:
 <u>Hémorhéologie et agrégation érythrocytaire</u>. Volume 2, applications cliniques J.F. Stoltz (Ed.).Paris: Editions Médicales Internationales, 1988, pp. 65-74.
- 11. DONNER M., SIADAT M, STOLTZ JF. Erythrocyte aggregation: approach by light scattering determination. Biorheology 25, 367-375, 1988.
- 12. CHABANEL A., SAMAMA M. Evaluation of a method to assess red blood cell aggregation. Biorheology 26, 785-797, 1989.
- MILLS P. QUEMADA D., DUFAUX J. Etude de la cinétique d'agrégation érythrocytaire dans un écoulement Couette. <u>Rev Phys Appl 15</u>, 1357-1366, 1980.
- 14. SNABRE P, BITBOL M, MILLS P. Cell disaggregation behavior in shear flow. Biophys J 51, 795-807, 1987.

- 15. SCHMID-SCHONBEIN H, VOLGER E, KLOSE HJ Microrheology and light transmission of blood III. The velocity of red cell aggregate formation. Pflügers Arch 254, 299-317, 1975.
- 16. KLEINER GJ, MERSKEY C, JOHNSON AJ, MARKUS WB. Defibrination in normal and abnormal parturition. <u>Brit J Haematol</u> 19, 159-165, 1970
- 17. LE DEVEHAT C, KHODABANDEHLOU T, VIMEUX M, BOUTONNAT Y. Transcutaneous oxygen pressure and hemorheology in diabetes mellitus. In: <u>Hémorhéologie et agrégation érythrocytaire</u>. Volume 3, Théorie et applications cliniques J.F. Stoltz, M. Donner, A. L. Copley (Eds.).Paris: Editions Médicales Internationales, 1991, pp. 268-273.