Haemorheological changes during pregnancy.
Huisman, Adrianus

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
1986

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Haemorheology is concerned with whole blood viscosity and its determinants, i.e. plasma viscosity, haematocrit and shear-dependent flow behaviour of the red cells due to their tendency to aggregate at low and to deform at high shear rates. The basic principles and definitions of haemorheology are explained in Chapter 1, section 1.1. In section 1.2. the haemodynamic relevance of the changes in whole blood viscosity are discussed. The haemodynamic significance of whole blood viscosity depends on the shear forces exerted on the blood. Under normal circulatory circumstances the local shear forces are always so high, that whole blood viscosity will be low and hardly able to cause circulatory troubles. However, whole blood viscosity may become important when the shearing forces fall below a certain level and are not compensated for by vasomotor control.

The reduced intervillous blood flow in patients with pregnancy-induced hypertension and intra-uterine growth retardation is partly ascribed to an increase in structural viscosity. Because the driving pressure in the intervillous space is low and because the uteroplacental circulation has no autoregulation, an increased blood viscosity might contribute to the intervillous blood flow reduction (section 1.2.). However, there exists much confusion with regard to the haemorheological changes during normal pregnancy and in pregnancies complicated by pregnancy-induced hypertension and intra-uterine growth retardation and their relevance for the uteroplacental circulation. The obstetrical literature with regard to these haemorheological changes is reviewed in section 1.3. This study was primarily undertaken to investigate whole blood viscosity and its determinants during normal pregnancy (section 1.4.).

Therefore we investigated the occurrence and the changes in red cell aggregation, plasma viscosity and whole blood viscosity in 24 women during the course of their normal pregnancy. Red cell aggregation was measured by means of a syllectometer, plasma and whole blood viscosity by means of a Contraves LS 30 rotational viscometer. In Chapter 2 the selection of patients and the methods used for sampling, anticoagulation, storage and transport of blood as well as reflection photometry and rotational viscometry are discussed in detail.

Red cell aggregation was found to increase during the whole course of normal pregnancy in spite of the physiological haemodilution.
This increase in red cell aggregation could be attributed, to a great extent, to the increase in fibrinogen concentration during pregnancy. The other plasma proteins with a high molecular weight and asymmetrical spatial structure, immunoglobulin M and $\alpha_2$-macroglobulin, had no influence on the changes in aggregation tendency (Chapter 3).

Plasma viscosity increased during the second and especially the third trimester of normal pregnancy, after a small decrease during the first trimester. The increase was due to the continuous increase in fibrinogen concentration during this period, in which total serum protein hardly showed a further decrease. It was concluded that plasma viscosity represents a balance between the rising fibrinogen and the falling total serum protein concentration (Chapter 4).

During normal pregnancy we found a decrease in whole blood viscosity at all shear rates until the 30th week, followed by a smaller increase between 30 and 37 weeks. The changes in whole blood viscosity were largely determined by the changes in haematocrit and to a smaller extent by the changes in plasma viscosity. The influence of plasma viscosity on the resulting whole blood viscosity increased at higher shear rates. At lower shear rates haematocrit was the most important determinant of whole blood viscosity. We did not find any influence of the increase in red cell aggregation on low shear blood viscosity as measured in a rotational viscometer (Chapter 5).

In Chapter 6 the results of a cross-sectional study are described, in which whole blood viscosity and its determinants were measured in a group of 15 pregnant women with pregnancy-induced hypertension and/or intra-uterine growth retardation and in a control group, matched for parity and gestational age. In the pathological group we found statistically higher haematocrit values and whole blood viscosity values measured at all shear rates.

The findings in Chapter 3-6 are discussed in Chapter 7. Additional data are given, showing the unsuitability of in vitro measurements with rotational viscometers for discriminating between a normal and an enhanced red cell aggregation tendency. It is suggested that the influence of red cell aggregation on low shear blood viscosity levels off below a certain aggregation half time.

In this chapter the significance of changes in structural viscosity in vivo is also discussed. In our opinion the decrease in haematocrit
during normal pregnancy not only compensates for the enhanced red cell aggregation, but even diminishes the resistance to flow in the intervillous space. On the other hand, the haemoconcentration seen in pregnancies complicated by pregnancy-induced hypertension may result in an increased resistance to flow. In combination with the lowered driving pressure in the intervillous space this increased resistance may lead to a reduced intervillous blood flow in these pregnancies. Finally, some speculations are made on the possible effects of haemodilution therapy on the intervillous blood flow.