Maternal mean platelet volume and subsequent development of adverse neonatal outcomes in pregnancies affected by abnormal maternal fetal Doppler velocimetry

Thesis

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Introduction

Introduction

Pre-eclampsia (PE) and intrauterine growth restriction (IUGR) are the main causes of foetal–maternal morbidity and mortality, complicating approximately 15% of pregnancies. Many studies have shown the importance of some biochemical and hematological parameters in monitoring gestational complications. Platelets have been demonstrated to have an important role in the mechanisms of altered placentation. ***(Piazze et al ., 2006)***.

It is now widely accepted that platelets are important blood elements involved in haemostatic events which, when inappropriately activated, contribute to a number of thrombotic and cardiovascular disorders.***(Lau et al.,1991.)***.

Mean platelet volume (M.P.V) has been shown to reflect platelet activity and a determinant of platelet function. Large platelets are metabolically, haemostatically and enzymatically more active than small platelets and produce more thromboxane A2**.** ***(Thompson et al., 1982)***. Mean platelet volume (MPV) reflects changes in either the level of platelet stimulation or the rate of platelet production.

Women at risk to develop pre-eclampsia and IUGR exhibit platelet (PTL) activation both in early pregnancy and before pregnancy. Platelet activation has been associated with changes in plasma and mean platelet volume (MPV), conditions giving rise to homodynamic maladaptation and gestational hypertensive disease ***(Spaanderman et al., 2000)***.

Moreover, this condition has been associated with numerous other clinical syndromes, including chronic hypertension, myocardial infarction, and stroke, all of these are more frequently observed among formerly pre-eclamptic women ***(Wilson et al., 2003).***

Doppler velocimetry is a non-invasive method for the evaluation of the utero–feto–placental circulation. The accessibility of Doppler colors flow mapping has enabled a precise identification of the uterine arteries, umbilical artery (UA) and middle cerebral artery (MCA) ***(Lees et al., 1997***).

The persistence of high resistances in the uterine arteries may reflect the failure of the physiological changes in the spiral arteries, thus being a risk factor for the consequent maternal–foetal pathologies such as pre-eclampsia (PE), intrauterine growth retardation (IUGR) and abruptio placentae ***(Harrington et al .,1996).***

In women with abnormal Doppler velocimetry, mean platelet volume (MPV) and platelet function may be altered with specific patterns of change associated with subsequent adverse pregnancy outcome. Impaired placentation and increased impedance to flow may cause endothelial changes due to increased shear stress or alterations in circulating platelets ***(Wallenburg & Rotmans., 1982).***

Several studies supporting the view of pregnancy related hypertensive diseases are superimposed on a pre-existing haemostatic or hemodynamic disorder ***(Spaanderman et al .,2000)***. In assumption, association of pregnancy complications with increased uteroplacental resistance cannot be solely explained by abnormal uteroplacental vessel histopathology

(Aardema et al.,2001), but the pattern of changes in platelet morphology and function may be disease specific. These tests of uteroplacental vessel histopathology are too labour-intensive, expensive and not sufficiently specific to be applicable to clinical screening or risk assessment. ***(Gioia et al., 2007).***

Mean platelet volume (MPV) was higher in women with abnormal uterine arteries Doppler velocimetry compared to those with normal Doppler velocimetry due to increased consumption of platelets in the uteroplacental circulation leading to a reduction in the number of circulating platelets, and a compensatory increase in bone marrow platelet production. Platelet consumption results in the physiological release of younger platelets which are known to have a higher mean platelet volume (MPV) and aggregation tendency ***(Karpatkin et al ., 1969)*** .

It was suggested that women with altered fetal-maternal Doppler velocimetry in umbilical artery (UA) (high pulsatility index, absent or reversed end diastolic flow (ARED), blood flow cephalisation) and/or bilateral increased resistance in uterine arteries, mean platelet volume (MPV) and platelet function are altered with specific patterns of change associated with subsequent adverse pregnancy outcome(neonatal O2 support448 hrs or intubation and/or Ph<7.2 at umbilical blood gas analysis (UBGA)) ***(Missfelder-lobos et al., 2002)***. So periodical monitoring of hematological markers such as mean platelet volume (MPV) may be associated with Doppler velocimetry in order to enhance management (time and mode of delivery) capabilities in pregnancies with elevated uterine resistances, ameliorating their maternal–neonatal outcome. ***(Piazze et al ., 2007).***

AIM OF THE STUDY

The aim of the study is to investigate a possible association between maternal mean platelet volume and development of adverse neonatal outcome in pregnancies affected by altered maternal- fetal Doppler velocity.

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UA; Umbilical Artery.

MCA; Middle Cerebral Artery.

IUGR; Intrauterine growth restriction.

FVWs; Flow velocity waveforms.

EDV; end-diasfotic velocity.

MV; mean velocity

(S/D) ratio; systolic / Diastolic ratio.

PI; Pulsatility index.

RI; Resistance index.

CW; Continuous wave Doppler.

PW; Pulsed wave Doppler.

EDV; End diastolic velocity.

GA; Gestational age.

ACA; Anterior cerebral artery.

PCA; Posterior cerebral artery

MPV; Mean platelet volume.

GP; Glycoprotein.

ATP; Adenosine triphosphate.

ECs; Endothelial cells.

PGI2; prostaglandin I2.

EDRP; Endothelium derived relaxing factor.

vWF; Von Willebrand Factor.

SEM; Subendothelial microfibrils.

TXA2; Thromboxane A2.

5-HT; 5-hydroxy-tryptamine.

A-C; Apgar score minus color.

Doppler ultrasound

Introduction:

At the moment, the ultrasound represents the most important mean for the study of the uteroplacental and fetoplacental circulation.

Doppler velocimetry is a non-invasive method for the evaluation of the utero-feto-placental circulation the accessibility of Doppler colour flow mapping has enabled a precise identification of the uterine arteries, Umbilical Artery (UA) and Middle Cerebral Artery (MCA).

Several studies have demonstrated that doppler ultrasound represents an important diagnostic tool in modern obstetrics ***(Allfirevic et al., 1995***) indeed; the American College of Obstetrics and Gynecology has endorsed the use of Doppler ultrasound of the umbilical artery in high-risk pregnancies.

Information obtained with Doppler ultrasound helps obstetricians in managing patients in the following situations:

1) Pregnancies complicated by intrauterine growth restriction (IUGR).

2) Pregnancies in which the fetus is at risk for anemia because of red blood cell alloimmunization.

3) Multiple gestations.

4) Pregnancies treated with prostaglandin inhibitors to monitor the ductus arteriosus.

Blood flow velocity of the fetal vascular system can be either pulsatile or continuous. The arteries always have a pulsatile pattern, whereas the veins have either pulsatile or a continuous pattern. Figure (1) shows a typical Doppler arterial blood FVW. Figure (2) shows FVW of an umbilical artery and vein.

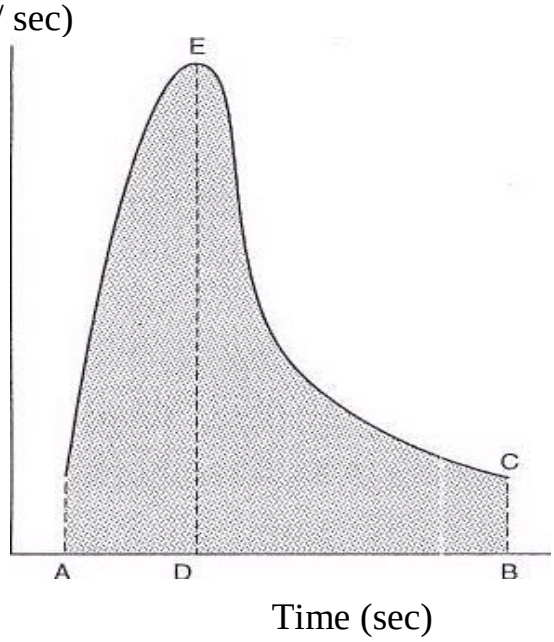

Figure **1.** Typical Doppler flow velocity waveform of a fetal artery, A represents the beginning of the waveform that coincides with the beginning of the cardiac systole. DE is the peak systolic velocity. CB is the end- diastolic velocity.