Evaluation of platelet aggregation in flow and platelet aggregometry during pregnancy

Editor—I read with interest the paper by Vincelot and colleagues. The authors presented the PFA (platelet function analyser) as a device giving reproducible results similar to an in vitro aggregation test. This is not the case. The PFA was designed to assess platelet-related haemostasis as whole blood flows under high shear rate conditions.[2] Briefly, the system consists of a disposable test cartridge in which citrated whole blood is aspirated through a capillary and the microscopic aperture cut in a membrane that had been coated with either collagen and ADP, or collagen and epinephrine. The instrument determines the time required for occlusion of the aperture (closure time). The test is sensitive to abnormalities in platelet adhesion and aggregation occurring under high shear rate conditions, similar to those encountered in a stenotic blood vessel (5000–6000 s\(^{-1}\)). The molecular mechanism evaluated in this system, initial binding of von Willebrand factor (vWF) by GP Ib followed by GPIIb/IIIa-dependent binding of vWF, is different from that of fibrinogen-mediated platelet aggregation. At the low shear rates associated with the stirred suspensions of platelets used in aggregometers (shear rate <100 s\(^{-1}\)), fibrinogen predominates over vWF in driving aggregation by binding to GPIIb/IIIa.[3] However, at very high shear rates, fibrinogen is no longer efficient at mediating aggregation, whereas vWF can bind to GP Ib and GPIIb/IIIa.[4] This distinction may be important because it has been reported that antibodies directed against GP Ib, GPIIb/IIIa and vWF prolong the PFA closure time, whereas antifibrinogen antibodies do not affect it.[5] In contrast, in the absence of fibrinogen, platelet-rich plasma failed to support aggregation.[6] Nevertheless, we now know that the clinical sensitivity and specificity of the PFA in healthy subjects are no different from aggregometry.[7]

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Editor—Thank you for the opportunity to answer Dr Fattorutti’s comments. He clearly poses the question of which test, if any, is able to evaluate platelet performance during the coagulation process, and what is its clinical significance. His approach suggests that there are clear cut differences in the pathways of platelet aggregation: either fibrinogen-dependent (under low shear rates conditions), or pathways dependant on vWF, GPIb, GPIIb/IIIa interaction (under high shear rates). Such a dichotomy is of interest in understanding the biological mechanisms of in vitro platelet aggregation. But it is probably a simplified approach of what is happening clinically in vivo, as well as in vitro, compared with the use of more global biological tests such as the PFA-100 system or thrombelastography. Although the PFA-100 was designed primarily to evaluate platelet function during high shear rate conditions, it is also used on whole blood without excluding or modifying (as in platelet aggregometry) the in vivo natural environment of platelets, such as erythrocytes and plasma.

Pregnancy is a unique situation for which the PFA-100 may be useful to evaluate platelet competence. In women with pregnancy-induced thrombocytopenia, fibrinogen levels are increased and thus the evaluation of platelet defects is less dependent on fibrinogen. In pre-eclamptic patients, the alteration in platelet function is more complex, and depends on the reduction of circulating platelet number and function. This alteration in function is not unique to pre-eclampsia. In most pregnant patients, an increase in ADP-induced platelet aggregation with increased ATP secretion is observed.[8-9] In more severe cases of pre-eclampsia, however, the decrease in collagen, ADP or epinephrine-induced platelet aggregation results from a depletion of platelet content and from the effects of associated disseminated intravascular coagulation.[10-11] Use of PFA-100 in such circumstances, using the same agonists as the platelet aggregation test, is thus of interest, but remains to be proven. The PFA-100 needs to be validated by comparison with aggregation tests, and its use in predicting the risk of haemorrhage needs to be demonstrated before recommending its use. Until now, no test of platelet function has been able to do so.

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