

Analysis of the sensitivity of the overall haemostatic potential (OHP) assay to components of the coagulation system

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Aim:

To determine the sensitivity of the OHP assay parameters to changes in components of the coagulation system. To assess changes seen with a modified OHP using tissue factor as the coagulation trigger.

Methods:

In the standard OHP we use a small amount of thrombin to trigger fibrin generation in platelet poor plasma (PPP) with rt-PA added to initiate fibrinolysis. In order to model *in vivo* events more closely, we developed a modified version of the assay using tissue factor (TF) as the coagulation trigger. We then analysed changes seen in assay parameters after spiking PPP, to alter levels of components of the coagulation system including: antithrombin, fibrinogen, prothrombin and factors V, VII, VIII and X. Results were compared with reference intervals we have established in a healthy Australian population. Method comparisons were analysed using a repeated measures ANOVA.

Results:

Fibrinogen levels (0 to 10g/L) showed a direct correlation with all OHP parameters: OCP (overall coagulation potential), OHP, OFP (overall fibrinolysis potential), maximum OD (Max OD), maximum slope of the OCP curve (Max slope) and delay in onset of fibrin generation. Factors II, VIII and X showed similar correlations for fibrin generation parameters but fibrinolysis was not altered until the individual factor levels were $\leq 5\%$ and therefore clot formation was markedly reduced. Samples from individuals with elevated FVIII levels were associated with increased fibrin generation and reduced fibrinolysis. Lowering of the high FVIII levels reduced fibrin generation into the normal range but fibrinolysis remained reduced in these hypercoagulable individuals. Standard OHP assay parameters were not influenced by factor V and VII until levels were $\leq 5\%$, however the TF triggered assay showed correlation for all assay parameters with FV and FVII levels. Reduced antithrombin levels showed more rapid fibrin generation, consistent with a hypercoagulable state.

Conclusions:

We have shown that the OHP is influenced by various components of the coagulation system with both hypocoagulable and hypercoagulable states demonstrated. Fibrin generation and fibrinolysis parameters show different responses to alterations in coagulation factor levels. The modified OHP, triggered by TF, may be more sensitive than the standard assay to abnormalities of Factor V and VII.