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Letter to the Editors-in-Chief

Diagnostic utility of comparing fibrinogen Clauss and prothrombin time derived method

A prothrombin time (PT) derived method has been described to measure plasma fibrinogen concentration. This method is not a direct determination of plasma fibrinogen but an estimation of the fibrinogen concentration from the absorbance changes at 450 nm (delta OD) during the clotting process of the PT on an automated photo optical coagulometers [1,2]. Although this assay is quick, economical and easily available to laboratories with suitable instruments, different papers state opposite conclusions: some studies conclude that the method is accurate and precise for most routine purposes [3] but other authors consider this assay inaccurate and lacks standardization [4,5]. The aims of this study were to compare the results obtained with the determination of fibrinogen by the Clauss and the PT derived methods and to assess the utility of comparison of both methods to identify polymerisation abnormalities.

We have compared fibrinogen levels determined by Clauss method (Multifibren U, Dade Behring) and PT derived (Thromborel S, Dade Behring) in 411 normal subjects and in 50 orally anticoagulated patients using a BCS coagulometer (Dade Behring, Malburg, Germany). Correlation between methods was performed by Pearson correlation test and Bland-Altman plots. Linear regression was used to assess the goodness of correlation. We also included in the study 23 patients sent to our laboratory with a suspected diagnosis of dysfibrinogenemia. In these patients we performed basic coagulation test (PT and aPTT), Clauss and PT derived fibrinogen, thrombin time (TT), reptilase time (RT), fibrinogen antigen concentration by radial immunodiffusion (Nor-Partigen fibrinogen, Dade Behring) and by heat precipitation methods. Magnitude of the polymerisation defects was measured as studied by Francis and Armstrong [6].

The mean $\pm$ standard deviation value for Clauss method was 320 ± 124 and 421 ± 154 mg/dl and for PT derived 289 ± 126 and 487 ± 194 mg/dl for normal and orally anticoagulated subjects, respectively. Pearson correlation were 0.94 in control samples and 0.96 in anticoagulated patients. Bland-Altman analysis shows a good agreement for fibrinogen measurement by both methods although suggests the presence of differences in anticoagulated patients. However, a simple linear regression study showed a coefficient of 0.93 (CI: 0.89–0.97) in controls and of 0.76 (CI: 0.70–0.83) in orally anticoagulated patients. Theses results indicate that PT derived gave higher values (24%) than Clauss method in the group of anticoagulated patients than in the normal group (7%).

The diagnosis of dysfibrinogenemia was confirmed in 6 out of the 23 patients sent with this suspicion. Fibrinogen antigen by radial inmunodifussion and heat precipitation assay showed similar values. A clear contrast was observed between the values obtained with the fibrinogen Clauss and the PT derived. Besides, in three out of six patients (cases 4, 5 and 6), all belonging to the same family, we also found a slight hypofibrinogenemia. Results are shown in Table 1.

Although PT derived fibrinogen assay has been demonstrated to be rapid, economical, and easily available, it should not be used without restriction [2]. Previous studies reported that PT-derived fibrinogen values were higher than the Clauss method specially in oral anticoagulated patients [1–3]. Therefore this test seems inadequate in this group of patients. On the other hand, PT-derived fibrinogen has not been validated for the diagnosis of dysfibrinogenemia, so it cannot be recommended at this time on a routine basis [7]. However, PT-derived fibrinogen comparison with Clauss method results may have additional diagnostic utility identifying polymerisation abnormalities when there is a discrepancy between both determinations. In these cases we should think about

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Table 1 Results of the tests performed in patients with dysfibrinogenemia

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Clauss fibrinogen (mg/dl) (nr: 200–350)	60	80	93	64	60	97
PT derived fibrinogen (mg/dl)	365	389	395	315	311	411
Antigen fibrinogen mg/dl (inmunodiffusion/heat precipitation) (nr: 180–350)	190/180	230/260	210/240	120/140	83/100	100/120
Fibrinogen activity/antigen	1:3.1	1:2.8	1:2.2	1:1.8	1:1.4	1:1.0
Thrombin time (s) (nr: 17–24)	34.5	37.4	40.3	39.5	45.1	34.7
Reptilase time (s) (nr: 18–22)	41.5	43.2	45.4	40.9	52.6	42.2
Fibrin monomer polymerisation ratio (normal < 3)	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal

Nr: normal range.

the diagnosis of dysfibrinogenemia and set up ancillary tests.

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