Evaluation of the diagnostic utility of individual parameters in the disseminated intravascular coagulation (DIC) panel for use in under-resourced settings

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Introduction

- Disseminated intravascular coagulation (DIC) is caused by a number of inflammatory and pro-coagulant stimuli resulting in dysregulation of normal coagulation homeostasis and is a strong predictor of mortality.
- The pathogenesis includes increased procoagulants e.g. tissue factor and phospholipids, suboptimal natural anticoagulant activity and dysregulation of fibrinolysis with systemic deposition of fibrin clots with consumption of platelets and coagulation factors, ischaemic injury in vital organs and ultimately in a bleeding diathesis.
- A single diagnostic DIC marker is better but no single test is sufficiently specific and robust to confirm the presence of a DIC.
- The diagnosis is made on clinical suspicion supported by appropriate tests grouped together in a DIC panel: laboratory test results are interpreted according to various diagnostic algorithms (Table 1). Identification of the underlying precipitating disorder is key to appropriate investigation and management.
- Studies have documented that the laboratory abnormalities detected in DIC, in decreasing order of frequency, are thrombocytopenia, elevated fibrin degradation products (FDPs), prolonged prothrombin time (PT), prolonged activated partial thromboplastin time (aPTT) and a low fibrinogen.
- The DIC panel at our centre in South Africa at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) includes: PT, aPTT, Thrombin Time, D-dimers, fibrinogen, antithrombin and platelet count with correction studies of prolonged time-to-clot assays.
- As the cost of health care continues to rise and reimbursement rates decrease, there is a growing need to cut overall costs, enhance quality and cost-effectiveness of services but maintaining safety and care of the patient. This is especially true in resource poor environments.

Methodology

A retrospective review of all CMJAH DIC screens in 2015/16 was conducted. The ISTH DIC score was applied. A score of >5 equated to a DIC. A logistic regression analysis was performed and a predictive Z-score was derived to assess the diagnostic utility of each parameter in the DIC panel.

Results:

- A total of 341 screens of which 169 were diagnostic of an underlying DIC.
- Parameters with statistically significant predictive value for DIC: platelet count, D-dimers, antithrombin and aPTT.
- Parameters without statistically significant predictive value: fibrinogen and Thrombin Time (TT) (Table 2).
- Only 23 of the 169 (14%) patients with a DIC had a fibrinogen level below the normal reference range (2-4.0g/dl). Only 10 (6%) of these patients had a fibrinogen below 1g/dl to qualify for ISTH DIC point allocation. Acute promyelocytic leukaemia (APL) was present in 4 of the patients with a DIC and hypofibrinogenemia and 1 patient was post liver transplant. Hypoalbuminemia i.e. liver synthetic dysfunction was present in 13 (56%) of the hypofibrinogenemic patients with a DIC.
- S3 (31%) of the 169 DIC patients had a prolonged Thrombin Time (TT) and 84 (49%) had a prolonged aPTT. Incomplete correction of the TT related to elevated D-dimers in the range of 1.4-20mg/l with a laboratory. 14 (26%) of the patients with a normal aPTT had a prolonged TT which corrected with normal pool plasma in only 50%. The reason for the discordance between the prolongation of aPTT and TT and incomplete correction of TT may relate to heparin contamination of samples as TT is more sensitive to Heparin interference.

Conclusion

- Fibrinogen is part of the ISTH DIC scoring system although it is not very useful in most cases as it is an acute-phase reactant and remain normal despite ongoing consumption. The sensitivity of a hypofibrinogenemia for the diagnosis of DIC is only 28% and occurs only in very severe cases. The Clauss method for fibrinogen measurement is recommended if a DIC is suspected although FDPs can interfere with this assay. Patients with severe sepsis who would get an additional DIC score point due to fibrinogen levels below 1g/L, are uncommon.
- Thrombin Time (TT) is not included in the ISTH DIC scoring system but may be used in conjunction with a reptilase time to exclude heparin contamination of samples in patients with prolonged aPTT. The PT or aPTT is prolonged in about 50-60% of cases of DIC at some point although normal results do occur in DIC due to activated coagulation factors in the circulation and the TT can provide additional information in these situations.
- To improve cost-efficiency without compromising patient care in the screening of DIC, we recommend reconsidering fibrinogen and thrombin time analysis in the routine DIC panel in our setting. Fibrinogen measurement in patients with acute promyelocytic leukaemia (APL) is still advocated. Thrombin Time analysis in specific patients with normal aPTT results may add value.

References: