Usefulness of Pretest Clinical Scores (“the 4Ts”) and Their Correlation with the Rapid ID-heparin / PF4 Antibody Testing for the Diagnosis of Heparin Induced Thrombocytopenia.

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Introduction: Heparin treatment may mediate immune thrombocytopenia (HIT) and paradoxical thrombosis (thrombolysis) due to the formation of antibodies against heparin and platelet factor 4 complexes. The BCSH Guidelines (2006) recommend assessing the clinical probability of HIT prior to lab testing.

Aim: To evaluate the usefulness of a pretest clinical scoring system (the 4Ts)1 in combination with a rapid particle gel immunosassay (ID-PaGIA) in diagnosing the probability of HIT at a single centre.

Materials & Methods:
A. Total patients: n = 111 unselected
• Surgical: n = 57 (56 cardiopulmonary bypass surgery [CPB])
• Medical: n = 54
B. The “4Ts” includes (i) the severity, (ii) timing, (iii) association with thrombus and (iv) the likely cause of thrombocytopenia, and scores patients into low (0 - 3), intermediate (4 - 5) and high (6 – 8) risk groups of having HIT.
C. Particle Gel Immuno Assay: ID-PaGIA shows agglutination of polymer particles coated with Heparin/PF4 complex (HPF4) in the presence of specific anti-HPF4 antibodies of any immunoglobulin class.

Table 1. Management advice (as printed in the HIT request form along with the “4Ts” scores to aid the clinicians)

Table 2. The “4Ts” characteristics of HIT+ patients

Table 3. Correlation of 4Ts & PaGIA testing

Discussion:
• 4Ts and PaGIA had 100% concordance in ruling out HIT in low risk cases (100% negative predictive value). PaGIA was positive for only 39% (29/75) of intermediate & high 4Ts. Higher 4Ts scores may not always be predictive of HIT.
• PaGIA showed a FN rate of 24% and FP rate of 1.4% when judged against the clinical decision of having HIT. It gave weak / doubtful results in 4 cases; on repeat testing after a few days, results were negative in 1 and clear positive in 3 cases. The level of anti-HPF4 antibodies may vary and account for this. (PaGIA alone may not be sufficient to diagnose HIT)
• 4Ts scoring is difficult. Alternative causes of thrombocytopenia are commonly present - therefore most patients fall into intermediate or high risk groups (88%). However patients in high risk group were found to have significant risk of HIT (59%).

• All CPB patients with positive HIT testing showed a specific pattern of PC evolution. (P1 & P2 pattern of PC evolution has been reported to increase the diagnostic sensitivity of HIT in CPB patients 1-3).
• PaGIA in combination with 4Ts has been reported to be a reliable strategy to rule out HIT 4. PaGIA is a simple and quick test (results in < 1 h) making it clinically useful.

• Finally, incorporation of 4Ts and management advice to the HIT request form prompts clinicians to consider alternative anticoagulation even before HIT testing in high risk cases; and in low risk cases will aid the decision whether to investigate. (Patients scored as low risk do not seem to need lab testing - 32 avoidable requests in this audit)

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References:
2. ID-PaGIA heparin/PF4 antibody test (Dinamap, Dakkoht, Scotland).

Figure 1. Platelet evolution in CPB surgeries

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