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Short Communication

Is it Time to Renew the Guidelines for Diagnosis of HIT?

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Heparin-induced thrombocytopenia (HIT) is one of the major adverse drug reactions with high rate of morbidity and mortality in affected patients. Regardless of the high frequency of anti-PF4/Heparin antibody in patients receiving heparin (8 - 50%), only sensitive patients develop the clinical complications of HIT (approximately 0.2 to 3%) [1]; therefore, a challenging approach is necessary in order to prevent overdiagnosis of the disease.

The first step in HIT diagnosis is clinical evaluation of the patient according to one of the clinical scoring tools; 4Ts score and HIT expert probability (HEP) score [2]. 4Ts clinical scoring system which was developed by Warkentin consists of three categories as: low 4Ts (≤ 3), intermediate 4Ts (4 - 5) and high 4Ts (6 - 8), has been validated during several studies [3]. According to a recent meta-analysis, the low 4Ts score carries a high negative predictive value (99.8; 95%CI, 97 - 100) if conducted by expert observers [4]. However, there are several shortcomings for this scoring system. First: there is significant inter-observer variability which not only causes the intermediate and high 4Ts scores to be poorly effective in predicting disease, but also to be a reason for insufficiency of low 4Ts score for the exclusion of HIT in clinical practice [5]. In addition; strict considering, precise calculating and consistently documenting of 4Ts score by clinicians are a matter of doubt [5]. The other clinical score, HEP score, as defined by Cuker., *et al*. shows improved inter-observer correlation, but it is currently undergoing validation [6].

Since HIT is a clinicopathologic syndrome and considering the limitations of clinical scoring tools, the diagnosis of HIT is impossible without laboratory evidence of anti-PF4/heparin antibodies [1]. Based on a recent official recommendation of the Platelet Immunology SSC Working Group on HIT, "a diagnosis of HIT requires a clinical scenario in which HIT is judged to be the most plausible diagnosis, generally meeting at least an intermediate probability for HIT (judged by a clinical scoring system), plus either a strong-positive EIA-IgG or, preferably, a positive test for platelet-activating antibodies" [7].

Platelet-activating assays are regarded as "gold standard", however they are performed in few, specialized laboratories in a timely manner [8]. On the other hand, immunoassays are the most common tests which are widely used and are essential in the work up of suspected patients for HIT. Anti- PF4/heparin ELISA assay is the most available test with high sensitivity, but it suffers from 1) limited specificity due to incapability in distinguishing between pathogenic and non-pathogenic antibodies, and 2) it generally takes a turn-around time, not providing the results on the same day. These limitations lead to a clinically-based only management decisions by physicians with a high probability of over-diagnosis or on the other hand, postponing the decision until laboratory results are available which may result in a devastating outcome.

Recently, several rapid immunoassays (RIs) have been developed to overcome the limitations of ELISA. The results of RIs are provided in less than half an hour. All tests, detecting antiPF4/heparin (or other polyanions) antibodies but they differ widely based on the test principles, the class of recognized antibodies and the used thresholds used. Particle-gel immunoassay (PaGIA), IgG-specific chemiluminescent assay (IgG-CA), polyspecific chemiluminescence assay (Poly-CA), lateral flow immunoassay (LFIA), latex particle-enhanced assay

(HemosIL-Ab), particle immunofiltration assay (PIFA) are the current assays used as RIs [9]. There are several single-center studies for evaluating the characteristics of these tests, reporting the performance of each test in comparison with ELISA and/ or platelet activating assays. Quite recently, in two systematic reviews and meta-analyses, the diagnostic accuracy of (rapid) immunoassays has been evaluated [9,10]. Nagler., *et al*. have classified RIs into three categories of 1) combined high sensitivity and high specificity, 2,3) borderline and inadequate diagnostic accuracy respectively [10]. According to a meta-analysis by Sue., *et al*. IgG specific RIs appears to cause improvement in HIT diagnostic accuracy (high sensitivity and greater specificity in comparison with ELISA) [9]. The overall results of these studies show that the negative test results of RIs are only most valuable in patients with low and intermediate clinical probability scores and the reliability of its negative results in the cases with high 4Ts score, however rare but is still challenging. Due to the importance of timely and precisely diagnosis of HIT in prevention of misdiagnosis and further morbidity and mortality events, the relatively significant high rate of false negative results of RIs in patients with high probability clinical risk (4Ts ≥ 6) need to be considered. Some authors propose flowchart-based guidelines for the interpretation of the results for some the RIs; they also strongly recommend that these tests apply to only patients with a low or intermediate risk [11].

With respect to the discussion above, it appears that now is the time to review the HIT diagnostic guidelines with integration of RIs in the diagnostic algorithm.

Bibliography

1. Arepally GM and Ortel TL. "Heparin-induced thrombocytopenia". *New England Journal of Medicine* 355.8 (2006): 809-817.

2. Nagler M and Bakchoul T. "Clinical and laboratory tests for the diagnosis of heparin-induced thrombocytopenia". *Thrombosis and Haemostasis* 116.5 (2016): 823-834.

3. Lo GK., *et al*. "Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings". *Journal of Thrombosis and Haemostasis* 4.4 (2006): 759-765.

4. Cuker A., *et al*. "Predictive value of the 4Ts scoring system for heparin-induced thrombocytopenia: a systematic review and meta-analysis". *Blood* 120.20 (2012): 4160-4167.

5. Favaloro EJ. "Toward improved diagnosis of HIT". *Blood* 126.5 (2015): 563-564.

6. Cuker A., *et al*. "The HIT Expert Probability (HEP) Score: a novel pre-test probability model for heparin-induced thrombocytopenia based on broad expert opinion". *Journal of Thrombosis and Haemostasis* 8.12 (2010): 2642-2650.

7. Warkentin TE., *et al*. "Laboratory testing for heparin-induced thrombocytopenia: a conceptual framework and implications for diagnosis". *Journal of Thrombosis and Haemostasis* 9.12 (2011): 2498-2500.

8. Warkentin TE. "Demand on-demand testing for the diagnosis of heparin-induced thrombocytopenia". *Thrombosis Research* 140 (2016): 163-164.

9. Sun L., *et al*. "Diagnostic accuracy of rapid immunoassays for heparin-induced thrombocytopenia". *Thrombosis and Haemostasis* 115.5 (2016): 1044-1055.

10. Nagler M., *et al*. "Diagnostic value of immunoassays for heparin-induced thrombocytopenia: a systematic review and meta-analysis". *Blood* 127.5 (2015): 546-557.

11. Leroux D., *et al*. "Prospective evaluation of a rapid nanoparticle-based lateral flow immunoassay (STic Expert® HIT) for the diagnosis of heparin-induced thrombocytopenia". *British Journal of Haematology* 66.5 (2014): 774-782.

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