Prospective evaluation of a rapid nanoparticle-based lateral flow immunoassay (Stic Expert HIT®) for the diagnosis of Heparin-Induced Thrombocytopenia.

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INTRODUCTION and AIM OF THE STUDY

Heparin-induced thrombocytopenia (HIT) is a severe complication of heparin treatments associated with a high risk of venous and arterial thrombosis. HIT is often difficult to diagnose in clinical practice since most patients present several potential causes of thrombocytopenia. A scoring system named 4Ts and based on four criteria (i.e. Thrombocytopenia; Timing of platelet count fall; Thrombosis or other sequelae; Other causes of thrombocytopenia) is currently used to evaluate the probability of HIT before laboratory testing. Recently, a rapid lateral flow immunoassay (LFI) based on the use of PF4/polyanion complexes linked to both an antigen and of gold nanoparticles coated with antibodies specific to both has been developed (Stic Expert HIT®). This test is IgG specific since gold particles are immobilized on the microliter strip by anti-human IgG and become visible as a colored line when IgG antibodies to PF4/polyanion complexes are present in the patient sample (1).

RESULTS (1)

1. Positive diagnosis of HIT

The diagnosis of HIT was confirmed in 42 patients i.e. 12.5% of suspected HIT.

2. The "4Ts" score and exclusion of HIT

> HIT was excluded (negative SRA) in 94 of 97 patients identified as LR. Therefore, the negative predictive value (NPV) of the "4Ts" score was 96.8%.
>
> (1) Importantly, these 3 patients identified as having developed HIT despite a low "4Ts" score had undergone cardiac surgery with cardiopulmonary bypass.

DISCUSSION - CONCLUSION

> One major advantage of the LFI Stic Expert HIT® is the possibility of obtaining a result in less than 40 minutes. A strategy based on results of both the 4Ts score and this assay can therefore be proposed for the management of patients with suspected HIT in emergency conditions.
>
> The Stic Expert HIT® can be performed both on serum and plasma and a negative result is able to confidently rule out the diagnosis of HIT since NPV and negative LR values are excellent (>89% and <0.1 respectively).
>
> These performances are particularly useful in LR or IR patients, for whom heparin treatment can be continued safely if the Stic Expert HIT® is negative.

PATIENTS AND METHODS (2)

PLASMA (n = 332)

R1 R2

+ + + + + + + + 73 1 2

+ + 59 3 2

+ 4 244

SEUM (n = 257)

R1 R2

+ + 80 8 0

+ 4 244

+ 0 2 188

The interreader reproducibility was excellent whether the test was performed on plasma (kappa test ratio = 0.95) or on serum (kappa = 0.93).

All doublet (+/-) results were considered as positive.

An excellent concordance (kappa = 0.86) was evidenced between data obtained with fresh plasma and serum.

4. Performances of Stic Expert® to exclude HIT compared to asserachrom HPIA®

Plasma

No 245 47

Yes 188 37

Serum

No 246 49

Yes 0 2

The pretest probabilities were defined according to the frequencies of HIT in our 3 groups of patients (Low, Intermediate and High Risk).

The post-test probabilities were then calculated according to the positive and negative likelihood ratios (LR+ and LR-) of the Stic Expert® HIT and data obtained with plasma samples (Theorem of Bayes).

5. Performances of the "4Ts" score combined with Stic Expert® to exclude HIT

Stic Expert HIT® was performed on Serum and Plasma in each center with a reading done independently by two different technicians or biologists.

The diagnosis of HIT was confirmed when both SRA and HPIA ELISA were positive.

PATIENTS AND METHODS (1)

Suspected HIT

All patients with clinical suspicion of HIT were included in the study. Consecutive patients were enrolled between February 2010 and October 2012 in 10 different centers. 43 patients were excluded from the study because of clinical information or plasma/serum samples were missing. 337 patients were thus analyzed in this prospective study.

Clinical history was recorded and the probability of HIT was evaluated using the <4Ts > score (2) and then compared to the results of the Stic EXPERT HIT®.

Stic Expert HIT® was performed on Serum and Plasma in each center.

Centralized assays (Tours Hospital, France) :

- Asserachrom HPIA IgG (Stago, France)

- Sanitron Release Assay (SRA)

The diagnosis of HIT was confirmed when both SRA and HPIA ELISA were positive.

The authors have no relevant financial relationship to disclose.

Aims of this study

- To evaluate the performances of this rapid assay in a large prospective cohort of patients with suspected HIT.

- To compare the results obtained with serum and plasma samples.

- To evaluate the inter-reader reproducibility of assay.

The pre-test probability of HIT is about 10% (Intermediate risk) and of HIT is positive (LR+ = 43%). If Stic Expert® HIT is negative (LR- = 0.05), and will be lower than 1% if Stic Expert® HIT is negative (LR- = 0.03).