Evaluation of a New, Automated Quantitative Factor XIII Assay

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Evaluation of a New, Automated Quantitative Factor XIII Assay.

K. Alhomsi[1], R. O. Salem[1], K. A. Morin[2], E. M. Van Cott[1]
[1]Massachusetts General Hospital, Department of Pathology, Boston, MA.
[2]Instrumentation Laboratory, Lexington, MA.

Introduction

There is a need for a quantitative, easy-to-perform Factor XIII (FXIII) assay. The most commonly used FXIII assay is a manual, qualitative assay that can only detect severe deficiencies of < 2% FXIII activity. Alternatively, a chromogenic FXIII assay exists that measures FXIII activity. Inherited FXIII deficiencies reported to date have shown decreased antigenic and activity levels, where no known cases have shown decreased activity with normal antigenic levels. In acquired deficiencies, the measured antigenic levels of FXIII (subunit A) is proportional to the activity levels, although they may not be identical, particularly after replacement therapy (Lim 2004). In addition, there is some evidence that heterozygous FXIII deficiency might be associated with bleeding symptoms (Ivaskevius, 2007).

HemosIL® Factor XIII Antigen (Instrumentation Laboratory) is a new, automated latex enhanced immunoassay for the quantitative determination of FXIII antigen (subunit A) in human citrated plasma. It is a liquid, ready-to-use reagent that simplifies the screening of genetic and acquired FXIII deficiency.

Methods

HemosIL Factor XIII Antigen (FXIII Ag) assay was performed on an ACL TOP® Hemostasis Testing System. A normal range study for FXIII Ag was performed by analyzing 45 normal samples to establish a reference range. A patient population of 74 samples was assayed with FXIII Ag, and also with an established quantitative chromogenic FXIII activity assay (Berichrom XIII, Dade Behring) on an AMAX 400 (Trinity Biotech).

Objective

- Evaluate a new, automated quantitative FXIII antigen assay by comparing it against an established, chro mogenic method.
- Test the ability of the assay to diagnose low FXIII to explain positive bleeding history in patients with no other bleeding disorders
- Validate the FXIII Ag assay on the ACL TOP System

Patients

- Twenty-three patients undergoing FXIII testing, one of whom had congenital FXIII deficiency
- Twenty patients with a personal or family history of bleeding and normal von Willebrand factor results
- Eleven patients with normal FVIII levels
- Twenty unselected inpatients

Results

The mean FXIII value was 91.6 % using the new antigen assay and 93.6% using the activity assay, with no significant difference using a paired, two-tailed T-test ($p = 0.36$). A Bland-Altman plot revealed no discernible bias between the two methods (Figure 1). Linear regression revealed an R value of 0.8 (Figure 2).

Low FXIII activity (≤70%, range 28-70) was present in seventeen of the seventy-four patients. If considering the activity results to be the 'gold standard,' fifteen of seventeen antigen results were also ≤ 70% for a sensitivity of 88% (15/17) (Table 1). The two discordant pairs were: 77% antigen versus 63% activity, and 82% antigen versus 63% activity. Among the fifty-seven specimens with >70% activity, antigen results were also >70% in fifty-five, for a specificity of 95% (55/57) (Table 1). The two discordant pairs were 55% antigen versus 79% activity, and 62% antigen versus 79% activity.

The normal range for the FXIII Ag assay was calculated to be 70.2 - 146.8%, while the normal range for the FXIII activity assay was 60 - 150%. Based on these ranges, thirteen discordant pairs exist in total. Of the samples that fell within range for the activity assay, one sample surpassed the high limit of the antigen assay normal range. Eleven pairs had disagreement due

to activity values that fell outside the low limit of the normal range; however seven of the eleven had differences of < 10%. Of the samples that fell out of the normal range for the activity assay, one sample, which fell out of range on the high end, was within range for the antigen assay (Table 1).

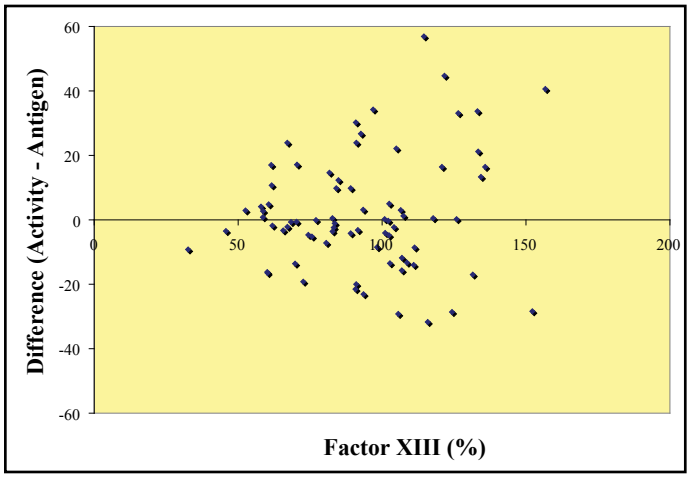

Figure 1
Bland-Altman plot showing no discernible bias between the antigen and activity methods.

No difference was observed when comparing the results of the FXIII Ag assay on the ACL TOP versus the FXIII activity assay.

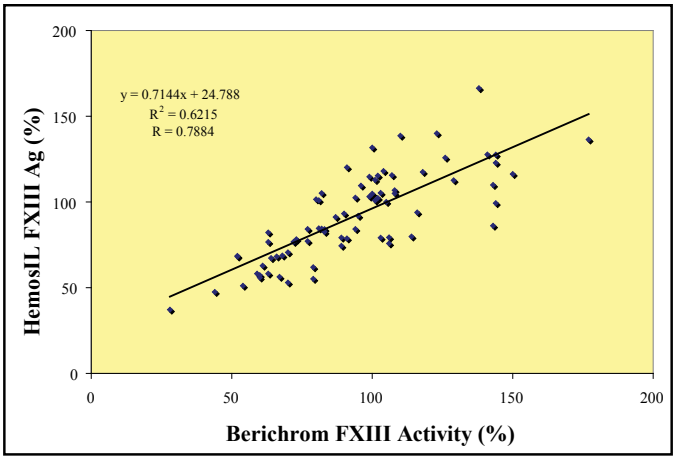

Figure 2
Linear regression for the antigen method versus the activity method.

Linear regression analysis demonstrates an r value of 0.8 and a slope of 0.7 when comparing the FXIII Ag assay to the activity assay.

Table 1
Classification of Results

Reference Method Result Category	No. of Cases	Berichrom FXIII Activity	HemosIL FXIII Ag
> 70% (n = 57)	55	> 70%	> 70%
	2	> 70%	≤ 70%
≤ 70% (n = 17)	15	≤ 70%	≤ 70%
	2	≤ 70%	≥ 70%
Within normal range (n = 67)	55	Within normal range	Within normal range
	1	Within normal range	Outside high limit
	11	Within normal range	Outside low limit
Outside normal range (n = 7)	6	Outside normal range	Outside normal range
	1	Outside high limit	Within normal range

Conclusions

HemosIL FXIII Ag assay appears to be an improvement over the manual, qualitative assay in that, it is quantitative and automated.

FXIII Ag performs adequately when compared to a quantitative activity assay in terms of numerical agreement and clinical classification.

References

Ivaskevius V, Seitz R, Kohler HP et al. International registry on FXIII deficiency: a basis formed mostly on European data. *J Thromb Haemost* 2007; 914-921.

Lim W, Moffat K, Hayward CPM. Prophylactic and perioperative replacement therapy for acquired FXIII deficiency. *J Thromb Haemost* 2004; 2:1017-1018.