Factor XIII levels in haemophilia: Treatment implications

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Introduction

Haemophilia is characterised by abnormal thrombin generation resulting in the formation of unstable clots and characteristic bleeding symptoms associated with haemophilia. Recent laboratory studies indicate that adding standard factor concentrates combined with FXIII maximally enhances clot stability in whole blood and plasma from individuals with haemophilia[1, 2]. It is unclear whether the clot promoting effect of adding FXIII results from a correction in unexpectedly low FXIII levels in patients or due to the effect of enhancing FXIII to supraphysiological levels.

The aim of this study was to perform a retrospective survey of FXIII measurements made in patients with haemophilia over 3 years to establish whether levels were within a normal range. It was hypothesized that FXIII levels would not differ from the reference range.

Methods

FXIII antigen was evaluated using the HemosIL FXIII antigen assay (ACL Top, Intrumentation Laboratory, Bedford, MA). A database search (following approval) extracted FXIII measurements from patients with haemophilia. The results were compared to a reference established on in-house samples from 50 healthy adults (0.61-1.77 Arbitrary Units (AU) x 10^3/L).

Results

23 FXIII results were collected from 22 patients **(table 1)**. Two measurements were from a patient with moderate haemophilia A, and one of the measurements performed during an acute and significant haemorrhage was excluded from analysis.

FXIII levels lay within the normal reference range for all patients and there was no difference in mean values comparing individuals with mild, moderate and severe haemophilia (Mann-Whitney P>0.3) **(table 1)**. Of note, FXIII levels show correlation with age (Spearman rank p<0.016), reflecting reports in the general population[3] **(figure 1)**.

> *It is unclear whether the clot promoting effect of adding FXIII results from a correction in unexpectedly low FXIII levels in patients or due to the effect of enhancing FXIII to supraphysiological levels*

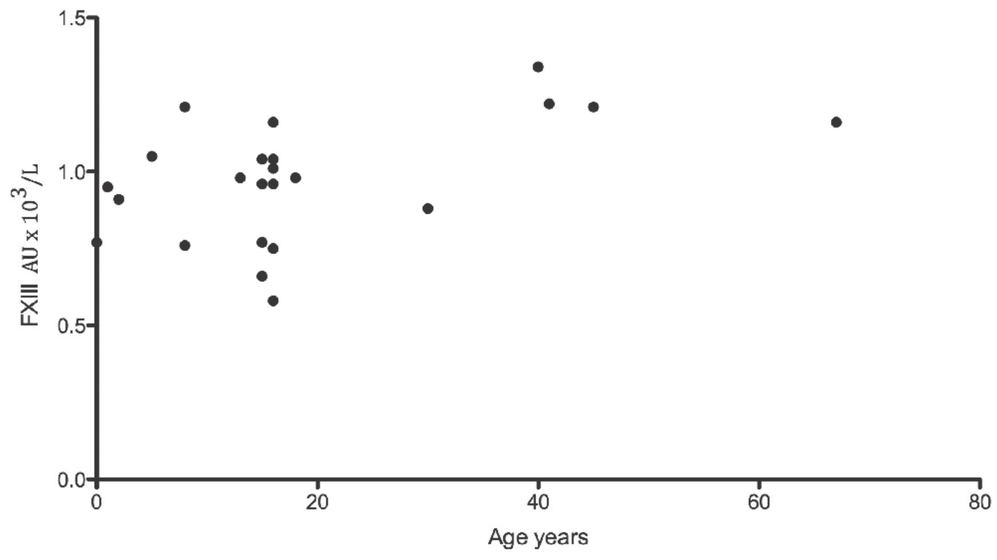
Conclusions

In this retrospective survey, FXIII levels in individuals with haemophilia do not differ from the normal range. This indicates that adding FXIII to factor deficient whole blood or plasma in laboratory studies improves clot stability by raising FXIII levels to a supra-physiological level, rather than by correcting an underlying FXIII deficiency.

Table 1: Patient demographics and FXIII results

Number	Age	Haemophilia	Severity	FXIII (AU x 10^3/L)
1	18	A	Moderate	0.98
2	67	A	Mild	1.16
3	15	A	Severe	0.96
4	1	A	Moderate	0.95
5	15	A	Severe	1.04
6	16	A	Severe	1.01
7	45	B	Moderate	1.21
8	16	A	Severe	0.75
9	16	A	Mild	1.04
10	41	B	Mild	1.22
11	5	A	Moderate	1.05
12	8	A	Moderate	0.76
13	13	A	Mild	0.98
14	40	A	Moderate	1.34
15	16	A	Mild	1.16
16	15	A	Mild	0.66
17	16	A	Mild	0.96
18	15	A	Mild	0.77
19	2	A	Moderate	0.91
20	8	A	Moderate	1.21
21	0	A	Severe	0.77
22	30	A	Severe	0.88

Figure 1: Demonstrates correlation between FXIII level and age in population with haemophilia



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WFH2012 46--Tu
Clotting Factor Concentrates
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DOI: 10.3252/pso.eu.WFH2012.2012
Poster presented at: WFH 2012 World Congress