Clinical and laboratorial evaluation of recombinant FVIII Fc fusion protein treatment in hemophilia A patients: a real-life experience in a single center

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INTRODUCTION AND OBJECTIVES

The mainstay of treatment for hemophilia A (HA) is replacement therapy with FVIII concentrates. An adequate laboratory control is necessary for optimization of dosing. New modified rFVIII Fc fusion protein (rFVIIIFc) was recently approved for hemophilia A treatment, and in our hemophilia center we started using it thanks to a humanitarian aid from the World Federation of Hemophilia. The aim of this study was to evaluate the clinical efficacy of the product and laboratory behavior using the available methods

TABLE 1: CHARACTERISTICS OF PATIENTS AND CLINICAL BEHAVIOR

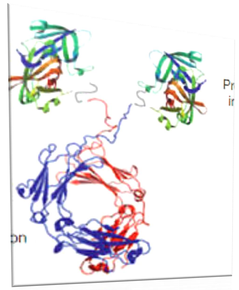
Severe Hemophilia A patient (n)	Moderate Hemophilia A patient (n)	Median age	Dose (IU/Kg^{-1})	Clinical response
21	3	27.5 (11 – 58)	40.4 (20 – 59)	Excellent = 17 (70.8%) Very good = 5 (20.8%) Good = 1 (4.2%) Regular = 1 (4.2%)

TABLE 2: DIFFERENCES BETWEEN METHODS IN POST INFUSION PLASMA SAMPLES

Level FVIII 1h post (IU/dl^{-1}) OSA	Level FVIII 1h post (IU/dl^{-1}) CSA	Mean diference Between methods 1h post (%)	Level FVIII 3h post (IU/dl^{-1}) OSA	Level FVIII 3h post (IU/dl^{-1}) CSA	Mean diference Between methods 3h post (%)	Level FVIII 24h post (IU/dl^{-1}) OSA	Level FVIII 24h post (IU/dl^{-1}) CSA	Mean diference Between methods 24h post (%)
70	**102.3**	**29.8 (17.1 – 57.4)**	**70.2**	**98.9**	**28.1 (15.1 – 56.3)**	**26.5**	**27.8**	**5.2 (2.3 – 30)**

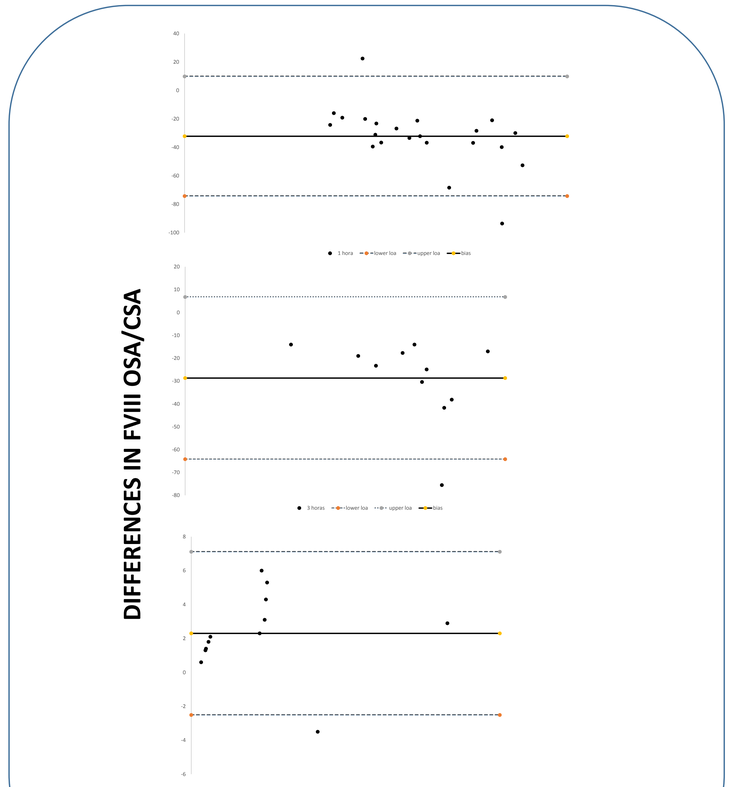
MATERIALS AND METHODS

We treated 24 patients with hemophilia A (21 severe and 3 moderate) the median age was 27.5 years (range=11-58), patients came to our center for treatment of bleeding episodes, post surgery or secondary prophylaxis. The dose used vary from 20 to 59 IU kg^{-1} and the initial regimen for prophylaxis was every four days. We evaluate the clinical efficacy and monitoring FVIII levels using one stage-OSA (aPTT-SP reagent, HemosIL, Italy) and chromogenic substrate assay-CSA (Electrochrome, HemosIL, Italy) before the infusion of FVIII concentrates and after 1, 3 , and at different times up to 96 hours.



RESULTS

rFVIIIFc was well tolerated and efficacious for treatment and prophylaxis; no adverse event was observed. Laboratory: Mean incremental recovery for the OSA was 1.7 IU/dl per IU/Kg and for the CSA was 2.3 IU dl^{-1} per IU Kg^{-1}; mean difference between methods ~ 29.6% (17-52%). In 25% (6/24) the difference is higher reaching 50% in some cases, this could have clinical implications in order to avoid overdosing. At FVIII levels around 20 IU dl^{-1} the differences between methods decreases (~5%) while at FVIII levels less than 5 IU dl^{-1} (troughs levels) the chromogenic result was lower than the OSA.



BLAND ALTMAN ANALYSIS OF FVIII ACTIVITY MEASURED BY OSA AND CSA IN 1 HOUR, 3 HOUR AND 72 HOUR POST INFUSION PLASMA SAMPLES

CONCLUSIONS

The rFVIIIFc is an excellent treatment option however there are some issues to be considered regarding the laboratorial behavior. Based in these results prophylactic regimen was modified in some patients. Clinical and laboratory results could allow us to avoid overdosing and to modify prophylactic regimen in order to optimize the use of this product.

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