INTRODUCTION

- **BACKGROUND**
  Guidelines for management of haemophilia recommend that subjects perform regular and appropriate physical activity. In moderate and mild haemophilia A subjects, exercise induces an endogenous factor VIII (FVIII) half-life. In severe haemophilia A subjects, exercise induces a transient increase of von Willebrand factor Antigen (VWF:Ag) with no significant difference in FVIII mean half-life. VWF:Ag increase is notably higher in non-O blood group subjects.

- **AIMS**
  To evaluate the impact of VWF:Ag on FVIII PK (null mutations) in young adults with severe haemophilia A performing moderate-intensity physical activity.

METHODS

- **STUDY PROTOCOL**
  The study involved 4 visits by participants: two 9 h visits (visit 1: «rest» and visit 2: «exercise», and two 1 h visits, the following morning (Fig. 1). Blood specimens were collected before infusing FVIII and at 15 min, 1h, 3h, 6h, 9 h and 24h. During the visit 1, participants remained sedentary, while during the visit 2: «exercise», and two 1 h visits, the following morning (Fig. 1).

- **EXCLUSION CRITERIA**
  - Subjects with non-O blood group (n=5).
  - Subjects with non-O blood group had a greater increase in VWF:Ag (+34%, range: +18 to 58,4%) when performing moderate physical activity as compared to subjects with O blood group subjects; and from 10h14±3h15 to 11h19±3h15 (p=0,6250) in non-O blood group subjects.
  - A threshold value of +24% in VWF:Ag level discriminated subjects with increased half-lives from subjects with decreased half-lives.

RESULTS

- **SUBJECTS CHARACTERISTICS**
  12 young adults age 19 to 31 years (median: 23,5 years) participated to visit 1 and visit 2. Median age was 23.5 y (range 19-31 y). Median HJHS score was 4.5 (range 0-13), median global gait score was 1 (range 0-4). Median body mass index (BMI) was 23.7 kg/m² (range 18.9-32.9 kg/m²). FVIII prophylaxis varied from 1-7/wk (median 7/wk) of 500-2000 IU (median 600 IU), and 6-32 IU/kg (median 8.5 IU/kg/day). All patients used Hemilise F5®, except one, who used Xyntha®.

- **LABORATORY ASSAY**
  FVIII activity was measured with the one-stage clotting assay and VWF:Ag with an immunoturbidimetric assay on platelet-poor-plasma. Differences between rest and exercise were compared with two-way ANOVA with Bonferroni post-test and Wilcoxon matched-pairs signed -Ranks test. A p value <0,05 was considered significant.

- **SUBJECT RECRUITMENT:** The study was approved by the medical Ethics Committee of the CHU Sainte-Justine. All subjects gave written, informed consent for participation in the study.

INCLUSION CRITERIA

- FVIII <10%, null mutation
- 18-30 years old
- on a prophylaxis treatment regimen with recombinant FVIII product
- a Haemophilia Joint Health Score (HJHS) <15 at the knee or ankle joint

EXCLUSION CRITERIA

- presence of inhibitors
- clinical signs of active bleeding

CONCLUSIONS

The extent of VWF:Ag rise during moderate-physical activity contributes to FVIII half-life variation. This pilot study suggests a potential influence of ABO blood group in the modulation of therapeutic FVIII replacement through a higher VWF:Ag rise during exercise. The limitation of the study being the small sample size, a larger study is currently being conducted in order to validate these results.

REFERENCES


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