Plasma Tissue Factor Pathway Inhibitor (TFPI) Levels in Healthy Subjects and Patients With Hemophilia A and B

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INTRODUCTION
- Hemophilia A, caused by a deficiency of the coagulation factor VIII (FVIII), can result in spontaneous bleeding into joints, muscles, and internal organs.
- About 30% of patients treated with recombinant FVIII (rFVIII) develop anti-FVIII inhibitors and rely on bypassing agents such as recombinant activated factor VII (rFVIIa) and activated prothrombin complex concentrate. Other bypass agents such as anti-tissue factor pathway inhibitor (TFPI) monoclonal antibody (mAb) and the bispecific antibody ACE910 have been used in clinical trials.
- TFPI is a potent inhibitor of factor Xa (FXa) and the FVIIa-activating complex. About 30% of patients treated with recombinant FVIII (rFVIII) also have free TFPI levels in plasma.

RESULTS
The individual plasma samples used for the analyses were as follows:
- Healthy Subjects (n=30)
- Hemophilia A (n=15) with and without inhibitors (n=9) were from HRF Inc (Raleigh, NC).
- FVIII (n=12), severe hemophilia B (n=9), or severe hemophilia A and B (n=15) were treated by hemophilia care centers in the US for the detection.

Statistical Analyses
- Statistical significance was assessed using GraphPad Prism 5 (1-way analysis of variance, Dunnett multiple comparison test), and 2-tailed P values <0.05 were considered significant.

METHODS
Study Samples
- The individual plasma samples used for the analyses were as follows:
  - Individual and pooled human plasma anticoagulated with 3.2% sodium citrate (BioreclamationIVT, Westbury, NY) from healthy donors (n=30; 15 men and 15 women, ranging in age from 18-71 years) was used.
  - Plasma samples from 30 patients with severe hemophilia A (n=12), severe hemophilia B (n=8), or severe hemophilia A with inhibitors (n=9) were from HRF Inc (Raleigh, NC). FVIII and FIX activity were confirmed to be <1%.

CONCLUSIONS
- The plasma TFPI levels in healthy individuals showed no statistical differences with regard to sex or to Hispanic, black, or white race (Figure 3; Figure 4).
- No correlation between age and plasma TFPI levels (Figure 5).

REFERENCES

Acknowledgments
This is a poster presentation. The plasma TFPI levels in healthy individuals and patients with severe hemophilia A and B were determined using the ELISA assay described above. The free TFPI ELISA assay shows very good precision, accuracy, and reproducibility and should capture coagulation-related forms of TFPI from plasma.

DISCLOSURES
All authors are employees of Bayer.

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