MONITORING RARE BLEEDING DISORDERS AND THEIR RESPONSE TO THERAPEUTIC TREATMENTS WITH A MICROCHIP FLOW-CHAMBER ASSAY

P. Acuña [1], E. G. Arias-Salgado [1], E. Monzón Manzano [1], M. Martín Salces [1], M.T. Álvarez Román [1], M.I. Rivas Pollmar [1], S. García Barcenilla [1], T. Cebanu [1], E. Gonzalez Zorrilla [1], N. Butta [1], V. Jiménez Yuste [1]
[1]Service of Hematology, Hospital Universitario La Paz, Madrid, Spain, Madrid, Spain

1- INTRODUCTION

The management of congenital rare bleeding disorders (RBDs) and von Willebrand disease (VWD) is difficult due to the wide spectrum of clinical phenotypes and to several procoagulant responses to different treatments.

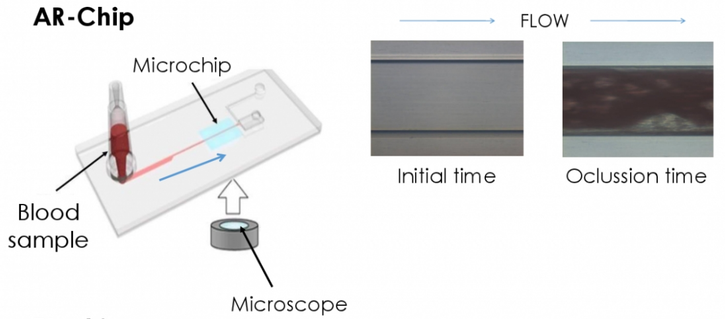
2- AIM

To test the usefulness of a microchip flow-chamber system (T-TAS®) for analyzing haemostatic and coagulation status in RBDs and type-3 VWD, and the response to different treatments.

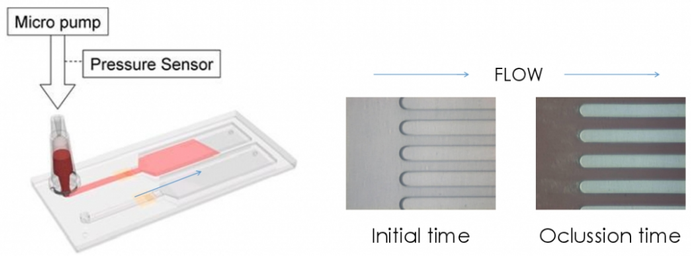
3- METHODS

We recruited one patient of each deficiency:
FVII (5%), FXI (<15%), FX (5%), FXIII (5%), VWD type-3 (0% VWF / 0.4% FVIII) and five healthy controls. Microchips coated with either collagen plus thromboplastin [(AR)-chip] or collagen [platelet (PL)-chip] were used to evaluate fibrin-rich platelet thrombus formation or platelet thrombus formation.

AR-Chip



PL-chip



4- RESULTS

Using AR-chips, deficiencies of FVII (Fig.1A) and FXI (Fig.1B) caused an anomalous clot formation. *In vitro* treatment of samples with replacement factor restored coagulation profile in FVII and FXI deficiencies. Anti-TFPI corrected the deficiencies although less effectively. FX deficiency prevented clot development and treatment with PCC or anti-TFPI scarcely improved it (Fig.1C). Lack of FXIII did not affect clot formation (Fig. 1D).

The impairment in coagulation (Fig.2A) and primary haemostasis (Fig.2B) observed in type-3 VWD was partially corrected by pdFVIII/VWF, whereas anti-TFPI was almost ineffective.

5- CONCLUSION

Analysis with *a flow* chamber-based assay to measure thrombus formation *in vitro* may be useful for the evaluation of the coagulation profile in RBDs and VWD and for monitoring effects of therapeutic treatments. Anti-TFPI was effective for correcting FVII and FXI deficiencies but have poor effects for amending FX deficiency and VWD.

Authors are extremely grateful to Zacros (Tokio, Japan) for their support

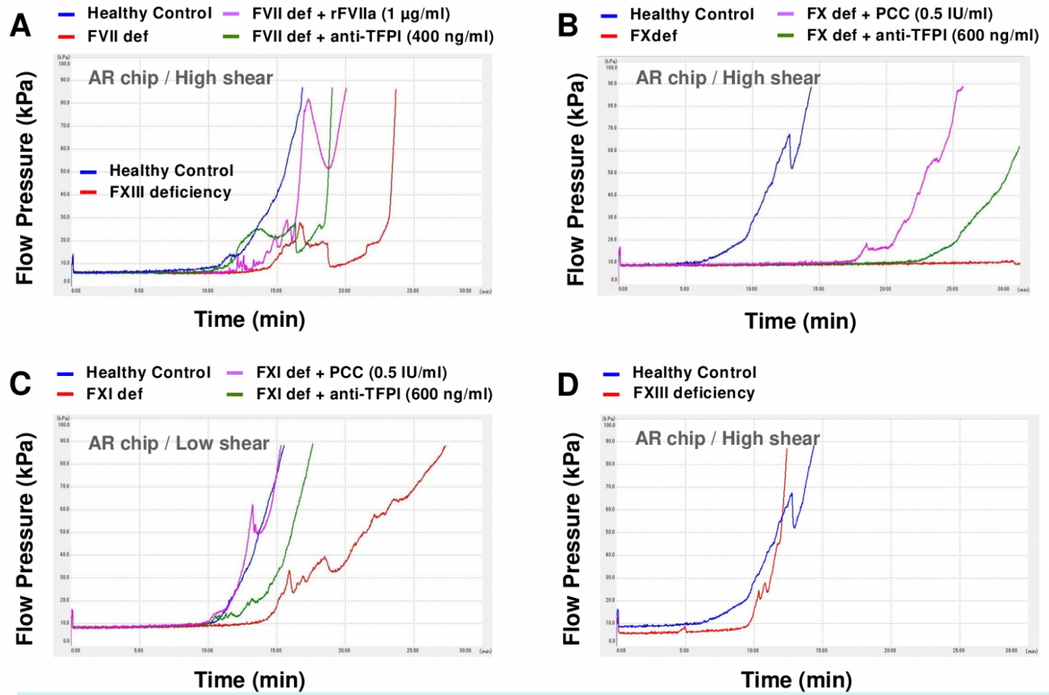


Fig.1: Time/pressure curves of T-TAS assay using AR-chips: (A) FVII deficiency, (B) FXI deficiency, (C) FX deficiency, (D) FXIII deficiency before or after spiking with indicated treatment. PCC: Prothrombine complex concentrate; rFVIIa: recombinant activated Factor VII; anti-TFPI: Tissue Factor Pathway Inhibitor neutralizing antibody.

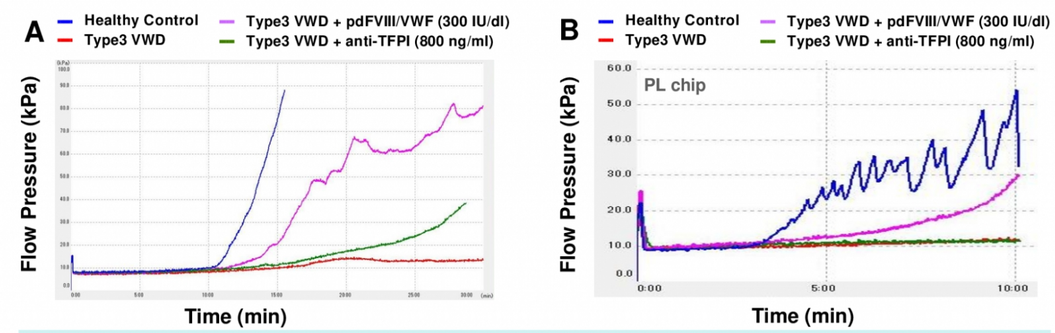


Fig.2: Time/pressure curves of T-TAS assay using AR-chip (A) or PL-chip (B) with healthy controls or type-3 VWD patient, before or after spiking with indicated treatment. pdFVIII/VWF: plasma-derived Factor VIII - Von Willebrand Factor; anti-TFPI: Tissue Factor Pathway Inhibitor neutralizing antibody.