

Combined Point of Care Tools Are Able to Improve Treatment Adherence and Health-Related Quality of Life in Patients with Severe Hemophilia: An Observational Prospective Study

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Introduction: Ultrasound (US) assessment of joints is an evolving point of care tool for the detection of early joint arthropathy (Napolitano M, Kessler CM. Hemophilia A and B. Consultative Hemostasis and Thrombosis, Kitchens, 4th edition); population pharmacokinetic (pop-PK) studies are adopted as a useful instrument to set the prophylaxis regimen for patients with hemophilia, they may improve adherence (Nagao A. et al. Thromb Res. 2019 Jan; 173:79-84) and reduce the annual bleeding rate (ABR). Adherence to continuous intravenous administrations of factor VIII or Factor IX products is challenging, thus patients may experience breakthrough bleedings while on prophylaxis. Repeated US examinations of joint status have recently been advocated to attempt to remedy sub-optimal medication adherence (Di Minno A et al., Blood Rev. 2019 Jan;33:106-116). Aim of the current prospective analysis was to evaluate the impact of combined US assessment and pop-PK study on adherence to treatment and health related quality of life in patients with severe hemophilia A(HA) and B (HB) under regular prophylaxis.

Material and methods: This prospective observational study was performed at a single tertiary center from January 2017 to June 2019. Research was conducted following the Helsinki Declaration. All patients included in the study provided a written informed consent for study participation. Patients with severe HA and HB routinely underwent, as part of regular 12-months follow-up visits, the following: US joints evaluation of elbows, knees and ankles using the HEAD-US protocol, treatment adherence evaluation by VERITAS-Pro questionnaire, health -related quality of life assessment by the standardized EQ-5D, EQ-VAS and pop-PK study (WAPPS-Hemo, McMaster University) as needed (i.e. in case of changes in life style, planned treatment switch); each patient visualised US and his estimated PK profile during medial encounters. Compliance to the prescribed treatment was also determined by analysis of patient diaries with infusion logs. Statistical analysis was performed using the SPSS software version 25.0 (SPSS Chicago, IL). Statistical tests were 2-sided, with a significance threshold of 0.05.

Results: Twenty consecutive males with severe haemophilia were included in the current analysis, 13 with severe HA, 2 with HA with previous inhibitors and 5 HB, with a median age of 30 (range 14- 56) years and a median ABR of 5 (range:0-12). Nine patients were under primary prophylaxis, 8 under secondary prophylaxis and 3 under tertiary prophylaxis, they all self-infused at home. Four patients had one target joint and 3 patients had multiple target joints. For each enrolled subject, HEAD-US score, VERITAS-pro, EQ5D and EQ-VAS score were assessed at enrolment (T0) and at 12 (T12) and 24 (T24) months follow-up visits, respectively. Pop-PK was assessed in 11 patients: in 7 (5 HA, 2 HB) it was assessed twice, before and after treatment switch to extended half-life (EHL) products, in 4 it was assessed once to modify prophylaxis treatment schedules for a more active life-style (N=2) or weight changes (N=2). Median ABR was 4 at T12 and 3.8 at T24. Reported breakthrough bleeds at T12 were 14, mainly trauma-related (N= 8) or affecting target joints (N=4), they were not reported at T24 in patients with PK-driven modified schedules (N=4) and in 4 patients under EHL treatments. Mean HEAD-US score at T0 resulted 8 (range:0-16), at T24 it was 6 (range:0-16). Mean Veritas-Pro score values were

42.7 at T0, 40.1 at T12 and 38.7 at T24. At T0, EQ-5D mean utility score was 0.82 (range: 0.68-1), at T24, the mean was 0.87 (range:0.72-1). In detail, at 24 months follow-up, there was a statistically significant ($p<0.05$) improvement in adherence to treatment with particular reference to the dimensions of communication and skipped doses. A tendency toward improved HEAD-US score, higher adherence and better quality of life scores, was observed in particular in patients switched to EHL products at T24, at a mean of 10 months after switching (range: 6-22 months).

Conclusion: Several combined measures of haemophilia treatment monitoring, allowing visual assessment of joints status and PK profile estimates by patients have here shown to improve treatment adherence and quality of life in patients with HA and HB, this may be not only related to new available treatments but also to an increased awareness and education of patients.

Disclosures

Napolitano: *BIOFVIIIx*: Consultancy; *Novonordisk*: Consultancy, Speakers Bureau; *Shire*: Other: Expert Testimony, Speakers Bureau; *Kedrion*: Other: Expert Testimony, Speakers Bureau; *Octapharma*: Speakers Bureau; *Bayer*: Consultancy, Other: Expert Testimony. **Di Minno:** *Novo Nordisk*: Speakers Bureau; *CSL*: Speakers Bureau; *Sanofi*: Speakers Bureau; *Bayer*: Consultancy, Honoraria, Speakers Bureau; *Kedrion*: Speakers Bureau; *Pfizer*: Speakers Bureau.