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ADHERENCE TO PROPHYLAXIS WITH HELIXATE NEXGEN IN CHILDREN, ADOLESCENTS AND ADULTS WITH SEVERE HAEMOPHILIA A – AN ITALIAN PROSPECTIVE OBSERVATIONAL MULTICENTRE SHAPE STUDY

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Introduction

- Prophylaxis in haemophilia patients reduces the incidence of bleeds and the development of arthropathy [1]. Prophylaxis is as well beneficial for patient's quality of life [2,3,4]. Strict adherence to treatment is crucial to obtain the efficacy of such regimen [5]. In the literature no prospective studies evaluating adherence in persons with haemophilia (PWH) are available.
- The primary purpose of this study was to collect prospective data on adherence to primary and secondary prophylaxis in haemophilia patients using Helixate NexGen® over 36 months.
- This Study was sponsored by CSL Behring S.p.A., Italy.

Methods

- The study population included subjects of any age with severe Haemophilia A (FVIII:C<1%) who were prescribed long-term prophylaxis regimen (at least one infusion/week for at least 46 weeks per year) with Helixate NexGen® for at least 6 months prior to the study enrolment.
- Adherence was measured as percentage change of administered concentrate with respect to the prescribed amount.
- Therapeutic adherence was classified under groups at 5 different levels (see definition in box on the right side).
- A subject was defined as adherent if his adherence level was high or medium, while the subject was defined as non-adherent in case of low, minimum or absent compliance.
- Demographic and clinical data were collected via electronic CRF. The orthopaedic status was assessed with the WFH Orthopaedic Joint Score (OJS [6]) or the Hemophilia Joint Health Score (HJHS [7]).

Definition Adherence

- **High adherence: if % change was within ± 11%**
- **Medium adherence: if % change ranged from ± 11% (included) to ± 25%**
- Low adherence: if % change ranged from ± 25% (included) to ± 33%
- Minimum adherence: if % change ranged from ± 33% (included) to ± 50%
- Lack of adherence: if % change was >= ± 50%

Results

Socio-demographic and Clinical Data

- Forty-two PWH from 14 Italian Haemophilia Centres were enrolled; 40 patients fulfilled all inclusion criteria:
  - 12 children (30%)
  - 9 adolescents (22.5%)
  - 19 adults (47.5%)
- Patients had a median number of 1 bleed in the previous year (range 0-60): children 1.5 (range 0-51); adolescents 0 (range 0-60); adults 1 (range 0-19)
- The absolute number of bleeding events reported during the second year was significantly lower than that of the first year: 158 vs. 43 in children/adolescents and 62 vs. 34 in adults: (Chi^2=29.21, p<0.0001).
- The mean orthopaedic joint score was in
  - adults (M_{OJS}=10.15±9.8) and in kids (M_{HJHS}=1.63±2.2)

Classification of Adherent Patients

	Age Groups											
	Children < 12 years			Adolescents 12-17 years			Adults ≥ 18 years			Total		
Level of Adherence	N	%	I.C. (95%)	N	%	I.C. (95%)	N	%	I.C. (95%)	N	%	I.C. (95%)
No	1	8.3	[-45.8 - 62.5]	1	11.1	[-50.5 - 72.7]	2	10.5	[-32.0 - 53.1]	4	10	[-19.4 - 39.4]
Minimum	2	16.7	[-35.0 - 68.3]	-	-		2	10.5	[-32.0 - 53.1]	4	10	[-19.4 - 39.4]
Low	1	8.3	[-45.8 - 62.5]	1	11.1	[-50.5 - 72.7]	2	10.5	[-32.0 - 53.1]	4	10	[-19.4 - 39.4]
Medium	3	25	[-24.0 - 74.0]	3	33.3	[-20.0 - 86.7]	3	15.8	[-25.5 - 57.1]	9	22.5	[-4.8 - 49.8]
High	5	41.7	[-1.5 - 84.9]	4	44.4	[-4.3 - 93.1]	10	52.6	[21.7 - 83.6]	19	47.5	[25.0 - 70.0]
	12	**100**		**9**	**100**		**19**	**100**		**40**	**100**	

Differences between Adherent and Non-Adherent Patients

- **70% of patients were classified adherent to prophylaxis.**
- At least *one bleed* occurred in "adherent" patients as follows:
  - 50% in the year before enrolment
  - 34.4% in the first year
  - 31.3% in the second year
  - 28.1% in the third year
- In "adherent" patients HJHS scores decreased from M_{HJHS}2.3±3.2 to M_{HJHS}0.1±0.4, while OJS scores remained the same.
- The presence of target joints dropped from 67.9% at baseline to 48.1% in the "adherent" group, while remaining stable in the "non-adherent" group.
- During observation, the mean number of school/work days lost decreased more in adherent patients (from 3.4±6.8 to 0.2±0.9) in comparison to non-adherent patients (from 8.5±12.6 to 2.8±4.0).

Conclusion

This study is the first study to our knowledge that has prospectively assessed adherence in haemophilia patients on long-term prophylaxis. It is also the first study evaluating adherence in Italian haemophilia patients. Adherence to prophylaxis appears to be high in Italian haemophilia patients and it correlates with a reduction in bleeding events, number of target joints and school/work days lost over time. The percentage of having at least one bleed dropped in the adherent group during the three years of the study.

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