Low bleeding rates in youth and young adults on low-dose daily prophylaxis for severe hemophilia A

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INTRODUCTION

Although prophylaxis is now a recommended standard of care for severe hemophilia A (HA),[1] the optimal way of delivering prophylaxis has not yet been determined.

Low-dose daily prophylaxis (LDDP) may be a cost effective way to maintain adequate factor VIII through levels in severe HA but the impact of such a regimen on annualized bleeding rates (ABR) and adherence are not well documented.

This study describes the outcomes achieved with LDDP in a cohort of 17 patients with severe HA who were followed prospectively for 2 to 3 years.

METHODS

Recruitment: Males (14 to 29 years) with severe HA were recruited as part of a larger prospective, non-interventional study of HRQoL in patients with severe HA in Canada (see poster P-M-222). This study focuses on the 17 subjects on LDDP. All were treated at the same Haemophilia Treatment Centre and they represent all of the subjects receiving LDDP in the larger study.

Outcomes: Primary: Bleeding and treatment logs were collected using the Helitrax™ electronic diary and were reviewed and validated on a quarterly basis. Adherence to treatment was reported as the percentage of prophylactic infusions administered over the number of infusions prescribed, based on the diaries.

Secondary: Information on joint health (Hemophilia Joint Health Score version 2.0 – HJHS) and Health-Related Quality of Life (HRQoL) was collected prospectively

RESULTS

Sample:

- 17 participants, aged 14 to 29 years
- Mean age = 22 (SD=4.06) years
- All had been on LDDP for ≥ one year prior to entering the study because of break-through bleeding on previous regime (3 times/week regimen)
- 4 had an active target joint at study entry

Doses:

- 500 IU per day in 15 cases and 1000 IU per day in 2 cases
- Median daily dose of 7.1 IU/kg/day (range 4 to 13 IU/kg/day)
- Median annual dose of 2591 IU/kg/year (range 1460 to 4745 IU/kg/year)

Adherence

- Over the entire observation period: 56% to 98% (median 85%, mean 81%)
- First 3 months on study: 58% to 99% (median 88%, mean 82%)
- Last 3 months of the study: 48% to 101% (median 80%, mean 77%)

Bleeding and ABR (see Table 1)

- Over 516 months of cumulative observation in 17 subjects: 76 bleeds in the 6 index joints (elbows, knees and ankles), and 51 other types of bleeds
- Median ABR in the 6 index joints of 0.7 (range 0.0 to 9.6)
- Median ABR for all bleeds of 1.6 (range 0.0 to 11.8)

HJHS

- Median HJHS = 16, on a scale of 0 to 144, where 144 indicates extreme joint damage
- Range of 0 to 34 (SD=8.5) at study entry
- Range of 0 to 38 (SD=9.0) at end of study

HRQoL

- Assessed by the Physical Component Summary (PCS) and Mental Component Summary (MCS) scales of the SF-36v2. Note: these scores are standardized to an expected mean of 50 in the general population.
- At study entry: mean PCS 49.11 (SD 5.65) and MCS 51.03 (SD 7.83)
- At end of study: mean PCS 51.75 (SD 5.92) and MCS 47.93 (DS 9.45)
- The differences between entry and exit were not significantly different (PCS t= -1.68, p= 0.113) (MSC t =1.75; p= 0.099)

Table 1

	ABR for Index Joints in Year 1	ABR for Index Joints in Year 2	ABR for Index Joints in Year 3	ABR for Index Joints /year	ABR for All Bleeds in Year 1	ABR for All Bleeds in Year 2	ABR for All Bleeds in Year 3	ABR for All Bleeds /year
Median	1.1	1.0	0.0	**0.7**	2.0	2.0	0.9	**1.6**
Minimum	0.0	0.0	0.0	**0.0**	0.0	0.0	0.0	**0.0**
Maximum	11.5	9.2	8.0	**9.6**	11.5	13.8	10.0	**11.8**
Standard Deviation	2.68	2.47	2.81	**2.65**	3.57	3.34	3.67	**3.53**

CONCLUSIONS

- Although non-interventional, our study of a small cohort of patients on a LDDP regimen shows results comparable to published reports of standard dose prophylaxis in terms of adherence to treatment and QoL.[2,3,4] In addition, we did not have any participants withdraw from LDDP throughout the study.
- Bleeding as assessed by ABR is low and comparable to published data. [4]
- The median annual utilisation of 2591 IU/kg in our cohort represents 33% less factor use than a typical regimen of 25 IU/kg thrice weekly (3900 IU/kg/year). This might be an important economical issue in developing as well as developed countries.
- LDDP may be an advantageous way of tailoring prophylaxis but our data would ideally need to be confirmed in a randomized prospective study.

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Acknowledgements:
Funding for this research was provided by CSL Behring Canada. NL Young is supported by a Canada Research Chair from CIHR.