Successful daily tertiary prophylaxis without increase in factor VIII consumption in a group of severe hemophilia A adolescents

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INTRODUCTION AND OBJECTIVES

Late start of long-term prophylaxis in severe hemophilia A (sHA) patients leads to musculoskeletal impairments. Effective tertiary prophylaxis is challenging to achieve. Some patients may need a more physiological regimen, with frequent infusions of factor VIII (FVIII) concentrate. This study aimed to evaluated the efficacy of daily prophylaxis, FVIII concentrate consumption and the impact of this type of prophylaxis on sHA adolescents patients daily life.

MATERIALS AND METHODS

We retrospectively assessed all sHA (FVIII:C < 1 IU/dL) adolescents (12 to 18 years of age) followed at Hemocentro Unicamp on different tertiary prophylaxis regimens who switched to daily prophylaxis at any moment. We analyzed the number of bleeding episodes by calculating the annualized bleeding rate (ABR) and annualized joint bleeding rate (AJBR), and the FVIII concentrate monthly consumption in the period under daily prophylaxis in comparison to the previous 12 months. The adherence to treatment and the patient's perception of improvement in prevent bleeding episodes and the impact of daily infusion in their routine were assessed by 2 simple questions formulated by our institution. Each answer was given a score from zero to ten. Data analysis was carried out in Prism 7 using Wilcoxon matched-pairs signed rank test.

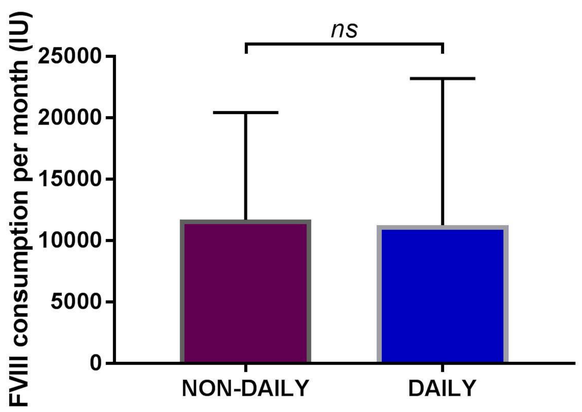


Figure 2. Median FVIII concentrate monthly consumption in the group of 6 adolescents, before and during daily prophylaxis.

Table 1. Patients Characteristics

Patient	Age (y)	BMI (kg/m²)	Number of joints with HA	Previous history of inhibitors	Previous prophylaxis regimen	Daily prophylaxis (DP)	Months with DP	Adherence
1	19	16.23	6	No	21 IU/kg every other day	10.2 IU/kg	4	Irregular
2	14	23.98	2	No	19.6 IU/kg 3x/week and 17.5 IU/kg every other day	16.9 IU/kg and 12.5 IU/kg	24	Good
3	16	17.15	1	Yes	14.8 IU/kg every other day	13 IU/kg	28	Good
4	16	22.17	2	No	21 IU/kg 2x/week	7.8 IU/kg	15	Good
5	13	16.16	2	No	22.7 IU/kg every other day	16.6 IU/kg	7	Irregular
6	14	26.21	2	No	20 IU/kg 3x/week	8 IU/kg	20	Good

BMI (body mass index); HA (haemophilic arthropathy); DP (Daily prophylaxis)

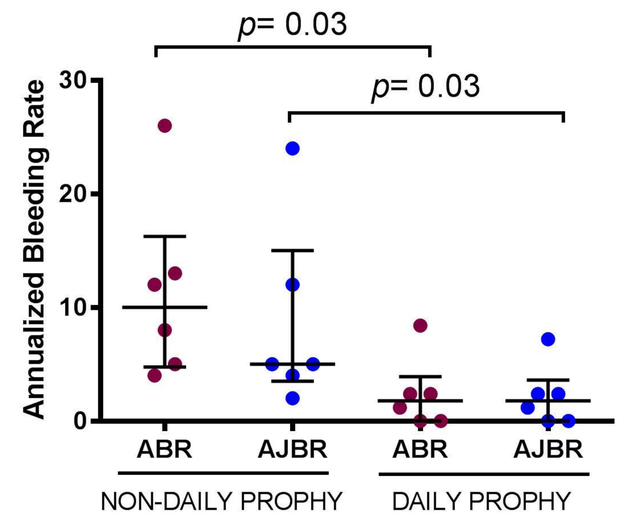
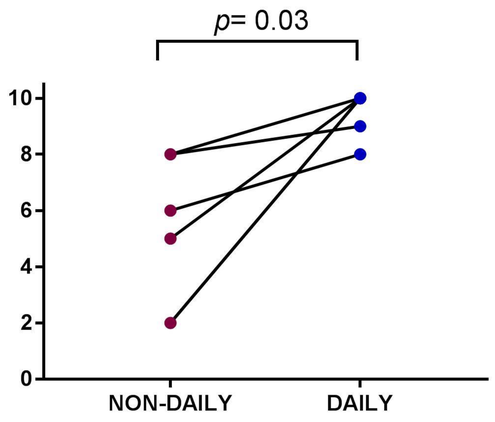


Figure 1. Annualized bleeding rate (ABR) and annualized joint bleeding rate (AJBR) before and during daily prophylaxis.



Questions formulated:

1. What was your confidence level in doing daily activities with the previous prophylactic regimen (from 0 to 10)?
2. What is your current confidence level in doing daily activities with daily prophylaxis (from 0 to 10)?

Figure 3. Patient´s perception of pros and cons of daily prophylaxis.

RESULTS

In total, 6 of 33 (18%) sHA adolescents of our Hemophilia Treatment Center (HTC) were under daily prophylaxis and were analyzed in this study (Table 1). Median age was 15y (SD ± 2.16; range 13-19). Three patients were previously using 14.8-22.7 IU/kg of FVIII concentrate every other day. One patient was using two different dosing schedules in a twelve-month period (19.6 IU/kg three times per week and 17.5 IU/kg every other day). The additional two patients were using around 20 IU/kg two or three times per week. After switching to daily prophylaxis, patients received 500-1000 IU of FVIII concentrate per day. Mean dose was 12.14 IU/kg/day (SD ± 3.23; range 7.8-16.9). The mean period of daily prophylaxis was 19.6 months (SD ± 11.3; range 4-29). Three patients continue under this treatment so far. Two of them quit daily prophylaxis because of bad compliance and the additional one switched back to three times per week prophylaxis after medical evaluation. During the time of daily prophylaxis, four patients (66%) kept good adhesion, with more than 90% of the period taking daily infusions as prescribed. When we analyzed the bleeding frequency during daily prophylaxis (Figure 1), we observed a statistically significant reduction in the ABR in comparison to the previous prophylactic regimen. The median ABR was 10 bleeds/year (4-26) in non-daily *vs.* 1.8 (0-8.4) in daily prophylaxis (p= 0.03). Similar result was observed for joint bleeds, with median AJBR of 5 (2-24) in non-daily *vs.* 2.16 (0-7.2) in daily prophylaxis (p= 0.03). No significant difference was observed in FVIII concentrate monthly consumption (Figure 2), with median of 11,698 IU/month (6,500 to 20,416) in non-daily, and 11,258 IU/month (2,428 to 23,206) in daily prophylaxis (p=0.56). Concerning to the patient´s perception about the pros and cons of daily prophylaxis, (Figure 3), we observed a statistically significant improvement in the score, with median of 5.5 (SD ± 2.7; range 2-8) in non-daily *vs.* 10 (SD ± 0.83; range 8-10) in daily prophylaxis (p= 0,03).

CONCLUSIONS

In this study, all patients had different severities of musculoskeletal damage. Despite that, all patients presented a reduction in bleeding frequency after switching to daily prophylaxis, without increase in FVIII consumption. Although adolescents constitute a challenging group of patients to achieve good adhesion to intensive treatment, we observed in this group that daily prophylaxis is feasible and can be well tolerated. All patients reported that the treatment burden of daily infusions was compensated by the improvement in their independence for daily activities.