

Daytime of prophylaxis and bleeding frequency: Real life data from the electronic diary smart medication™

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Background:

Patients with severe haemophilia A and B are usually advised to do their prophylactic infusions in the morning in order to achieve best efficacy during daytime, thus maxim activity. Aim of this study was to explore from real life data, collected with the electronic diary smart-medication™, whether daytime of prophylactic infusions has an influence on bleeding frequency. It was also analysed whether the bleeding location has influence on the urgency of treatment. Finally the recorded prophylaxis patterns were compared to bleeding frequency.

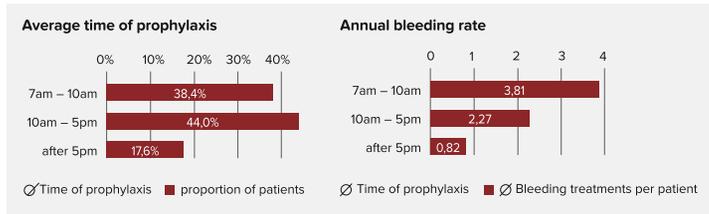
Methods:

192 patients completed their documentation in 2014 and were analysed with respect to treatment regimen, time and frequency of factor infusions and bleeding frequency. Prophylaxis was defined as regular factor infusion at least once weekly. In case of bleeding, patients were asked to indicate the approximate delay between onset of symptoms and transfusion of factor VIII/IX.

Results:

125 of 192 patients were on regular prophylaxis (Tab. 1). 38% of all patients applied their prophylactic infusions between 7 am and 10 am (Fig. 1), 44% between 10 am and 5 pm and 18% after 5 pm. Average number of bleeding treatments recorded were 3.81 (±4.19), 2.27 (±2.67) and 0.82 (±1.72) in the respective groups (Fig. 1).

FIG 1: AVERAGE TIME OF PROPHYLAXIS (A) AND ANNUAL BLEEDING RATE (B)

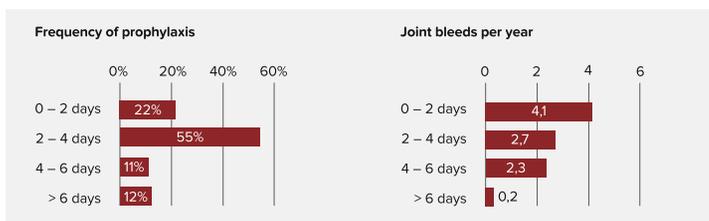


TAB. 1: ANNUAL FACTOR VIII/IX CONSUMPTION ACCORDING TO TREATMENT REGIMEN IN ALL PATIENTS, PER PATIENT AND PER PATIENT IN RELATION TO BODYWEIGHT (BW)

	n =	Total annual factor consumption IU	Annual factor consumption per patient IU	Standard deviation	Annual factor consumption IU/kg BW	Standard deviation
Prophylaxe	125	21.481.700	172.000	131.000	2.761	1.945
Mixed P/OD	52	7.589.350	146.000	138.000	2.222	2.181
On Demand	15	586.000	39.000	42.000	542	521

Treatment patterns varied within the prophylaxis group (Fig. 2). Highest annual bleeding rates (4.1 ± 4.2) were found in patients with prophylactic treatment every or every second day. Less bleeding (2.7 ± 3.3, 2.2 ± 2.1 and 0.2 ± 0.4) in patients with prophylaxis every 3-4, 5-6 and weekly, respectively.

FIG 2: ANNUAL BLEEDING RATE ACCORDING TO PROPHYLAXIS REGIMEN



The mean time for prophylactic infusions was 9:57 (hh:min) in small children (0-9 years of age), 11:16 in adolescents (10-19 years), 12:53 in young adults (20-29 years), 14:34 in patients aged 30-39 years and 13:51 in patients aged > 39 years.

TAB 2: AGE OF PATIENTS, TIME OF PROPHYLAXIS AND BLEEDING RATE

Age of patients	Number of patients (%)	∅ Time of prophylaxis	∅ Bleeding treatment per patient
0 – 9 years	15 (13,5%)	09:56:53	3,93
10 – 19 years	32 (28,8%)	11:16:16	3,22
20 – 29 years	29 (26,1%)	12:53:48	1,59
30 – 39 years	21 (18,9%)	14:33:45	2,62
> 39 years	14 (12,6%)	13:50:46	2,21
Σ	111 (100%)	12:27:52	2,65

Time between bleeding onset and home treatment could not be indicated in approximately one third of patients (Tab.3). Time to treatment was shorter in joint than in soft tissue bleeds, but did not differ between joints. The majority of joint bleeds were ankle, followed by elbow and knee bleeds.

TAB 3: DELAY BETWEEN ONSET OF SYMPTOMS AND INFUSION OF FACTOR VIII OR IX IN RELATION TO BLEEDING LOCATION

Treatment delay	Soft tissue bleeds N (%)	All joint bleeds N (%)	Elbow N (%)	Knee N (%)	Ankle N (%)
< 1 hour	347 (29)	163 (37)	55 (40)	41 (36)	67 (36)
1 – 2 hours	114 (13)	79 (18)	20 (15)	20 (16)	39 (21)
2 – 4 hours	88 (10)	49 (11)	18 (13)	13 (11)	18 (10)
> 4 hours	126 (14)	22 (5)	4 (3)	4 (3)	14 (8)
Not indicated	209 (24)	131 (30)	40 (29)	45 (36)	46 (25)
Sum	884	444	137	123	184

Conclusion:

- Patients who administered their prophylaxis in the morning recorded more bleeding episodes than those applying it later during daytime. The reasons for choice of time have not been recorded, but by this data assumption, that early day treatment prevents bleeding more effectively, is not supported.
- As earlier time of prophylactic infusions seemed to be associated with younger age, a possible explanation for these observations could be that in real life setting children bleed more frequently than adults despite intensive prophylaxis.
- Approximately one third of all recorded bleeds were joint bleeds, the majority were ankle, followed by elbow and finally knee bleeds. Time delay between symptoms and factor infusion was shorter in joint bleeds than in soft tissue bleeds.
- In nearly one third of all treatments the time since onset of symptoms was not indicated.
- Possibly symptoms started during sleep or were rather chronic and increased slowly without exact determination of onset.
- Higher bleeding rates were found in patients with frequent, such as daily prophylaxis, demonstrating the individual need for intensified prophylaxis in patients with high bleeding tendency.
- All data were acquired automatically from patient smart medication™ entries and did not require cumbersome and erroneous transfer from paper diaries.