

Annual Bleeding vs. Factor VIII/IX consumption – what is the optimal dose according to electronic diary smart-medication™

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Background:

Bleeding frequency differs widely among patients with the same coagulation defect and the same severity of factor VIII or IX deficiency. Increasing factor consumption leads to less joint or muscle bleeds. To achieve close to zero spontaneous bleeds, an individual minimum dose for prophylaxis is required. Further increase of the prophylactic dose has no benefit. The electronic treatment diary smart medication™ allows online adjustment of the individual required dose and may lead to the optimal individual treatment pattern.

Methods:

195 patients completed electronic documentation with smart medication™ in 2014. Three were excluded due to additional Novoseven treatment, so that 192 were analyzed according factor VIII/IX consumption and subsequent bleeding frequency. For the following analysis, only joint bleeds were considered.

Results:

The average annual factor consumption was 2442 IU/kg BW (± 2038 IU/kg). An average of two joint bleeds ($\pm 3,9$) were documented. Four groups were identified. Patient with low factor consumption and low number of bleeds (green), patients with high factor consumption and low number of bleeds (yellow), patients with high number of bleeds and low factor consumption (blue) and patients with high number of bleeds and high factor consumption. Limits for group definition were drawn according to the overall mean values (Fig. 1) in comparison to mean + standard deviation (Fig. 2). In Table 1 patients groups with non, one, two or above two annual joint bleeds were compared.

TAB.1: ANNUAL JOINT BLEEDS IN RELATION TO FACTOR CONSUMPTION

Joint bleeds n/ year	Patients n	Patients %	Total factor VIII/IX 106 IU/year	Total factor VIII/IX %/year	Factor VIII/IX IU/year/ Patient
0	97	51	12,1	41	125.000
1	32	17	5,3	18	167.000
2	18	9	3,2	11	176.000
<2	45	23	9,1	31	201.000

Summary:

- According to the respective limit, the majority (45% and 77,6%) of all patients were in the green group with low or moderate bleeding and reasonable factor consumption.
- Second largest was the yellow group (less frequent bleeds, high dose, 12,5% to 31%) which may allow online controlled dose reduction in some patients.
- Few belonged the blue group (frequent bleeds, low factor consumption, 7,8% to 9,9%) demonstrating the need for higher dosing, maybe as shift from on demand to prophylactic treatment.
- The smallest group was the red group (Frequent bleeds, and high dose treatment, 2,1% up to 13,5%) These patients need further attention, other than an increase of treatment dose.
- Theoretically, a shift of resources from the yellow to the blue group may improve the general outcome without an increase of overall factor requirements.
- By comparing patients with no or low frequent bleeds, the general assumption - the higher the annual dose, the less bleeds can be observed - was not confirmed, rather than an increase of dosing in case of high bleeding tendency. This underlines the individual heterogeneity in the hemophilia cohort and the requirement for online observation by smart medication™.
- All data were acquired automatically from patient smart medication™ entries and did not require cumbersome and erroneous transfer from paper diaries.

FIG. 1: MEAN AS LIMIT FOR BLEEDS AND FACTOR CONSUMPTION

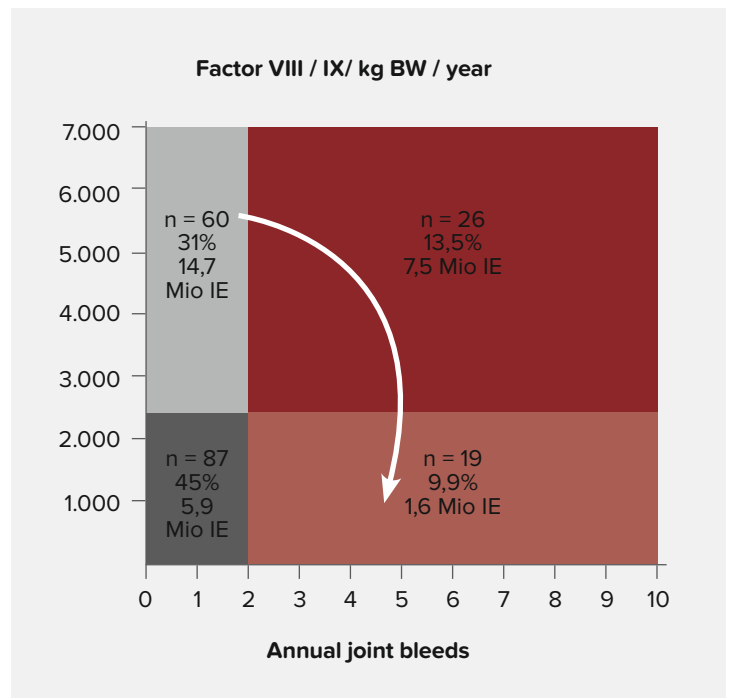


FIG. 2: MEAN + STDEV AS LIMIT FOR BLEEDS AND FACTOR CONSUMPTION

