

Background

Phenotypes of severe haemophilia A (HA) and severe haemophilia B (HB), i.e. the bleeding characteristics, are different. Patients with HB show less and milder joint and muscular bleeds than patients with HA. However, currently it is discussed whether patients with HB are possibly at higher risk for intracranial bleeds (Klamroth et al. 2010).

Methods

All patients with severe HA or HB (<1 % FVIII/FIX) treated at the haemophilia care centre in Muenster were eligible for inclusion. Regimens of replacement therapy, factor concentrate consumption and bleeding episodes within the last five years of observation (2007 - 2011) were evaluated. Intracranial bleeds were captured over the whole life span of the patients. Prerequisites for inclusion into the evaluation were complete documentation and absence of any additional coagulation disorder other than HA or HB. Bleeds were calculated per patient (fig. 1, table 5), consumption of factor concentrates was calculated per kg body weight (bw) because of its increase during the perennial investigation period (fig. 2, table 5). Values are given as means ± sem if not otherwise stated.

Table 1: Cerebral Bleeds per patient and per year of life

Regimen	n	Cerebral bleeds per patient	Cerebral bleeds per year of life
HA			
All	97	11	0.0041
BB	15	0	0
DT	57	8	0.0055
HB			
All	20	1	0.0019
BB	2	0	0
DT	15	1	0.0026

Figure 1: Bleeds of patients with HA compared to HB
Number of bleeds per patient and year, mean ± sem. Patients were treated on demand (OD), with continuous prophylaxis (CP) or regimens were changed (RC).

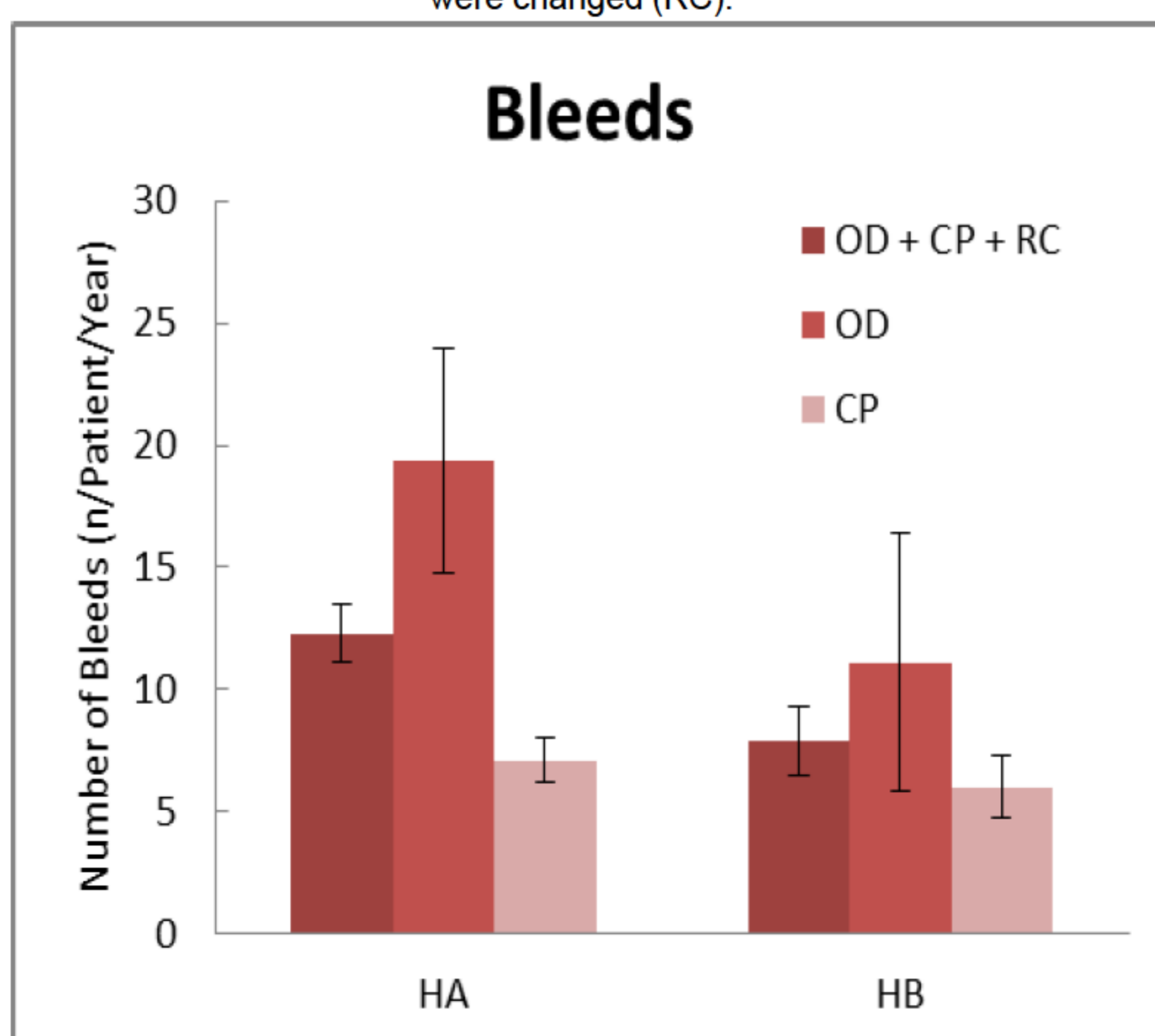


Table 2: Increase in body weight during study period

	HA Patients					HB Patients				
	2007	2008	2009	2010	2011	2007	2008	2009	2010	2011
Mean	62.5	64.3	66.1	70.3	71.1	66.6	68.7	70.8	73.9	76.5
SEM	2.9	2.9	3.0	3.1	2.9	7.1	6.7	6.7	6.7	5.6
n	99	101	96	91	88	20	20	20	19	20

Table 3: What is continuous prophylaxis (CP)?

CP Assessment	Regimen	EDs per Year (%)
EDs per Year		
365	7 x per week	100 %
182	3.5 x per week	50 %
156	3 x per week	43 %
104	2 x per week	29 %
52	1 x per week	15 %*

*Regimen was assessed as CP if ≥15 % of EDs were prophylactic.

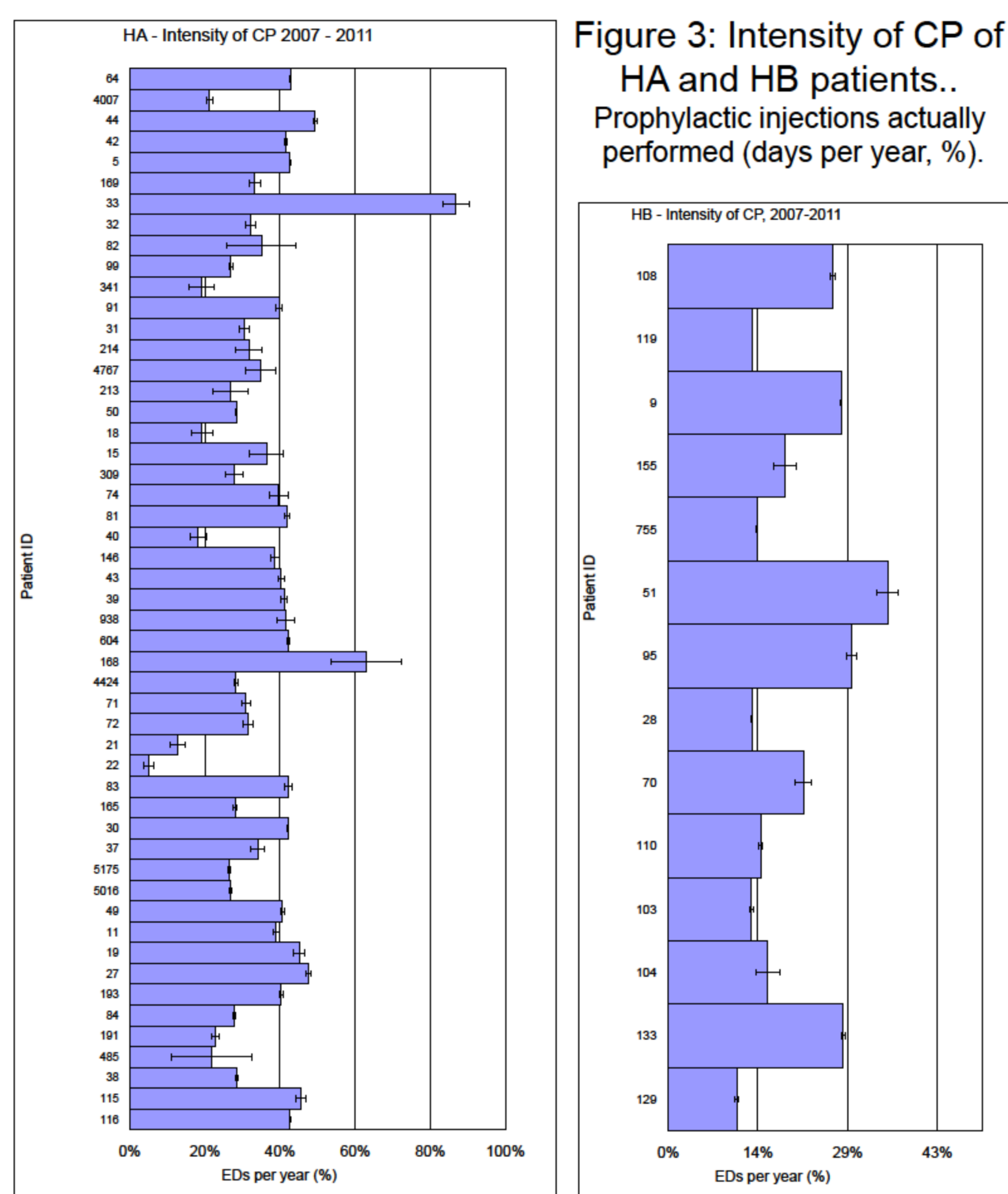
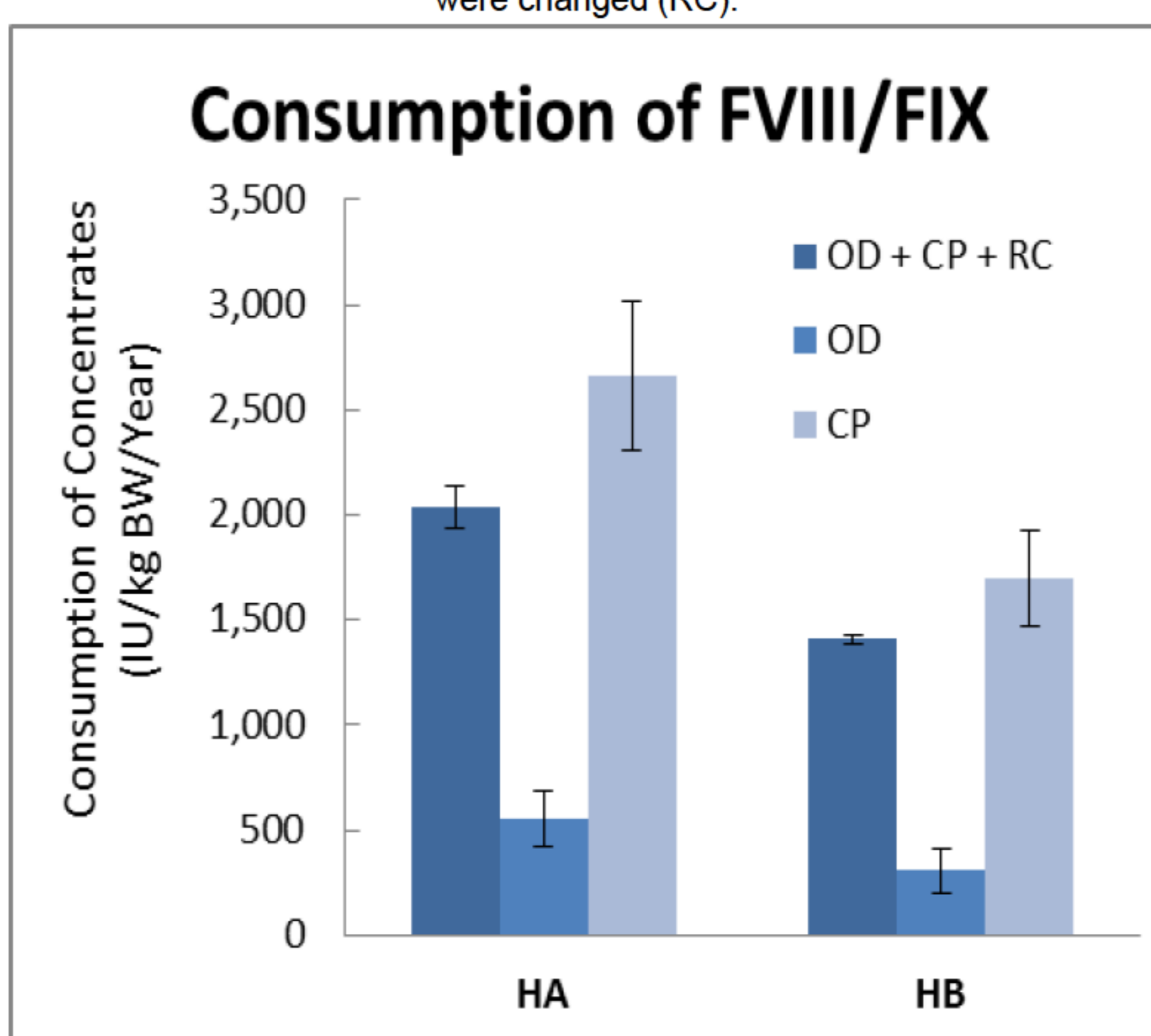


Table 4: Subgroup analysis of bleeds and factor consumption. Number of bleeds and FVIII/FIX consumption per patient and year, IU per kg bw and year, mean ± sem (n). Patients were treated on demand (OD), with continuous prophylaxis (CP) or regimens were changed (RC).

Bleeds	HA	HB
	Mean ± SEM (n)	
OD + CP + RC	12.3 ± 1.2 (101)	7.9 ± 1.4 (20)
OD	19.4 ± 4.6 (18)	11.1 ± 5.3 (2)
CP	7.1 ± 0.9 (58)	6.0 ± 1.3 (15)

Consumption	HA	HB
	Mean ± SEM (n)	
OD + CP + RC	2,032 ± 202 (101)	1,409 ± 207 (20)
OD	556 ± 131 (18)	305 ± 102 (2)
CP	2,662 ± 350 (58)	1,698 ± 226 (15)

Figure 2: Consumption of concentrates of HA or HB patients. FVIII/FIX consumption. IU per kg bw and year, mean ± sem. Patients were treated on demand (OD), with continuous prophylaxis (CP) or regimens were changed (RC).



Results

A total of 101 patients with severe HA and 20 patients with severe HB were included initially. 38 HA patients (4 HB patients) were treated on demand (OD) and 63 HA patients (16 HB patients) preventatively (continuous prophylaxis, CP). Numbers decreased during the 5-years investigation period due to losts-of-follow-ups and regimen changes (see specifications in tabs. and figs.). Body weight (table 2) increased by about 7 % in the HA and HB cohort in equal measure. Patients with HA suffered on average 57 bleeds (12.3 ± 1.2 bleeds per patient and year), patients with HB received 39 bleeds (7.9 ± 1.4 bleeds per patient and year (tab. 4, fig. 1). Consumption of factor concentrates per year amounted to 2,515 ± 150 IU/kg bw for patients with HA and to 1,712 ± 267 IU/kg bw for patients with HB. Intracranial bleeds were less frequent in HB patients compared to HA patients (0.002 vs 0.004 bleeds per year of life, tab. 1). Analysis of subgroups demonstrates during CP similar bleeding rates for HA and HB (7.1 ± 0.9 vs 6.0 ± 1.3 bleeds per patient and year), but a higher consumption is observed of FVIII concentrates compared to FIX (2,662 ± 350 IU vs 1,698 ± 226 IU). However, during OD treatment a significantly lower bleeding rate (19.4 ± 4.6 vs 11.1 ± 5.3) under HB compared to HA was noticed (tab. 4).

Conclusion

Data confirm a milder bleeding pattern of patients with severe HB compared to patients with severe HA.

No indication was found that a higher risk for intracranial bleeds must be feared for patients with HB. Intracranial bleeds did not occur more frequently under HB compared to HA.

The longer half life of FIX compared to FVIII cannot be referred to as a reliable explanation for this observation.

Literature

Klamroth R, Orlovic M, Kubicek-Hofman C, Gottstein S. Haemophilia A and Haemophilia B – Are there relevant clinical differences? Hämostaseologie 2010; 30 (Suppl 1): S26-S27.

Disclosure

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