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Treatment and Management Patterns of Patients with Von Willebrand Disease in the United States

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Abstract

Background: Few data exist regarding patient management strategies for von Willebrand disease (VWD), the most frequently inherited bleeding disorder. The objective of this study was to retrospectively assess patterns of VWD patient management in the United States.

Methods: 41 physicians were recruited using the Centers for Disease Control and Prevention's list of hemophilia treatment centers (HTCs) and the American Medical Association's physician database (16 HTC-, 25 non-HTC-affiliated). Patient charts were randomly sampled by quota method.

Results: Charts of 225 VWD patients treated from 1/2005–12/2007 were reviewed (94/74/57 for VWD types 1/2/3, respectively). The proportion of white patients was higher at non-HTCs than HTCs, and among type 1 than type 2 patients. Females comprised 65% of patients, (77% of type 1, 55% of type 2, and 58% of type 3 patients) However, bleeding episodes requiring treatment occurred in 53% of male but only 36% of female patients. The proportion of patients treated with desmopressin or von Willebrand factor/factor VIII (VWF/FVIII) concentrates for bleeding (148 events) and surgery (140 episodes) within VWD type were: 31% and 47% of type 1, 55% and 36% of type 2, 44% and 39% of type 3 patients, respectively. Of the 140 surgical events requiring desmopressin or VWF/FVIII concentrates, 61% occurred in the non-HTC setting.

Conclusion: In addition to revealing interesting disparities in VWD patient demographics, these data indicate VWD patients receive care generally aligned with treatment guidelines, with the exception of the number of surgeries performed outside of the HTC setting, where access to laboratory monitoring of factor levels may be limited.

Keywords: Bleeding disorder; Desmopressin; Factor concentrate; Hemophilia treatment center; Von Willebrand disease

Abbreviations: FVIII: Factor VIII; HIPAA: Health Insurance Portability and Accountability Act; HTC: Hemophilia Treatment Center; NHLBI: National Heart Lung and Blood Institute; RCo: Ristocetin Cofactor; VWD: Von Willebrand Disease; VWF: Von Willebrand Factor

Introduction

Von Willebrand disease (VWD) is the most common inherited bleeding disorder, with an estimated prevalence ranging from 0.6% to 1.3% [1]. Therapies approved for VWD in the United States include desmopressin (eg, intravenous DDAVP®, intranasal Stimate®) and von Willebrand factor/factor VIII (VWF/FVIII) concentrates (Humate-P®, CSL Behring, Kankakee, IL; Alphanate® SD/HT, Grifols Biologicals, Los Angeles, CA; and Wilate®, Octapharma USA, Hoboken, NJ). Adjunct therapies include antifibrinolytic agents and topical agents such as fibrin glue [1].

Treatment for VWD depends on several factors, such as VWD type, severity, type of bleeding event (episodic or surgical), and historical response to desmopressin [1]. For VWD patients responsive to desmopressin, most bleeding episodes can be controlled by desmopressin and antifibrinolytic agents. In approximately 20% of patients, however, replacement therapy with plasma-derived VWF/FVIII concentrates may be needed to treat acute bleeding episodes and prevent bleeding during invasive or surgical procedures [2,3]. Because of the complicated nature of VWD, physicians generally provide individualized therapy based on a patient's particular need.

In 2008, clinical practice guidelines developed by an expert panel were published by the National Heart Lung and Blood Institute (NHLBI). These guidelines entitled "The Diagnosis, Evaluation and Management of von Willebrand Disease,"[4] confirmed the need to individualize treatment approaches in patients with VWD. When caring for patients with severe disease, or for patients having major bleeding or surgical interventions, the guidelines also recommended the preferred use of health care facilities with availability of 24 hour laboratory services and teams of physicians, such as those found at specialized coagulation centers (hemophilia treatment centers [HTCs]), skilled in the management of bleeding disorders [4]. A large study has shown that treatment at an HTC is associated with reduced mortality for patients with hemophilia [5]. Although no similar study has been done in patients with VWD, it is likely that sites specializing in the care of patients with coagulation disorders may offer optimal management strategies and clinical outcomes for patients with VWD.

In general, few data exist on the actual treatment patterns of VWD patients in the US, either within HTCs or from community-based physicians. In this study, retrospective VWD treatment data were

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collected from a sample of physicians from HTCs and community-based practices. The objectives of this study were 1) to better understand where and how VWD patients were receiving care, and 2) to assess potential age, gender, or race-related differences in the treatment of VWD in the US.

Methods

Study design and patient charts

Data regarding diagnosis and treatment of VWD were collected in a retrospective chart review of patient medical records dated January 2005 through December 2007. The study was conducted in the spring of 2008. A nationally representative quota sample of hematologists and hematologists/oncologists who treat VWD patients, whether affiliated with an HTC or not, was recruited from the Centers for Disease Control and Prevention's list of HTCs and the national American Medical Association's physician database. Treating physicians were eligible to participate if they had been in practice for 2 to 30 years, and confirmed their medical specialty, willingness, and ability to provide detailed treatment information based on actual patient chart reviews.

To achieve sufficient numbers of patients with each type of VWD in the study, a quota sampling design was employed, with a prespecified target enrollment of 225 patients. The enrollment goals by VWD types 1, 2, and 3 were prespecified at 42%, 33%, and 25%, respectively, of the total sample. This distribution does not represent the natural distribution of VWD types, but ensured that a large enough sample size of type 2 and type 3 patients could be collected for meaningful analysis of treatment patterns within each subtype. Patients treated for VWD were chosen based on random selection criteria (birth month and month of office/center visit). Patients currently participating in clinical trials were excluded.

The data collection forms utilized were in compliance with the requirements of the Health Insurance Portability and Accountability Act (HIPAA). Institutional Review Board exemption was obtained from each participating site. A bleeding event as defined by the data collection form was designated as one of the following: urinary tract, hemarthrosis, skeletal, gastrointestinal tract, head and neck, post-traumatic, menorrhagia, or other (to be specified by the physician). A surgery event as defined by the data collection form was defined as any use of a VWD product to prevent bleeding during surgery.

Data collection forms

Three survey instruments were employed: a VWD patient case record form, a physician office profile form, and a physician telephone interview questionnaire. The specific information collected on these forms included patient information (gender, blood group, demographics, referral status), VWD diagnosis (diagnosing physician, family history, tests performed, VWD type), and VWD treatment for both the initial treatment and during the previous 3 years (product[s] used, purpose, dosing information). See Table 1 for a tabular listing of the actual data collected.

Data analysis

Descriptive statistics were employed to summarize study data. Differences observed in patient demographic data between HTCs and non-HTCs, and among VWD types 1, 2, and 3, were tested using an independent t-test for means and an independent z-test for percentages, both with an α=0.05 level of significance.

Patient information	Gender, Blood group, Demographics, Referral status
VWD diagnosis	Diagnosing physician, Family history, Tests performed, VWD Type
Initial VWD treatment	Products used, Dates, Purpose (surgery/bleed*), Reason, Dosing, Number of doses given, Bottle/vial used, Treatment site
VWD treatment in previous 3 years	Products used, Dates, Purpose (surgery/bleed*), Reason, Dosing, Frequency of administration, Number of doses given, Bottle/vial used, Treatment site

VWD: Von Willebrand Disease.

*The type of bleed was coded by the physician as urinary tract, hemarthrosis, skeletal, gastrointestinal tract, head and neck, post-traumatic, menorrhagia, or other.

Table 1: Summary of Data Collected in Retrospective Chart Survey.

Results

Patient characteristics

The prespecified enrollment quota of 225 patients was fulfilled. Data for these 225 VWD patients (94 [42%] with type 1, 74 [33%] with type 2, and 57 [25%] with type 3) were collected from 41 physicians (16 affiliated with HTCs, 25 not affiliated with HTCs). Overall, 65% of patients were female, 64% were white, and 70% were aged >20 years (Table 2). Of the 225 patients, 130 (58%) were treated at HTCs. Patient characteristics were generally similar between those receiving care at HTCs and non-HTCs and across disease types, with the following exceptions: the proportion of white patients was higher at non-HTC (77%) than HTC (55%) sites and among type 1 (72%) than type 2 (57%) VWD patients. In addition, the proportion of females was higher for type 1 VWD (77%) than type 2 (55%) and type 3 (58%) VWD. On average, patients with type 1 VWD were older than those with type 3 VWD (mean ages: 31 vs. 26 years; Table 2). Finally, a higher proportion of patients seen at HTCs (65%) had type 2 or type 3 VWD compared to the patients followed at non-HTC sites, where 48% had type 2 or type 3 VWD.

Treatment patterns: desmopressin and vwf/fviii concentrate use for bleeding and surgical events

Across all VWD types, the most commonly prescribed treatments were desmopressin at HTC sites (42% of patients) and VWF/FVIII concentrates at non-HTC sites (47% of patients). All bleeding and surgical events reported were treated with either desmopressin or VWF/FVIII concentrates, but no events were treated with both. Of note, a greater percentage of patients receiving care at an HTC had received antifibrinolytic therapy with aminocaproic acid (15%) compared with non-HTC patients (4%).

Of the 225 patients, 95 (42%) received desmopressin and 93 (41%) received VWF/FVIII concentrates for the treatment of bleeding (n=148 events) and/or surgery (n=140 events) during the 3 year study period. The following data pertaining to treatment patterns by patient sex, age, VWD type, and treatment site focus on these patients and their corresponding bleeding and/or surgical events.

Treatment patterns by gender

Among the 95 patients requiring treatment of a bleeding episode(s) with desmopressin or VWF/FVIII concentrates, 53 (56%) were female and 42 (44%) were male; this moderate gender imbalance was largely due to the preponderance of female patients in the sample population, particularly with respect to type 1 VWD. However, a greater percentage

	All VWD Patients n=225	HTC Status		VWD Type		
		HTC n=130	Non-HTC n=95	Type 1 n=94	Type 2 n=74	Type 3 n=57
Gender, n (%)						
Female	146 (65)	82 (63)	64 (67)	72 (77)†	41 (55)	33 (58)
Male	79 (35)	48 (37)	31 (33)	22 (23)	33 (44)	24 (42)
Age, n (%)						
Mean, years	28	25	33	31‡	27	26
≤20 years	67 (30)	52 (40)	15 (16)	25 (27)	26 (35)	16 (28)
21–30 years	66 (29)	39 (30)	27 (28)	23 (24)	20 (27)	23 (40)
31–40 years	53 (24)	22 (17)	31 (33)	26 (28)	17 (23)	10 (18)
≥41 years	39 (17)	17 (13)	22 (23)	20 (21)	11 (15)	8 (14)
Ethnicity, n (%)						
White	145 (64)	72 (55)	73 (77)*	68 (72)§	42 (57)	35 (61)
Hispanic	43 (19)	27 (21)	16 (17)	16 (17)	17 (23)	10 (18)
Black	27 (12)	22 (17)	5 (5)	8 (9)	11 (15)	8 (14)
Other	4 (2)	3 (2)	1 (1)	2 (2)	4 (6)	4 (4)
VWD type, n (%)						
Type 1	94 (42)	45 (35)	49 (52)	-	-	-
Type 2	74 (33)	47 (36)	27 (28)	-	-	-
Type 3	57 (25)	38 (29)	19 (20)	-	-	-

HTC: Hemophilia Treatment Center; VWD: Von Willebrand Disease.

*P<0.05 vs. HTC, †P<0.05 vs. type 2 and type 3, ‡P<0.05 vs. type 3, §P<0.05 vs. type 2.

Table 2: Summary of Patient Demographics.

of male patients were treated for bleeding episodes than female patients (53% compared with 36%; Table 3). These gender differences were more pronounced for type 1 and 2 patients compared with type 3 patients. Figure 1 shows the percentage of women and men who required treatment for bleeds or surgery.

Among the 93 patients who required desmopressin or VWF/FVIII concentrate for surgery, 62 (67%) were female and 31 (33%) were male, as would be expected from a patient sample in which approximately two-thirds were female. The frequency of obstetric and gynecologic procedures was 21% (13/62) of surgeries in type 1 cases, 11% (5/45) in type 2 cases, and 18% (6/33) in type 3 cases (Table 4).

Treatment patterns by age

Among the 95 patients requiring treatment of a bleeding episode(s) with desmopressin or VWF/FVIII concentrates, 42 (44%) were ≤ 20 years of age and 53 (56%) were ≥ 21 years of age. Among the 93 patients who required such treatment for surgery, 11 (12%) were ≤ 20 years of age and 82 (88%) were ≥ 21 years of age. Treatment patterns were generally similar between the younger and older patient subgroups for both bleeding (Figure 2A) and surgical (Figure 2B) events.

Treatment patterns by vwd type

In patients with type 1 VWD, 41 bleeding events required treatment with desmopressin or VWF/FVIII concentrate (Table 3). A substantially higher proportion of bleeding events was treated with desmopressin (88%) than with VWF/FVIII concentrate (12%). A similar treatment pattern was observed for surgical events in patients with type 1 VWD (87% vs. 13%, respectively).

For type 2 VWD patients, a modest difference was observed for the treatment of bleeding events (44% treated with desmopressin, 56% treated with VWF/FVIII concentrates), while twice as many surgical events were treated with VWF/FVIII concentrates (67%) than with desmopressin (33%). In type 3 VWD patients, VWF/FVIII concentrate was used to treat 95% of bleeding episodes and used in 97% of the surgical events.

Treatment patterns for htc and non-htc sites

Of the 148 bleeding events reported, 86 (58%) occurred in patients treated at HTCs and 62 (42%) in non-HTC patients (Table 3). The majority of bleeding events in patients with type 1 VWD were treated with desmopressin at both HTCs (92%; Figure 3A) and non-HTCs (81%; Figure 3A). In patients with type 2 VWD, whereas similar percentages of bleeding events were treated with desmopressin and VWF/FVIII concentrate at HTCs (48% vs. 52%, respectively; Figure 3A), nearly twice as many bleeding events were treated with VWF/FVIII concentrate than with desmopressin at non-HTCs (65% vs. 35%, respectively; Figure 3A). In patients with type 3 VWD, the vast majority of bleeding events were treated with VWF/FVIII concentrates at both HTCs (87%; Figure 3A) and non-HTCs (100%; Figure 3A).

Of the 140 surgical events reported, 54 (39%) were in patients treated at HTCs and 86 (61%) were in non-HTC patients (Table 3). Most surgical events in patients with type 1 VWD were treated with desmopressin at both HTCs (82%; Figure 3B) and non-HTCs (89%; Figure 3B). In patients with type 2 VWD, more surgical events were treated with VWF/FVIII concentrate than desmopressin at both HTCs (59% *vs.* 41%, respectively; Figure 3B) and non-HTCs (71% vs. 29%, respectively; Figure 3B); the difference in product choice was more pronounced at non-HTCs. In patients with type 3 VWD, the most surgical events were treated with VWF/FVIII concentrates at both HTCs (100%; Figure 3B) and non-HTCs (92%; Figure 3B).

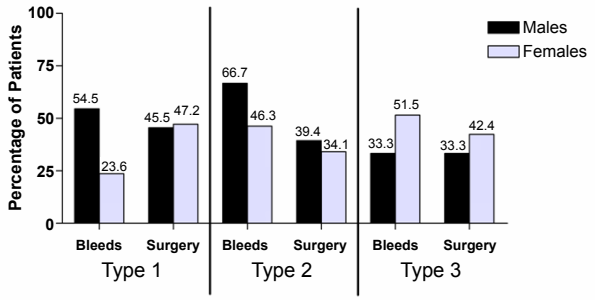

Figure 1: Treatment Patterns by Gender within VWD Type: Percentage of Males and Females That Required Treatment for Bleeding or Surgery.

VWD=von Willebrand disease.

	Patients With Bleeds, n (%)	Bleeds, n	Patients Having Surgery, n (%)	Surgeries, n
All VWD, n=225	95 (42)	148	93 (41)	140
Gender				
Female, n=146	53 (36)	87	62 (42)	96
Male, n=79	42 (53)	61	31 (39)	44
HTC status				
HTC, n=130	59 (45)	86	39 (30)	54
Non-HTC, n=95	36 (38)	62	54 (57)	86
VWD type				
Type 1, n=94	29 (31)	41	44 (47)	62
Type 2, n=74	41 (55)	63	27 (36)	45
Type 3, n=57	25 (44)	44	22 (39)	33
Age				
≤20 y, n=67	42 (63)	63	11 (16)	15
>20 y, n=158	53 (34)	85	82 (52)	125

Table 3: Bleeding and Surgical Events That Required Treatment with Desmopressin or VWF/FVIII Concentrates*

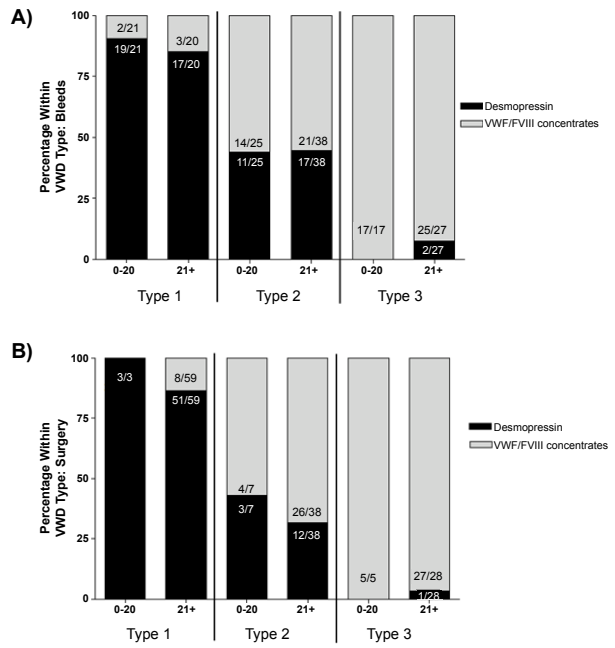

Figure 2: Treatment Patterns by Age within VWD Type. A) Bleeding Events (n=148), and B) Surgical Events (n=140) That Required Treatment with Either Desmopressin or VWF/FVIII Concentrates.

Desmopressin includes DDAVP and Stimate. VWF/FVIII concentrates include Humate-P®, Alphanate® SD/HT, and Koate®-DVI. Note: Numbers refer to bleeding/surgical events. FVIII=factor VIII; VWD=von Willebrand disease; VWF=von Willebrand factor.

Dosing patterns: desmopressin and vwf/fviii concentrate use for bleeding

As shown in Table 5, patients with type 1 VWD generally received desmopressin to treat their bleeding events. Patients with type 2 and type 3 VWD had more bleeding events that required VWF/FVIII concentrates compared with type 1 patients. In addition, while patients with type 2 and type 3 VWD appeared to receive similar mean dosage of VWF/FVIII concentrates, on average those with type 3 disease required more doses (6.3 doses) than those with type 2 VWD (4.4 doses).

Discussion

VWD is a bleeding disorder of variable severity for which guidelines for optimal diagnosis and treatment have recently been issued [4]. However, most of the recommendations are based on expert opinion and practice rather than on evidence from scientific studies; thus optimal treatment has yet to be fully demonstrated and implemented. To expand the knowledge of existing treatment and management patterns of VWD patients, we conducted an analysis of data from a retrospective patient chart study performed on a sample of patients with VWD receiving treatment at either HTCs or non-HTCs.

Analysis of the characteristics of the patients comprising our study population demonstrated that women constitute 65% of patients receiving care for VWD, and that this proportion is essentially the same in the HTC and non-HTC setting. Among patients followed with type 1 VWD, more than 75% were female. In many studies, females with VWD are overrepresented, despite the autosomal dominant inheritance, probably because they are more likely to seek medical attention for menorrhagia or bleeding related to other reproductive issues. While females constitute the majority of VWD patients requiring treatment in this study, similar proportions of female (43%) and male patients (39%) required treatment for surgical procedures; and a larger proportion of male patients (53%) required treatment for bleeding events compared to female patients (36%). The higher proportion of males requiring treatment for bleeds suggests that male patients who present for treatment are more likely to be those with active bleeding problems and more severe forms of VWD (ie, types 2 and 3) than female patients.

Pediatric patients constituted a greater proportion of the total VWD patients treated at HTC (38%) than at non-HTC (14%) sites; overall 80% of the pediatric patients were treated at HTCs. Patients who are diagnosed at a younger age may be directed to seek treatment from HTCs, which offer comprehensive care and early intervention. Also, patients diagnosed earlier in life are likely to have a more severe phenotype, prompting referral to coagulation specialists.

Surgery Type (n=number of patients)	Type 1 n=44	Type 2 n=27	Type 3 n=22
Appendectomy	1	2	2
Arthroscopy	1	-	2
Benign prostatic hyperplasia	-	1	-
Biopsy	5	2	-
Caesarean section*	3	1	1
Cervical cerclage*	-	-	1
Carpal tunnel surgery	-	2	-
Cholecystectomy	4	4	-
Circumcision	-	1	1
Coeliotomy	1	-	-
Colectomy	1	-	-
Colonoscopy	1	1	1
Cosmetic	-	2	-
Dental	14	5	1
Dilatation and curettage*	3	2	-
Evacuation hemarthrosis	-	-	2
Gastrointestinal tract surgery	-	1	1
Hammer toe revision	-	1	-
Hemorrhoidectomy	-	2	-
Endoscopy	1	-	-
Exploratory laparotomy	1	-	-
Ganglion cyst removal	1	-	-
Gastric bypass	1	-	-
Hernia repair	1	-	-
Hysterectomy*	4	1	1
Inguinal lymphadenectomy	1	-	-
Labor*	2	-	-
Leiomyomectomy*	-	-	2
Nasal surgery	1	1	-
Orthopedic	5	7	7
Pannectomy	1	-	2
Post traumatic	-	1	-
Rhinoplasty	1	2	3
Thoracentesis	-	-	1
Tonsillectomy/adenoidectomy	4	4	2
Trauma	-	-	2
Tubal ligation*	1	1	1
Not reported	3	1	-
Total no. of surgeries	62	45	33

VWD: Von Willebrand Disease.

*Obstetrics or gynecology related.

Table 4: Summary of Surgeries by VWD Type.

Product	No. of Bleeds	Dosage Median (Range)	No. of Doses Median (Range)
Type 1*			
Intravenous desmopressin	29	0.3 (0.3–2.0) µg/kg	1 (1–9)
Intranasal desmopressin	4	300 (300–300) µg/kg	1 (1–3)
VWF/FVIII concentrates	4	40 (30–50) IU/kg	8 (8–8)
Type 2†			
Intravenous desmopressin	21	0.3 (0.3–1) µg/kg	2.0 (1–6)
Intranasal desmopressin	4	150 (150–300) µg/kg	2.5 (2–3)
VWF/FVIII concentrates	28	50 (10–70) IU/kg	4.0 (1–15)
Type 3‡			
Intravenous desmopressin	0	Not reported	Not reported
Intranasal desmopressin	0	—	—
VWF/FVIII concentrates	37	50 (10–70) IU/kg	6.0 (1–30)

FVIII: Factor VIII; VWF: Von Willebrand Factor.

Note: VWF/FVIII concentrates include Humate-P®, Alphanate® SD/HT, and Koate®-DVI.

*Dosing data not reported/available for 3 events treated with DDAVP and 1 event treated with VWF/FVIII concentrates; †Dosing data not reported/available for 3 events treated with DDAVP and 7 events treated with VWF/FVIII concentrates; ‡ Dosing data not reported/available for 2 events treated with DDAVP and 5 events treated with VWF/FVIII concentrates.

Table 5: Summary of Desmopressin and VWF/FVIII Concentrate Dosing to Treat Bleeding Events by VWD Type

White patients comprised a larger percentage of type 1 patients than type 2 and type 3 patients, which may represent race-based physiologic differences. Previous investigators have shown that there are higher VWF:Ag levels in African American women compared with Caucasian women, even when blood type has been taken into account [6]. In one study of women with menorrhagia, the prevalence of VWD was 15.5% in Caucasian women compared to 1.4% in African American women (P=0.0037) [7]. While genetic studies have demonstrated distinct differences in poymorphisms of the VWF gene in African Americans when compared to Caucasian populations [8], the full genetic contribution to the clinical phenotype of VWD in different racial groups has not yet been fully described.

Interestingly, whites also comprised a greater proportion of patients treated in non-HTC sites compared to HTC sites which may represent disparity in access to care or patterns of health care insurance, for non-white patients with milder forms of VWD.

As expected, VWF/FVIII concentrate use was least among patients with type 1 VWD, who generally have milder manifestations and higher baseline VWF:Ristocetin cofactor (RCo) levels, and greatest in those with type 3 disease. Desmopressin was used by a greater proportion of patients with type 1 VWD, for whom it is typically effective. Regardless of where patients were treated, at an HTC or non-HTC, approximately the same percentage received desmopressin or concentrate for types 1 and 3, for either surgery or bleeding episodes. Type 1 patients were much more likely to receive desmopressin, and type 3 patients were much more likely to receive concentrate, regardless of where they were treated. This observation is reassuring, as it is consistent with the recommendations from the NHLBI guidelines. Treatment was more variable for type 2, with a trend for more concentrate use for both bleeding events and surgery at non-HTCs compared with HTCs. A somewhat unexpected and potentially concerning finding is that desmopressin was reportedly used occasionally to treat bleeding events and surgery in a few type 3 VWD patients, both at HTCs and non-HTCs.

For bleeding events treated with VWF/VIII concentrate in types 2 and 3 VWD patients, the median dose was 50 IU/kg , and patients received a median of 4 doses (type 2 patients) or 6 doses (type 3 patients). These doses also appear to be consistent with treatment recommendations from the NHLBI guidelines.

Although 41% of all VWD patients required treatment during the 3-year study period for a surgical intervention, only 16% of pediatric patients underwent surgery compared with 52% of adult patients. Gynecologic procedures were the most common, followed by dental procedures, orthopedic surgeries, tonsillectomies, and cholecystectomies. Some of the major surgeries covered by desmopressin in type 1 and type 2 patients included cholecystectomies (2), hysterectomies (4), tonsillectomies (5), and a gastric bypass procedure (1).

Antifibrinolytic therapy with aminocaproic acid was used in 15% of patients treated at HTCs compared with 4% of patients treated at non-HTC sites for mucosal bleeding. This treatment choice probably represents greater familiarity with use of antifibrinolytics by physicians at HTCs.

No comparable study of treatment patterns has been reported for VWD patients. The findings of this retrospective study of a large population of VWD patients treated by HTC- and non–HTC-affiliated physicians are noteworthy in that they indicate that VWD patients in the US were receiving care that was generally aligned with NHLBI guidelines when they were published in 2008, regardless of treatment site or patient age. The notable exception is that an unexpectedly high number of surgical procedures were carried out at non-HTC sites where laboratory testing of FVIII and VWF:RCo levels may not be readily available. This practice may place patients at greater risk of

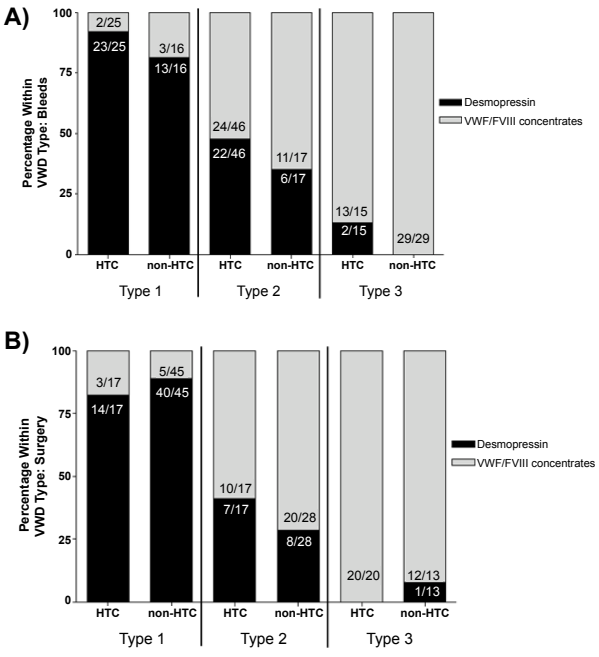

Figure 3: HTC vs NON-HTC Treatment Patterns within VWD Type. A) Bleeding Events (HTCs n=86, non-HTCs n=62), and B) Surgery Events (HTCs n=54, non-HTCs n=86) Requiring Desmopressin or VWF/FVIII Concentrate.

Desmopressin includes DDAVP and Stimate. VWF/FVIII concentrates include Humate-P®, Alphanate® SD/HT, and Koate®-DVI. FVIII=factor VIII; HTC=hemophilia treatment center; VWD=von Willebrand disease; VWF=von Willebrand factor.

inadequate treatment and bleeding, or place them at increased risk of the complications of overtreatment. Since data were not available on clinical outcomes, it is not known whether lack of ancillary support services at non-HTC sites significantly impacted the care of these patients.

The limitations of this study are mostly related to the retrospective nature of this analysis. Although selection bias by the reporting physician was possible, the method of patient selection was pre-determined by the study design (month of birth and month of office visit) and was implemented to minimize selection bias. In addition, the analysis is limited in that it was based on review of patients' medical charts and documentation of VWD treatment in the medical record; bleeding episodes treated by patients on home-based treatment regimens would not always be documented in the physician's record. For this reason, the study may underestimate the number of bleeding episodes that were actually treated over the course of the study, and likely explains why the majority of bleeds were treated with intravenous desmopressin and not the intranasal form that is generally used as home-based therapy. Nevertheless, these data provide an interesting overview of the demographics of the VWD patient population seeking care within the United States, and the management strategies employed to treat bleeding in these patients.

Several findings that merit attention include the racial differences noted among the patient population diagnosed with type 1 VWD, which await further clinical and genetic studies [8,9]. The racial differences noted in the source of care for VWD patients point to disparities that also may require further investigation. Finally, the high proportion of VWD patients of all types having surgery at non-HTC sites, which may lack full laboratory and support services for recommended monitoring of replacement factor levels, is a cause for concern although clinical outcome studies will be needed to better understand the impact of this practice.

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