

The Successful Use of Desmopressin With Tranexamic Acid in Children With Mild Type 1 Von Willebrand Disease Who Undergo Circumcision

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Abstract

Background: Desmopressin (DDAVP) is a synthetic vasopressin analog, and increases endogenous von Willebrand factor (VWF) by secreting it from the vascular endothelial cell. Circumcision is one of the oldest and most commonly performed operations in the world. This study reported the specific uses of DDAVP together with tranexamic acid in children with mild type 1 von Willebrand disease (VWD) undergoing circumcision. The aim of this study was to report the successful use of DDAVP in two doses and tranexamic acid in six children with VWD undergoing circumcision.

Methods: Our study evaluated two doses of DDAVP therapy in circumcision operation of six male children diagnosed with mild type 1 VWD with a good response to DDAVP before they underwent circumcision, with a mean age of 7.3 years. The subcutaneous preparation of DDAVP was utilized. Under medical supervision, patients were subcutaneously injected DDAVP at a dose between 0.3 and 0.2 µg/kg based on their weight. Oral tranexamic acid was instituted at a dosage of 15 mg/kg three times per day for 5 days. The first dose was given 24 hours before circumcision. The first and second doses of DDAVP were given 1 hour before the circumcision and 24 hours after the circumcision, respectively.

Results: This study included six male children aged 4 - 10 years with mild type 1 VWD, weighting 22 - 30 kg. The DDAVP dose (mean, range) based on the patient's weight was 0.25 (0.23 - 0.28 µg/kg). The calculated dose was repeated two times for each patient. Laboratory values (mean, range, U/dL) of baseline VWF:Ag, VWF:RCo and FVIII:C in mild type 1 VWD patients were 37 (32 - 42), 38 (34 - 42), and 50 (44 - 56), respectively.

Conclusion: Single infusions of DDAVP for common bleeding episodes do not usually require laboratory monitoring. There are limited published data to guide clinical practice about the optimal dosing and timing of these agents to prevent or resolve bleeding using DDAVP at minor surgeries as circumcision operation. Castaman et al showed almost all minor surgeries and deliveries occurring during follow-up were successfully managed with DDAVP in patients with type 1 VWD. We used two doses in circumcision like O'Brein. Comparison of the results across studies is difficult, as surgical techniques, timing, and frequency of DDAVP dosing, and use and dosing of antifibrinolytics all varied by institution. Two doses of DDAVP allowed adequate perioperative bleeding prophylaxis management in children with mild type 1 VWD who underwent circumcision surgery with presenting bleeding complications.

Keywords: VWD; Desmopressin; Circumcision

Introduction

Desmopressin (DDAVP) is the treatment of choice for the majority of patients with type 1 von Willebrand disease (VWD). DDAVP (1-desamino-8-D-arginine vasopressin), a synthetic vasopressin analog, increases endogenous von Willebrand factor (VWF) by secreting it from the vascular endothelial cell, its natural site of synthesis and storage [1]. The severity of the bleeding tendency is usually proportional to the degree of the VWF defect, although the large majority of cases diagnosed appear to have mild disease. DDAVP is usually effective in patients with type 1 and baseline VWF and FVIII levels higher than 10 IU/dL. The intravenous or subcutaneous dose is 0.2 - 0.3 µg/kg. Treatment can be repeated every 12 - 24 h depending on the type and severity of the bleeding [2, 3].

Circumcision is one of the oldest and most commonly performed operations in the world. It is a religious covenant for Jewish males and was recommended by the Muslims' prophet Mohammed to his society [4]. Although its life-threatening effect for VWD is well described and it is only a recommendation for Muslims in Turkey, their families consider that circumcision is a very important step to become a member of society and it is a social obligation for men [5].

In the current literature, limited data regarding DDAVP management of circumcision in mild type 1 VWD are available.

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Table 1. Results of DDAVP Challenge Test With Subcutaneous Administration

ID	DDAVP dose (µg/kg)	Baseline VWD parameters			1-h post-DDAVP response			4-h post-DDAVP response								
		FVIII:C	VWF:Ag	VWF:RCo	C/Epi	C/ADP	FVIII:C	VWF:Ag	VWF:RCo	C/Epi	C/ADP	FVIII:C	VWF:Ag	VWF:RCo	C/Epi	C/ADP
1	0.2	46	38	32	194	119	168	158	112	124	96	128	100			
2	0.24	48	39	31	195	124	168	144	110	118	92	122	110			
3	0.3	47	40	36	192	122	198	142	112	98	80	132	92			
4	0.26	43	38	30	194	119	158	144	128	90	72	108	88			
5	0.25	48	37	32	202	120	178	162	130	88	70	126	94			
6	0.3	46	42	31	198	118	198	166	144	92	68	132	98			

VWF: von Willebrand factor; RCo: Ristocetin cofactor activity; Ag: antigen; FVIII:C: factor VIII coagulant activity; C/Epi: collagen/epinephrine; C/ADP: collagen/adrenosine diphosphate.

The aim of this study was to report the successful use of DDAVP in two doses and tranexamic acid in six children with VWD undergoing circumcision.

Patients and Methods

Our study evaluated two doses of DDAVP therapy during circumcision operation of six male children, whose mean age was 7.3 (4 - 10) years, diagnosed with mild type 1 VWD with a good response to DDAVP treatment before they underwent circumcision [6]. It was a prospective blind observational study. Ethics Board approval and parents' informed consent were received. The study was undertaken in Pamukkale University. The most common bleeding symptoms were epistaxis (100%) and bruising (50%). Criteria for the diagnosis of mild type 1 VWD were von Willebrand factor antigen (VWF:Ag), von Willebrand factor ristocetin cofactor (vWF:RCo) levels between 31 and 49 IU/dL and disproportionately low ratio of VWF:RCo to VWF:Ag (VWF:RCo/VWF:Ag > 0.7), and at least one bleeding symptom.

The subcutaneous preparation of DDAVP (4 µg/mL; Minirin®, Ferring, Kiel, Germany) was utilized. Under medical supervision, patients were subcutaneously injected DDAVP between at a dose of 0.3 to 0.2 µg/kg based on their weight. Oral tranexamic acid was instituted at a dosage of 15 mg/kg three times per day for 5 days. The first dose was given 24 h before circumcision.

The first and second doses of DDAVP were given 1 h before the circumcision and 24 h after the circumcision, respectively. No measurement for plasma factor level was done. Circumcision was carried out under general anesthesia. The prepuce was incised circumferentially and excised using Gomco clamp or open technique.

Patients were discharged 24 h after circumcision and they had not any type of bleeding complication in subsequent week.

Results

This study included six male children aged 4 - 10 years with mild type 1 VWD, weighting 22 - 30 kg. The DDAVP dose (mean, range) based on the patient's weight was 0.25 (0.23 - 0.28 µg/kg). The calculated dose was repeated two times for each patient.

Laboratory values (mean, range, U/dL) of baseline VWF:Ag, VWF:RCo and FVIII:C in mild type 1 VWD patients were 37 (32 - 42), 38 (34 - 42), and 50 (44 - 56), respectively. All the mild type 1 VWD patients achieved initial and sustained response (VWF:RCo levels > 40% for a minimum of 1 h and normal PFA-100 CT for 4 h to DDAVP delivered by a subcutaneous route in Table 1) [7, 8].

In the period of 5 days after circumcision, bleeding was not observed in any patient.

Discussion

Circumcision is a very important ritual for Muslim and Jewish

populations. Almost all parents of patients with VWD are willing to have their children circumcised.

Short-term DDAVP prophylaxis was successfully applied ranging from 91% to 100% to prevent excessive bleeding following surgery or invasive procedures in patients with type 1 VWD [9, 10]. In our study, clinical responses were excellent with no bleeding episode.

Single infusions of DDAVP for common bleeding episodes such as epistaxis, simple dental extraction or menorrhagia do not usually require laboratory monitoring [11]. There are limited published data to guide clinical practice about the optimal dosing and timing of these agents to prevent or resolve bleeding using DDAVP at minor surgeries as circumcision operation. Castaman et al showed almost all dental extractions, minor surgeries and deliveries occurring during follow-up were successfully managed with DDAVP in patients with type 1 VWD [12].

Previous studies showed that patients with mild/moderate type 1 VWD undergoing an adenotonsillar procedure were treated with the same hemostatic regimen consisting of one single dose of DDAVP and an extended use of antifibrinolytic therapy [13-15]. Due to the prolonged risk period of postoperative bleeding with tonsillectomy, O'Brein recommended to use DDAVP preoperatively and 24 h after surgery [16].

We used two doses in circumcision like O'Brein. Comparison of the results across studies is difficult, as surgical techniques, timing, and frequency of DDAVP dosing, and use and dosing of antifibrinolytics all varied by institution.

In conclusion, the two doses of DDAVP allowed adequate perioperative bleeding prophylaxis management in children with mild type 1 VWD who undergo circumcision surgery with presenting bleeding complications.

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