Original Article

Effect of Desmopressin on Platelet Aggregation and Blood Loss in Patients Undergoing Valvular Heart Surgery

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Abstract

Background: Blood loss after cardiac surgery can be caused by impaired platelet (PLT) function after cardiopulmonary bypass. Desmopressin or 1-deamino-8-D-arginine vasopressin (DDAVP) is a synthetic analog of vasopressin. DDAVP can increase the level of von Willebrand factor and coagulation factor VIII, thus it may enhance PLT function and improve coagulation. In this study, we assessed the effects of DDAVP on PLT aggregation and blood loss in patients undergoing cardiac surgery.

Methods: A total of 102 patients undergoing valvular heart surgery (from October 2010 to June 2011) were divided into DDAVP group (n = 52) and control group (n = 50). A dose of DDAVP (0.3 μg/kg) was administered to the patients intravenously when they were being re-warmed. At the same time, an equal volume of saline was given to the patients in the control group. PLT aggregation rate was measured with the AggRAM four-way PLT aggregation measurement instrument. The blood loss and transfusion, hemoglobin levels, PLT counts, and urine outputs at different time were recorded and compared.

Results: The postoperative blood loss in the first 6 h was significantly reduced in DDAVP group (202 ± 119 ml vs. 258 ± 143 ml, P = 0.023). The incidence of fresh frozen plasma (FFP) transfusion was decreased postoperatively in DDAVP group (3.8% vs. 12%, P = 0.015). There was no significant difference in the PLT aggregation, urine volumes, red blood cell transfusions and blood loss after 24 h between two groups.

Conclusions: A single dose of DDAVP can reduce the first 6 h blood loss and FFP transfusion postoperatively in patients undergoing valvular heart surgery, but has no effect on PLT aggregation.

Key words: Blood Loss; Blood Transfusion; Cardiac Surgery; Desmopressin; Platelet Aggregation

Introduction

Desmopressin or 1-deamino-8-D-arginine vasopressin (DDAVP) can increase the serum levels of von Willebrand factor (vWF) and coagulation factor VIII, so it can enhance platelet (PLT) function and improve coagulation. DDAVP has been used to treat many inherited bleeding diseases, and it also has been shown to be effective in treating some acquired bleeding disorders. Poor PLT function is one of the main causes for bleeding and allogeneic blood transfusion after cardiopulmonary bypass (CPB). The objective of this study was to observe the effect of DDAVP on blood loss and the rate of PLT aggregation after cardiac surgery with CPB to evaluate the role of DDAVP in hemostasis in cardiac surgery.

Methods

Study subjects and drugs

The study protocol was approved by the Ethics Committee of Fuwai Hospital and signed informed consent was obtained from the patients. From October 2010 to June 2011, a total of 102 adult patients undergoing elective surgery for valvular heart disease were enrolled in the study. The inclusion criteria were as follows: The American Society of Anesthesiologists classification was level II–III; no coronary heart disease or decompensated heart failure was present; no blood disease was present; preoperative routine coagulation tests and PLT counts were normal; and no anticoagulant or hemostasis treatment was administered for 1-week prior to surgery. The exclusion criteria were an emergency surgery or a repeat cardiac surgery.

Desmopressin (acetate desmopressin, manufactured by Squire Sanders Pharmaceutical Co., Ltd., Shenzhen City, Guangdong Province, China. Batch No.: 20100607) was used in the study.

Anesthesia procedures

Once the patients were in the operating room, they were routinely monitored via electrocardiography and blood oxygen saturation (at the radial artery). An oxygen mask was deployed. Radial artery catheterization was performed under

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local anesthesia for invasive blood pressure monitoring. The induction of anesthesia was carried out as follows: Intravenous (IV) injection of midazolam and/or etomidate, fentanyl or sufentanil, pipecuronium bromide or rocuronium bromide. The drug dose was adjusted based on the patient's heart function and the hemodynamic changes during the induction. Endotracheal intubation was carried out for mechanical ventilation, and deep vein puncture was performed for the placement of a central venous catheter. The anesthesia was maintained with inhalation and IV combined anesthesia, and pipecuronium bromide or rocuronium bromide was intermittently injected to maintain muscle relaxation. All of the patients underwent open heart surgery for valve replacement or valvuloplasty under general anesthesia, had a midline incision and had hypothermic CPB; a synthetic anti-fibrinolytic drug (tranexamic acid, at a total dosage of 30 mg/kg) was routinely administered during surgery as a preventive measure. The patients' own blood was recycled.

Study design

The enrolled patients were randomly divided into DDAVP group (n = 52) and control group (n = 50), and a double-blind method was utilized. During surgery, approximately 30 min before the cardiac resuscitation (at the time of rewarming), DDAVP (0.3 μg/kg) was administered to the patients in DDAVP group; the drug was diluted to 50 ml and administered slowly via IV injection over 10 min. The patients in the control group received an IV injection of an equal volume of saline.

Measurement indicators and methods

Venous blood was collected at the following 3 times points: Prior to surgery (after anesthesia), during drug administration and 2 h after drug administration to measure the PLT aggregation rate. An AggRAM four-way PLT aggregation measurement instrument (Helena Inc., USA) was used, and adenosine diphosphate, arachidonic acid and ristocetin (Helena Inc., USA) were used as aggregation agents. Blood loss and transfusion at 6 h and 24 h after surgery, the hemoglobin levels and PLT counts before surgery and 24 h after surgery and the intraoperative and postoperative urine outputs were recorded. Postoperative myocardial infarction and thrombotic events were also recorded.

Statistical analysis

The SPSS 17.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis, and measurement data were expressed as means ± standard deviation. A t-test was conducted to compare the PLT aggregation rates, the blood loss, the hemoglobin levels, the PLT counts and urine output between the two groups. A Chi-square test was conducted to compare the incidence of blood transfusion. A value of $P < 0.05$ was considered to be statistically significant.

Results

There were no significant differences in age, sex, weight, operation time or CPB time between the two groups of patients [Table 1].

Table 2 shows the comparison of the blood loss at 6 and 24 h after surgery and the postoperative incidence of transfusion between the two groups. Compared with the control group, the blood loss at 6 h after surgery was significantly reduced in DDAVP group. There were no significant differences in blood loss at 24 h after surgery. The postoperative incidence of fresh frozen plasma (FFP) transfusion was significantly decreased in DDAVP group. There were no differences in red blood cell (RBC) and PLT transfusion rate between the two groups [Table 2].

No significant differences were observed between the two groups in the rates of PLT aggregation prior to surgery, prior to drug administration and 2 h after drug administration ($P > 0.05$) [Table 3].

There were no significant differences in hemoglobin levels and PLT counts prior to surgery and at 24 h after surgery between the two groups ($P > 0.05$) [Table 4].

There were no significant differences in intraoperative urine output (1146 ± 391 ml vs. 997 ± 370 ml), urine output at 6 h after surgery (1444 ± 689 ml vs. 1376 ± 638 ml) and urine output at 24 h after surgery (3939 ± 1053 ml vs. 3833 ± 938 ml) between the DDAVP group and the control group ($P > 0.05$).

Table 1: Comparison of the general data of the two groups of patients (total n = 102)

Items	DDAVP group (n = 52)	Control group (n = 50)	P
Age (years)	49 ± 10	53 ± 9	0.086
Sex (percentage of females)	59.6	58	0.87
Weight (kg)	63 ± 12	59 ± 11	0.13
Operation time (min)	215 ± 67	205 ± 76	0.49
Cardiopulmonary bypass time (min)	110 ± 49	101 ± 50	0.35
Aortic clamping time (min)	79 ± 42	74 ± 40	0.52
Time to close the chest (min)	61 ± 17	60 ± 18	0.68
Postoperative mechanical ventilation time (min)	785 ± 213	1009 ± 889	0.08

DDAVP: Desmopressin, or 1-deamino-8-D-arginine vasopressin.

Table 2: Comparison of blood loss at 6 and 24 h after surgery and the incidence of postoperative blood transfusion

Items	DDAVP group (n = 52)	Control group (n = 50)	P
Blood loss at 6 h after surgery (ml)	202 ± 119	258 ± 143	0.023
Blood loss at 24 h after surgery (ml)	525 ± 242	574 ± 307	0.44
Incidence of postoperative RBC transfusion (%)	7.7 (4/52)	12 (6/50)	0.69
Incidence of postoperative FFP transfusion (%)	3.8 (2/52)	12 (6/50)	0.015
Incidence of postoperative PLT transfusion (%)	3.8 (2/52)	4 (2/50)	0.89

RBC: Red blood cell; FFP: Fresh frozen plasma; DDAVP: Desmopressin or 1-deamino-8-D-arginine vasopressin; PLT: Platelet.

Table 3: Comparison of the PLT aggregation rate prior to surgery, prior to drug administration and 2 h after drug administration

Items	PLT aggregation rate (%)		
	ADP*	AA†	Ristocetin
Prior to surgery			
DDAVP group	50.5 ± 19.3	48.5 ± 33.6	62.6 ± 26.5
Control group	52.3 ± 22.4	47.7 ± 30.1	63.8 ± 30.8
P	0.77	0.93	0.78
Prior to drug administration (during cardiopulmonary bypass)			
DDAVP group	44.3 ± 19.2	29.6 ± 24.6	56.5 ± 26.8
Control group	40.1 ± 22.1	18.7 ± 19.5	58.7 ± 26.9
P	0.47	0.09	0.63
2 h after drug administration			
DDAVP group	33.7 ± 18.8	11.8 ± 15.9	54.8 ± 19.8
Control group	32.7 ± 19.5	7.8 ± 10.9	47.8 ± 26.5
P	0.85	0.29	0.29

*Adenosine diphosphate, †Arachidonic acid. DDAVP: Desmopressin, or 1-deamino-8-D-arginine vasopressin; PLT: Platelet.

Table 4: Comparison of the Hb level and PLT count prior to surgery and at 24 h after surgery

Items	Prior to surgery			24 h after surgery		
	DDAVP group (n = 52)	Control group (n = 50)	*P*	DDAVP group (n = 52)	Control group (n = 50)	*P*
Hb (g/L)	138 ± 18	137 ± 13	0.764	112 ± 14	107 ± 16	0.138
PLT (10^9/L)	188 ± 42	175 ± 40	0.095	122 ± 34	113 ± 32	0.192

Hb: Hemoglobin; PLT: Platelet; DDAVP: Desmopressin or 1-deamino-8-D-arginine vasopressin.

The patients were followed-up until discharge. There were no postoperative complications, such as myocardial infarction, thrombotic events or death, in the two groups of patients.

Discussion

Desmopressin, or 1-deamino-8-D-arginine vasopressin is a synthetic arginine vasopressin analog that increases the levels of plasma coagulation factor VIII and vWF[1,2] and improves PLT function.[3] Therefore, in addition to the treatment of congenital bleeding disorders, such as mild hemophilia A and von Willebrand disease, DDAVP can also be used in clinical practice to treat the bleeding caused by abnormal PLT function after cardiac surgery with CPB.[4]

In this study, DDAVP was used in patients undergoing heart valve surgery with CPB, and the results indicate that a single administration of DDAVP effectively reduces blood loss at the early stage (6 h) after cardiac surgery, which is consistent with the time (approximately 6 h) that DDAVP is active in the body. However, blood loss at 24 h after surgery was not significantly reduced, which suggests that patients with postoperative blood loss may require additional drug administration at 6 h after surgery. The reduction of FFP transfusion in DDAVP group indicated DDAVP can improve hemostasis in the cardiac patient after CPB.[5] There was no significant difference in the incidence of RBC transfusion between the two groups after surgery, which is consistent with the meta-analysis results of Carless *et al*. in 2004.[6]

Former studies reported that DDAVP had no significant effect on PLT count or PLT aggregation but could enhance PLT adhesion to the vessel wall.[7,8] This study found that there was no significant difference in the PLT aggregation between the groups, which was consistent with the result of a relevant clinical study.[9] But Weber *et al*.[10] reported recently that DDAVP could significantly improve PLT aggregation. They selected bleeding patients with suspected isolated CPB-induced PLT dysfunction after cardiac surgery. In our study, we observed unselected valvular surgery patients without confirmed PLT dysfunction, which may lead to different results that DDAVP had no effect on PLT aggregation. In other words, the effect of DDAVP on PLT aggregation (if it exists) may be hidden by other factors. In addition, different techniques used to detect PLT aggregation (whole-blood impedance aggregometry vs. light transmission aggregometry) may be one of the reasons leading to different outcomes.

Desmopressin, or 1-deamino-8-D-arginine vasopressin has a certain antidiuretic effect, so it may reduce a patient's urine output. In this study, we recorded intraoperative and postoperative urine output, and the results indicated no significant difference in the patients' urine output between the DDAVP group and the control group. Prior studies suggested that the antidiuretic effect of DDAVP is minor, and if fluid intake is managed under monitoring within 24 h of drug administration, then the incidence of fluid overload and severe hyponatremia is rare; in the rare cases of fluid overload and severe hyponatremia, the patients were mostly pediatric patients who received repeated drug administrations.[11] Therefore, DDAVP can be safely used for intraoperative and postoperative hemostasis in patients undergoing cardiac surgery with cardiopulmonary bypass.

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