Desmopressin acetate decreases blood loss in patients with massive hemorrhage undergoing gastrointestinal surgery

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ABSTRACT

Background/Aims: *Intraoperative blood loss of more than 400 ml during gastrointestinal surgery is an independent predictor of mortality. Desmopressin acetate (1-deamino-8-D-arginine vasopressin [DDAVP]) could reduce perioperative blood loss. Few studies have prompted concerning the effects of DDAVP on gastrointestinal surgery. This study aimed to investigate whether DDAVP can decrease blood loss in patients with massive hemorrhage undergoing gastrointestinal surgery.*

Materials and Methods: *A multiple-center, double-blind clinical trial was conducted; patients who underwent gastrointestinal surgery were recruited from three hospitals and were randomly assigned to two different groups. Patients in the treatment group received desmopressin in a dosage of 0.3 μg kg^{-1}, 30 min once a day after the surgery; patients in the control group received 50 ml saline for 30 min. The primary outcome was the changes of hemoglobin at 24 h after the surgery, and the secondary outcomes included coagulation function, urine volume, serum creatinine, and safety.*

Results: *There were 59 patients enrolled between June 1, 2015, and June 1, 2017. At 24 h after the surgery, the decrease in hemoglobin in the DDAVP group was significantly lower than that in the Normal Saline (NS) group (–5.0±6.9 g l^{-1} versus –10.2±9.3 g l^{-1}, p=0.03). Sonoclot® showed that the platelet function in the DDAVP group was higher than that in the NS group at 24 h (2.56±0.59 versus 1.91±0.72, p<0.05). There was no difference in urine volume and serum creatinine at 24 h between the two groups.*

Conclusion: *DDAVP could reduce post-operation blood loss in patients with massive hemorrhage undergoing surgery by improving the platelet function. We observed no difference in urine volume and serum creatinine in two groups.*

Keywords: *Desmopressin acetate, gastrointestinal surgery, post-operation blood loss, antidiuretic effect*

INTRODUCTION

Intraoperative blood loss more than 400 mL during gastrointestinal surgery is an independent predictor of mortality (1, 2). Postoperative anemia is related to poor postoperative outcome, and the benefits of blood transfusion for patients after gastrointestinal surgery are still controversial (3, 4). Patients with gastrointestinal surgery often have hypercoagulable state, with a high incidence of thrombotic events. Therefore, application of hemostatic agents after operation is particularly cautious (5). Some studies have shown that desmopressin acetate (1-deamino-8-D-arginine vasopressin, DDAVP) could reduce blood transfusion without increasing the risk of thrombotic events (6, 7). DDAVP is a chemically synthesized vasopressin derivative that could promote the release of factor VIII (FVIII) and von Willebrand factor (VWF), improve the platelet function, and reduce perioperative blood loss. However, because of the antidiuretic effect of DDAVP, its effects on urine volume and renal function are still unclear. There are few clinical studies concerning the effects of DDAVP on hemostasis after gastrointestinal surgery. Hence, this study aimed to investigate whether desmopressin acetate can decrease blood loss in patients with massive hemorrhage undergoing gastrointestinal surgery and its antidiuretic influences after gastrointestinal surgery.

MATERIALS AND METHODS

Trial Design and Study Participants

This study was a randomized, double-blinded, controlled trial, was approved by the Institutional Ethics Committee of the Sixth Affiliated Hospital of Sun Yat-sen University (approval number: E2015016) and was subsequently approved by the other hospitals. This study was conducted between June 1, 2015, and June 1, 2017. The trial is registered at the Chinese Clinical Trial Registry: ChiCTR1900022678.

Inclusion criteria were as follows: 1) patients who agreed to participate in the study and signed the informed con-

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sent form; 2) aged 18-75 years; and 3) patients with 400-1000 mL of intraoperative blood loss who underwent gastrointestinal surgery.

The criteria for exclusion were the following: 1) patients with secondary surgery; 2) pregnant and lactating patients; 3) platelet count $<5\times10^9$ l^{-1}; 4) patients with hematologic disease; 5) international normalized ratio (INR) >2.0; 6) patients who were diagnosed with unstable angina, pectoris, and myocardial infarction within six months and had a history of congenital heart disease, pulmonary heart disease, and cardiac insufficiency; 7) patients with hypertension (blood pressure >180/110 mmHg); 8) patients with hemorrhagic stroke; 9) patients with type 2B von Willebrand disease; 10) patients with serum bilirubin, alanine aminotransferase, aspartate aminotransferase, urea nitrogen, and serum creatinine that were 1.5 times higher than normal; 11) patients with fasting blood glucose >15 mmol l^{-1}; 12) serum sodium <120 g l^{-1}; 13) patients with serum albumin <25 g l^{-1}; 14) patients with hyperadrenocorticism, hyperthyroidism, and hypothyroidism; 15) patients with idiopathic edema; 16) patients with bladder outlet obstruction, or urine flow <5 mL/s; 17) patients with central or renal diabetes insipidus; 18) patients with a history of blood transfusion within one month; 19) patients with bladder cancer or prostate cancer; 20) patients allergic to DDAVP; 21) patients treated with DDAVP within three months; 22) patients with a history of drug and alcohol dependence or abuse; 23) patients who participated in other clinical trials within three months; and 24) patients who refused to participate or did not sign the informed consent form.

Withdrawal criteria were as follows: 1) patients who had active bleeding or postoperative drainage greater than 200 ml/h, lasting for 3 h; 2) patients who had adverse drug reactions, which should be included in the safety analysis; 3) patients who used other hemostatic drugs during the period; 4) patients with postoperative urinary retention; 5) allergic patients; 6) patients who used other drugs that could cause vasopressin release; 7) patients who automatically withdrew from the trial for any reasons; and 8) patients whose efficacy and safety judgment were affected because of incomplete data.

Randomization and Masking

The purpose and requirements of the trial were explained to potential participants or their authorizer after the operation, and after written informed consent, they were randomly assigned to either DDAVP group or NS group in a 1:1 ratio in each hospital. Randomization used sequentially numbered, computer-generated sealed envelopes, with stratified block randomization (block size=10). The random number was written on the opaque sealed envelopes. The study nurse who did not participate in the other parts of this trial prepared the medication according to random envelope in an independent dispensary, and then, the envelope was locked in an independent safe box. Both DDAVP and NS were colorless and transparent; they were prepared in a standard 50-mL syringe. All the investigators, researchers, patients and their families, and the clinical staffs were blinded to treatment allocation. Data were collected by the clinicians who did not enroll the subjects.

Procedures

The patients in the treatment group received desmopressin in the dosage of 0.3 mg kg^{-1} for 30 min once a day after the surgery. In the control group, patients were intravenously administered with 50-mL saline for 30 min once a day. Drugs such as etamsylate, aminobenzoic acid, reptilase, hemocoagulase agkistrodon, prothrombin complex, indomethacin, tricyclic antidepressants, chlorpromazine, and carbamazepine were forbidden, but antibiotics and blood transfusion could be used during the study if needed. Patients were monitored in the intensive care unit. The infusion was interrupted if a patient experienced any of the following conditions: serum sodium lower than 130 mmol l^{-1}, plasma osmotic pressure lower than 270 mOsm kg^{-1}, hypotension, tachycardia, nausea, and vomiting or any other serious adverse events as judged by the investigators. If the adverse event had been controlled, the drug could be resumed. To protect the patients' safety, the study was discontinued if the patients had active bleeding or postoperative drainage greater than 200 mL/h lasting for 3 h.

Outcomes

The primary observational indicator was the changes of hemoglobin at 24 h after operation. Hemoglobin change = hemoglobin (g l^{-1}) at 24 h + unit of packed red blood cell (RBC) transfusion × 24 (g l^{-1})/(body weight × 0.08) – hemoglobin at 0 h. One unit of packed RBCs contained about 24 g of hemoglobin. Body weight × 0.08 indicated the blood volume. The secondary observational indicators were the volume of abdominal drainage, coagulation and hemostasis function, renal function, postoperative blood transfusion events, urine volume, serum sodium, adverse events, and safety events (cardiovascular events, gastrointestinal reactions, hyponatremia, and other treatment-related adverse effects) at 24 h after the surgery. The hemostatic effect of DDAVP depends on the FVIII

(VIII:C) in plasma; the half-life of VIII:C is 8-12 h. Therefore, we also observed the change of hemoglobin and the other outcomes as mentioned above at 8 h.

Statistical Analysis

On the basis of previous study, the level of hemoglobin before the surgery was 14±2.0 g/dL, and it decreased to 11.5±1.5 g/dL 24 h after the operation. The sample size was calculated assuming that the level of hemoglobin would have a decrease of 3±2 g/dL in the control group and 2±2 g/dL in the DDAVP group. The sample size for each group was 63 patients (80% power, two-sided type I error 0.05). Considering a possible dropout rate of 20%, 150 patients had to be included. During the period of this study, with the development of surgical techniques, intraoperative blood loss had gradually decreased. The amount of intraoperative blood loss in most of the patients with gastrointestinal surgery was less than 200 ml. Hence, we had to stop the study early because of difficulties in finding eligible patients. Finally, 59 patients were randomized in this study.

The statistical analysis was carried out by using the Statistical Packages for the Social Sciences (SPSS) 21.0 software (IBM Corp.; Armonk, NY, USA). The numeration data were expressed by frequency, and the measurement data were expressed by the mean ± standard deviation (SD). The measurement data and numeration data were statistically analyzed with the *t*-test and the chi-squared or (χ^2) test, respectively. p<0.05 was considered statistically significant.

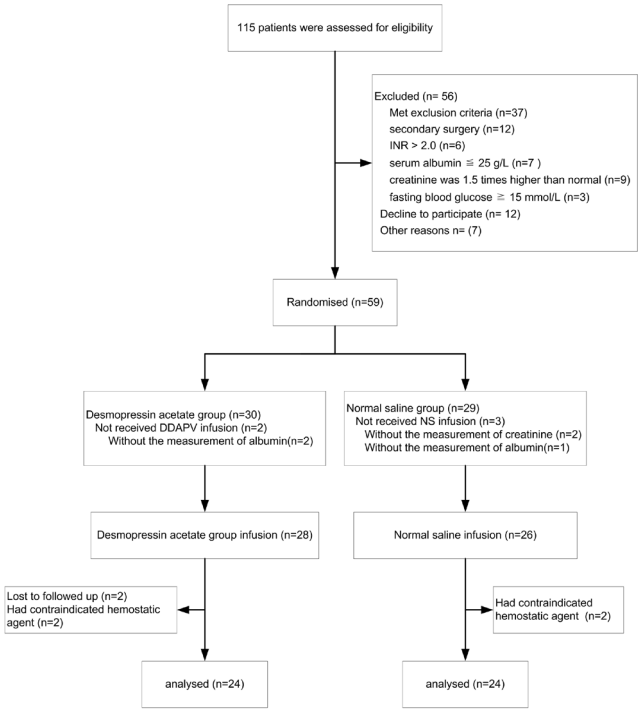

Figure 1. Flow chart of the patients.

RESULTS

A total of 59 patients were enrolled in this study, and they were randomly divided into two groups, including 30 patients in the DDAVP group and 29 patients in the NS group. In the DDAVP group, six cases were excluded, and five cases in the NS group were not included. Finally, a total of 48 cases were included in the analysis (Figure 1). Most of the patients in this study had colon cancer: 51.2% in the DDAVP group and 50.0% in the NS group. There were no significant differences between the two groups in preoperative diagnosis. There was no significant difference in the proportion of patients who had received chemotherapy in two groups (25% versus 20.8%, p=0.73). The time between the operation and the last chemotherapy was more than one month. None of the patients in this study received the preoperative radiotherapy. There were no differences between the two groups in the male/female ratio, body mass index, intraoperative blood loss, postoperative hemoglobin, platelet, prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen (FIB), INR, serum calcium, serum sodium, and Sonoclot® coagulation indicators (all p>0.05) (Table 1).

At 8 h after the surgery, a decrease in hemoglobin in the DDAVP group was significantly lower than that in the NS group (–2.5±5.2 g l^{-1} versus –6.9±8.4 g l^{-1}, p<0.05). There was no significant difference in serum sodium, serum calcium, and coagulation indicators between the two groups (p>0.05), as shown in Table 2. The results of Sonoclot® coagulation indicators suggested that the platelet function in the DDAVP group was significantly higher than that in the NS group (1.99±0.84 versus 1.08±0.51, p<0.05), as presented in Table 3. In terms of renal function, there was no significant difference in serum creatinine, cystatin C, urine volume, and urine specific gravity between the two groups, p>0.05, as shown in Table 2.

At 24 h after the surgery, there was no significant difference between the DDAVP group and the NS group in hemorrhagic drainage volume, total liquid volume, liquid balance volume, PT, APTT, FIB, INR, serum calcium, serum sodium, serum creatinine, urea nitrogen,

Table 1. Baseline clinical characteristics and laboratory values in both groups.

Baseline clinical characteristics	DDAVP group	NS group	p
Gender			
Male	17	13	0.37
Female	7	11	
Age (years)	63.9±11.68	64.5±10.00	0.70
Body mass index (kg m^{-2})	22.03±3.46	22.03±3.46	0.83
Intraoperative blood loss (ml)	495.83±142.89	533.33±189.98	0.43
Preoperative diagnosis, n (%)			
Rectal cancer	3 (12.5)	4 (16.7)	0.68
Colon cancer	13 (51.2)	12 (50.0)	0.77
Gastric cancer	3 (12.5)	4 (16.7)	0.68
Esophageal cancer	3 (12.5)	3 (12.5)	1.00
Others	2 (8.3)	1 (4.2)	0.60
Preoperative chemotherapy, n (%)	6 (25)	5 (20.8)	0.73
Preoperative radiotherapy n (%)	0 (0)	0 (0)	1.00
RBC (1012 l^{-1})	3.46±0.60	3.75±1.51	0.43
HCT (%)	0.30±0.05	0.29±0.12	0.85
PLT (109 l^{-1})	199±58	175±62	0.16
HB (g l^{-1})	98±17	103±24	0.35
Serum sodium (mM)	138±3	139±4	0.42
Serum calcium (mM)	1.82±0.32	1.88±0.36	0.50
APTT (seconds)	33.64±9.43	32.33±7.69	0.60
PT (seconds)	10.24±0.72	12.27±7.08	0.21
FIB (g l–1)	2.77±0.71	3.18±3.20	0.54
INR	1.18±0.15	1.20±0.23	0.69
D2 (μg ml^{-1})	2.24±1.55	2.58±1.96	0.53
Scr (μM)	69.90±22.63	61.60±22.98	0.21
Urea nitrogen (μM)	4.90±2.82	4.20±2.60	0.41
Cys-c (mg l^{-1})	0.96±0.43	1.00±0.81	0.83
AST (U l^{-1})	24.43±15.00	25.58±14.68	0.79
ALT (U l^{-1})	25.21±14.94	28.52±21.90	0.55
ALB (g l^{-1})	31.50±5.30	31.14±4.87	0.81
ACT (seconds)	160.65±32.19	157.05±46.36	0.78
CR (clot signals min^{-1})	22.63±6.24	21.27±6.78	0.51
PLT function	1.05±0.61	0.90±0.83	0.53

DDAVP: 1-deamino-8-D-arginine vasopressin; RBC: red blood cells; HCT: hematocrit; PLT: platelet; HB: hemoglobin; APTT: activated partial thromboplastin time; PT: prothrombin time; FIB: fibrinogen; INR: international normalized ratio; D2: D-dimer; Scr: serum creatinine; AST: glutamic-oxaloacetic transaminase; ALT: glutamic-pyruvic transaminase; ALB: albumin; ACT: activated coagulation time; CR: clot rate; PLT function: platelet function.

cystatin C, urine volume, and urine specific gravity at 24 h after the surgery (all p>0.05, Table 4). Hemoglobin was decreased 24 h after the surgery in the two groups, and the decrease of hemoglobin in the DDAVP group was significantly lower than that in the NS group (–5.0±6.9 g l^{-1} versus –10.9±9.3 g l^{-1}, p<0.05), as tabulated in Table 4. The results of three Sonoclot® coagulation indicators showed that the platelet function in the DDAVP group was remarkably higher than that in the NS group (2.56±0.59 versus 1.91±0.72, p<0.05), and there was no significant difference in the activated coagulation time and the clot rate between the two groups (p>0.05, Table 3).

In the DDAVP group, four patients got plasma infusion (550±443 mL) within 24 h after the surgery, and five patients in the NS group underwent plasma infusion (680±228 mL). In the DDAVP group, two patients received packed RBC infusion (500±141 mL) within 24 h after the surgery, and seven patients in the NS group received packed RBC infusion (235±75 mL).

Table 2. Outcomes at 8 h after treatment in two groups.

Outcomes at 8 h	DDAVP[a] group	NS group	p
Changes in hemoglobin (g l^{-1})	–2.5±5.2	–6.9±8.4	0.04
Drainage volume (mL)	221.88±271.58	262.50±269.379	0.61
Total fluid volume (mL)	1187.00±519.16	1358.63±941.45	0.44
Fluid balance (mL)	320.95±704.61	233.35±849.13	0.71
Urine volume (mL)	745.42±449.376	655.00±298.136	0.41
RBCb (1012 l^{-1})	3.38±0.64	3.61±0.91	0.31
HCTc (%)	0.27±0.08	0.30±0.12	0.40
PLTd (109 l^{-1})	195.67±65.25	176.17±55.60	0.28
Serum sodium (mM)	138.63±3.91	139.69±3.80	0.35
Serum calcium (mM)	1.83±0.30	1.93±0.37	0.34
APTTe (seconds)	31.16±6.25	30.90±6.19	0.89
PTf (seconds)	10.44±0.58	10.65±0.99	0.42
FIBg (g l^{-1})	2.98±0.81	2.50±0.96	0.07
INRh	1.16±0.12	1.18±0.23	0.65
D2i (μg mL^{-1})	2.59±1.78	3.31±2.56	0.30
Scrj (μM)	74.18±27.30	63.34±22.71	0.15
Urea nitrogen (μM)	5.17±2.90	5.92±7.25	0.67
Cys-c (mg l^{-1})	1.04±0.46	0.95±0.37	0.52
Urine specific gravity	1.02±0.01	1.02±0.01	0.51

DDAVP: 1-deamino-8-D-arginine vasopressin; RBC: red blood cells; HCT: hematocrit; PLT: platelet; APTT: activated partial thromboplastin time; PT: prothrombin time; FIB: fibrinogen; INR: international normalized ratio; D2: D-dimer; Scr: serum creatinine.

Table 3. Sonoclot® indicators at 8 and 24 h after treatment in two groups.

Sonoclot® indicators	NS (8 h)	DDAVP (8 h)	p	NS (24 h)	DDAVP (24 h)	p
ACT (seconds)	163.24±39.96	167.4±29.85	0.71	152.19±30.73	159.7±37.68	0.49
CR (clot signals min^{-1})	22.47±5.91	22.90±4.30	0.79	20.43±4.42	19.13±4.19	0.34
PLT function	1.08±0.51	1.99±0.84	0.00	1.91±0.72	2.56±0.59	0.00

DDAVP: 1-deamino-8-D-arginine vasopressin; ACT: activated coagulation time; CR: clot rate; PLT function: platelet function.

Table 4. Primary and secondary outcomes at 24 h after treatment in two groups.

Primary and secondary outcomes	DDAVP group	NS group	p
Primary outcome			
Changes in hemoglobin (g l^{-1})	–5.0±6.9	–10.2±9.3	0.03
Secondary outcomes			
Drainage volume (mL)	369.79±433.26	429.58±405.00	0.62
Total fluid volume (mL)	3233.15±1131.55	3410.88±1789.16	0.69
Fluid balance (mL)	932.84±1340.94	836.17±1368.90	0.80
Urine volume (mL)	1865.79±718.11	1911.25±975.23	0.86
RBC (1012 l–1)	3.27±0.51	3.65±1.28	0.18
HCT (%)	0.39±0.59	0.28±0.11	0.37
PLT (109 l–1)	196.07±67.30	166.79±64.76	0.13
Serum sodium (mM)	137.84±5.16	138.95±3.29	0.39
Serum calcium (mM)	1.89±0.24	1.96±0.38	0.26
APTT (seconds)	32.04±5.46	31.10±7.18	0.44
PT (seconds)	16.14±11.76	14.20±1.73	0.43
FIB (g l–1)	3.72±1.93	3.40±2.26	0.62
INR	1.17±0.15	1.19±0.22	0.74
D2 (μg mL–1)	3.05±2.41	3.35±3.84	0.76
Scr (μM)	77.78±32.98	65.25±21.09	0.15
Urea nitrogen (μM)	5.73±3.37	5.01±2.17	0.43
Cys-c (mg l–1)	1.00±0.54	1.00±0.39	1.00
Urine specific gravity	1.02±0.01	1.02±0.01	0.83

DDAVP: 1-deamino-8-D-arginine vasopressin; RBC: red blood cells; HCT: hematocrit; PLT: platelet; APTT: activated partial thromboplastin time; PT: prothrombin time; FIB: fibrinogen; INR: international normalized ratio; D2: D-dimer; Scr: serum creatinine.

In the DDAVP group, hyponatremia occurred in three patients at 8 h after the surgery, in which the concentrations were 133, 133, and 132 mmol l^{-1}, respectively. In the NS group, hyponatremia occurred in two patients at 8 h after the surgery, in which the concentrations were 132 and 131 mmol l^{-1}, respectively. There was no significant difference in the incidence of hyponatremia between the two groups (12.5% versus 8.3%, p=1.00). At 24 h after the operation, in the DDAVP group, hyponatremia occurred in five patients with a concentration range of 130-134 mmol l^{-1}. There were only two cases who had hyponatremia in the NS group, in which the concentrations were 132 and 133 mmol l^{-1}, respectively. There was no significant difference between the two groups (20.8% versus 8.3%, p=0.41). No hypotension, tachycardia, nausea, or vomiting was found in 48 patients.

As shown in Figure 2, the urine volume at 3 h after operation in the DDAVP group was significantly lower than that in the NS group (45.83±34.16 mL versus 71.67±42.88 mL, p<0.05).

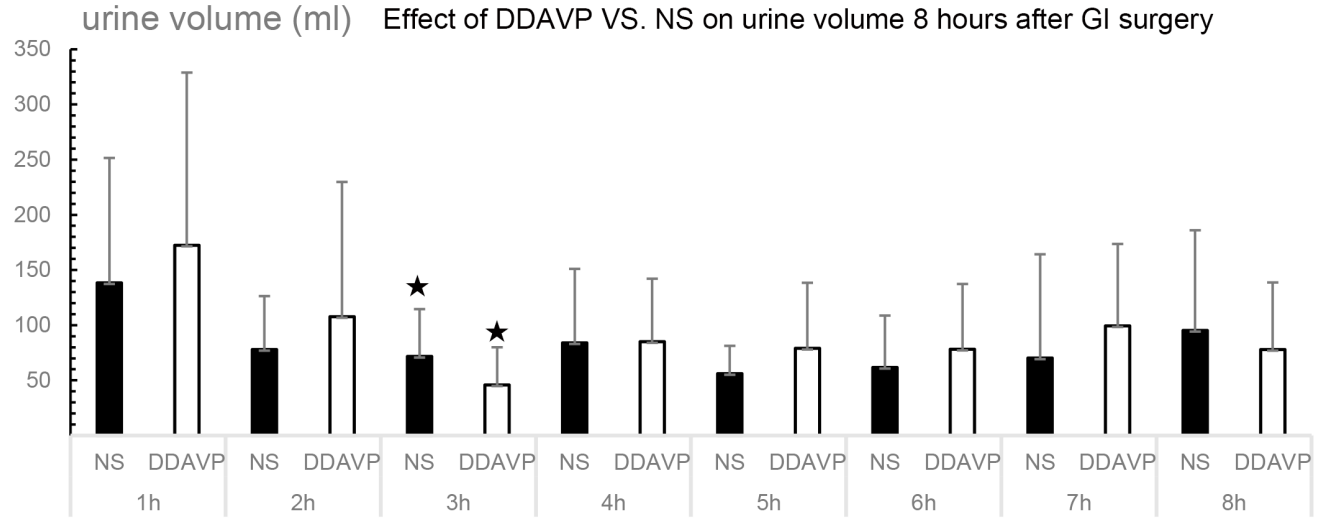

Figure 2. Effect of DDAVP VS NS on urine volume at 8 hours after GI surgery.

DISCUSSION

Postoperative bleeding occurred in 0.5-26.6% of patients that received gastrointestinal surgery (8). Multiple factors contribute to the causes of postoperative bleeding that include vascular factors and nonvascular factors. Vascular factors include capillary hemorrhage and incomplete vascular management. Nonvascular factors include intraoperative blood loss, hemodilution, consumption of coagulation factors, and acquired platelet dysfunction (9, 10). Postoperative bleeding associates with increased allogeneic blood transfusion and mortality. The standard treatment strategy includes blood transfusion and hemostatic agents. However, previous studies have shown that perioperative allogeneic blood transfusion is associated with poor prognosis, including colorectal, esophageal, and gastric cancer (3, 11, 12). In addition to autologous blood transfusion, the use of hemostatic agents is a routine treatment strategy for reducing allogeneic blood transfusion. Patients with gastrointestinal surgery often have hypercoagulable state, which increases the risk of thrombosis; thus, the choice hemostatic agents after operative should be particularly cautious.

A number of randomized controlled trials and meta-analyses have shown (6, 13-15) that the administration of 0.3-mg kg^{-1} DDAVP in perioperative period could reduce the perioperative blood loss and allogeneic blood transfusion in cardiac surgery, vascular surgery, joint surgery, and hepatobiliary surgery, without increasing the risk of thrombosis. In most studies, patients received DDAVP before the surgery. Few studies have prompted concerning the effects of DDAVP on hemostasis after gastrointestinal surgery. Thus, we performed this study to investigate whether DDAVP can decrease blood loss after the gastrointestinal surgery in patients who had 400-1000 mL of intraoperative blood loss.

This study was a multicenter, double-blind clinical trial, in which 48 patients with the volume of 400-1000 mL intraoperative blood loss in gastrointestinal surgery were included. They were randomly assigned to two groups. Considering the effect of packed RBC transfusion on hemoglobin concentrations, the change of hemoglobin was calculated by the formula, as mentioned above. Compared with the NS group, DDAVP treatment was found to reduce the loss of hemoglobin in patients at 8 and 24 h after gastrointestinal surgery. The results of Sonoclot® tests showed that DDAVP could improve the platelet function. Our study reveals that DDAVP could reduce the loss of hemoglobin after the surgery by enhancing the platelet formation function. Our finding was supported by several studies. As Swieringa (16) showed that in patients with postoperative bleeding after cardiac surgery, after DDAVP treatment, the procoagulant activity significantly increased from 3.0% (interquartile range (IQR): 1.8-4.0%) to 3.4% (IQR: 2.8-4.9%) (p=0.013), while there was no significant difference in PT, APTT, INR, and platelet counts. Another study conducted by Andrew (17) to detect the platelet aggregation function after DDAVP treatment in patients with acute intracerebral hemorrhage. They found that DDAVP increased the platelet aggregation function; the aggregation time was shortened from 192±18 s to 124±15 s, which was similar to our find-

ings. Colucci (18) showed that DDAVP could enhance the platelet formation function and increase platelet-dependent thrombin generation by selectively enhancing Na+/Ca^{2}+ exchange *in vivo*.

DDAVP could selectively act on vasopressin receptor 2 and increase the content of cyclic adenosine monophosphate in renal tubular cells, resulting in decreased urine volume and increased urine osmotic pressure, which led to water retention and decreased blood osmotic pressure and hyponatremia (19). Our study revealed that there was no significant difference in total urine volume after DDAVP treatment. There was no significant difference in serum creatinine, urea nitrogen, and cystatin C between two groups at 8 and 24 h after treatment. Although the urine volume at 3 h after DDAVP treatment was significantly lower than that in the NS group, there was no significant difference in liquid balance between the two groups, which indicated that treatment with DDAVP did not cause a risk of water retention in the patients after gastrointestinal surgery. In terms of hyponatremia, the DDAVP group had a higher incidence of hyponatremia at 24 h after the surgery than the NS group; however, no statistical difference was found in study, maybe for our small sample size. There are few studies concerning the adverse effects of DDAVP as a hemostasis agent, only reported in a small number of research works. Stoof and his team (20) observed the side effects of desmopressin in patients with bleeding disorders. In this study, 108 patients were included, in which four (4%) patients had hyponatremia (<135 mmol l^{-1}) 24 h after treatment, while no severe hyponatremia (<125 mmol l^{-1}) occurred. Their study also showed that 38% of patients had hypotension, 9% of patients had tachycardia, and the duration was less than 24 h, which could be recovered by themselves. The probability of hyponatremia was similar to that of our study, but no hypotension and tachycardia were found in our study.

This study had several limitations. Firstly, it was a multicenter study, but with small sample size, because there were fewer patients with intraoperation blood loss more than 400 mL in the three hospitals for the development of medical technology. Hence, we had to stop the study early because of difficulties in finding eligible patients. Thus, further study with larger population needs to be conducted to confirm our findings. Secondly, we did not check the concentration of VWF and FVIII in patients, which will enhance thrombus formation and evaluate the effect of desmopressin treatment on post-operation bleeding. Thirdly, the main limitation of this study was the lack of thrombotic complications.

In conclusion, DDAVP could reduce blood loss after abdominal surgery by improving the platelet function. The urine volume decreased significantly 3 h after DDAVP treatment, while the total urine volume and the renal function were not significantly affected.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of the Sixth Affiliated Hospital of Sun Yat-sen University (approval number: E2015016).

Informed Consent: Written informed consent was obtained from the patients/next-of-kin who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Q.Y.K.; Design – Q.Y.K.; Supervision - Q.Y.K.; Resource - Q.Y.K.; Materials – L.C.W., Y.F.H., L.C., R.X., X.F.L., Q.Y.K.; Data Collection and/or Processing – L.C.W., Y.F.H., X.F.L.; Analysis and/or Interpretation – L.C.; Literature Search – L.C.W., Y.F.H.; Writing – L.C.W.; Critical Reviews – R.X., Q.Y.K.

Conflict of Interest: The authors have no conflict of interest to declare.

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