The Effectiveness of Prophylactic Desmopressin in Coronary Artery Surgery

KORONER ARTER CERRAHİSİNDE PROFİLAKTİK DESMOPRESSİNİN ETKİNLİĞİ

Erdem ÖZKISACIK*, Fatih İSLAMOĞLU*, Tahir YAĞDI*, Mehmet BOĞA*, Tanzer ÇALKAVUR*, Yüksel ATAY**, Mustafa ÖZBARAN*, Suat BUKET*

* Dept. of Cardiovascular Surgery, Medical School of Ege University,
** Dept. of Haemotology, Medical School of Ege University, İzmir, TURKEY

Summary

Purpose: The aim of this study was to investigate the hemostatic effects of Desmopressin acetate (DDAVP) that has been implicated as a promising agent to reduce blood loss in patients undergone cardiopulmonary bypass.

Materials and Methods: 40 patients undergoing coronary artery bypass grafting, randomized equally into desmopressin and control groups. Desmopressin group received 0.3mg/kg desmopressin at the end of cardiopulmonary bypass. Coagulation factors, platelet aggregation response to various inducing agents, bleeding and transfusion needs were all measured at different control times.

Results: Fibrinogen level of both groups significantly reduced at postoperative 2nd hr, whereas a significant rise was observed at postoperative 24th hr with an intergroup difference favoring control group (p=0.031). In desmopressin group, the activation time of factor VIII shortened during all postoperative period being significant (p=0.131) at postoperative 24th hr. Postoperative von Willebrand factor (vWF) levels of desmopressin group were significantly higher than the preoperative ones. Control group did not show such important changes in factor VIII and vWF measurements. Platelet aggregation times of both groups prolonged at postoperative 2nd hr. Control group showed significant elevation in ADP induced aggregation time at 2nd hr and significant reductions of platelet activation percents in response to ADP, epinephrine, collagen and ristocetin at 2nd hr. Postoperative blood loss as well as blood transfusion need did not differ between two groups.

Received: Feb. 8, 2000

Correspondence: Fatih İSLAMOĞLU
Dept. of Cardiovascular Surgery
Medical School of Ege University
İzmir, TURKEY

Özet

Amaç: Bu çalışma kardiyopulmoner bypass uygulanan hastalarda kan kaybını azaltıcı bir ajan olarak öne sürülen desmopressin asetatın (DDAVP) hemostatik etkilerini araştırmak amacı ile düzenlenmiştir.

Materyal ve Metod: Ege Üniversitesi Tıp Fakültesi Kalp ve Damar Cerrahisi Anabilim Dalı'nda koroner arter bypass cerrahisi uygulanan 40 olgu kontrol ve desmopressin olarak iki eşit gruba ayrılmıştır. Desmopressin grubundaki olgulara kardiyopulmoner bypass sonunda 0.3mg/kg dozda desmopressin intravenöz olarak verilmiştir. Her iki grup için belirlenmiş ölçüm zamanlarında koagülasyon faktörleri, çeşitli ajanlara trombosit agregasyon cevabı, kanama ve transfüzyon ihtiyacı gözlenmiş ve karşılaştırılmıştır.

Bulgular: Postoperatif 2. saatte her iki grubun fibrinojen düzeyleri anlamlı olarak azalırken, postoperatif 24. saatte fibrinojen düzeylerinde kontrol grubunda daha belirgin olmak üzere (p=0.031) bir yükselme gözlenmiştir. Desmopressin grubunda faktör VIII aktivasyon zamanı postoperatif dönem süresince azalmış ve bu azalma özellikle postoperatif 24. saatte anlamlı olmuştur (p=0.131). Desmopressin grubunun postoperatif von Willebrand faktör (vWF) düzeyleri, preoperatif düzeylerden daha yüksek olmuştur. Kontrol grubunda ise faktör VIII ve vWF düzeylerinde önemli değişiklikler olmamıştır. Her iki grubun trombosit agregasyon zamanlarında postoperatif 2. saatte anlamlı uzama olmuştur. Kontrol grubunun ADP ile uyarılmış agregasyon zamanı postoperatif 2. saatte uzamış ve yine 2. saat ADP, epinefrin, kollajen ve ristosetine yanıt olan trombosit aktivasyon yüzdelerinde anlamlı azalma görülmüştür. Postoperatif kan kaybı ve kan transfüzyon ihtiyacında gruplar arası anlamlı bir fark görülmemiştir.

Conclusion: We suggest that despite the improved platelet functions, desmopressin does not have obvious beneficial effects on postoperative hemostasis in patients without any bleeding disorder and undergoing elective cardiac surgery.

fCey **Words:** Desmopressin acetate, Coagulation, Cardiopulmonary bypass

T Klin J Med Res 2001, 19:1-9

Sonuç: Çalışmamızın sonuçları trombosit fonksiyonlanndaki artışa rağmen, desmopressin uygulamasının her hangi bir kanama bozukluğu olmayan ve elektif kardiyak cerrahi yapılan olgularda postoperatif hemostaz üzerine belirgin faydalı bir etkisinin olmadığını göstermektedir.

Anahtar Kelimeler: Desmopressin asetat, Koagülasyon, Kardiyopulmoner bypass

T Klin Araştırma 2001, 19:1-9

The harmful effects of CPB on coagulation factors emerge through denaturation, dilution, extracorporeal circulation surfaces, and hypothermia. f>ilution reduces the concentration of coagulation factors. Extracorporeal surfaces cause the attachment of plasma proteins and fibrinogen, thereby lead platelet adhesion and activation (1). It was asserted that reversible platelet inhibitors like dipyridamole could protect the platelet functions, however, its inhibitory effect does not easily reverse in a short time due to relative longevity of biologic half-life (2). Prostaglandins have more impressive and short lasting inhibitory effects on platelets, nevertheless vasodilator potentials of these agents can need concomitant vasoconstrictive drug administration (3). Fibrinogen receptor antagonists acting on GPIIb/IIIa receptors can be promising in protection of platelet functions (4). Heparin coated surfaces could be ineffective due to rapid corporation *of* heparin into circulation in ionic bounded surfaces, and prolonged residence of heparin, thereby loss of platelet functions in covalent bounded ones <S).

Hypothermia in CPB causes delay in fibrin for-^nation by slowing enzymatic reactions. CPB also activates fibrinolytic system and inadequate anticoagulation causes to increase in fibrinolysis (6,7). "T~he beneficial effect of antifibrinolytic manage-^^rient with aprotinin on preventing postoperative ^j-t^leeding caused by fibrinolysis is obvious. ^^^Xprotinin reduces bleeding by both preventing fib-.^^rinolysis and protecting platelet functions (8). ^j^jj-Iowever, it is still blamed as a causative factor of ^^^^arly graft thrombosis in many reports, therefore it s not used in CABG operations in our clinic.

Desmopressin acetate (DDAVP) is a synthetic ,^-K^asopressin analogue lacking any vasoconstrictor activity on smooth muscles. Besides its primary indication in diabetes insipidus and enuresis due to inherent antidiuretic activity, it is also used in patients with mild hemophilia A who will undergo surgical procedures or with von-Willebrand disease. Salzman et al. showed that DDAVP reduced postoperative blood loss in patients undergoing CPB, by providing an elevation in plasma concentration of factor VIII:C and von-Willebrand factor (vWF). This elevation is possibly in association with release of factor VIII and vWF from liver and endothelial cells, and a change in distribution of vWF multimers (9, 10). It has been also shown that DDAVP shortened the bleeding time and reduced the blood loss in other conditions having a bleeding tendency and involving platelet defects without a defect in function or structure of vWF, such as uremia, certain thrombopathic states, and aspirin ingestion (11). In this respect, the hemostatic effects of DDAVP can be summarized as to increase in plasma concentrations of factor VIII:C , vWF and t-PA, to improve in adhesive functions of platelets and to shorten the bleeding time (12).

In this study we evaluated the effectiveness of intraoperative DDAVP administration on preventing postoperative blood loss in a prospective trial involving 40 patients randomized into study and placebo groups.

Patients and Methods

We studied 40 patients undergoing elective CABG. The patients were prospectively randomized and allocated equally into study (ultrafiltration) and control groups. The work was approved by ethic committee of the hospital and informed consents were obtained from all patients. The patients who underwent emergency surgery, having

diagnosed systemic disorder such as, hemostatic defect, hypertension, diabetes and renal failure were excluded. Not one of patients was excluded after enrollment. A11 operations were performed by same surgeon (SB). There was not any significant difference between two groups regarding age, gender, cross clamp, CPB times and number of distal anastomosis (Table 1). The acetylsalicylic acid (ASA-Aspirin) therapy that is a common practice for patients with coronary artery disease, was ceased at least one week before the surgery. None of the patients had received preoperative or perioperative prophylactic antibiotic regimen that can interfere with platelet functions. The patients in DDAVP group received desmopressin acetate (Octostim 1mL amp.15mg/L, Er-Kim, Istanbul-Turkey), 0.3mg/kg body weight in 50 mL saline solution intravenously, over 20 min. when CPB had been concluded, soon after the administration of protamine. The control group had received only 50 mL saline solution at the same time period. Blood samples were drawn through a flushed arterial catheter at the following times: immediately before operation, postoperative 2nd hour (two hours after the administration of DDAVP), and 24 hours after the operation (postoperative day 1). Blood samples were used for measurement of prothrombin time (PT), activated partial thromboplastin time (APTT), hematocrit, fibrinogen (mg/dL), factor VHI activation time (sec), vWF (mU/mL); studies of platelet aggregation in response to adenosine di phosphate (ADP), collagen, epinephrine and ristocetin. The measurement of vWF was performed by an ELISA method (Boehringer, Mannheim, Germany). The citratted blood samples taken for platelet aggregation tests were processed with centrifugation to obtain platelet enriched plasma (TRP). The platelet aggregation curves were obtained through invitro induction of TRP samples with ADP, collagen, epinephrine and ristocetin. The activation percents and times (sec) were obtained by using these curves. The delivered blood and blood products as well as postoperative blood loss of patients were observed at postoperative 2nd and 24th hours, and as total amount by measurement of drainages intraoperatively and postoperatively, and were compared statistically between two groups. Blood pressure and diuresis of patients were noted during first 24 -hour. Approximately 300 to 400 mL of autologous blood was taken from all patients but one in DDAVP group and two in control group before the heparinization, if hematocrit level of the patient was above 40%, and was readministered after the delivery of protamine. The postoperative volume replacement was performed with either blood, if hematocrit level was below 28%, or fresh frozen plasma, if there was a drainage exceeding 2 mg/kg/h and hematocrit level was above 28%.

A11 operations were performed through median sternotomy. The membrane oxygenator was primed with 2 L of lactated Ringer's solution. CPB was established via standard aortic and single venous cannulation using a Sarns modified roller pump (Sarns, Ann Arbor, MI, USA). During CPB, oxygenation was achieved with a D 708 Simplex adult hollow-fibre oxygenator (Dideco, Mirandola, Italy), and a 40 mm blood filter (Dideco, Mirandola, Italy) was used on the arterial line. During bypass, the hematocrit was maintained between 20% and 25%, non-pulsatile pump flow between 2.0 and 2.5 L/min/m2, and mean arterial pressures between 50 and 65 mmHg. After the aortic cross-clamping, all patients received intermittant, moderately hypothermic blood cardioplegia. Topical hypothermia was also used in all operations. Body temparature was maintained between 28 and 30°C during CPB. Distal anastomoses were performed during a complete period of aortic cross-clamping and proximal anastomoses were performed with partial aortic clamping during rewarming. Only internal mammarian artery and greater saphenous vein grafts were used in all cases. Any cell-saver application was not needed along the course of study. There was not any reoperation for bleeding.

Statistical analyses were performed by SPSS/PC+(ver 5.01) computer program. The probability (p) less than 0.05 was considered significant. The mean and standard error of mean values of all parameters were calculated and indicated. The comparison of parameters for which repeated measurements was made, was performed through "Mann-Whitney U Test". "The Wilcoxon Matched Pair Signed Rank Sum Test" was performed to evaluate the significance coefficients of parameters in each group. The consistency of proportional data was determined by the chi-square test, corrected for continuity, or by "Fisher's Exact Test".

Results

There was not any significant difference between two groups, regarding basic demographic and operative characteristics (age, sex, body surface area, graft number and pump time) (Table 1). The two groups did not differ in comparison of preoperative values of hematocrit, PT, APTT, fibrinogen, factor VIII activation time, vWF and platelet activation tests.

There was a constant decline in hematocrit level of both groups in postoperative all controls compared with the basal value. The mean hematocrit levels of DDAVP and control groups at postoperative 2nd hour were 31.23±2.31% and 30.66±1.92% respectively, being similar between two groups.

Both groups showed significant and similar increases in PT measurements at postoperative 2nd and 24th hours compared with preoperative basal values (p=0.0015 and p=0.0022 for DDAVP and control groups respectively, at postoperative 2nd hour) (Table 2).

Although there were slight increases in APTT

Table **1.** Basic operative and demographic data of the patients (DDAVP: desmopressin group, CPB: cardiopulmonary bypass.)

	Control ri=20	DDAVP n=20	P
Sex (male/female)	15/5 (75/25 %)	1674(80/20%)	0.91
Age (years)	56.50±10.88	57.61±9.75	0.56
Body Surface Area (m^2)	1.77±0.13	L81io.11	0.51
CBPtime(min)	66.08i24.89	75.00±28.69	0.64
Cross-clamp time (min)	49.00±18.48	46.76±14.50	0.73
Number of Anastomosis	2.83±0.83	3.15±0.7	0.44

Table **2.** Alterations in measurements of prothrombin time, fibrinogen, F VIII activation time and vWF levels (F VIII: factor VHt, vWF: von-Willebrand factor, DDAVP: desmopressin group, PO 2: postoperative 2^{nd} hour, PO 24: postoperative 24^{th} hour; bold values indicate significance.)

	Control	DDAVP	
Prothrombin time (preoperative) (sec)	12.39±1.22	12.23i0.87	0.5862
Prothrombin time (PO 2)	16.27±1.87	15.9011.30	0.0862
P	**0.0022**	**0.0015**	0.647
Prothrombin time (PO 24)	14.62±1.26	14.06i0.84	0.9783
P	**0.0029**	**0.0015**	0.212
Fibrinogen (preoperative) (mg/dl)	305.95i46.67	298.60i45.78	0.5315
Fibrinogen (PO 2)	263.85i62.31	231.18i41.70	0.1917
P	**0.0121**	**0.0024**	0.127
Fibrinogen (PO 24)	432.69i68.56	384.33i26.44	**0.0143**
P	**0.0022**	**0.0030**	**0.031**
F VIII activation time (preoperative) (sec)	49.30i4.82	48.08i2.04	0.5495
F VIII activation time (PO 2)	46.87i4.52	46.61i2.65	0.9783
P	0.1823	0.1422	0.953
F VIII activation time (PO 24)	46.74i4.96	46.43il.95	0.7855
	0.3465	**0.0131**	0.903
VWF (preoperative) (mU/ml)	13.79i0.40	13.5610.31	0.0865
VWF (PO 2)	13.99.020	14.49il.37	0.6437
P	0.2294	**0.0022**	0.120
VWF (PO 24)	13.97i0.32	13.74i0.19	0.0681
P	0.1823 ' •	**0.0464**	0.118

measurements at postoperative controls compared with preoperative ones, the difference did not reach a significant level between two groups as well as in each of two groups.

The fibrinogen levels of both groups significantly reduced at postoperative 2nd hour (p=0.024 and p=0.0121 for DDAVP and control groups respectively). Although the early reduction had not differed significantly between two groups, fibrinogen level of control group at postoperative 24th hour was significantly higher than that of DDAVP group (p=0.0143) (Table 2). This later rise compared with preoperative values was also significant in each group (p=0.0022 and p=0.0030 for control and DDAVP group, respectively), but there was an intergroup difference favoring control group (p=0.0031)(Table2).

Activation time of factor VIII shortened along the course of study being the differences were not significant between two groups and in each group, however, at postoperative 24th hour, the DDAVP group showed more significant shortening in activation time compared with initial level (p=0.0131) (Table 2).

There was a significant elevation in vWF level of DDAVP group at postoperative 2nd hour (p=0.022) and on postoperative day 1 (p=0.0464) compared with initial value, whereas the differences were not significant in control group as well as between two groups (Table 2).

Tests of platelet aggregation time in response to ADP, collagen and ristocetin were showed significant prolongations in both groups at postoperative 2nd hour. There was also a significant prolongation in platelet aggregation time in response to epinephrine of control group at 2nd hour compared with initial level (277.33±105.29 versus 187.75±41.97 sec; p=0.0376), whereas the prolongation was not significant in study group (218.15±49.19 versus 190.46±34.10 sec; p=0.182). The evaluations at postoperative 24th hour did not show significant differences in both groups. The aggregation times of platelets, in response to collagen and ristocetin, of both groups showed significant prolongations at postoperative 2nd hour compared with initial level (p=0.0GT5 and p=0.0022 for collagen; p=0.0088 and p=0.0310 for ristocetin in DDAVP and control groups respectively). Although it was seemed that the prolongation was more prominent in control group, any significant difference was not detected. The aggregation times of both groups shortened again from 2nd hour to 24th hour, but yet, remained longer than the preoperative ones, being similar between two groups.

The platelet aggregation time in response to ADP was significantly prolonged at postoperative 2nd hour in both DDAVP (183.61±32.25 sec; p=0.0277) and control (281.00±123.41 sec; p=0.0037) groups compared with initial levels (145.23±35.48 and 139.83±21.98 sec for DDAVP and control groups, respectively). The prolongation in aggregation time of control group was significantly higher than that of DDAVP group (p=0.0192). The aggregation times of both groups shortened again at postoperative 24th hour, but remained longer than the preoperative ones and the difference between two groups was not significant (Figure 1).

The platelet activation percents of platelets induced by ADP, epinephrine, collagen and ristocetin showed significant reductions in control group at postoperative 2nd hour (p=0.0499, p=0.0076, p=0.0342, and p=0.0254 for ADP, epinephrine, collagen, and ristocetin consecutively), whereas the DDAVP group did not have such obvious changes. The change in activation percents of DDAVP group that obtained through aggregation slopes, was less than that of control group, and was not significant along the course of study. The activation percents of both groups at 24th hour did not show significant differences in comparison with preoperative and later ones.

The mean postoperative blood loss in first two-hour were 48.30±24.43 and 78.33±50.60 mL in DDAVP and control groups respectively, and two groups did not differ. The blood loss of DDAVP and control groups on postoperative day 1 were 418.33±116.37 and 533.33±231.25 mL, respectively; as similar. Consequently, the total blood loss of DDAVP group was similar to that of placebo group (462.50±123.44 versus 575.83±231.02 mL).

Twelve patients in control group had received 15 units of blood totally, whereas 13 patients in DDAVP group received 9 units. Although the mean postoperative blood transfusion needs of DDAVP group at 2nd hour (0.38±0.5 versus 0.75±0.96

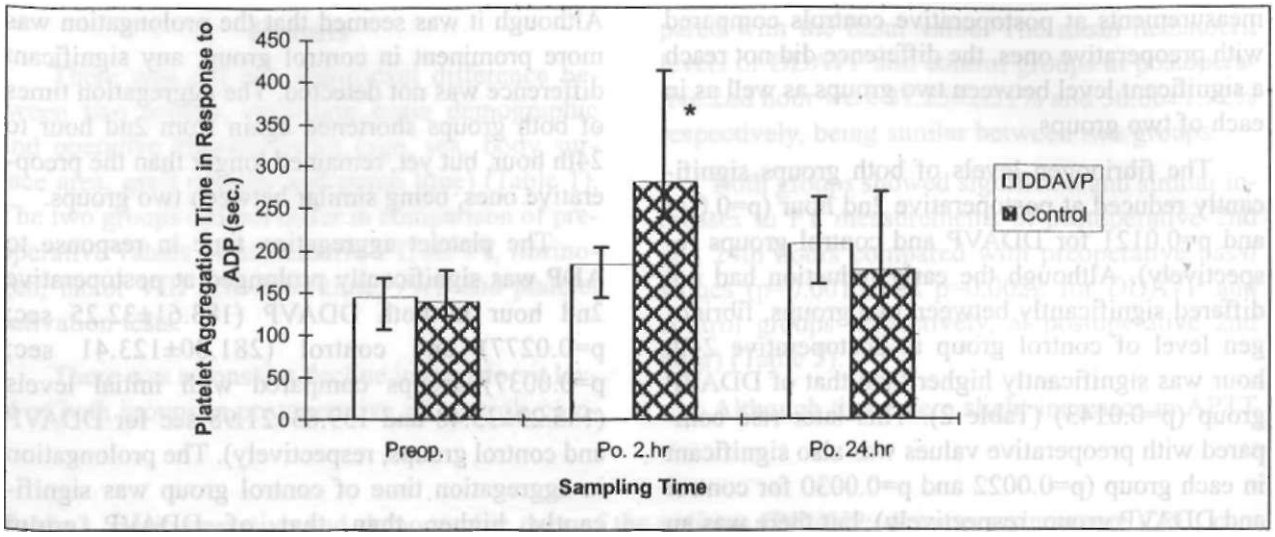

Figure 1. Alterations in platelet aggregation times of desmopressin and control groups, in response to ADP. (DDAVP: desmopressin, Preop: preoperative, Po 2. hr: Postoperative 2nd hour, Po 24.hr: postoperative 24th hour, ADP: adenosine di phosphate; asterisk indicates significance: p=0.0192.)

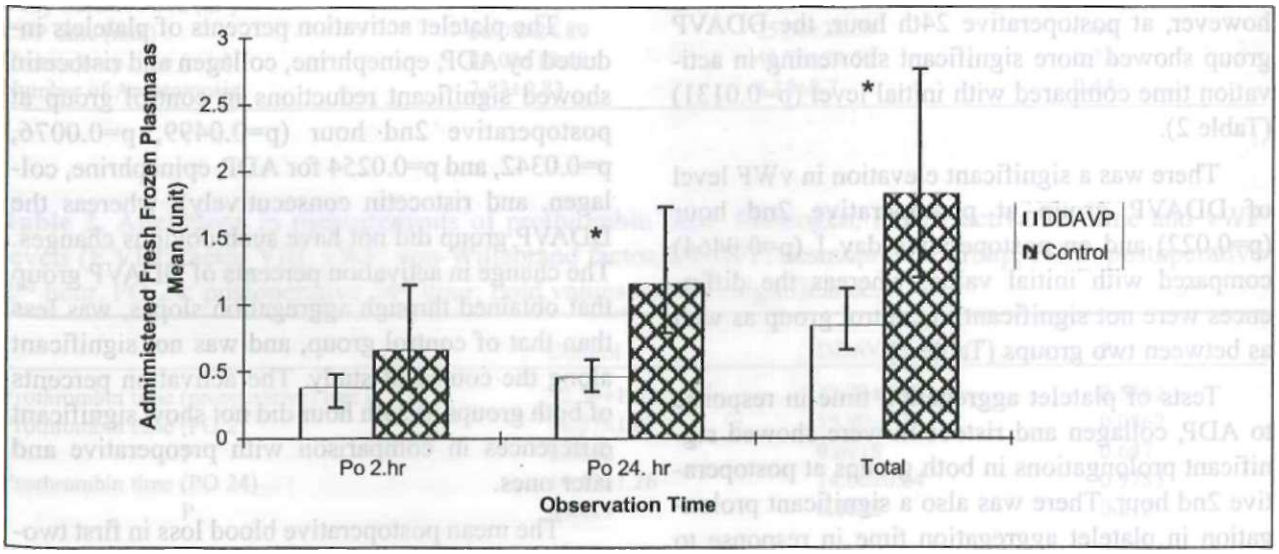

Figure 2. The comparison of fersh frozen plasma need between desmopressin and control groups. (DDAVP: desmopressin, Po 2.hr: Postoperative 2nd hour, Po 24. hr: postoperative 24 th hour; asterisks indicate significance: p=0.0072 at Po24.hr and p=0.0020 as total).

units) and on postoperative day 1 (0.32±0.48 versus 0.5±0.52 units) as well as totally (0.69±0.75 versus 1.25±1.05 units) seemed fewer than those of control group, the differences did not reach a significant level. Twelve patients in control group had received 22 units of fresh frozen plasma (FFP) totally, whereas 13 patients in DDAVP group received 11 units. Despite the similar FFP needs of both groups until postoperative 2nd hour, the DDAVP group needed significantly fewer FFP than the control group at the end of postoperative day 1 (0.46±0.51 versus 1.16±0.57 units; p=0.0072), and as total amount (0.84±0.68 versus 1.83±0.93 units; p=0.002) (Figure 2).

Discussion

Despite the widespread and improved success of open heart surgery, patients placed on CPB have an increased susceptibility to postoperative bleeding. Reoperation for bleeding control and sometimes life threatening hemorrhage occur during the postoperative period. The hemorrhagic tendency accompanying CPB is a complex reflection of multiple hemostatic defects, including heparin and protamine excess, heparin rebound, low platelet count, functional deficits of platelets, low fibrinogen, primary fibrinolysis, and disseminated intravascular coagulation (DIC) (9, 10).

Whether the DDAVP can treat excessive bleeding after CPB or not is still being a subject of many studies (9, 10). Like antidiuretic hormone (ADH), epinephrine, and insulin desmopressin releases some important hemostatically active substances from vascular endothelium, such as factor V m , prostacyclin, t-PA and vWF (12). Factor VIII coagulation activity increases up to 2 to 20 times as much as basal level within 30 to 90 min of DDAVP injection. Release of large vWF multimers leads more sustained factor VIII activity, after desmopressin has been eliminated. Although prostacyclin, by preventing platelet activation and t-PA, can block the hemostatic process, the overall effect of DDAVP favors hemostasis (12). DDAVP is administered in 0.3 mg/kg doses by intravenous, intranasal or subcutaneous routes. The biologic half life of 55 min belies the clinical effects that last at least 6 hours (13). Although there are some controversial reports of coronary thrombosis temporarily associated with DDAVP management, blaming the DDAVP as thrombogenic and therefore dangerous in patients with ischemic heart disease, we did not observe such an effect.

Czer and colleagues reported that the 23 patients who demonstrated postoperative drainage greater than 100 ml/hr for at least 2 hours and received DDAVP, 20 mg intravenously had needed fewer blood products (15±13 versus 29±19 units) than other 16 patients who received no drug. A11 patients had received dipyridamole prior to surgery. The nonrandomization and lack of blinding were deficient points of this study (11). In a later double blind, prospective study de Prost and coworkers demonstrated that DDAVP had no hemostatic effect in patients with substantial bleeding and prolonged bleeding times after cardiac surgery (14). Lo Cicero and colleagues reported that 74 patients who had received DDAVP because of postoperative excessive bleeding needed more blood products than 91 patients of control. However, this result could be expected since desmopressin receiving patients were selected on basis of excessive bleeding (15). Salzman et al. in a double blind randomized trial, concluded that DDAVP management was effective in reducing blood loss and transfusion requirements, thus confirmed results of former nonrandomized trial of Czer et al. However, this study was also debatable, because the selected patients had suffered excessive blood loss (9).

The objective of our study was to confirm the efficacy of DDAVP in reducing blood loss and transfusion requirements in patients undergoing CABG. Postoperative total blood loss of both groups was within normal limits that were accepted in most of centers. Although postoperative hemorrhage of DDAVP group seemed less than that of control group, there was not an intergroup difference. Blood requirements also were similar between two groups, however, DDAVP group needed fewer units of fresh frozen plasma in postoperative period.

Except the significant elevation in vWF level of DDAVP group that observed at only postoperative 2nd hour, all other coagulation parameters did not significantly differ between two groups. We also, did not observe any significant difference regarding intraoperative blood loss of both groups, measured as drained volume (mL). Besides the lack of demonstrable correlation between intraoperative blood loss and the level of vWF in the samples obtained two hours after the treatment, the deficiency of coagulation factors in remarkable degrees that enable to cause bleeding after CPB is described as a very rare event (16). Both groups of our study showed significant prolongations in platelet aggregation time at postoperative 2nd hour, however these changes were less prominent in DDAVP group than those in control group. Especially, the ADP induced platelet aggregation time of DDAVP group showed significantly less prolongation at 2nd hour than that of control group ($p=0.0192$). These findings suggest the better and improved platelet

functions provided by DDAVP management. Although the plasma level of vWF, that has an important impact on platelet aggregation on subendothelial as well as artificial surfaces, significantly elevated in DDAVP group, there was not a considerable difference in plasma concentration between both groups. It might be reasonable to explain this observation with the study of Cattaneo and colleagues, that asserted the role of possible mechanisms independent of release vWF, in hemostatic effect of DDAVP (17). Cattaneo and colleagues were also showed in a later study describing meta analysis of 17 double blind placebo controlled trials, comprising 1200 patients overall, that DDAVP reduced the postoperative blood loss in 39% of patients with excessive blood loss and the efficacy lessened to 9% when all the patients with both normal and excessive bleeding were taken into account (18).

Cattaneo and colleagues also claimed that shear-induced platelet aggregation was potentiated by desmopressin (19). Since shear-induced platelet aggregation can cause thrombotic occlusions in stenotic arterial vessels, the potential hazardous effects of DDAVP on arterial thrombosis must be investigated thoroughly. It was indicated in most of the studies that desmopressin had not a proved beneficial effect on postoperative bleeding in patients who underwent elective, uncomplicated surgical procedures and without any known bleeding disorder. It was also suggested as a common consequence of aforementioned studies that DDAVP might be useful if one of these conditions was present such as, high bleeding risk, reoperation, complicated and combined operations, pump time exceeding two hours and any diagnosed bleeding disorder due to inherent factors or preoperative drug management. Moreover, desmopressin might be more protective than the aprotinin in patients receiving acetyl salisilic acid (aspirin) treatment at the time of coronary artery bypass surgery (20).

The postoperative bleeding and other complications gradually subsided in open heart surgery due to less traumatic extracorporeal circuit and oxygenator systems come into current practice with the advent of newer technologies and improved trial in surgical skill, and preoperative as well as postoperative care. The preoperative preservation of autologous blood by predonation technique renders the occasion of whole autologous blood transfusion after the operation, therefore considerably reduces the postoperative bleeding as well as blood transfusion need (21).

The conclusions of our study and former ones suggest that, despite the improved platelet functions, the administration of DDAVP in patients undergoing elective CABG and without any diagnosed bleeding disorder, does not confer a reduction in both intraoperative and postoperative blood losses. It could be recommended, however, in patients undergoing complicated or emergent operation with increased risk of bleeding and excessive blood loss.

REFERENCES

1. Edmunds LH Jr, Ellison N, Colman RW, Niewiarowski S, Rao AK, Addonizio VP Jr, Stephenson LW, Edie RN. Platelet function during cardiac operation: comparison of membrane and bubble oxygenators. J Thorac Cardiovasc Surg 1982; 83(6):805-12.
2. Teoh KH, Christakis GT, Weisel RD, Wong PY, Mee AV, Ivanov J, Madonik MM, Levitt DS, Reilly PA, Rosenfeld JM et al. Dipyridamole preserved platelets and reduced blood loss after cardiopulmonary bypass. J Thorac Cardiovasc Surg 1988; 96(2):332-41.
3. Musial J, Niewiarowski S, Rucinski B, Stewart GJ, Cook JJ, Williams JA, Edmunds LH Jr. Inhibition of platelet adhesion to surfaces of extracorporeal circuits by disintegrins. RGD-containing peptides from viper venoms. Circulation 1990; 82(l):261-73.
4. Niewiarowski S, Edmunds LH Jr. Fibrinogen receptor antagonists in cardiopulmonary bypass. J Thorac Cardiovasc Surg 1993; 106(5):931-3.
5. Lindon JN, Salzman EW, Merrill EW, Dincer AK, Labarre D, Bauer KA, Rosenberg RR. Catalytic activity and platelet reactivity of heparin covalently bonded to surfaces. J Lab Clin Med 1985; 105(2):219-26.
6. Levin EG, Marzec U, Anderson J, Harker LA. Thrombin stimulates tissue plasminogen activator release from cultured human endothelial cells. J Clin Invest 1984; 74(6): 1988-95.
7. Kucuk O, Kwaan HC, Frederickson J, Wade L, Green D. Increased fibrinolytic activity in patients undergoing cardiopulmonary bypass operation. Am J Hematol 1986; 23(3):223-9.
8. Bidstrup BP, Royston D, Sapsford RN, Taylor KM. Reduction in blood loss and blood use after cardiopulmonary bypass with high dose aprotinin (Trasylol). J Thorac Cardiovasc Surg 1989; 97(3):364-72.

9. Salzman EW, Weinstein MJ, Weintraub RM, Ware JA, Thurer RL, Robertson L, Donovan A, Gaffhey T, Bertele V, Troll J et al. Treatment with desmopressin acetate to reduce blood loss after cardiac surgery. A double-blind randomized trial. N Engl J Med 1986; 29:314(22): 1402-6.

10. Rocha E, Llorens R, Paramo JA, Areas R, Cuesta B, Trenor A M. Does desmopressin acetate reduce blood loss after surgery in patients on cardiopulmonary bypass? Circulation 1988; 77(6): 1319-23.

11 .Czer LS, Bateman TM, Gray RJ, Raymond M, Stewart ME, Lee S, Goldfinger D, Chaux A, Matloff JM. Treatment of severe platelet dysfunction and hemorrhage after cardiopulmonary bypass: reduction in blood product usage with desmopressin. J Am Coll Cardiol 1987; 9(5): 1139-47.

12. Mac Gregor R, Roberts EN, Provose CV, Broomhead AF, Ozolius M,, Litka P. Fibrinolytic and haemostatic responses to desamino-D-arginin vasopressin administered by intravenous and subcutaneous routes in healthy subjects. Thromb Haemost 1988; 59:34-9.

13. Manucci PM. Desmopressin: a nontransfusional form of treatment for congenital and acquired bleeding disorders. Blood 1988; 72:1449-55.

14. de prost D, Barbier-Bohm G, Hazebroucq I, Ibrahim H, Bielsky MC, Hvass U, et al. Desmopressin has no benificial effect on excessive postoperative bleeding or blood product requirements associated with cardiopulmonaery bypass. Thromb Haemost 1992; 68:106-10.

15. Lo Cicero JL III, Massad M, Materno J. Effect of desmopressin acetate on hemorrhage without identifiable cause in coronary bypass patients. Am Surgeon 1991; 57:165-8.

16. Mammen EF, Koets MH, Washington BC, Wolk LW, Brown JM, Burdick M, Selik NR, Wilson RF. Hemostasis changes during cardiopulmonary bypass surgery. Semin Thromb Hemost 1985; 11(3):281-92.

17. Cattaneo M, Moia M, Delle Valle P, Castellana P, Mannucci PM. DDAVP shortens the prolonged bleeding times of patients with severe von Willebrand disease treated with cryoprecipitate. Evidence for a mechanism of action independent of released von Willebrand factor. Blood 1989 Nov 1; 74(6): 1972-5.

18. Cattaneo M, Harris AS, Stromberg U, Mannucci PM. The effect of desmopressin on reducing blood loss in cardiac surgery-a meta-analysis of double-blind, placebo-controlled trials. Thromb Haemost 1995; 74(4): 1064-70.

19. Cattaneo M, Lombardi R, Bettega D, Lecchi A, Mannucci PM. Shear-induced platelet aggregation is potentiated by desmopressin and inhibited by ticlopidine. Arterioscler Thromb 1993; 13:393-7.

20. Catalyurek H, Oto O, Acikel U, Hazan E, Silistreli E, Ay N, Berber B, Ozmen O. The effects of desmopressin and low dose aprotinin on postoperative mediastinal drainage in patients receiving aspirin therapy before coronary artery bypass surgery. GKDC Dergisi 1999; 7:75-8.

21. Love TR, Hendren WG, O'Keefe DD, Daggett WM. Transfusion of predonated autologous blood in elective cardiac surgery. Ann Thorac Surg 1987; 43(5):508-12.