DESMOPRESSIN IN SCOLIOSIS SURGERY

R.Emre ACAROĞLU* Oktay ÖZDEMİR* Ömür ERÇELEN*
Ahmet ALANAY* A.Mazhar TOKGÖZOGLU

Reconstructive spinal surgery in scoliotic patients is known to be associated with excessive blood loss. Effects of Desmopressin (1-deamino-8-D-arginin vasopressin) on blood loss and urinary output in patients undergoing anterior and/or posterior scoliosis surgery was studied on 21 patients. Patients were randomized into desmopressin (DDAVP) (n = 12) and placebo (n = 9) groups. The amount of blood loss, urine output, haematocrit values, and the required blood and fluid intake were monitored at 0, 30, 60, 90, 120, 150, 180 min. during the operation using a cell saver and at the 24 th hour after surgery. Results were evaluated using two factor ANOVA (DDAVP vs. Placebo and Anterior vs. Posterior).

A significant difference in the number of operated levels was found between the anterior and posterior surgery groups along with a significant difference in the average duration of the operations. The blood loss parameters during surgery, total blood loss, blood loss/number of operated levels, required amount of fluid intake, haematocrit values, and diuresis parameters were found not to be sensitive to either the type of surgery or to the presence of DDAVP treatment.

The preliminary results of our random-prospective study indicate that DDAVP treatment probably does not have a significant effect on the blood loss in scoliosis surgery, but does not cause any significant side effects either. These findings need to be revalidated by increasing the number of patients included in this study.

Key words: *Scoliosis surgey. Desmopressin.*

INDRODUCTION

Scoliosis surgery is known to be associated with significant blood loss as patients may lose their estimated blood volume or more (9, 10). The duration of operation, number of operated levels, surgical dechnique used, type of bone grafts utilized, type of anesthesia, arterial blood pressure during surgery, and positioning of the patients are factors known to effect the blood loss (8). Furthermore, in patients with idiopathic scoliosis abnormalities in platelet aggregation have bee identified (16).

DDAVP is an analogue of the natural hormone Vasopressin with an antidiuretic/pressor ratio 2000 to 3000 times more than the original hormone. It causes the release of Von Willebrand factor from the endothelial cells along with tissue type pasminogen activator and prostaglandins (5, 13). The increase in Von Willebrand factor is thought to be associated with the hemostatic activity in certain types of Von Willebrand's disease as well as chronic liver and kidney failures (1, 7).

Several studies have reported beneficial effects of DDAVP on blood loss in cardiac surgery especially in patients undergoing extra-corporeal circulation (4, 12, 14, 15), but the effectivenes during spinal surgery has been controversial in the limited number of experimental studies published. kobrinsky and coworkers have reported a significant decrease in blood loss in patients undergoing spinal fusion with Harrington instrumentation (6), while Guay and coworkers arrived in an exactly opposite conclusion (3). the incidence and severity of published peri-operative side effects, especially on the urinary output has also been a matter of controversy. Hence, the objectives of this study were 1) to re-evaluate the efficacy of DDAVP for reduction of blood loss in scoliosis surgery, and 2) to evaluate the side effects associated.

MATERIALS AND METHODS

The study group consisted of twenty-one patients with scoliotic deformities of the spine. These patients were randomized into a study group (DDAVP) (n = 12) or a control group (Placebo) (n = 9). Patients undergoing anterior and/or posterior surgeries were assigned to each group using blocked randomization. Distribution of the study population according to etiology of deformity and type of surgery can be seen in Table 1. All patients were treated by two surgeons, and a double blind study design was used in which the operating surgeon is not aware of the group patient is assigned at the time of surgery. Either 0.3 microgram

* Departments of Orhopaedics and Traumatology, Hematology Anesthesiology Hacettepe University Faculty of Medicine

Table 1: Distribution of the study population

No of Patients	Anterior	Posterior	Total
DDVP	6	6	12
Plasebo	4	5	9
Total	10	11	21

per kg body weight DDAVP in 200 ml saline solution or only 200 ml saline solution were given to the patients in 20 min. using an IV route during the induction of anesthesia, usually beginning before the positioning of the patients on the operating table. A cell saver device (Shiley products, Chicago, USA) was used in every surgery so as to monitor the blood loss during surgery as well as to decrease the necessary amount of bank blood transfusion. Hypotensive anesthesia and epinephrine injections were not used in any patient throughout this study. Total blood loss, total urinary output and haematocrit levels were monitored at 0, 30, 60, 90, 120 and 150 min. during surgery and at the 24th hour after surgery. Total blood loss values were corrected of total estimated blood volume. Urinary output values were corrected as per kg body weight. Total required fluid and blood infusions were also corrected as per kg body weight.

Results were analyzed using the SPSS package (Microsoft Corp.) installed on a PC. Two factor ANOVA was performed so as to evaluate the sensitivity of the above defined variables to treatment (DDAVP vs. Placebo) as well as to the type of surgery utilized (Anterior vs. Posterior). Etiologic factors and different types of operation or instrumentation were not analyzed as independent variables at this stage of the study because of the limitations due to the number of patients in each given variable.

RESULTS AND DISCUSSION

Significant differences were noted in the number of operated levels and the duration of operation by the type of surgery, both parameters appearing higher in the posterior surgery group ($p < 0.05$). These parameters were not significantly different in the treatment (DDAVP) group compared to the placebo. This finding should be considered as the rationale of the present statistical design used in this study.

Table 2: Blood loss and replacement parameters ($p > 0.05$ for all parameters)

	DDAVP Anterior	DDAVP Posterior	Plasebo Anterior	Pasebo Posterior
Total Blood Loss (ml)	874 ±1158	1275 ±767	362 ±298	637 ±411
Total Blood Loss/no. of levels (ml)	237 ±409	88 ±60	71 ±44	52 ±28
Required Bank Blood Replacement (ml/kg)	6 ±16	13 ±6	0 ±0	8 ±11
Required Blood Replacement (ml/kg)	24 ±34	29 ±16	11 ±10	15 ±14
Required total Fluid Replacement (ml/kg)	72 ±51	66 ±14	37 ±6	37 ±18

The measurements total blood loss, total blood loss per kg body weight, and total blood loss normalized by the estimated total blood volume, as well as the tota required fluid and blood replacements can be seen in the study groups can be seen in Table 2. Neither of these variables were found to be significantly different in either of the study groups. Total amount of bank blood transfused to our patients also did not demonstrate any significant dependence on either the treatment or the type of surgery (Table 2). These findings indicate that DDAVP treatment so as to reduce blood loss, and decrease the amount of bank blood transfusions during any tpe of scoliosis surgery should not be considered as an effective alternative to other methods such as the utilization of hypotensive anesthesia or use of autologous predonated blood in patients undergoing major reconstructive spinal surgery. The lack of any significant statistical interaction between the type of treatment and the type of surgery ($p > 0.05$) indicates that the effects of DDAVP on blood loss parameters is not sensitive to the type of surgery patients underwent.

Blood loss at different intervals during surgery was analyzed in an effort to identify any possible time frame in which the treatment is effective. Loss of hemostatic effects of DDAVP during surgery because of dilution associated with excessive blood loss may effect the study results based on total blood loss parameters, and may be thought to obscure any significant effect during the early stages of the operation. the results of measurements of total blood loss total blood loss per kg in our study groups can be seen in Fig. 1. Any significant difference in blood loss between study groups could not be demonstrated during any stage of the operations ($p > 0.05$). Haematocrit levels were also found not to be significantly sensitive to DDAVP treatment at any stage (Fig 2). these findings indicate that DDAVP treatment does not significantly decrease blood loss during any stage of the surgery and therefore may not be a valid alternative for blood preservation even in operations with short duration.

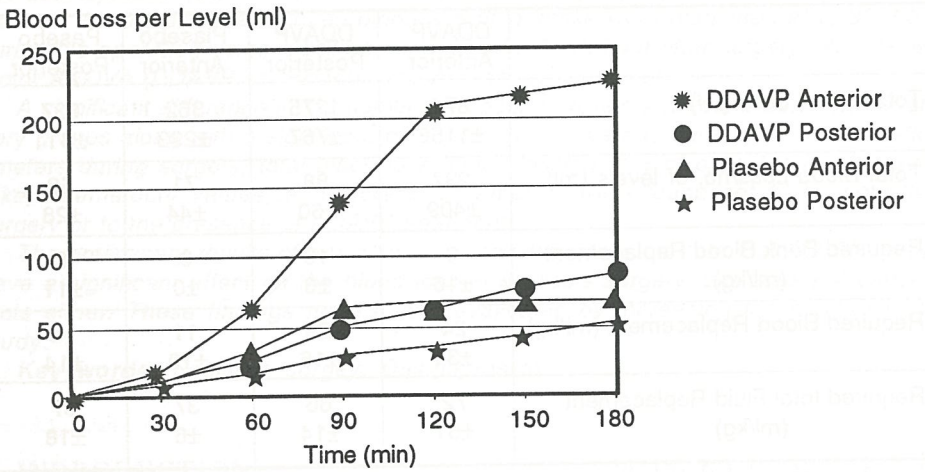

Figure 1: Bloods loss per operated levels by the duration of operation ($p > 0.005$ for all study groups)

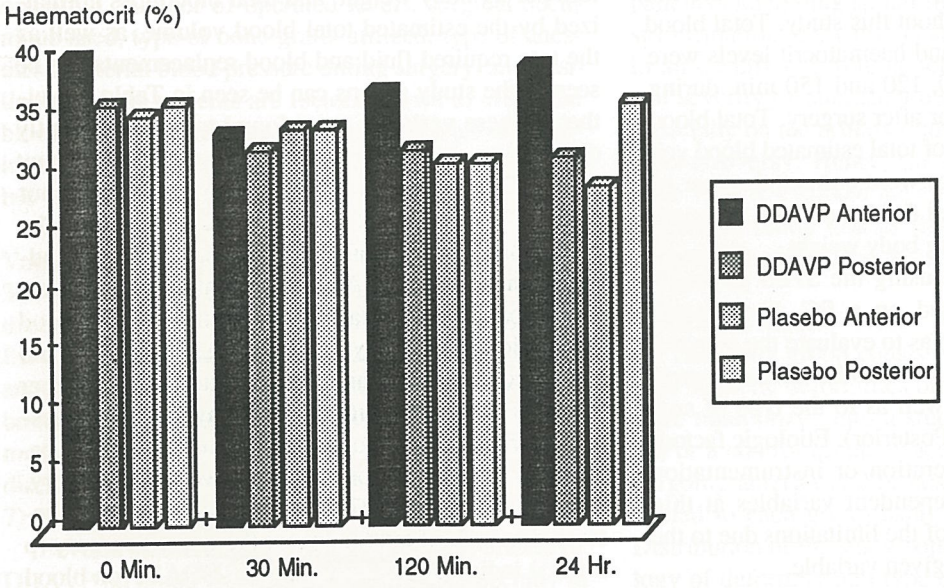

Figure 2: Haematocrit values by time ($p > 0.05$ for all study groups)

Guay and associates have demonstrated significant differences in the urinary output of their patients during the operation as well as at the 24th hour. The results of our measurements of total urinary output per kg body weight at the 24th hour can be seen in table 3. These values are slightly higher compared to those reported by Guay et al. (3), and the urinary output could not be demonstrated to be sensitive to the modality of treatment in our study. This discrepancy may be explained by the findings of Flordal and Ljungstrom denoting that the long lasting antidiuretic effect of desmopressin seen in healthy individuals may be absent in surgical patients, possibly because of the compansatory increase in glomerular filtration rate (2).

The inadequacy of

Table 3: Urinary Output per kg Body Weight in 24 Hours ($p > 0.05$)

	DDAVP Anterior	DDAVP Posterior	Plasebo Anterior	Pasebo Posterior
Urinary output	56	27	40	44
in 24 hours (ml/kg)	+/-41	+/-7	+/-11	+/-9

the number of patients in the study groups may be postulated as a limitation in this study. Future work on this subject will include the expansion of the study to a larger population as well as the evaluation of any possible effects of DDAVP on hematological parameters in patients, and any possible correlations between these parameters and blood loss.

CONCLUSIONS

The coclusions of this study were: 1) DDAVP could not be demonstrated to be effective in reduction of blood loss in patients undergoing scoliosis surgery, and, 2) DDAVP does not have any significant side effects, especially on urinary outputs of patients.

REFERENCES

1. Agnelli G, Berettini M, deCunto M, Nenci GC; Desmopressin induced improvement of abnormal coagulation in chronic liver disease. Lancet 1983; 1:645.
2. Flordal PA, Ljunstrom KG; Renal effects of high dose desmopressin and dextran. A study in normal subjects and in patients undergoing total hip replacement. Acta Anesthesiol Scand 1993; 37, 1-6.
3. Guay J, Reinberg C, Poitras B, David M, Mathews S, Lortie L, Rivard GE; A trial of desmopressin to reduce blood loss in patients undergoing spinal fusion for idiopathic scoliosis. Anesth Analg 1992; 75, 405-10.
4. Hackman T, Gascoyne RD, Naiman SC; A trial of desmopressin (1-desamino-8-D-arginine vasopressin) to reduce blood loss in uncomplicated cardiac surgery. N Eng J Med 1989; 321, 1437-43.
5. Horrow JC; Desmopressin and antifibrinolytics. Int Anesthesiol Clin 1990; 28, 230-6.
6. Kobrinsky NL, Letts RM, Patel LR, Israels ED, Monson RC, Schwetz N, Cheang MS; 1-Desamino-8-D-arginine (desmopressin) decreases operative blood loss in patients having Harrington rod spinal fusion surgery. Ann Intern Med 1987; 107, 446-50.
7. Mannucci PM, Remuzzi G, Pusineri F, Lombardi R, Valsecchi C, Mecca G, Zimmerman TS; Deamino-8-d-arginine vasopressin shortens the bleeding time in uremia. N Eng J Med 1983; 308, 88-93.
9. Relton JES, Conn AW; Anaesthesia for the surgical correction of scoliosis by the Harrington method in children. Can J Anaesth 1963; 10, 603-15.
10. Relton JES, Hall JE; An operative frame for spinal fusion: A new apparatus designed to reduce haemorrhage during operation. J Bone Joint Surg 1967; 49B, 327-32.
11. Richardson DW, Robinson AG; Desmopressin. Ann Intern Med 1985; 103, 228-39.
12. Rocha E, Lorens R, Paramo JA, Arcas R, Cuesta B, Trenor AM; Does desmopressin acetate reduce blood loss after surgery in patients on cardiopulmonary bypass? Circulation 1988; 77, 1319-23.
13. Ruggeri ZM, Manucci PM, Lombardi R, Federici AR, Zimmerman TS; Multimetric composition of factor VII/Von Willebrand factor following administration of DDAVP: Implications for pathopysiology and therapy of Von Willebrand's disease subtypes. Blood 1982; 59, 1272-8.
14. Salzman EW, Weinstein MJ, Weintraub RM; Treatment with desmopressin acetate to reduce blood loss after cardiac surgery. A double blind randomized trial. N Eng J Med 1986; 314, 1402-6.
15. Shear MD, Wadsworth LD, Rogers PC, Sheps S, Ashmore PG, The effect of desmopressin acetate (DDAVP) on postoperative blood loss after cardiac operations in children. J Thorac Cardiovasc Surg 1989; 98, 217-9.
16. Yarom R, Muhlrad A, Hodges B, Robin GC; Platelet pathology in patients with idiopathic scoliosis: Ultrastructural morphometry, aggregations, x-ray spectrometry, and biochemical analysis. Lab Invest 1980; 43, 208-16.