Autologous blood transfusion in hip replacement

No effect on blood loss but less increase of plasminogen activator inhibitor in a randomized series of 80 patients

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80 patients underwent total hip replacement (THR) for primary coxarthrosis. In a randomized study, half of them donated 2 units of blood before operation. One unit was collected 4 weeks and one 2 weeks before the scheduled THR. All except 1 patient tolerated the predonations well. Total blood losses were similar in both groups. Additional bank blood was given in 7/38 in the predonation group, compared to 29/40 in the control group.

Hemostatic parameters were studied in 10 consecutive patients in each group. Plasminogen activator inhibitor 1 (PAI-1), a possible risk parameter for thromboembolism, was significantly more increased postoperatively in the control group, which received only homologous blood. Platelet count, prothrombin complex, antithrombin III and von Willebrand factor antigen were significantly reduced and C reactive protein increased after surgery in both groups.

We recommend predonation of 2 autologous units before a primary THR. In most cases, such predonation makes homologous blood transfusion unnecessary. The use of predonated blood causes no reduction of blood loss in THRs, but the increase in PAI-1 seen after homologous transfusions is avoided.

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A reduced postoperative blood loss after a total hip replacement (THR) has been reported after autologous transfusions (Elawad et al. 1991a). The aim of our study was to investigate the effect of preoperative donation of blood on blood loss during THR and to analyze the effects of predonation and blood transfusion on several hemostatic parameters.

Patients and methods

80 patients with primary coxarthrosis who were to undergo THR were randomly allocated by sealed envelopes to preoperative blood donation or no donation (Table 1). Patients with hepatitis, severe coronary artery disease or heart failure, hematologic diseases, hemoglobin concentration less than 110 g/L or body weight less than 50 kg were not eligible for the study.

In the autologous group, 2 units (0.9 L) of blood were collected, one of the units 4 and the other 2 weeks before the scheduled operation. The blood was stored at +4 °C not more than 6 weeks and was handled according to existing routines and regulations for homologous blood. The autologous units were tested for infectious disease markers as was the homologous blood, although it is not permitted in Sweden to use "crossing over" of autologous units for homologous use. All autologous blood, as well as the homologous blood was retransfused as packed red blood cells (leucocyte-depleted blood), if needed. All patients received iron supplementation consisting of 100 mg Fe^{2+} given orally 2 times a day after the first donation until the day of operation. All patients except 1 woman, who felt dizzy after the first donation and refused to donate another unit, tolerated the predonation well. 2 women who were allocated to predonation were excluded: 1 woman refused to participate

Table 1. Patient data. Mean (SD)

	Autologous group (n 38)	Control group (n 40)
Men / women	15 / 23	6 / 34
Body weight	77 (14)	72 (14)
Age	71 (5)	71 (5)
Prosthesis		
BiMetric	10	7
Charnley	27	30
Stanmore	1	3
Duration of surgery (min)	107	97

as she wanted to be operated on as soon as possible and the other was excluded because of a low hemoglobin (110 g/L) on the day before donation. Operations were performed under spinal anesthesia. During the operation, all patients received an infusion of 0.5–1 L Macrodex for thromboprophylaxis and plasma expansion. They were also given 0.5 L Macrodex on the first and the third postoperative days. The patients were operated in a lateral position, using a posterior approach. Therefore practically all blood lost stayed in the wound and was easily collected in the swabs and the suction device. Blood loss was estimated in 2 ways: measurement and calculation. Intraoperative blood loss—i.e., the amount of blood in every swab used and the volume of blood *measured* in the suction device—were assessed visually by experienced nurses. The postoperative blood loss was collected in graded drainage bags until the first postoperative morning. Blood loss was *calculated* from the pre- and postoperative hemoglobin levels and the amount of erythrocyte hemoglobin transfused in order to include hematomas, intravascular thrombus formation and hemolysis (Flordal et al. 1992). The hemoglobin concentration was measured 6 weeks before operation, preoperatively and 3 days after surgery.

The last 20 randomized patients, 10 from each group, were studied regarding parameters of platelet function, coagulation and fibrinolysis before blood donation—i.e., in the morning 6 weeks before operation, in the morning before surgery, 2 hours postoperatively and the following morning. Venous samples were taken with minimal stasis from an antecubital vein using the Vacutainer system. Blood anticoagulated with EDTA was analyzed for hemoglobin, platelet count and mean platelet volume (MPV). In plasma obtained from blood anticoagulated with citrate (10:1, v/v), the activated partial thromboplastin time (APTT, Cephotest, Nycomed, Norway), antithrombin III (ATIII, Coatest S-2238, Kabi Diagnostica, Sweden) and prothrombin complex (PK, prothrombin complex assay, Stago, France) were determined. The rest of the plasma was frozen at –70 °C and later analyzed for factor VIII procoagulant activity (FVIII, Coatest S-2222), von Willebrand factor antigen (vWF:Ag, electro-immunoassay according to Laurell), C-reactive protein (CRP) and plasminogen activator inhibitor (PAI-1). The activity of PAI-1 was analyzed with the chromogenic substrate technique (Spectrolyse, Biopool AB, Umeå, reference interval 1.3–14.2 U/mL established at 8.00–11.00 a.m. in 50 healthy controls). The total coefficient of variation for control plasmas analyzed was 7.5% at the level of 17 U/mL. The analysis was performed with microfilter technique, according to the manufacturer's instructions. The bleeding time (modified after Ivy) was measured using the Surgicutt device and 40 mm Hg stasis. Predeposited packed red cells not used by the patients were discarded.

The study was approved by the local ethics committee. All patients gave their consent after oral and written information.

Statistics

Differences between groups were tested with the Mann-Whitney U-test. Differences between groups and changes over time in hemostatic parameters were tested with two-way repeated measures ANOVA. The Fisher exact test was used to test frequencies. Correlations were computed by Pearson's method. The power of clinical and hemostatic parameters to predict blood loss was tested by multiple linear regression with stepwise backward variable elimination. A p-value less than 0.05 was considered significant.

Results

The measured and calculated total blood losses did not differ between the autologous group and the control group (Table 2). Nor did the total transfusion volumes differ between the groups. The mean total volume of Macrodex given during the operation day was 800 (SD 250) mL in the autologous group and 870 (250) mL in the control group (p 0.2). The mean homologous transfusion requirements were 0.3 and 1.8 units, for the autologous group and the control group, respectively ($p < 0.001$). 7 patients in the autologous

Table 2. Amounts of transfusion, blood loss (mL) and hemoglobin concentration (g/L)

	Autologous group (n 38)	Control group (n 40)	P
Number of patients given transfusions (0, 1, 2, 3, ≥4 units)			
0	5	11	
1	6	2	
2	21	19	
3	1	3	
≥4	5	5	
Homologous units	12	73	
Blood loss (mL), Mean (SD)			
Intraoperatively	720 (340)	640 (350)	0.2
Postoperatively	630 (250)	620 (210)	0.9
Total blood loss	1350 (440)	1260 (410)	0.2
Calculated blood loss	1840 (770)	1980 (890)	0.6
Hemoglobin concentration (g/L), Mean (SD)			
6 weeks preop.	139 (12)	136 (10)	0.3
Preoperatively	127 (12)	135 (10)	0.02
3 days postop.	103 (10)	104 (10)	0.7

Table 3. Hemostatic parameters before predonation (6 weeks before operation), preoperatively, 2 hours postoperatively and on the first postoperative day. A autologous group (n 10), C control group (n 10). Means (SD) and significance of change over time

		–6w before op.	Preop.	2 h postop.	First postop. day	Change in perioperative period, p-value	Difference between groups, p-value
Bleeding time (1.8–7.0 min)	A	4.8 (1.2)	3.8 (0.9) [a]	4.5 (2.4)	6.2 (5.3)		
	C	6.1 (3.3)	4.7 (1.8) [a]	4.9 (1.3)	6.6 (5.2)	0.1	0.6
Platelet count (150–400x10^9/L)	A	226 (54)	247 (64)	177 (35)	177 (58)		
	C	248 (37)	298 (31)	202 (28)	169 (40)	< 0.001	0.5
MPV (8.35–10.35)	A	9.7 (1.2)	9.4 (1.4)	8.8 (1.2)	9.3 (1.0)		
	C	8.8 (0.5)	8.5 (0.4)	8.8 (0.5)	9.1 (0.5)	0.02	0.02
PK (70–130%)	A	108 (17)	113 (10)	89 (13)	82 (11)		
	C	116 (11)	111 (16)	90 (15)	78 (17)	< 0.001	0.6
APTT (20–30 sec.)	A	26 (2)	28 (6)	27 (2)	27 (2)		
	C	25 (1)	26 (2)	26 (3)	27 (2)	0.5	0.4
FVIII (55–145%)	A	141 (42)	154 (40) [a]	114 (48)	162 (77)		
	C	160 (46)	152 (38)	158 (140)	144 (53)	0.7	0.6
vWF:Ag (40–180%)	A	170 (42)	169 (39)	126 (31)	178 (30)		
	C	197 (68)	205 (71)	150 (71)	162 (48)	0.002	0.3
AT-III (85–125%)	A	102 (16)	100 (22)	70 (11)	74 (10)		
	C	106 (15)	94 (18)	72 (14)	73 (15)	< 0.001	0.6
PAI-1 (1.3–14.2 U/mL)	A	11.6 (7.6)	10.7 (4.0)	7.3 (4.6)	14.7 (7.9)		
	C	29.1 (30.2)	14.0 (10.6)	19.9 (20.4)	42.7 (38.4)	0.02	0.01
CRP (< 10mg/L)	A	1.5 (2.1)	2.6 (4.2)	1.4 (2.1)	45.6 (16.9)		
	C	2.6 (4.4)	3.0 (6.9)	1.9 (4.6)	47.1 (30.6)	< 0.001	0.7

[a] Difference from 6 weeks preop. $p < 0.05$.

group (n 38) received homologous packed red cells after they had been given their own 2 predonated units, compared to 29 in the control group (n 40), ($p < 0.001$). Predonation of blood resulted in a 4 (95% confidence interval 1.7–11) times reduction of the need for homologous transfusion. 2 predonating patients were given 1 and 5 patients 2 units of homologous blood. The total blood loss was higher in men (1560 (560) mL) than in women (1210 (330) mL), but when expressed as a percentage of each patient's estimated blood volume (Nadler et al. 1962), no difference was found.

There was a correlation between operating time and total blood loss (r 0.41, p 0.0002).

The hemoglobin concentrations did not differ between the two groups 6 weeks before operation. Preoperatively, however, the predonating group had lower hemoglobin concentrations (p 0.002), but there were no differences postoperatively, despite similar blood losses and transfusion volumes (Table 2).

The bleeding time was longer 6 weeks before operation than preoperatively and there was no difference between the groups. After operation, the mean bleeding time was close to the limit of the pathological level in 17/20 and abnormal (> 7 minutes) in 3/20 patients (Table 3).

The platelet counts decreased during surgery in both groups (p 0.001). There was a negative correlation between bleeding time and platelet count (p 0.003).

FVIII increased after the predonations (p 0.04) while other hemostatic parameters were unchanged.

vWF:Ag, PK and antithrombin III decreased during surgery in both groups ($p < 0.001$).

CRP increased postoperatively, with no difference between the groups.

PAI-1 increased postoperatively in the control group (p 0.01; Figure 1) and there was a significant difference between the groups.

No hemostatic parameters or patient factors were identified that could predict the total blood loss.

Discussion

We could not confirm the finding of Elawad et al. (1991a) that predonation of blood would reduce blood loss in THR. In our study, blood loss and the amount of the blood transfusion were similar in the group who received predonated blood and in the one who did not. A similar result was reported by Holman et al. (1993).

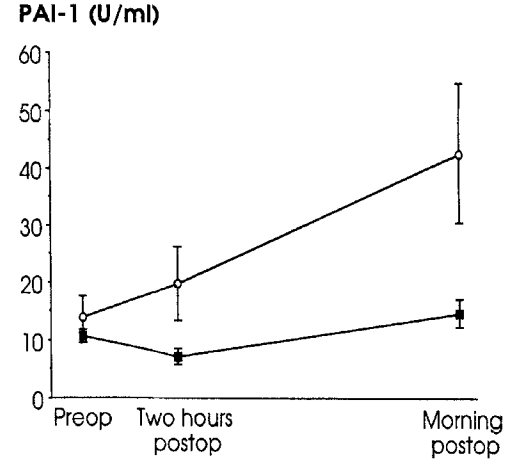

Figure 1. Plasminogen activator inhibitor 1 (PAI-1) in 20 patients undergoing total hip replacement. Significantly higher values are seen in the homologous group (○) than in the autologous group (■). Means and SEM.

The mean bleeding time in all the patients, regardless of the type of transfusion, was significantly shorter the day before surgery than 6 weeks earlier. This could be explained by the fact that the antiinflammatory drugs, used by half of the patients, were excluded 10 days before surgery.

During surgery, the level of vWF:Ag decreased. Normally it rises after trauma, but as has been shown earlier, it is reduced by blood loss and plasma expansion with dextran (Flordal et al. 1991). The mean AT-III levels were about 70% of the normal value postoperatively in both groups (Bredbacka et al. 1987, Flordal et al. 1991).

PAI-1 determinations indicated that fibrinolysis was significantly more inhibited in the group with homologous tranfusion postoperatively. There were no differences in the general health status or laboratory values between the groups that could explain the various PAI-1 levels. PAI-1 increase is the cause of so-called postoperative fibrinolytic shutdown (Risberg 1988), known to be associated with an increased risk of postoperative venous thromboembolism in general (Gordon-Smith et al. 1974) and orthopedic (Eriksson et al. 1989) surgery. Our result indicates that homologous transfusions may be a cause of this fibrinolytic shutdown.

It is still not clear whether autologous transfusions are cost-effective and result in net savings in elective orthopedic operations. Elawad et al. (1991b) reported that the use of autologous blood is cost-effective, while Birkmeyer et al. (1993) found the contrary, which is mainly due to overcollection and wastage. The issue of disposition of predonated blood which is not retransfused to donor patients remains unsolved.

To reduce overcollection and wastage, we recommend that the amount of autologous blood donated before a THR should be two units (Biesma et al. 1994). This reduces four-fold the need for homologous blood transfusion. It also prevents the prothrombotic PAI-1 increase seen in patients receiving homologous transfusions.

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