Local wound and systemic coagulation/ fibrinolysis responses in hip arthroplasty

Influence of allogeneic and autologous blood transfusion

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22 patients undergoing elective hip arthroplasty were studied. In 12 patients, a closed-loop autotransfusion system, without anticoagulant, was used and 10 had an ordinary wound drainage allowing repeated blood sampling from the wound. Plasma concentrations of antithrombin (AT), fibrin, soluble (SF) and fibrin D-dimer were determined preoperatively, 3, 8, and 24 hours after start ing surgery.

Wound drainage blood had increased concentrations of SF and fibrin D-dimer and decreased concentrations of AT compared to reference values and systemic concentrations in patients. Plasma concentrations of SF, fibrin D-dimer and AT did not differ between patients receiving retrieved blood and those receiving stored red blood cell concentrates (RBCs). Patients receiving blood transfusions had lower AT concentrations at 8 hours after starting surgery than those not receiving such a transfusion.

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During the last decade, the use of per- and postoperative autotransfusion at the time of total hip replacement (THR) surgery has become popular. In advanced autotransfusion systems—e.g., the Cell Saver system (Haemonetics, Boston, Mass., USA)—the blood is anticoagulated, washed and filtrated (Ottesen and Frøysaker 1982). In less sophisticated systems, only filtered blood, sometimes anticoagulated, is used (Faris et al. 1990, 1991).

Stryker Consta Vac (Stryker, Kalamazoo, Mich., USA) is a closed-loop system in which no anticoagulant is used. We have found a pronounced hypercoagulability of the retrieved blood, using Stryker Consta Vac (Kristiansson et al. 1995). Reinfusion of such blood, however, seems not to have adverse effects (Faris et al. 1991, Wixon et al. 1994).

The aims of this study, were first, to characterize the coagulation/fibrinolysis pattern at the local trauma site, as reflected by the concentrations of antithrombin (AT), fibrin, soluble (SF), and fibrin D-dimer in blood from an ordinary wound drainage in patients undergoing THR, secondly, to compare this local pattern with concentrations in the systemic circulation and, finally, to compare systemic concentrations of SF, AT and fibrin D-dimer in patients receiving allogeneic to those receiving autologous blood components.

Patients and methods

Patients (Table 1)

Group A, 8 women and 2 men, aged a median of 72 (57–78) years undergoing THR with spinal (5) or epidural block (5) were studied with regard to local and systemic concentrations of AT, SF and D-dimer. To obtain frequent blood sampling, ordinary wound drainage (Bellovac/exudrain/abdovac, Astra Tech, Mölndal, Sweden) was used. These patients were not subjected to autotransfusion of retrieved blood. They received ordinary red blood cell concentrates (RBCs), when the hemoglobin level was less than 110 g/L. 4 patients needed RBCs.

Group B comprised 12 patients (6 women), aged 72 (59–87) years, undergoing THR with epidural (9) or spinal block (3). In these patients, the Stryker Consta Vac autotransfusion system was used. The Stryker Consta Vac drainage was connected at the end of the operation, using a suction level of 60 mmHg. The blood is collected via a polyvinylchloride tubing system, which drains through a 240-µm prefilter into an 800-mL container. After salvage, the blood is transferred from the container into a transfusion bag and immediately passed via a 40-µm screen filter before transfusion. Blood was retransfused when hemoglobin was less than 110 g/L. The retrieved blood remained in the container for a median duration of 2.7

Table 1. Characteristics of patients in group A, and B, medians (ranges)

	Group A (n 10)	Group B (n 12)
Women/men	8/2	6/6
Epidural/spinal	5/5	9/3
Age, years	72 (57–78)	72 (59–87)
Height, cm	168 (162–189)	168 (141–185)
Weight, kg	70 (60–100)	66 (49–100)
Preoperative hemoglobin, g/L	128 (114–142)	133 (120–140)
Peroperative bleeding, mL	1010 (150–2100)	740 (300–3200)
Red blood cell concentrates, mL	0 (0–900)	0 (0–1800)
Duration of surgery, hours	1.8 (0.8–2.8)	2.5 (1.5–4.2)
Hospital stay, days	6 (5–10)	8 (4–14)

Group A received no retrieved blood but were given red blood cell concentrates alone.
Group B received retrieved blood in combination with red blood cell concentrates.
Significant differences between the groups were not found (Wilcoxon two-sample test and Fisher's exact test, when appropriate)

Table 2. Characteristics of patients in Group C and D, medians (ranges)

	Group C (n 6)	Group D (n 16)
Women/men	4/2	8/8
Epidural/spinal	4/2	10/6
Age, years	72 (57–78)	74 (59–87)
Height, cm	173 (163–189)	168 (141–185)
Weight, kg	75 (60–100)	68 (49–100)
Preoperative hemoglobin, g/L	130 (120–142)	122 (114–140)
Peroperative bleeding, mL	610 (150–1745)	890 (300–3200)
Red blood cell concentrates, mL	0	600 (0–1800) [a]
Duration of surgery, hours	2.0 (0.8–2.8)	2.5 (1.5–4.2)
Hospital stay, days	6 (5–10)	8 (4–14)

Group C received no blood transfusion.
Group D received retrieved blood and/or red blood cell concentrates.
[a] $p < 0.05$ (Wilcoxon two-sample test and Fisher's exact test, when appropriate)

(2–4) hours. A median of 250 (120–450) mL retrieved blood was retransfused to the patients. In 5 patients, retrieved blood had to be supplemented with RBCs. The criterion for receiving a blood transfusion was the same as in Group A.

Of the 22 patients, 6 needed no blood transfusion. These patients were compared to the other 16 (Table 2).

All patients were scheduled for THR, because of primary arthrosis, and the Charnley prosthesis was used.

The patients were given non-steroidal anti-inflammatory drugs on demand. No patient was on corticosteroids or other immunosuppressant drugs. Meperidine, 25–50 mg intramuscularly, was used as premedication.

There were no postoperative infections.

Epidural anesthesia was performed with bupivacaine, 5 mg/mL, combined with adrenaline, 5 µg/mL (Marcain® Adrenalin, Astra, Stockholm, Sweden) while spinal anesthesia was performed with hyperbaric bupivacaine, 5 mg/mL (Marcain®, Astra, Stockholm, Sweden). A lumbar approach was used for regional blocks and the level of anesthesia varied between Th VII–Th X.

Dextran 70 (Macrodex®, Kabi Pharmacia, Uppsala, Sweden), 500 mL, as thromboprophylaxis, and cefuroxime, 1.5 g, as infection prophylaxis, were given to all patients peroperatively. Local anesthetics (bupivacaine) were administered via the epidural catheter postoperatively for pain relief. Patients without an epidural catheter received meperidine on demand.

The study was approved by the local Ethics Committee at Karolinska Institute, Huddinge University Hospital. All patients gave informed consent. A randomization between allogeneic and autologous blood was not regarded as appropriate, since most patients refused RBCs, unless necessary.

Experimental protocol and sampling

All samples were obtained in 5-mL citrated vacutainer tubes (Becton Dickinson, Plymouth, UK). The tubes were rotated several times and, after 30 minutes of centrifugation at 2000 G, the plasma samples were aliquoted into plastic tubes (Cerbo AB, Trollhättan, Sweden) and frozen at –70 °C, pending analysis.

Local samples were aspirated from the wound drainage system (Bellovac® exudrain, Astra Tech, Mölndal, Sweden), using a sterile 10-mL syringe. The samples were then transferred to a single citrated vacutainer tube (Becton Dickinson, Plymouth, UK) and handled, as described above.

Samples from the local injury site in Group A were obtained 1, 2, 3, 4, 6, 8, and 24 hours after starting surgery. Venous blood samples from the systemic circulation of patients were obtained via venipuncture preoperatively (before anesthesia) and 3, 8, and 24 hours after the start of surgery.

Analytical procedures

AT (Abildgaard et al. 1977) and SF (Wiman and Rånby 1986) were analyzed with amidolytic methods, using chromogenic substrates with kits from Chro-

mogenix (Mölndal, Sweden). Concentrations of fibrin D-dimer (Elms et al. 1983) were analyzed by ELISA with a kit from Biopool (Umeå, Sweden). Reference values for AT, SF and fibrin D-dimer are 0.86–1.30 IU/mL, < 25 nmol/L and 20–90 µg/L, respectively, and the coefficients of variation interassays are less than 12% for each assay.

Statistics

Patient data are presented as medians and ranges. Patient characteristics in various groups of patients are compared, using the Wilcoxon two-sample test and Fisher's exact test, when appropriate.

Coagulation/fibrinolysis parameters are expressed as mean (SEM) and, when appropriate, as 95% confidence interval. Comparisons between groups and between different time-points were performed using a one-way analysis of variance (ANOVA), with repeated measures. Scheffes F-test was used as a post hoc test. A p-value of less than 0.05 was considered significant.

Results

Wound drainage blood

Concentrations of AT in the wound drainage blood did not change but were lower than reference values. At 1 hour after starting surgery, the AT concentration was 0.38 (SEM 0.02) (0.34–0.43) IU/mL and the lowest values were found at 8 hours after starting surgery, 0.35 (0.02) (0.30–0.39) IU/mL.

All drainage AT concentrations were lower than those in the systemic concentrations, p = 0.0008 for all comparisons. The most pronounced differences were seen after 24 hours, 0.37 (0.02) (0.33–0.40) vs. 0.77 (0.42) (0.67–0.86) IU/mL (p = 0.0008).

SF concentrations were > 200 nmol/L in all samples, with 4 exceptions (range 78–171) mmol/L.

Wound drainage fibrin D-dimer concentrations were analyzed in 2 patients. The concentrations were increased (range 481600–1583000 µg/L), compared to reference values.

Group A vs. group B (Table 3)

Patients in Group B received 250 (100–450) mL retrieved blood. 5 patients also needed RBCs (Table 1).

Concentrations of coagulation/fibrinolysis parameters did not differ between group A and group B. In both groups the AT concentrations remained reduced after 24 hours, compared to preoperative values (p = 0.007). The most pronounced reductions were found 3 hours and 8 hours after the start of surgery in group A and group B, respectively.

Table 3. Mean (SEM) systemic concentrations of AT, SF and fibrin D-dimer, preoperatively (pre), 3, 8, and 24 hours after the start of surgery in group A and B

		Group A (n 10)	Group B (n 12)
AT, units/mL	pre	1.05 (0.06)	0.99 (0.05)
	3	0.73 (0.04)	0.82 (0.04)
	8	0.80 (0.05)	0.73 (0.04)
	24	0.77 (0.04)	0.78 (0.04)
SF, nmol/L	pre	17 (3)	18 (11)
	3	65 (20)	70 (19)
	8	42 (6)	70 (19)
	24	42 (6)	49 (13)
Fibrin D-dimer, µg/L)	pre	251 (36)	201 (24)
	3	3664 (799)	2923 (436)
	8	3383 (639)	3402 (590)
	24	1087 (252)	1166 (322)

Group A: retrieved blood was not transfused, 4 patients received red blood cell concentrates.
Group B: retrieved blood was transfused to all patients, 5 patients also received red blood cell concentrates.
Significant changes between the groups were not found (ANOVA)

Apart from preoperative values, SF concentrations were increased, compared to reference values. In group A, SF concentrations at 3 hours after the start of surgery were higher than preoperative values (p = 0.007). In group B, no significant changes in plasma SF concentrations occurred. Peak SF concentrations were found at 3 hours after the start of surgery in both groups.

All fibrin D-dimer concentrations (Table 3) were higher than reference values. In both groups, elevations were found after 3 and 8 hours, compared to preoperative values, but after 24 hours no difference was detected compared to preoperative concentrations. In group A, peak values occurred after 3 hours and in group B after 8 hours.

Group C vs. group D (Table 4)

For clinical reasons, 6 patients did not require a blood transfusion (group C). In Table 2, they are compared to patients receiving retrieved blood and/or RBCs with regard to patient characteristics (group D). No differences were found, except with regard to transfusion of blood.

Patients receiving no blood had higher AT concentrations at 8 hours than those receiving retrieved blood and/or RBCs (p = 0.04). Preoperative fibrin D-dimer levels (Table 4) were higher in group C than in group D (p = 0.04).

Side effects

No patient in either group had any symptoms that might be attributable to transfusion reactions.

Table 4. Mean (SEM) systemic concentrations of AT, SF and fibrin D-dimer, preoperatively (pre), 3, 8, and 24 hours after the start of surgery in group C and D

		Group C (n 6)	Group D (n 16)
AT, units/mL	pre	1.09 (0.09)	0.99 (0.04)
	3	0.75 (0.05)	0.79 (0.05)
	8	0.86 (0.06) [a]	0.72 (0.03)
	24	0.82 (0.04)	0.76 (0.04)
SF, nmol/L	pre	21 (3)	24 (8)
	3	71 (32)	67 (15)
	8	44 (8)	62 (14)
	24	42 (8)	48 (10)
Fibrin D-dimer, µg/L	pre	308 (41) [a]	191 (20)
	3	3200 (777)	3307 (548)
	8	3386 (893)	3396 (494)
	24	1289 (385)	1070 (249)

Group C: neither retrieved blood nor red blood cell concentrates were transfused.
Group D: retrieved blood and/or red blood cell concentrates were transfused
[a] $p < 0.05$, group C vs. group D (ANOVA)

Discussion

Our findings suggest that transfusion of non-anticoagulated retrieved blood does not influence the coagulation/fibrinolysis profile, as reflected by plasma concentrations of AT, SF and fibrin D-dimer in patients receiving such blood, compared to patients not receiving retrieved blood. The amount of retrieved blood retransfused in the present study, however, was fairly low. The surgical procedure per se and the use of stored RBCs might also have influenced the results. However, concentrations of AT, fibrin D-dimer and SF did not differ between the 7 patients receiving retrieved blood alone and the 4 receiving only RBCs (data not shown). The small number of patients precludes any firm conclusions.

We found a pronounced alteration in the coagulation/fibrinolysis parameters studied in samples from the wound, which reflects the trauma response at the local site of injury. No complications were seen in the patients investigated and only a very minor part of the local alteration affected the systemic circulation. In critically ill patients, the systemic response may be more pronounced than in the case with THR surgery. We found no relationship between plasma SF concentrations and outcome, as reflected by hospital stay. In critically ill patients, however, SF may be a predictor of the outcome (Bredbacka et al. 1993).

Our findings also suggest that the alterations with regard to plasma AT profile were less marked in patients receiving no blood transfusion. These patients, on the other hand, had increased preoperative plasma fibrin D-dimer concentrations.

In summary, the described changes in systemic concentrations of AT, SF and fibrin D-dimer could be related to the trauma response associated with orthopedic surgery (Bredbacka et al. 1987). We found no differences in coagulation/fibrinolysis parameters or clinical side-effects attributable to transfusion of retrieved blood. Thus, provided that comparatively small amounts of retrieved blood are retransfused to the patient, the described autotransfusion technique seemed not to influence the coagulation/fibrinolysis profile. This is in line with a recently performed study (Dalén et al. 1995), where only the concentrations of fibrin D-dimer and fibrinogen were analyzed. In our study also, plasma concentrations of SF and AT were determined and we believe that the present data show more complete characteristics of the coagulation/fibrinolysis profile of the retrieved blood.

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