Increased interleukin-6 in collected drainage blood after total knee arthroplasty

An association with febrile reactions during retransfusion

Martin Handel[1], Jochen Winkler[1], Rainer F Hörnlein[2], Hinnak Northoff[2], Peter Heeg[3], Martin Teschner[1] and Stefan Sell[1]

[1]Section of Orthopaedic Surgery, University Hospital, Tübingen, Germany, Departments of [2]Transfusion Medicine, University Hospital, Tübingen, Germany, [3]Hospital Infection Control, University Hospital, Tübingen, Germany. Correspondence: Dr. M. Handel, Berggasse 155, DE-72762 Reutlingen, Germany. E-mail martin.handel@freenet.de
Submitted 99-08-29. Accepted 00-10-19

ABSTRACT – We determined interleukin-6 (IL-6) concentrations in collected shed drainage blood intended for retransfusion in a prospective study in 81 patients after total knee replacement. We found large increases in IL-6 levels, averaging 6.5 (SD 3.9) ng/mL, in shed blood collected in the first 6 postoperative hours. 3 patients had febrile reactions after collected blood was retransfused. The IL-6 levels in the drainage blood of these patients were very high (9.6–13.4 ng/mL). In the blood collected after 6 hours, IL-6 concentrations increased to 47 (SD 33) ng/mL ($p < 0.001$). These results suggest a relation between increased interleukin-6 concentrations in shed drainage blood and the occurrence of febrile reactions after retransfusion of such blood.

Autologous retransfusion of postoperatively collected drainage blood is a widely used, safe and effective method for avoiding heterologous blood transfusion in orthopedic surgery (Groh et al. 1990, Gannon et al. 1991, Dalen et al. 1992, Harrap et al. 1992, Kristensen et al. 1992, Xenakis et al. 1997). Occasional febrile reactions during retransfusion are the only side-effects so far reported (Faris et al. 1991, Dalen et al. 1992). Laboratory values and blood cultures of collected drainage blood were similar in patients with and without febrile reactions during retransfusion. Interleukin concentrations in collected drainage blood, however, have not been analyzed in this connection.

We determined interleukin-6 (IL-6) levels in shed blood collected for retransfusion to assess whether febrile reactions during retransfusion are associated with an increase in interleukin concentrations.

Patients and methods

81 patients (52 women) having a mean age of 69 (48–87) years, undergoing total knee arthroplasty at our hospital between August 1998 and February 1999, took part in this study. Inclusion criteria were severe osteoarthrosis treated with unilateral total knee replacement. Exclusion criteria were malignant disease, coagulopathy and clinical signs or laboratory evidence of infection. The patients gave informed consent and the study was approved by the Ethics Committee at the University Hospital of Tübingen.

A "SureTrans" retransfusion system (made by Davol Inc., Cranston, USA) was used during the study for wound drainage blood collection and retransfusion. This system allows for multiple retransfusions, with the same device. The retransfusion was given in the first 6 hours after connecting the system (batch A), during which the collection container was completely emptied into the retransfusion container. Patients were under continuous clinical supervision including body temperature, pulse and blood pressure monitoring during the retransfusion. Thereafter, drainage blood was collected for an additional 6 hours with the same system (batch B).

IL-6 concentrations (ng/mL) in collected drainage blood of all 81 patients during the first and second postoperative 6-hour collection intervals

		0–6-hour collection interval			6–12-hour collection interval		
	n	Mean	*SD*	(range)	Mean	*SD*	(range)
Patients with febrile reactions	3	11	*2.0*	(9.6–13)	98	*1.2*	(97–99)
Patients without febrile reactions	78	6.4	*3.9*	(0.8–18)	45	*31*	(6.4–157)
Total	81	6.5	*3.9*	(0.8–18)	47	*33*	(6.4–157)

Blood samples for an alaysis were taken after 6 hours (batch A) and 12 hours (batch B) from the retransfusion container. Aerobic and anaerobic blood cultures derived from batches A and B were analyzed using a 6 mL blood sample for each. The cultures were incubated for 7 days at 37 °C.

To determine the IL-6 concentrations, 10 mL of blood samples were drawn into serum tubes and centrifuged for 10 minutes at 1000 g. The resulting serum was then stored at –70 °C, pending analysis. IL-6 concentrations were determined with an enzyme-linked immunosorbent assay (ELISA) "Quantikine" (R&D Systems, Minneapolis, USA).

Statistics

The IL-6 values in batches A and B were compared using the Wilcoxon signed-rank test (because the Kolmogorov-Smirnov test gave a significant difference from a Gaussian distribution). IL-6 levels in patients with febrile reactions were compared to those in patients without febrile reactions using the Mann-Whitney rank-sum test.

Results

Febrile reactions during retransfusion of shed drainage blood collected during the first 6 postoperative hours were seen in 3 of 81 patients which was the reason for termination of the retransfusion. Subsequently, symptoms (shivers) and increased body temperatures, which developed during the retransfusion, regressed within 30–45 minutes. There was no growth in the blood cultures in any of these patients.

We found marked increases in interleukin-6 concentrations in all patients (Table). The IL-6 levels in the 3 patients who had febrile reactions during retransfusion were still higher, between 9.6 and 13.4 ng/mL ($p = 0.03$).

The mean IL-6 levels in the whole patient population were higher during the second collection interval between the 6th and 12th postoperative hours than the IL-6 levels at 6 hours ($p < 0.001$). A difference between the two patient groups as regards their IL-6 levels remained, even during the second 6-hour collection interval ($p = 0.02$).

Discussion

Serum IL-6 levels rapidly rise shortly after major surgery (Ohazato et al. 1992). Maximum levels have been reported by Hogevold et al. (1996) in patients 20 hours after total hip replacement. A marked release of interleukins takes place in the wound area, which explains why even higher levels of IL-6 can be seen locally than in blood (Krohn et al. 1998). Foreign body reactions caused by drain tubes and collection bags may increase its release (Arnold et al. 1995). These three mechanisms explain the very high levels of IL-6 found in collected shed blood taken from the retransfusion systems. During retransfusion, the patient is exposed to these high levels. IL-6 is a potent pyrogen which, reaching the brain, induces a rise in body temperature (Opp et al. 1989, Blatteis et al. 1990). Hence, one can assume that IL-6 causes febrile reactions. The very high IL-6 levels in our patients who had febrile reactions accords with this view. However, other cytokines are also probably involved in these reactions

Faris et al. (1991) reported an increases in the incidence of febrile reactions, from 2% after retransfusion of blood collected within the first 6 hours to 22%, if the blood collected over 12 hours was

retransfused. None of the blood parameters which they evaluated during their study gave a conclusive answer as to why the increase occurred. The 7-fold increase in IL-6 blood levels that we observed in the second 6-hour collection interval may explain this finding since patients would then be given blood containing even higher IL-6 levels during the second retransfusion interval. This is additional evidence supporting a link between IL-6 levels in collected drainage blood and febrile reactions during its retransfusion.

When the postoperative blood collection period for autologous retransfusion is extended, febrile reactions can be expected to increase due to rising IL-6 levels in collected drainage blood.

This study was done under the patronage of the Fortüne-Program of the University of Tübingen, application number 554.

Arnold J P, Haeger M, Bengtson J P, Bengtsson A, Lisander B. Release of inflammatory mediators in association with collection of wound drainage blood during orthopaedic surgery. Anaesth Intensive Care 1995; 23: 683-6.

Blatteis C M, Quan N, Xin L, Ungar A L. Neuromodulation of acute-phase responses to interleukin-6 in guinea pigs. Brain Res Bull 1990; 25: 895-901.

Dalén T, Skak S, Thorsen K. Blood salvage in total knee arthroplasty with Solcotrans postoperative drainage. Acta Orthop Scand (Suppl 248) 1992; 63: 53-4

Faris P M, Ritter M A, Keating E M, Valeri C R. Unwashed filtered shed blood collected after knee and hip arthroplasties. J Bone Joint Surg (Am) 1991; 73:1169-91.

Gannon D M, Lombardi A V Jr, Mallory T H, Vaughn B K, Finney C R, Niemcryk S. An evaluation of the efficacy of postoperative blood salvage after total joint arthroplasty. A prospective randomized trial. J Arthroplasty 1991; 6: 109-14.

Groh G I, Buchert P K, Allen W C. A comparison of transfusion requirements after total knee arthroplasty using the Solcotrans autotransfusion system. J Arthroplasty 1990; 5: 281-5.

Harrap R S J, Whyte G S, Farrugia A, Jones C. Some characteristics of blood shed into the Solcotrans postoperative orthopaedic drainage/reinfusion system. Med J Aust 1992; 157: 95-6.

Høgevold H E, Lyberg T, Kahler H, Reikerås O. Expression of beta-2-integrins and L-selectin by leukocytes and changes in acute-phase reactants in total hip replacement surgery. Eur Surg Res 1996; 28 (3): 190-200.

Kristensen P W, Sörensen L S, Thyregod H C. Autotransfusion of drainage blood in arthroplasty. Acta Orthop Scand 1992; 63: 377-80.

Krohn C D, Reikerås O, Mollnes T E, Aasen A O. Complement activation and release of interleukin-6 and tumor necrosis factor-alpha in drained and systemic blood after major orthopaedic surgery. Eur J Surg 1998; 164: 103-8.

Ohazato H, Yoshizaki K, Nishimoto N, Ogata A, Tagoh H, Monden M, Gotoh M, Kishimoto T, Mori T. Interleukin-6 as a new indicator of inflammatory status: detection of serum levels of interleukin-6 and CRP after surgery. Surgery 1992; 111: 201-9.

Opp M, Obal F Jr, Cady A B, Johannsen L, Krueger J M. Interleukin-6 is pyrogenic but not somnogenic. Physiol Behav 1989; 45: 1069-72.

Xenakis T A, Malizos K N, Dailiana Z, Koukoubis T, Zervou E, Golegou C, Soucacos P N. Blood salvage after total hip and total knee arthroplasty. Acta Orthop Scand (Suppl 275) 1997; 68: 135-8.