Mild hypothermia increases blood loss and transfusion requirements during total hip arthroplasty

Harald Schmied, Andrea Kurz, Daniel I Sessler, Sybille Kozek, Albert Reiter

Summary

Background In-vitro studies indicate that platelet function and the coagulation cascade are impaired by hypothermia. However, the extent to which perioperative hypothermia influences bleeding during surgery remains unknown. Accordingly, we tested the hypothesis that mild hypothermia increases blood loss and allogeneic transfusion requirements during hip arthroplasty.

Methods Blood loss and transfusion requirements were evaluated in 60 patients undergoing primary, unilateral total hip arthroplasties who were randomly assigned to normothermia (final intraoperative core temperature 36.6-36.9°C) or mild hypothermia (35.0-35.5°C). Crystalloid, colloid, scavenged red cells, and allogeneic blood were administered by strict protocol.

Findings Intra- and postoperative blood loss was significantly greater in the hypothermic patients: 2.2 (0.5) L vs 1.7 (0.3) L, p<0.001. Eight units of allogeneic packed red cells were required in seven of the 30 hypothermic patients, whereas only one normothermic patient required a unit of allogeneic blood (p<0.05 for administered volume). A typical decrease in core temperature in patients undergoing hip arthroplasty will thus augment blood loss by approximately 500 mL.

Interpretation The maintenance of intraoperative normothermia reduces blood loss and allogeneic blood requirements in patients undergoing total hip arthroplasty.

Introduction

Mild perioperative hypothermia (core temperature 34-36°C) results from intraoperative heat loss and anaesthetic-induced inhibition of normal thermoregulatory control. Postoperative restoration of a normal core temperature typically requires several hours, increasing the duration of hypothermia well beyond the time in surgery. Although intraoperative hypothermia can easily be prevented, it remains common; no prospective randomised study has shown adverse outcomes as a result of mild hypothermia.

In-vitro studies suggest that perioperative hypothermia may aggravate surgical bleeding by impairing platelet function and directly reducing clotting factor enzyme function. Hypothermia increases the bleeding time, an inhibition apparently related to defective thromboxane A2 release, upregulation of platelet surface protein GMP-140, and downregulation of platelet glycoprotein Ib-IX complex. Furthermore, hypothermia prolongs both the prothrombin (PT) and partial thromboplastin (PTT) times—most likely via direct inhibition of clotting factor enzyme function.

Despite in-vitro evidence that hypothermia impairs coagulation, the extent to which mild perioperative hypothermia increases bleeding during surgery remains unknown. Accordingly we tested the hypothesis that a policy of maintaining normothermia reduces blood loss and allogeneic transfusion requirements during hip arthroplasty. This is a relatively standardised operation associated with considerable microvascular blood loss.

Methods We evaluated blood loss and transfusion requirements in patients undergoing initial, unilateral total hip arthroplasties at the Hospital of Amstetten, Austria. The study was approved by review boards at the Hospital of Amstetten, the University of Vienna, and the University of California at San Francisco; written informed consent was obtained from participating patients. We studied 60 patients because a preliminary study indicated that this number would provide about an 80% chance of identifying a significant hypothermia-induced increase in
blood loss (two-tailed \( \alpha=0\cdot05 \)). Under the pilot study, 28 patients at the University of Vienna had been randomly assigned to normothermia (\( T_{\text{core}} 36-6 [0-4] ^\circ\text{C}, n=13 \)) or hypothermia (\( T_{\text{core}} 34-9 [0-8] ^\circ\text{C}, n=15 \)). Blood loss was 2-3 [0-8] and 1-8 [0-61] L in the respective groups (\( p < 0-07 \)).

In this study, patients were aged 40 to 80 yr, had American Society of Anesthesiologists physical status 1–3, and weighed 50–100 kg. None of the arthroplasties was for treatment of tumour. Patients having a history of excessive bleeding or bruising were excluded as were those having PTT of more than 35 s; PT less than 70% clot formation, fibrinogen less than 200 mg/dL, a platelet count less than 100 000/\( \mu\)L, or any contraindication to red-cell scavenging. Patients reporting ingestion of aspirin or non-steroidal anti-inflammatory drugs within 2 weeks of surgery also were excluded. Per surgical protocol, all patients were given low-molecular weight heparin (5000 IU every 8 h) starting 2 h before surgery (Depot Heparin, Immuino Inc, Vienna, Austria).

**Protocol**

Ambient temperature was maintained near 21°C. The patients were premedicated with 10 mg oral diazepam 1–2 h before surgery. General anaesthesia was induced by administration of thiopental sodium 3–5 mg/kg, fentanyl 250 lig, and vecuronium so as to allow the patients to be ventilated mechanically. Anaesthesia was subsequently maintained with nitrous oxide 60%, isoflurane 0-4–0-8% end-tidal concentration, and fentanyl: these drugs were administered in doses sufficient to keep arterial blood pressure within 20% of pre-induction values.

The patients were assigned to normothermia (core temperature maintained near 36-5°C) or mild hypothermia (core temperature allowed to decrease to about 35°C). Randomisation was based on computer-generated codes sealed in sequentially numbered, opaque envelopes. Patients assigned to normothermia were actively warmed with an upper-body forced-air cover and a warmer set to “high” (Bair-Hugger, Augustine Medical, Eden Prairie, MN, USA). Additionally, intravenous fluids in these patients were warmed to 37°C. In contrast, active skin and fluid warming was avoided in patients assigned to hypothermia.

Target minimum haematocrits were prospectively determined based on ages and cardiovascular status. The target haematocrit was 26% in patients aged less than 65 yr having no significant cardiovascular disease. The haematocrit was allowed to decrease to 28% in patients aged 65 yr or more or having cardiovascular disease. Significant cardiovascular disease was defined as previous myocardial infarction, angina, congestive heart failure, cardiomyopathy, hypertension (a diastolic blood pressure exceeding 90 mm Hg or requiring chronic drug treatment), or peripheral vascular disease. Haematocrit was maintained at 30% or more in patients having both cardiovascular disease and an age 65 yr or more. Preoperative acute normovolemic haemodilution, to a haematocrit of about 30%, was used in all patients. Removed blood was immediately replaced with an equal volume of colloid plasma expander (Haemacell, Behring Werke AG, Marburg, Germany). Nearly all intraoperative blood loss was scavenged using a Shiley Stat autotransfusion system (Dideco, Mirandola, Italy). The system was primed with 40 000 IU heparin (Immuino Inc) in 1000 mL solution, of which patients received 300 mL.

Crystalloid was infused throughout surgery at a rate of 10 mL/kg/h. The first 500 mL estimated blood loss were replaced with additional crystalloid at a ratio of 3 mL/mL blood loss. Additional blood loss was replaced with colloid, haemodilution blood, scavenged red cells, and allogeneic transfusions, if necessary, to maintain target haematocrit. All blood initially removed from the patients during haemodilution and all unused scavenged blood was re-infused by the end of recovery. Allogeneic packed red-blood cells were administered postoperatively as necessary to maintain the target haematocrit.

**Measurements**

Core temperatures (\( T_{\text{core}} \)) were recorded from the tympanic membrane (Malinckrodt Anesthesia Products Inc, St Louis, MO, USA). Intraoperative temperatures, end-tidal PCO\(_2\), and isoflurane concentrations, heart rates, and oscillometric blood pressures were recorded at 20-min intervals. Postoperatively, temperatures were recorded at 30-min intervals for 2 h.

Intraoperative fluid balance was tabulated at 20-min intervals, using aspirated suction volume, return to the cell scavenger, irrigation volume, and blood returned to the patients from the cell scavenger. Surgeons at the Hospital of Amstetten do not routinely use sponges; thus, most shed blood volume could be accurately—and objectively—recorded from aspirated volume.

Similar methods have been used in previous studies.\(^1\) Blood loss from the wound drains was subsequently recorded 3 and 12 h postoperatively, and the following morning.

Spun haematocrits were determined at 30-min intervals throughout surgery and used to guide intraoperative fluid and blood administration, as above. Blood haemoglobin concentrations were determined preoperatively, after haemodilution, at the end of surgery, and the next morning. Prothrombin and plasma thrombin times and blood fibrinogen, anti-thrombin 3, platelet, and haemoglobin concentrations were also determined by the clinical laboratory preoperatively, immediately after surgery, and on the first postoperative day. The PT and PTt were determined at 37°C; the PTt is reported in seconds (normal 27–35) and the PT is reported as percent clot formation (normal 70–140). Bleeding times were not measured because the correlation between bleeding time and blood loss in individuals is poor.\(^8\)

**Data analysis**

Results were analysed after completion of data collection and an audit confirming integrity of the randomisation process. An intention-to-treat analysis was used, ie, patients were considered to be in the temperature group to which they were assigned (even when target temperatures were not reached).\(^9\)

Time-dependent results were evaluated using one-way ANOVA with Dunnett's test for comparison to preoperative values. Results in the two treatment groups were compared using unpaired, two-tailed \( t \) tests. The number of patients in each group requiring allogeneic blood transfusion were compared using a Fisher exact test. Data are presented as means (SD); \( p < 0-05 \) identified statistically significant differences.

**Results**

The morphometric characteristics, duration of surgery, anaesthetic management, and haemodynamic responses were comparable in the two groups. By design, final intraoperative core temperature was approximately 1–5°C warmer in the patients assigned to extra warming. Among those assigned to extra warming, final intraoperative core temperature exceeded 36°C in all but one; among the unwarmed patients, all but two had final core temperature less than 36°C. 2 h postoperatively, \( T_{\text{core}} \) remained significantly cooler in the unwarmed patients (table 1).

**Table 1: Morphometric characteristics, duration of surgery, anaesthetic management, and haemodynamic responses**
Nonetheless, many more hypothermic patients required patients, relatively few required allogeneic transfusions.

Haemodilution and red-cell scavenging. Surgical bleeding and allogeneic transfusion requirements might have been further reduced had our management included other methods such as regional anaesthesia, deliberate hypotension, or use of autologous blood donated before surgery.

Excessive bleeding is only one reason to maintain intraoperative normothermia. It is well established that mild hypothermia causes postoperative shivering and decreases comfort. Recent evidence suggests that mild intraoperative hypothermia may also predispose toward myocardial ischaemia, aggravate surgical wound infections, and prolong drug action. Taken together, these factors indicate that surgical patients should be kept normothermic (core temperature \(\geq 36^\circ\text{C}\)) unless hypothermia is specifically indicated. We suspect that a policy of maintaining normothermia will also decrease allogeneic transfusions and the overall volume transfused was significantly greater in the unwarmed patients.

In addition to its direct cost (excess cost of blood in our hypothermic patients was about $US1050), the administration of allogeneic blood carries risks of infection, transfusion reaction, immune suppression, and may violate religious dictates of some patients.

There are three major pathways by which hypothermia might augment surgical blood loss: impaired platelet function, reduced intrinsic and extrinsic clotting, and increased fibrinolysis. Hypothermia significantly impairs platelet function, an inhibition apparently related to defective thromboxane \(A_2\) release, upregulation of platelet surface protein GMP-140, and downregulation of platelet glycoprotein Ib-IX complex. The platelet function defect (as assessed by bleeding time) is related to local temperature, rather than core temperature. Wound temperature, however, is largely determined by core temperature and will be distinctly higher in normothermic patients.

The prothrombin and partial thromboplastin times remain nearly normal in hypothermic patients when tested in the usual manner. The difficulty with these studies, however, is that the tests were performed at 37°C. There is considerable evidence that both the prothrombin and partial thromboplastin times are highly sensitive to the temperature at which the tests are performed. These tests may, therefore, fail to accurately assess individual clotting potential unless conducted at the patient's temperature. Most likely, both intrinsic and extrinsic clotting is substantially impaired by hypothermia in vivo.

The fibrinolytic system normally regulates the balance between formation of haemostatic plugs and restoration of blood flow after clot formation. The conversion of plasminogen to plasmin is the core of this mechanism, and is largely enhanced by tissue-type plasminogen activator. In contrast to platelet function and the coagulation cascade, fibrinolysis remains normal during mild hypothermia; these data suggest that hypothermia-induced coagulopathy does not result from excessive clot lysis.

We used two methods to reduce blood loss in our patients: haemodilution and red-cell scavenging. Surgical bleeding and allogeneic transfusion requirements might have been further reduced had our management included other methods such as regional anaesthesia, deliberate hypotension, or use of autologous blood donated before surgery.
Comparison of leg compression stocking and oral horse-chestnut seed extract therapy in patients with chronic venous insufficiency

C Diehm (representing the steering committee and investigators)*, H J Trampisch, S Lange, C Schmidt

Summary

Background Diseases of the venous system are widespread disorders sometimes associated with modern civilisation and are among the major concerns of social and occupational medicine. This study was carried out to compare the efficacy (oedema reduction) and safety of compression stockings class II and dried horse chestnut seed extract (HCSE, 50 mg aescin, twice daily).

Methods Equivalence of both therapies was examined in a novel hierarchical statistical design in 240 patients with chronic venous insufficiency. Patients were treated over a period of 12 weeks in a randomised, partially blinded, placebo-controlled, parallel study design.

Findings Lower leg volume of the more severely affected limb decreased on average by 43·8 mL (n=95) with HCSE and 46·7 mL (n=99) with compression therapy, while it increased by 9·8 mL with placebo (n=46) after 12 weeks therapy for the intention-to-treat group (95% Cl: HCSE: 21·1–66·4; compression: 30·4–63·0; placebo: 40·0–20·4). Significant oedema reductions were achieved by HCSE (p=0·005) and compression (p=0·002) compared to placebo, and the two therapies were shown to be equivalent (p=0·001); in this design, however, compression could not be proven as standard with regard to oedema reduction in the statistical test procedure. Both HCSE and compression therapy were well tolerated and no serious treatment-related events were reported.

Interpretation These results indicate that compression stocking therapy and HCSE therapy are alternative therapies for the effective treatment of patients with oedema resulting from chronic venous insufficiency.


Introduction

Chronic venous insufficiency cannot be deemed a minor health impairment; patients with venous system disease require hospital or sanatorium treatment, including surgical intervention, and often are propelled into early retirement. The therapeutic objective in managing venous insufficiency is intervention at an early and therapeutically favourable stage of the disease process in order to prevent time-consuming and expensive complications. Reducing the increased capillary permeability and associated oedema may improve microcirculation in the terminal vessels and—possibly—prevent or delay ulceration. Two