Acta Orthop. Belg., 2006, **72**, 18-23

ORIGINAL STUDY

Postoperative re-perfusion of drained blood in patients undergoing total knee arthroplasty : Is it effective and cost-efficient ?

John M. KIRKOS, Christos Th. KRYSTALLIS, Panayotis A. KONSTANTINIDIS, Kyriakos A. PAPAVASILIOU, Margaritis J. KYRKOS, Lazaros G. IKONOMIDIS

From the Aristotle University of Thessaloniki and the Kilkis General Hospital, Greece

The value of postoperative salvage and re-infusion of drained blood was assessed in 155 patients undergoing total knee arthroplasty for primary knee osteoarthritis. In group A (n = 77), standard vacuum drains were used. In group B (n = 78), an auto-transfusion system was used and the blood drained within 6 hours postoperatively was re-infused. Group B patients were further distributed into 2 subgroups, in one of which methylprednisolone was administered before blood re-perfusion. Patients who received autologous blood had higher levels of haemoglobin at 8 hours ($p < 0.05$) and 24 hours postoperatively ($p < 0.01$) and needed less allogeneic blood transfusion ($p < 0.01$). Methylprednisolone administration was found to attenuate the postoperative febrile reaction ($p = 0.01$).

Keywords : blood drainage ; blood salvage ; autologous transfusion ; cost effectiveness.

INTRODUCTION

Postoperative salvage and re-infusion of drained blood through a re-transfusion device, has become an attractive alternative to allogeneic transfusion, particularly in patients undergoing primary Total Knee Arthroplasty (TKA). The demand for blood that is required in patients undergoing TKA, the pressure that is exerted on blood banks mainly due to road traffic accidents, as well as the fear of transfusion-related viral infections (*8, 14, 20*) have contributed to a more liberal use of this procedure. Furthermore, the peri-operative transfusion of allogeneic blood has been found to increase the risk of infection and also the risk of noninfectious complications in patients undergoing TKA such as haemolytic, immunologic and allergic reactions (*7, 13, 17-19, 21*). The purpose of this prospective randomised controlled study was to evaluate the safety and efficacy of postoperative blood retrieval and re-infusion in patients undergoing TKA. The effect of this procedure on the patients' haemoglobin level and platelets count at 8 and 24 hours postoperatively and the patients' febrile movement after re-infusion of drained blood were also assessed.

■ John M. Kirkos, MD, Associate Professor.

■ Kyriakos A. Papavasiliou, MD, PhD, Resident in orthopaedic surgery.

■ Margaritis J. Kyrkos, MD, Research Fellow.

3rd Orthopaedic Department, Aristotle University of Thessaloniki, "Papageorgiou" General Hospital, N. Efkarpia 564 03 Thessaloniki, Greece.

■ Christos Th. Krystallis, MD, Associate Consultant.

■ Panayotis A. Konstantinides, MD, Orthopaedic Surgeon.

■ Lazaros G. Ikonomidis, MD, Resident in orthopaedic surgery.

Orthopaedic Department, Kilkis General Hospital, Kilkis, Greece.

Correspondence : Kyriakos A. Papavasiliou, 3 Natalias Mela Street, GR-546 46 Thessaloniki, Greece.

E-mail : kyrpap@hotmail.com.

No benefits or funds were received in support of this study

PATIENTS AND METHODS

This prospective randomised controlled study was approved by the Hospital's Scientific Research Board and was conducted in accordance with the World Medical Association Declaration of Helsinki of 1975, as revised in 1983. During 2002 we performed 155 total knee arthroplasties in patients with primary osteoarthritis of the knee**.** Preoperative evaluation of the patients was based on the ASA system. The decision to use a cemented or a non-cemented prosthesis was based on the clinical features (pre- and intra-operatively) of each patient, such as age, concomitant osteoporosis, anatomical axis of the affected knee, and bone stock quality.

Exclusion criteria were : 1. clinical signs of a systemic or local infection , 2. any malignant lesion near or at the site of the operative drain, and 3. any disease of the haemopoetic system or any disorder affecting blood coagulation. Furthermore, re-infusion of autologous blood with an auto-transfusion device was considered to be contraindicated ('additional exclusion criteria') and the patient was discarded from the study when a) the drained blood was contaminated, b) local haemostatic agents were used, and c) povidone-iodine or other local antiseptics and antibiotics had been used in the operative field.

The patients were randomly divided into two groups (the first patient to participate in the study or Patient #1 was classified in group B, the second or Patient #2 in group A and so on. If a group B patient was discarded from the study during the operation (see 'additional exclusion criteria'), the next patient to participate in the study was again classified in group B). The patients in both groups were comparable with respect to their age and gender.

Group A (n = 77) was used as a control group and included 10 male and 67 female patients ; theirs ages ranged from 53 to 79 years (mean age : 68.9 years). Eleven cemented and 66 non-cemented prostheses were implanted in group A patients. In all cases, the tourniquet used during the operation was released prior to wound closure in order to achieve complete haemostasis. This was followed by the intra-articular placement of two standard vacuum drain tubes.

Group B (n = 78) included 18 males and 60 females ; their ages ranged from 55 to 86 years (mean age : 69.1 years). Twenty cemented and 58 non-cemented prostheses were used in group B patients. A tourniquet was also used during the operation ; it was released after wound closure and application of a compression dressing. Two intra-capsular silicon drain tubes were placed and connected through a universal Y connector with the auto-transfusion system. No anticoagulant agent was added in the system's canister. The collection time for blood re-infusion was limited to 6 hours in order to prevent bacterial contamination and any subsequent risk of septicaemia *(11)*.

The auto-transfusion system that was used is a 'closed' system of collection and re-infusion of blood which contains a 260 micron pre-filter to prevent air and marrow fatty material from passing through into the transfusion bag. The system maintains a constant suction pressure of –90 mm Hg. The amount of blood that was collected within the first six hours postoperatively was transfused to the patients through a standard blood transfusion set with a 40 μm micro-aggregate filter. A standard 1000 ml blood transfer bag was connected to the system in order to collect and re-transfuse the blood by gravity.

Patients in both groups were operated on under spinal anaesthesia, by the same surgical team. Low molecular weight heparin was administered subcutaneously to all, starting from the evening before surgery and daily after operation. One preoperative dose was administered 12 hours before and the first postoperative dose 8 hours after the operation. The drain tubes were removed at 48 hours postoperatively. The patients' blood pressure and heart rate were monitored during the first 24 postoperative hours. The haemoglobin and platelet levels were evaluated preoperatively, at 8 and at 24 hours after surgery. Patients with Hb level < 10 g/dl were transfused with allogeneic blood. The patients' temperature was also recorded every 3 hours during the first 5 postoperative days.

As the salvaged autologous blood has been found to contain a number of by-products from the destruction of blood cells *(11)*, we tried to evaluate the stabilising effect of methylprednisolone on the blood cells' membranes by dividing group B patients into 2 subgroups. Subgroup B I (n = 53) received 125 mg of methylprednisolone as an intravenous bolus immediately after completion of the operation and before re-infusion of the autologous blood. The remaining 25 patients formed subgroup B II and did not receive methylprednisolone.

The statistical analysis, at first, was a descriptive analysis of all independent variables. All independent variables (1. transfusion, 2. age, 3. gender, 4. units of allogeneic blood transfused during operation and postoperatively, 5. use of cemented or non-cemented prostheses, 6. haemoglobin level and platelets count preoperatively, at 8 h and at 24 h postoperatively, 7. duration and mean level of hyperthermia considering as a

Table I. — Details of patients in groups A and B. The values are given as the means and standard deviations with the range of minimum and maximum values in parentheses (Hb = haemoglobin, PLT = platelets)

VARIABLE		RE-INFUSION OF DRAINED BLOOD		
		YES (group B)	NO (group A)	TOTAL
AGE (years)		69.08 ± 5.45 (55-86)	68.88 ± 5.11 (53-79)	68.98 ± 5.27 (53-86)
MALE		18	10	28
FEMALE		60	67	127
Hb (mg/dl)	Preoperative	13.03 ± 1.36 (9.4-15.8)	13.13 ± 1.41 (9.2-17.4)	13.08 ± 1.38 (9.2-17.4)
	8 h	11.37 ± 1.25 (8.7-14.3)	10.85 ± 1.46 (7-14.8)	11.11 ± 1.38 (7-14.8)
	24 h	10.67 ± 1.32 (8.1-13.7)	10.02 ± 1.37 (7.1-14.2)	10.35 ± 1.38 (7.1-14.2)
PLT (*10^3/mm^3)	Preoperative	246.6 ± 58.34 (146-425)	259.13 ± 62.48 (146-412)	252.07 ± 60.21 (146-425)
	8 h	194 ± 43.25 (105-307)	207.29 ± 58.45 (113-388)	199.81 ± 50.62 (105-388)
	24 h	184.53 ± 42.50 (128-328)	198.24 ± 62.67 (100-427)	190.52 ± 52.49 (100-427)
Units during operation		0	0.57 ± 0.938 (0-4)	0.57 ± 0.938 (0-4)
Units postoperatively		0.54 ± 0.86 (0-4)	1.06 ± 1.174 (0-4)	0.80 ± 1.06 (0-4)
Blood re-infused (ml)		686.5 ± 205.12 (300-1250)	0	686.5 ± 205.12 (300-1250)
Cemented/non-cemented prosthesis		20/58	11/66	31/124
Methylprednisolone Yes = B I/No = B II		53/25	0/0	53/25
Days with fever		1.05 ± 1.413 (0-5)	1.48 ± 1.56 (0-5)	1.27 ± 1.5 (0-5)
Fever (C°)		38.31 ± 0.34 (38-39.5)	38.40 ± 0.43 (38-40)	38.36 ± 0.39 (38-40)

'threshold' 38°C) were next correlated using Cross-tabulation and Bivariate correlation of Pearson and Spearman. The statistically significant correlated values were included in the regression analysis. The random distribution of individual values was checked by the 'RUNS test' (values higher than the default value of 0.05). The Kolmogorov-Smirnov test was also used to assess the normal distribution of the values recorded. Data processing was performed with the use of the SPSS program (version 11.5) for Windows.

RESULTS

Patients in group A received peri-operatively 0.57 and postoperatively 1.06 units of blood on average per patient (table I). Any blood transfusion that took place either after release of the tourniquet in the operation room or during the short stay (1 to 2 hours) in the postoperative care unit was categorised as 'peri-operative'. An average of 1.61 units per patient was transfused in this group. As a standard procedure, 125 mg of methylprednisolone was administered to all patients in group A, prior to the blood transfusion, in order to prevent anaphylactic reactions to the allogeneic blood.

The amount of salvaged and re-infused blood in group B patients ranged from 300 to 1250 cc (mean : 686.5 cc or 2.3 units per patient). There was no need for peri-operative allogeneic transfusion in any of group 'B' patients. An average of 0.54 unit of allogeneic blood per patient was transfused postoperatively in this group.

The preoperative haemoglobin levels in group A patients ranged from 9.2 to 17.4 g/dl (mean value : 13.13 g/dl). The postoperative levels ranged from 7 to 14.8 g/dl (mean value : 10.85 g/dl) at 8 hours after surgery and from 7.1 to 14.2 g/dl (mean : 10.02 g/dl) at 24 hours postoperatively.

The preoperative haemoglobin level in group B patients ranged from 9.4 to 15.8 g/dl (mean value : 13.03 g/dl). Their postoperative levels ranged from 8.7 to 14.3 g/dl (mean : 11.37 g/dl) at 8 hours after surgery and from 8.1 to 13.7 g/dl (mean of 10.67 g/dl) at 24 hours postoperatively.

Forty seven patients in group A developed hyperthermia up to 40°C for a period of 3 to 5 days. One patient responded to blood transfusion with a positive Wright serum reaction, another presented a pulmonary embolism and two developed allergic reactions.

Thirty nine patients in group 'B' developed hyperthermia up to 39.5°C ; 25 out of 53 patients in subgroup B I (fever up to 38.5°C) and 14 out of 25 patients in subgroup B II (fever up to 39.5°C for 3 to 5 days). Four complications were noted in group B patients. One patient presented severe haemolysis. Clotting occurred in the auto-transfusion system canister in three patients.

Statistical analysis showed a significant positive or negative correlation between auto-transfusion (or not) and the following variables : 1. number of allogeneic blood units that were transfused postoperatively ($p < 0.01$), 2. Hb level at 8 hours postoperatively ($p < 0.05$), 3. Hb level at 24 hours postoperatively ($p < 0.01$). Group B patients received fewer units of allogeneic blood postoperatively (mean : 0.54 in group B versus 1.06 in group A) and had higher levels of haemoglobin postoperatively ($p < 0.01$) (table I, fig 1).

The mean level of hyperthermia was lower (38.1°C) in group B compared to group A patients (38.4°C) and the duration of hyperthermia was shorter (mean value in group B : 1.05 days, versus 1.48 days in group A). Statistical analysis showed that methylprednisolone administration prior to re-infusion of shed blood decreased the mean level of hyperthermia ($p = 0.01$) during the postoperative period.

Female gender had a slightly negative correlation with the haemoglobin level pre-operatively ($p = 0.05$) and 8 hours postoperatively ($p = 0.01$). Female patients also needed more units of allogeneic blood than males. With increasing age, patients had lower Hb levels at 8 and at 24 hours ($p = 0.01$) postoperatively. The type of prostheses used (cemented or not) did not appear to affect the amount of blood loss (fig 1).

Furthermore the following statistical correlations were found : 1. the amount of blood that was re-infused positively influenced the Hb level at 8 hours post-operatively ($p = 0.01$) ; 2. the pre-operative Hb level had a negative correlation with the number of blood units that were needed postoperatively ($p < 0.05$), and 3. the number of units of allogeneic blood that were used had a positive correlation with the postoperative Hb measured at 8 and 24 hours ($p < 0.05$).

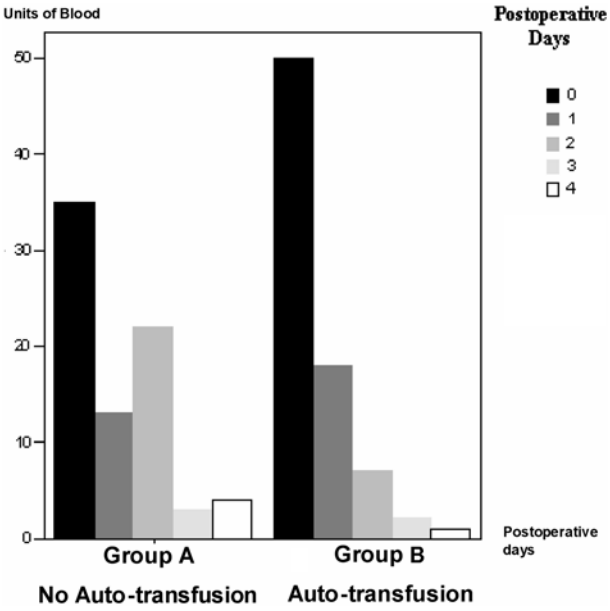

Fig. 1. — Numbers of blood units (both autologous and allogeneic) that were transfused postoperatively in group A and group B patients.

DISCUSSION

Transfusion of autologous blood has been used during recent years in both elective and emergency orthopaedic operations, mainly as a means of avoiding potential hazards associated with allogeneic blood transfusion. Even though the risk of transmission-related diseases has been dramatically diminished, auto-transfusion remains an attractive alternative to allogeneic transfusion, owing to the increasing pressure that is exerted on blood banks and to the risk of transfusion-related immunomodulation.

Blood transfusion is a rather expensive medical procedure, considering the lack of blood supplies and the need for screening for a number of infectious diseases. It is rather difficult to evaluate the

actual cost of blood transfusion, especially when taking into account possible transfusion-related infections. It has been calculated in our country that every blood unit costs approximately € 145. Each patient in group B received approximately 2.3 units of autologous blood, with an approximate mean cost reduction of € 333.5 which more than covered the cost of the autologous blood drainage and transfusion device, which was € 171.

It appears that the best predictor for the need for post-operative transfusion is the pre-operative Hb level (*1*). This is also well documented in our study. The saving of blood and the diminished need for allogeneic blood transfusion, when an auto-transfusion device is used, has been established in numerous studies. Martin *et al* (*13*) reported in a series of 197 patients undergoing TKA, that 59% of the mean volume of the postoperative blood loss (i.e. the blood that was collected in the re-transfusion device) in unilateral and 56% in bilateral TKA was recovered and re-infused with the use of an auto-transfusion system. Han and Sin (*9*) reported that 57% of the mean volume of the overall external blood loss (intra- and postoperative) and 74% of the mean volume of the postoperatively drained blood was re-infused in 39 patients that underwent unilateral TKA, and 59% and 79% respectively in 12 patients that underwent bilateral TKA. Newman *et al* (*16*) performed a randomised controlled study in order to evaluate the efficacy of a blood-saving and re-transfusion procedure. They reported that only 7 units of bank blood were used in the re-infusion group, compared with 50 in the control group ($p < 0.001$), which represented an overall saving of 86%.

The evaluation of a blood salvage and re-transfusion procedure in patients undergoing total knee arthroplasty for primary osteoarthritis is not an easy task. It is indeed impossible to conduct such a study in a completely blinded manner (*16*). It also appears that the amount of blood retrieved and re-transfused is unpredictable (in our series, it ranged from 300 to 1250 ml). In fact many patients still needed allogeneic blood transfusion despite the fact that they were transfused with autologous blood. Nevertheless the need for allogeneic blood was significantly lower ($p < 0.01$) in these patients.

The trigger point for allogeneic transfusion which was set in our study at 10 g/dl Hb is another weak point, which has certainly increased the number of units of allogeneic blood that were required postoperatively. During the time that our study was conducted, the standard procedure that was followed in our Department was to transfuse a patient whenever the Hb level dropped below the value of 10 g/dl. This should however not interfere with our conclusions, as the same transfusion trigger (10 g/dl) was used in both groups. With a lower transfusion trigger, the need for allogeneic blood transfusion would have also been less, and this could have reduced the difference in the need for allogeneic blood transfusion between group A and B patients. In fact, over the last two years, this threshold has been lowered to 9 g/dl or even less (*10*) when the patient is haemodynamically stable and symptom free.

One more weak point in this study is the fact that the tourniquet was released before wound closure in group A and after wound closure in group B. This may have affected external blood loss in various ways, as tourniquet release before wound closure will increase blood loss, but on the other hand it also allows for better haemostasis (*4*).

The complications that occurred in 4 out of 78 group B patients were noted when an attempt was made to reduce the diameter of the drain tubes in order to decrease the size of the large exit portals. This possibly resulted in increased damage to the red cells membranes . We therefore believe that the use of large exit portals is preferable.

Jensen *et al* (*11*) and Dalen *et al* (*5*) reported that the drained blood contains histamine, eosinophil cationic protein, eosinophil protein X, myeloperoxidase, plasminogen activator inhibitor type 1, activated complement factor C3 and various coagulation factors and split products. The drained blood is defibrinated and can be collected without the addition of anticoagulant factors and drugs (*6, 9, 15*). In our study, no anticoagulant was added in the reservoir and in contrast to several other articles (*6, 9, 15*) we noted hyperthermia up to 39.5°C in 38 patients. As the causes of febrile reactions were unknown, the most likely explanation is either a reaction to the by- products derived from the destroyed cells or

the effect of some exogenous pyrogens. Febrile reactions have also been reported by Martin *et al* (*15*) during the auto-transfusion procedure. The administration of methylprednisolone prior to re-infusion of salvaged blood attenuated the febrile reaction (mean level and duration of hyperthermia). Subgroup B I patients that received methylprednisolone prior to the auto-transfusion responded better than subgroup BII patients ($p = 0.01$).

The re-infusion of drained blood in patients undergoing total knee arthroplasty has been shown to be a safe method that minimises the risk of transfusion-related infectious diseases and the need for allogeneic blood. However, other efficient methods are also available to reduce the need for allogeneic blood in patients undergoing TKA. Fibrinolysis inhibition with tranexamic acid administered before tourniquet release and 3 hours postoperatively, intra-operative use of high dose aprotinin, pre-operative donation of autologous blood and fibrin based sprays also have documented efficiency, as well as preoperative administration of erythropoietin to increase the red cell stock (*2, 3, 12*).

REFERENCES

1. **Aderinto J, Brenkel IJ.** Pre-operative predictors of the requirement for blood transfusion following total hip replacement. *J Bone Joint Surg* 2004 ; 86-B : 970-973.
2. **Akizuki S, Yasukawa Y, Takizawa T.** A new method of hemostasis for cementless total knee arthroplasty. *Bull Hosp Jt Dis* 1997 ; 56 : 222-224.
3. **Benoni G, Fredin H.** Fibrinolytic inhibition with tranexamic acid reduces blood loss and blood transfusion after knee arthroplasty. *J Bone Joint Surg* 1996 ; 78-B : 434-440.
4. **Cushner FD, Friedman RJ.** Blood loss in total knee arthroplasty. *Clin Orthop* 1991 ; 269 : 98-101.
5. **Dalen T, Brostrom L, Engstrom KG.** Autotransfusion after total knee arthroplasty : effects on blood cells, plasma chemistry, and whole blood rheology. *J Arthroplasty* 1997 ; 12 : 517-525.
6. **Faris PM, Ritter MA, Keating EM, Valeri CR.** Unwashed filtered shed blood collected after knee and hip arthroplasties. A source of autologous red blood cells. *J Bone Joint Surg* 1991 ; 73-A : 1169-1178.
7. **Fernandez MC, Gottlieb M, Menitove JE.** Blood transfusion and postoperative infection in orthopedic patients. *Transfusion* 1992 ; 32 : 318-322.
8. **Glynn SA, Kleinman SH, Schreiber GB *et al.*** Trends in incidence and prevalence of major transfusion-transmissible viral infections in US blood donors, 1991 to 1996. Retrovirus Epidemiology Donor Study (REDS). *JAMA* 2000 ; 284 : 229-235.
9. **Han CD, Shin DE.** Postoperative blood salvage and reinfusion after total joint arthroplasty. *J Arthroplasty* 1997 ; 2 : 511-516.
10. **Helm AT, Karski MT, Parsons SJ *et al.*** A strategy for reducing blood-transfusion requirements in elective orthopaedic surgery. *J Bone Joint Surg* 2003 ; 85-B : 484-489.
11. **Jensen CM, Pilegaard R, Hviid K *et al.*** Quality of reinfused drainage blood after total knee arthroplasty. *J Arthroplasty* 1999 ; 14 : 312-318.
12. **Jeserschek R, Clar H, Aigner C *et al.*** Reduction of blood loss using high-dose aprotinin in major orthopaedic surgery. *J Bone Joint Surg* 2003 ; 85-B : 174-177.
13. **Jeter EK, Spivey MA.** Noninfectious complications of blood transfusion. *Hematol Oncol Clin North Am* 1995 ; 9 : 187-204.
14. **Kleinman SH, Glynn SA, Higgins MJ *et al.*** The RADAR repository : a resource for studies of infectious agents and their transmissibility by transfusion. *Transfusion* 2005 ; 45 : 1073-1083.
15. **Martin JW, Whiteside LA, Milliano MT, Reedy ME.** Postoperative blood retrieval and transfusion in cementless total knee arthroplasty. *J Arthroplasty* 1992 ; 7 : 205-210.
16. **Newman JH, Bowers M, Murphy J.** The clinical advantages of autologous transfusion. *J Bone Joint Surg* 1997 ; 79-B : 630-632.
17. **Nicholls MD.** Transfusion : morbidity and mortality. *Anaesth Intensive Care* 1993 ; 21 : 15-19.
18. **Nielsen HJ.** Detrimental effects of perioperative blood transfusion. *Br J Surg* 1995 ; 82 : 582-587.
19. **Nusbacher J**. Blood transfusion is mononuclear cell transplantation. *Transfusion* 1994 ; 34 : 1002-1006.
20. **Wang B, Schreiber GB, Glynn SA *et al.*** Does prevalence of transfusion-transmissible viral infection reflect corresponding incidence in United States blood donors ? *Transfusion* 2005 ; 45 : 1089-1096.
21. **Wylie BR.** Transfusion transmitted infection : viral and exotic diseases. Review. *Anaesth Intensive Care* 1993 ; 21 : 24-30.