Autologous blood transfusion in total knee replacement surgery

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We compared allogeneic blood usage for two groups of patients undergoing total knee replacement surgery (TKR). Patients were randomized to receive either their post-operative wound drainage as an autotransfusion (n=115) after processing or to have this wound drainage discarded (n=116). Allogeneic blood was transfused in patients of either group whose haemoglobin fell below 9 g dl⁻¹. Only 7% of patients in the autotransfusion group required an allogeneic transfusion compared with 28% in the control group (P<0.001). There was no hospital mortality and only 3% mortality from all causes at the study completion, which spanned 6 months to 3 yr. There was a higher incidence of infection requiring intervention in the allogeneic group (P<0.036). Total patient costs were £113 greater in the autotransfusion group.

We conclude that in this type of surgery post-operative cell salvage is a safe and effective method for reducing allogeneic blood use.

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The identification of transfusion transmitted diseases’ such as Human Immunodeficiency Viruses (HIV), Hepatitis C (Hep C) and new variant Creutzfeldt-Jakob (nvCJD) disease has led to an increasing number of tests which need to be performed before allogeneic blood transfusion. The current allogeneic blood supply is probably the safest ever produced. However, this statement does not take account of the evolution and subsequent identification of other illnesses, which may be transmitted by blood transfusion. The most recent problem relates to the transmission via blood transfusion of the prion thought to cause vCJD. This has led to the leucodepletion of all blood products within the UK. The increased cost of blood products has added considerable enthusiasm in medical circles to decrease their use, and subsequent patient exposure to allogeneic blood.

There is some inconclusive evidence,¹ suggesting that patients may suffer fewer peri-operative infections if they avoid allogeneic blood transfusion at the time of surgery. Using autotransfusion may be one way of maintaining peri-operative haemoglobin concentrations, reducing the need for allogeneic blood transfusion.²⁻⁵ If peri-operative transfusion practices were aimed at a ‘minimum’ haemoglobin concentration, rather than trying to maintain a pre-operative value, this would further decrease peri-operative transfusions.

Because of the paucity of evidence in the literature from randomized, controlled studies we decided to undertake a randomized controlled trial to confirm our findings from a small pilot study,⁶ which suggested that a marked reduction in allogeneic blood transfusion could be achieved safely by using post-operative red cell salvage (PRCS) and a haemoglobin ‘transfusion trigger’.

Patients and methods

This was a single-centre, randomized controlled study of patients undergoing TKR. After review and approval by the Local Research Ethics Committee, we obtained informed consent and studied 231 patients. Patients were allocated randomly to one of two treatment groups; one group received allogeneic blood (if their haemoglobin fell below a pre-set transfusion trigger of 9 g dl⁻¹) and the other group received autotransfusion of wound drainage if the volume was greater than 125 ml post-operatively.

The collected blood was washed and re-suspended in saline before re-infusion using a centrifugal cell washing machine (Cell Saver 5 Haemonetics). The patients in the cell salvage group were also transfused if their haemoglobin fell below the preset trigger after autotransfusion. We chose a transfusion trigger to standardize the transfusion incidence in both groups. Although the American Society of Anaesthesiology recommended a trigger of 7 g dl⁻¹, we felt this was perhaps too aggressive and it would be difficult to apply. Many anaesthetists would be reluctant to withhold blood at this level of anaemia knowing the correlation with an optimum oxygen delivery and haemoglobin of 10 g dl⁻¹.
Haemoglobin concentrations were measured on days 1, 2, 3, 4, and 7 in all patients. The TKR was conducted as routine. Data were collected by research nurses for post-operative length of stay, peri-operative and post-hospital discharge infection rates, adverse events, wound healing rates and quality of life (EuroQol EQ-5D).

One of the investigators scrutinized all adverse events in a blinded fashion to determine which were possibly related to transfusion effects, for example, wound infection, embolic events, myocardial ischaemic events, and cardiopulmonary complications.

Data were loaded onto an SPSS version 7.5 computer programme (SPSS Inc., Chicago, USA) and all statistical analysis was performed using this program. The level of statistical significance for all tests was set up at a $P$-value of $<0.05$. For bivariate analysis, a two-tailed test of significance was used. Patient characteristics were examined using Fischer’s Exact Test or the Independent Sample $t$-test. In respect to adverse events, the comparison was examined using chi-squared test.

Results

Of the 231 patients, 98 were males and 115 were randomized into the cell salvage group. Characteristics of patients in the two groups were comparable (Table 1). Although anaesthetic technique was not standardized, Table 2 depicts the type of anaesthesia used and the similarity between the groups. The majority of patients received a Johnson and Johnson prosthesis (75 in the autologous arm and 77 in the allogeneic arm) with the remaining patients in both groups having a De Puy prosthesis. All knee replacements were performed under tourniquet, with the pressure set according to systolic arterial pressure. Patients in both groups were transfused with allogeneic blood if their haemoglobin concentration fell below the preset trigger of $9\, \text{g}\, \text{dl}^{-1}$.

The study was analysed on an intention to treat basis. Of the 115 patients randomized into the autologous arm of the study, 85% received an autologous transfusion. The remaining 18 patients were not transfused because of lack of staff to operate the cell salvage equipment (13 patients), insufficient blood collection (four patients), and tourniquet failure (one patient).

Twelve patients in the autologous arm of the study received an allogeneic transfusion. Two were inappropriate,
as both patients had a haemoglobin concentration greater than 9 g dl⁻¹ and were asymptomatic, and could be classed as a procedure deviation. The remaining 10 patients had haemoglobin concentrations between 7.6 and 8.9 g dl⁻¹. Of the 10 patients whose transfusion was warranted, four of these were from the 18 patients in whom cell salvage failed and a further three patients had only a small amount of blood salvaged (<150 ml).

In the control group, 33 patients received allogeneic blood. The majority (76%) received two units, 6% three units, 6% four units, and 12% one unit.

There was no significant difference in length of stay, wound healing, serious adverse events or mortality, or health related quality of life (EuroQol) 6 months after surgery (Fig. 1). There was a significantly lower (7%) incidence of allogeneic blood transfusion in the cell salvage group, compared with 28% in the controls (P<0.001). There was no difference in post-operative mean haemoglobin concentration between the two groups (Fig. 2).

In relation to transfusion practice, we found significantly fewer re-admissions to hospital (P<0.008) and visits to general practitioners (P<0.043) in patients in the autologous blood transfusion group (Table 3). Infective complications were increased in allogeneic recipients (P=0.036), with increasing significance (P=0.025) if all patients receiving allogeneic blood were placed in the allogeneic group.

A comparison of the cost difference between allogeneic transfusion and autologous transfusion was made by one of the authors (DC). A summary of the findings is shown (Table 4).

### Discussion

This current study showed that a decrease in allogeneic blood use could be achieved by using PRCS. In a previous study,⁶ we showed that the use of PRCS could dramatically reduce patients’ exposure to allogeneic blood (from 82 to 18%), without clinical detriment, as all patients left hospital. In that study, as with this one, there was no statistical difference in the discharge haemoglobin concentrations. The design of our original pilot study did not apply a strict transfusion trigger to both groups; we were trying to show how the use of PRCS could improve transfusion practice over routine clinical practice. However, in this study we have assessed the difference in transfusion of allogeneic blood between the two groups whilst applying a strict transfusion trigger to both randomized groups. There is no doubt that by applying rational transfusion principles, a large decrease in allogeneic transfusion can be achieved without the use of any autologous transfusion methods.

The present study shows that further significant reductions can be achieved by the use of PRCS, decreasing overall use of allogeneic transfusion to below 7% in the autologous group. Despite publication of other studies showing a similar trend,²–⁶,⁸ our study is one of the largest randomized controlled trials yet performed. Criticism has also been levelled at the lack of outcome measures applied to many studies assessing the practice of PRCS. In our study, no patients failed to leave hospital from either group. It was reassuring that the end of study mortality (in some cases indicating a 2-yr follow up and/or a minimum of 6 months post-hospital discharge) was similar in both groups, when deaths from all causes were considered. This mortality rate compared very favourably with a large orthopaedic audit reported from the Mayo clinic.⁹

The data did not support a difference in immediate post-operative infection or earlier hospital discharge, as had been suggested by earlier publications. The well-recognized effect of immunomodulation because of allogeneic blood transfusion was not apparent. This may add weight to the

| Table 3 Readmission by group: conditions considered possibly related to blood products |
|---------------------------------|---------------------------------|
| **Males/females (Autologous group)** | **Males/females (Allogeneic group)** |
| Age/sex Problem | Age/sex Problem |
| 83 F Recurrent pulmonary embolism/ wound abscess: died | 72 M Cellulitis – ?DVT – doppler nad |
| 66 M Wound infection | 65 F DVT |
| 72 F Wound infection persisted: sinus explored which did not connect to knee replacement | 70 M Infected wound |
| 88 M Cellulitis |
| 70 F Wound infection | 65 M Acute anaemia: 4 units blood transfused |
| 78 F Superficial wound infection: antibiotics commenced |
| 60 M ? PE – heparinized overnight |
| 68 M Wound infection | |

| Table 4 Average per patient costs (£, 1998) of allogeneic and autologous blood transfusion |
|---------------------------------|---------------------------------|
| **Description** | **Cost of allogeneic transfusion (£)** | **Cost of autologous transfusion (£)** |
| Allogeneic blood | 27.96 | 12.20 |
| Staff time | 49.34 | |
| Capital and servicing | 24.12 | |
| Disposables | 00.74 | 80.12 |
| Total direct cost | 28.70 | 165.78 |
| Readmission | 34.65 | 11.66 |
| GP consultation | 01.55 | 00.72 |
| Total indirect costs | 36.20 | 12.38 |
| Total per patient cost | 64.90 | 178.16 |
argument that universal leucodepletion offers only minor benefit. The length of stay was consistent with data from other Welsh hospitals (personal communication, Department of Public Health). Assessment using EuroQol Health State score did not show a difference between groups (Fig. 1), in contrast to the proposal that patients receiving autologous blood have improved health and well being when compared with those receiving allogeneic blood. It was noted that the EuroQol scores improved in both groups when pre-operative and 12 weeks post-operative scores were compared.

The only area where we found a statistical difference between groups was in the post-hospital infective complications with allogeneic recipients having increased infection. This effect became even more significant if those who received rescue transfusion were included in the allogeneic group. These findings are supported by the reduced readmissions and visits to general practitioners by patients who had been randomized to receive an autologous transfusion.

We have shown that reducing allogeneic transfusion can be achieved safely by using a combination of PRCS and limiting the transfusion when the patient has haemoglobin greater than 9 g/dl\(^{-1}\). This may be considered as a conservative haemoglobin trigger and appropriate for even those patients with significant cardiac disease.\(^{10-15}\) Of course the group of patients undergoing this type of joint replacement are more elderly than the general population and thus more likely to suffer from heart disease. We believe therefore that such blood conservation techniques are clinically indicated in the light of present evidence. There is a need to seek safe alternatives to allogeneic blood, both to decrease the risk of future unknown blood-borne transmitted disease and to increase the availability of allogeneic blood supplies where there are no available alternatives.

Our cost analysis showed that autologous transfusion was overall more expensive, despite having lower re-admission and post-operative general practitioner costs. At the time of the study the unit cost of allogeneic blood was £50.83. In addition, staff time of £49.34 was estimated on a cell-salvage operator being present throughout the post-operative collection period. In practice, this is not necessary. Processing of the drained blood had a mean time of 20 min. These two factors would now make a cost comparison more favourable.

Moreover, although autologous transfusion was not shown to be cost-effective, it should be noted that this analysis was short term and ignores the value attached to reduced risk of transmission of virus related illness. A recent US study\(^{16}\) has estimated median willingness to pay for autologous blood to reduce this risk at $900 per patient, which is considerably more than the excess cost per patient in the experimental arm of the present study. It seems that the reluctance to adopt such techniques in routine practice is because of a number of factors. This includes cost, organization and, perhaps, motivation. The recent increase in cost of production of all red cell products, because of improved testing for Hep C and the leucodepletion of all blood products to decrease the risk of nvCJD transmission, may make post-operative red cell salvage more attractive.

We would hope that if cost is the most important driver, then significant reduction in red cell use, without increased morbidity or mortality, might aid motivation and organization of such transfusion alternatives.

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