An algorithm to reduce allogenic red blood cell transfusions for major orthopedic surgery

Robert Slappendel[1], Ris Dirksen[1], Eric W G Weber[3] and Dick B van der Schaaf[2]

Departments of [1]Anaesthesiology, [2]Orthopedics, Sint Maartenskliniek, Nijmegen, [3]Anaesthesiology, Academical Hospital Maastricht, Maastricht, The Netherlands.
Correspondence: r.slappendel@maartenskliniek.nl
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ABSTRACT In a previous prospective study, we confirmed that transfusion-related immunosuppression predisposes to postoperative infections, impairs the postoperative healing of wound and thereby prolongs hospitalization. This increases the well-known risks, such as transmission of infection or transfusion reactions, and has obliged us to revise our transfusion guidelines.

We used a relational database containing information about 28,861 orthopedic surgery patients was used to determine when and how to improve these guidelines for transfusions.

The survey showed the circumstances surrounding a high incidence of allogenic red cell infusions: failure to follow the guidelines, the preoperative use of non-selective NSAIDs, low preoperative Hb level, failure to retrieve blood, and high cut-off values for allogenic red cell transfusion. The first step was to determine the Hb level before giving red cell infusions and ensure compliance with predefined cut-off values. Subsequent measures included: use of COX 2-selective NSAIDs alone in the perioperative period; erythropoietin and iron therapy when the Hb level fell below 13 g/dL; use of cell salvage during and after surgery; administration of aprotinin to patients expected to have a high blood loss. The type of anesthesia had no blood-sparing effect.

Although these steps can not be regarded as a new approach, we show that by following a strict rules with appropriate steps and in a concerted fashion, the use of allogenic red blood cells was reduced by 80%. Moreover, the amount of blood saved had other effects—e.g., the incidence of deep wound infections was reduced by 40%. The outcome is described in an algorithm summarizing the steps in a comprehensive perioperative diagram for giving blood.

Inherent risks in homologous transfusions persist despite all efforts to minimize and avoid as many of these as possible. Apart from well-known risks, such as the transmission of infections or transfusion reactions, there is concern—especially in orthopedic surgery—about a causal relationship between allogenic red blood cell transfusions and immunomodulation. Transfusion-related immunosuppression is thought to increase the incidence of postoperative infections, delay healing of postoperative wounds and thereby prolong hospitalization (Murphy et al. 1991, Blumberg 1997, Bierbaum et al. 1999, Innerhofer et al. 1999, Borghi and Casati 2000). In our prospective study—which included 975 major orthopedic surgical procedures, such as total hip arthroplasty and knee replacement surgery, fusion surgery of the lumbar, thoracic or cervical spine—we confirm this view (Table 1).

These data on the consequences of infusion of allogenic red blood cells warrant guidelines for their proper use. Below we summarize how we developed our guidelines and the quantitative effect of each step that was added to our guidelines. We have now reduced the use of red cell transfusions by 80%.

Table 1. Incidence of postoperative infections, delayed postoperative wound healing, and duration of hospitalization in relation to treatment with an of allogenic red blood cell infusion (n = 975)

Blood transfusion	number of patients	Incidence of infections	Incidence of delayed wound healing	Duration of hospital stay (days)
None	867	3.8%	16%	8.3
1 or more	108	6.3%	31%	11.7

Table 2. Outcome of analysis of suitable routines for reducing the need for allogenic red blood cell transfusions

Period	Relevant routines
Preoperative	Hb, Ht, MCV
	Drugs that affect the clotting cascade
During surgery	Cut-off values for transfusion (transfusion trigger)
	Measures to activate the clotting cascade
	Cell saving
	Normothermia
Postoperative	Cut-off values for transfusion (transfusion trigger)
	Blood loss
	Cell saving

Use of database for development of transfusion guidelines

The basis for revising the guidelines for red cell transfusions was the previous inventory of detailed clinical data. Starting in 1991, details regarding all orthopedic surgical procedures in our Department were fed into a relational database. In each patient, we recorded the date of surgery, date of birth, hospital registration number, surgeon, anesthesiologist, type of surgery, diagnosis, duration of surgery, amount of blood lost during surgery, and the anesthetic procedure. This database is coupled to the database in the financial department that contains—e.g., details on the hospital stay and those in our laboratory about red cell transfusions, infections, etc. We analyzed the data about 28,861 patients to determine the most suitable routines for improving the guidelines in our Department. Table 2 outlines the outcome of the analysis of our database that showed us which areas should be focused on to improve our handling of blood loos afer orthopedic surgery.

Relevant routines and restrictions for reducing the number of transfusion of allogenic red blood cells

We realize that the use of steps to achieve our general aim of avoiding transfusion of allogenic red cells unnecessaryly is not new, but this review shows how a carefully-selected algorithm reducted the use of allogenic red blood cell transfusions by 80%. Here we will describe the various steps for minimizing the transfusion of allogenic red blood cells, and show how the improvement from each step was added to that of the preceding one. The algorithm summarizes these steps in a comprehensive diagram concerning the policy for dealing with perioperative blood loss (Figure 1).

Preoperative assessment

In our Department, the anesthesiologist is part of the team that evaluates each of the 4,500 patients a year scheduled for orthopedic surgery. The preoperative assessment is done at least 3–4 weeks before surgery. At this stage, the involvement of anesthesiologists permits an appropriate clinical evaluation in preparation for giving the anesthetic, and the management of special requirements for the surgical procedure. It also entails individualizing the guideline for dealing with blood loss. From the analysis of the relational database, we learned that two aspectswere of special interest: preoperative NSAIDs that can disturb coagulation of the blood during surgery, and preoperative laboratory studies for CBC to determine whether erythropoietin should be given. Other factors were also checked and the most relevant ones are included in the algorithm shown in Figure 1 and Table 2.

NSAIDs. Non steroidal anti-inflammatory drugs (= NSAIDs) used in the perioperative period for analgesia and reduction of edema in the surgical field have well-known undesired side effects, including COX 1-related effects that lead to impaired platelet aggregation. These data were shown in laboratory studies, and—in order to corroborate the relevance of these findings in the Department—we evaluated the blood loss for a specific surgical procedure (coxarthrosis: first hip replacement) during the period that we switched

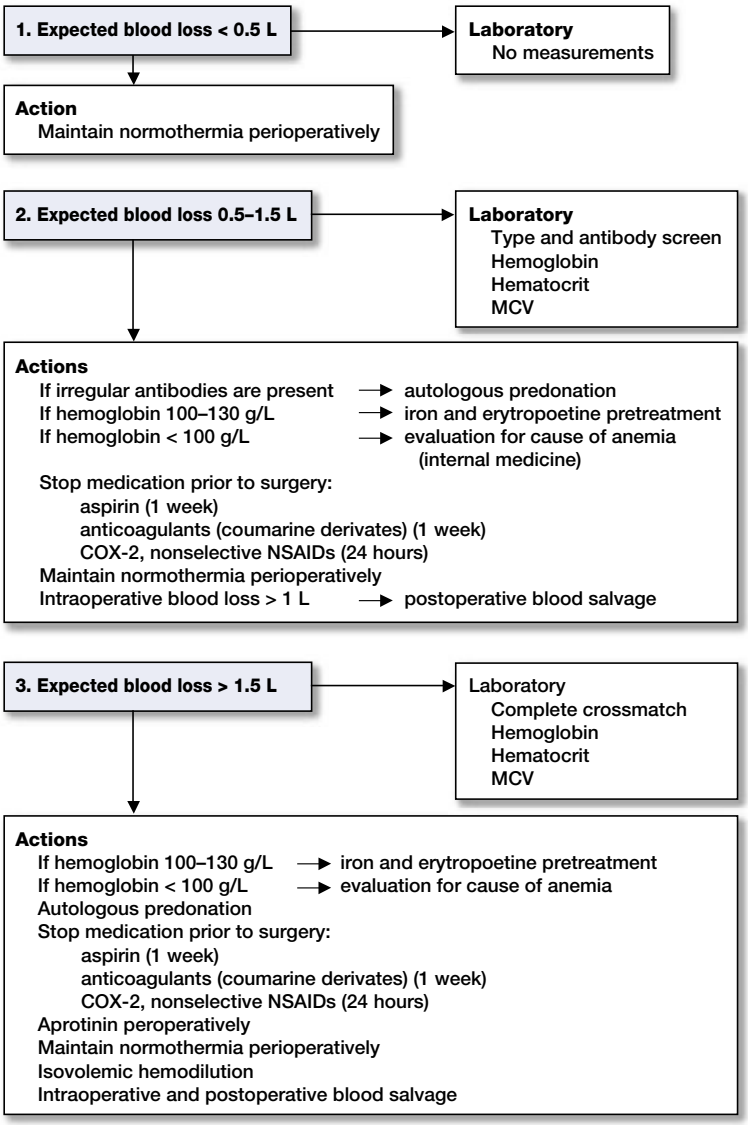

Figure 1. Polic concerning blood loss in elective orthopedic surgery in adult patients.

from non-specific to COX 2-selective NSAIDs. It was shown that the total blood loss declined by 26%, with no change in other factors—e.g., duration of surgery, antithrombosis prophylaxis unchanged (Table 3).

These data and the above considerations made us decide to evaluate the effect of NSAIDs on blood loss in clinical studies.

In the first double-blind randomized study, the blood loss of 50 patients, during and after total hip surgery who had been given ibuprofen or placebo for 2 weeks before the procedure (Slappendel et al. 2002b). We showed that after giving ibuprofen, the perioperative blood loss was 45% higher than after placebo—i.e., ibuprofen 1161 (SD 472) mL versus placebo 796 (SD 337) mL; $p < 0.001$). In a subsequent double-blind randomized study, we included 169 total hip surgery patients, in whom we compared blood loss after they had taken the NSAIDs indomethacin 50 mg (n = 83) or meloxicam 15 mg (n = 86) 1 hour before surgery. We found that when indomethacin was given preoperatively the mean peroperative blood loss was 623 (SD 243) mL and the postoperative blood loss 410 (SD 340) mL, while after meloxicam, the blood losses were 524 (SD 304) mL and 357 (SD 272) mL, respectively. The latter blood loss is 17% ($p = 0.001$) less than that after indomethacin. We conclude that these in vivo findings accord with the in vitro findings and showed that avoiding the use of nonselective NSAIDs will reduce blood loss by 17%.

Table 3. Peroperative blood loss in patients with coxarthrosis undergoing their first elective total hip operation

Year	1994	1997	2000
Number of procedures	226	362	420
NSAID [a]	D	D/M	M
Average blood loss per procedure (mL)	701	562	515
Duration of surgery (min)	65	71	63

[a] D diclofenac, M meloxicam

Recombinant human erythropoietin. Recombinant human erythropoietin has been approved for use in patients undergoing major orthopedic surgery in The Netherlands. Our cut-off value for giving this treatment is a hemoglobin of 100–130 g/L. We chose this value when the analysis of our database showed that 50% of all allogenic red cell transfusions had been given to patients in this group. The standard treatment consists of giving 40,000 IE erythropoietin at weekly intervals, regardless of age and gender (Goodnough et al. 1995); it is started 3 weeks before surgery, and the last dose is given immediately after surgery if the hemoglobin level is below 150 g/L. Since the variations in the response to erythropoietin are related to iron-restricted erythropoiesis, the increase in the consumption of iron due to enhanced erythropoiesis should be countered to avert iatrogenic iron depletion. Therefore, we also give 200 mg elemental iron daily. We checked the rise in HB in 127 patients, and found an average increase in Hb of 19 (SD 4.8) g/L in the blood.

During surgery

Intraoperative blood salvage. Today intraoperative blood salvage is commonly performed in hospitals where major surgery is done. In our Department, two cell savers 5 (Haemonetics) are used when the blood loss is expected to exceed 1.5 liters—e.g., during revision hip and spinal surgery.

Intersurgeon variations in blood loss. We keep records on the blood loss incorred by each surgeon. The data are presented to the group anonymously, and each surgeon is told about his/her results. In this way, meticulous techniques and appropriate salvage are maintained.

Medications used to reduce bleeding – Aprotinine. This substance—a naturally occurring serine protease inhibitor—modifies hemostasis and reduces bleeding. We give it intravenously when the estimated blood loss exceeds 2 liters (Samama et al. 2002)—e.g., in our department, it is given to patients undergoing major spinal fusion surgery of the lumbothoracic spine (scoliosis, M. Bechterew) or major revision hip surgery. Our regimen consists of: 1) a test dose; 2) 1×10^6 KIU/h after the induction of anaesthesia; and 3) an infusion at the rate of 0.5×10^6 KIU/h. We evaluated the effect in 43 patients undergoing surgery for scoliosis by one single orthopedic surgeon and found a reduction of 20% blood loss (Table 4).

Table 4. Use of aprotinin in patients undergoing major spinal surgery (scoliosis)

	No aprotinin	Aprotinin
Number of procedures	21	22
Duration of surgery (min)	205	221
Average blood loss (mL)	2772	2172
Mean number of units of red cells per patient	1.3	0.4

Factor VIIa. In some patients with severe bleeding, we give thrombocytes and coagulation factors for coagulopathies caused by specific deficiencies. More recently, we have started to treat patients with recombinant blood coagulation factor VIIa (rFVIIa, NovoSeven). It forms complexes with tissue factor (TF) which is present in the wound, and thereby acts as a catalyst in local blood coagulation. It was effective in some patients, but has not been used routinely. Although controlled trials are needed to show its value in those with massive blood loss the first case reports and experience suggest that it is beneficial (Slappendel et al. 2002a, Weiskopf 2002).

Normothermia. Two independent studies (Schmied et al. 1996, Winkler et al. 2000) have shown that normothermia is useful in total hip surgery. A reduction of 1.5 °C in body temperature at the end of surgery increased the perioperative blood loss by 500 mL. Although we did not evaluate the effect of normothermia, this finding made us strt using optimal warm air fields during surgery (Figure 2).

Figure 2. Marked warming during total hip surgery.

Table 5. Transfusion policy, based on the level as transfusion trigger, incorporates the most recent national (Dutch) transfusion guidelines

Within 4 hours of surgery		>4 hours after surgery	
Hb (g/L)	units of packed cells	Hb (g/L)	units of packed cells
Patients below the age of 60 years			
>64	0	>64	0
<64	1	<64	1
<48	2	<56	2
Patients over the age of 60 years			
>72	0	>80	0
<72	1	<80	1
<64	2	<72	2
Patients with cardiac disease			
<88	0	<88	1
<80	1	<80	2
<72	2	<72	2

Table 6. Mean transfusion rate, using three transfusion guidelines and transfusion triggers

Period	A	B	C
Number of surgical procedures	4620	5703	4264
Type of anesthesia % general/spinal/plexus	38/56/6	37/55/17	39/56/11
Male/female (%)	39/61	39/61	39/61
Average age (years)	40.6	37.1	42.5
Average duration of surgical procedure (min)	48.0	49.1	50.1
Number of allogenic red cell infusions	2218	1882	981
Mean transfusion rate	0.48	0.33	0.23

Table 7. Number of allogenic red cell infusions in patients undergoing total knee surgery

Year	1997	2000
Number of procedures	137	153
Number of allogenic red cell infusions	77	0

After surgery

Transfusion trigger. We have limited the use of cut-off values for allogenic red cell infusions in the post-operative period. In Dutch hospitals, about 60% of the units of allogenic red cells are requested when blood loss is expected (Buiting and Dinkelaar 1998, Van der Jagt et al. 2001). It is noteworthy that in 96.2% of the patients the actual infusion of allogenic red cells was give regardless of a low Hb content. The indication for these unrestricted infusions were based on "clinical signs", such as fatigue, pallor, or the blood was given "routinely". In our hospital, we took a simple, but major, step forward by forbidding the infusion of allogenic red cells when Hb and the Ht values were unknown. We adapted the trigger value from Dutch national guidelines (Slappendel et al. 1999, Weber et al. 2000), which were transformed into a practical format for that purpose (Table 5). During the first 4 hours afater surgery, we took into account the effect of hemodilution and permitted a lower Hb level (Table 5).

These guidelines were introduced in our Intensive Care Unit in May 1996, and came into use in the hospital several months later.

We evaluated the effectiveness of this simple measure by dividing the patients according to use of the guidline: period A (no guideline), period B (guideline used in ICU alone), period C (guideline used in hospital). The demographic data and type of surgery were similar in the patients in the three groups. We found that the number of units per procedure declined from 0.48 to 0.33 and 0.23 in periods A, B, and C, respectively (Slappendel et al. 1999, Weber et al. 2000) (Table 6).

Postoperative cell saving (Bellovac A.B.T.). The Bellovac A.B.T. system (A.B.T. = autologous blood transfusion) concerns a type of postoperative cell saving in which blood from the surgical wound is collected and filtered and then returned to the patient. This blood salvaging system has reducde the number of blood transfusions in our Department to zero in total knee replacement surgery. It is also used when patients undergoing total hip arthroplasty and revision hip arthroplasty have a blood loss exceeding 500 mL. Knee replacement surgery is done with a tourniquet and we found that the postoperative salvage drain was very beneficial (Table 7).

The effect of blood-sparing measures from 1995–2000. The use of this consecutive series of measures produced a steady decline in the administration of packed red cells (Table 8).

Table 8. Allogenic red cell infusions in the Sint Maartenskliniek in the period 1995–2001

Year	1995	1996	1997	1998	1999	2000	2001
Number of surgical procedures	3398	4246	4034	4253	4078	4242	4610
Total blood loss (L)	845	859	825	817	876	795	780
Average blood loss (mL)	265	209	201	192	210	187	169
Number of allogenic red cell infusions	1172	1022	918	734	867	382	340
Average transfusion rate	0.34	0.24	0.23	0.17	0.21	0.09	0.07

Discussion

An overwhelming number of therapeutic methods is available to reduce the need for allogenic red cell infusions. Rather than simply including measures at random, we decided to rely on our relational database and selected the conditions associated with allogenic red cell transfusions. With this approach, we obtained a tremendous decline of 80% in the use of red cells was achieved. The algorithm (Figure 1) shows the various steps.

The everyday practice in our hospital did not differ from that in any general hospital in The Netherlands. Systematic presentations on "how we did it" resulted in the introduction of these measures in several of the hospitals in the region and a steady annual decline of 5–7% in the use of allogenic red cell transfusions.

It is important to realize that a single blood-sparing measure has hardly any effect. However, the complete algorithm and specific measures for each hospital radically reduces the use of allogenic red cells. We stated above that one main reason for making a greater effort to reduce the number of allogenic red cell transfusions is that they are thought to be associated with immunosuppression, which increases the incidence of postoperative infections, delays healing of postoperative wounds and thereby prolongs hospitalization. An expected that finding of such a reduction in transfusions should be an effect on these figures as well. Analysis of our database showed a 42% decline in postoperative infections (Table 9).

Simple inexpensive measures help to reduce the need for allogenic red cell transfusions. The savings in health care costs can be used for further improvements, and eventually, such infusions may become anecdotal.

Table 9. Infection rate in the Sint Maartenskliniek 1997–2001

Year	1997	1998	1999	2000	2001
Number of surgical procedures	4034	4253	4078	4242	4610
Incidence (%) of postoperative wound infections	2.6	2.1	1.7	1.8	1.5

On the basis of our experience and other systematic improvements in the routines of patient care, we recommend restrictive guidelines for allogenic red cell infusions, automated relational databases that provide feedback on clinical practice, preoperative assessment that involves the anesthesiologists and permits preoperative planning using a comprehensive algorithm.

No competing interests declared.

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