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Tranexamic Acid Reduces Allogenic Transfusion in Revision Hip Arthroplasty

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Abstract

Background Revision THA is associated with high blood loss and a high probability of blood transfusion in the perioperative period. In November 2003, government legislation established the Blood Utilization Program at our center to reduce the rate and risks associated with allogenic transfusion.

Questions/purposes The purposes of this study were to (1) determine whether the allogenic transfusion rate in patients undergoing revision THA decreased in those who were reviewed preoperatively by the Blood Utilization Program versus those who were not; (2) determine whether tranexamic acid reduced the rate of transfusion; and (3) identify potential perioperative clinical parameters that are associated with an increased risk of blood transfusion.

Methods We included all 159 patients who underwent revision THA from January 2006 to October 2008 having either a socket and/or femoral stem revision except those having only a liner exchange. One hundred and one patients attended the Blood Utilization Program preoperatively and 58 patients did not (ie, they required urgent/emergency surgery).

Results The Blood Utilization Program referral made no difference in transfusion rate or transfusion amount; however, the transfusion rates and amount were decreased by 8% and one unit, respectively. In patients referred to the Blood Utilization Program, the intraoperative use of tranexamic acid (an antifibrinolytic) was associated with reduced transfusions, regardless of dosage; preoperative erythropoietin tended to reduce transfusions while preoperative oral iron supplements did not.

Conclusions To further increase the relevance of the blood utilization program, the guidelines for patients undergoing revision hip arthroplasty need to be redefined.

Level of Evidence Level III, therapeutic study. See the guidelines online for a complete description of level of evidence.

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Each author certifies that his institution has approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained from each subject prior to their inclusion in the study.

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Introduction

Revision THA is associated with substantial blood loss and a high probability of blood transfusion in the perioperative period [4]. In revision hip arthroplasty, the blood loss is approximately 4.0 ± 2.1 units. Transfusion rates of 2.9 ± 2.3 units for revision hip arthroplasty have been documented [5]. Transfusion of allogenic erythrocytes has been associated with risks of transmission of infectious diseases,

immune sensitization, transfusion related acute lung injury, fever, hemodynamic overload, and urticaria [5]. Moreover, it has been suggested that transfusion of allogenic blood independently predicts the development of postoperative infections [15]. Measures taken to allay concerns about the safety of blood transfusions have translated into increasing the cost of allogenic blood units. Additionally, blood banks regularly have blood shortages. In British Columbia, less than 3% of the population donates blood and the province imports 17–20% of its blood requirements. In November 2003, based on government legislation, the Blood Utilization Program was formally established at our center with the purpose of enhancing preoperative hemoglobin levels to reduce the rate and risks associated with allogenic transfusion.

The purposes of this study were to (1) determine whether the allogenic transfusion rate in patients undergoing revision THA decreased in those who were reviewed preoperatively by the Blood Utilization Program versus those who were not; (2) determine whether tranexamic acid reduced the rate of transfusion; and (3) identify potential perioperative clinical parameters that are associated with an increased risk of blood transfusion.

Table 1. Significant variables, intergroup analysis

Variable	Blood Utilization Program (n = 101)	Non-Blood Utilization Program (n = 58)
ASA rating		
1-2 (low risk)	54 (53%)	15 (26%)
≥ 3 (high risk)	37 (37%)	36 (62%)
Operative time (minutes)	166 ± 58	139 ± 48
Comorbidities		
CAD	17 (17%)	16 (28%)
Preop DVT	7 (7%)	1 (17%)
Preop CVA	3 (3%)	7 (12%)
Indication for surgery		
Aseptic loosening	61 (60%)	14 (24%)
Periprosthetic infection	11 (11%)	25 (43%)
Other	29 (29%)	19 (33%)
Preoperative Hb level	143 ± 11.1	131 ± 18.3
Revision of acetabular implant	61 (60%)	17 (29%)
Length of stay	7.8 ± 5.8	10.9 ± 9.6

Patients and Methods

We retrospectively reviewed the hospital records of all 220 patients who underwent revision THA from January 2006 to October 2008. All 159 patients who either had a socket and/or femoral stem revision were included in the study, whereas 61 patients who had a liner exchange alone were excluded. Of the 159 included patients 101 patients were reviewed by the Blood Utilization Program preoperatively; 58 patients were not. The non-Blood Utilization Program patients were admitted from the emergency room or had an urgent referral for a periprosthetic fracture or periprosthetic infection, so there was no time to refer them to the Blood Utilization Program. The mean age of the patients reviewed by the Blood Utilization Program was 68 years (range, 35–89 years) whereas non-Blood Utilization Program patients had a mean age of 70 years (range, 43–91 years). No patients were recalled specifically for this study; all data were obtained from medical records.

A higher percentage of Blood Utilization Program patients had a low ASA rating and a lower rate of comorbidities (Table 1). The Blood Utilization Program group had a higher proportion of patients undergoing revision THA for aseptic loosening versus the patients who were not in the Blood Utilization Program (Table 1). Sixty-one of 101 patients (60%) in the Blood Utilization Program had both the acetabulum and femoral prosthesis revised, whereas only 17 of 58 (29%) of the patients who were not in the Blood Utilization Program had both components revised. The mean hemoglobin at the time of referral to the Blood Utilization Program clinic for the 101 patients was 138, which increased to 143 just prior to surgery. The mean preoperative hemoglobin level for patients in the Blood Utilization Program just prior to surgery was higher ($p < 0.0001$) than that for patients not in the Blood Utilization Program (143 versus 131, respectively) (Table 2). Only 29 of 101 (29%) patients in the Blood Utilization Program had a preoperative hemoglobin level of less than or equal to 130, whereas 55 of 58 patients not in the Blood Utilization Program (95%) had a preoperative hemoglobin level of 130 or less.

The Blood Utilization Program at our center is conducted by a team led by an anesthesiologist. This program discourages the predonation of autologous blood, and selectively utilizes preoperative oral/intravenous iron therapy and erythropoietin as well as intraoperative use of tranexamic acid and intraoperative red blood cell salvage, in addition to evidence-based transfusion criteria. The use of hematinics is recommended postoperatively. Patients are referred to the BUP program on an average of at least 6 weeks prior to surgery.

A posterior approach was used for most of the revision THAs, whereas a lateral approach was used for select cases. A total of 53 patients underwent an extended trochanteric osteotomy and 26 patients required bone grafting.

The medical records and anesthesia data sheets were reviewed and the following preoperative data were recorded: patient age, gender, diagnosis, medical comorbidities,

Table 2. Blood Utilization Program versus Non-Blood Utilization Program transfusion

Variable	Blood Utilization Program (n = 101)	Non-Blood Utilization Program (n = 58)	p-value
Preoperative Hb level (mean)	138 to 143 ± 11.1	131 ± 18.3	($p < 0.0001$)
Preoperative Hgb ≤ 130	29/101 (29%)	55/58 (95%)	
Antifibrinolytic used	38 (38%)	18 (31%)	
# of patients received transfusion	53 (52%)	35 (60%)	($p = 0.4078$)
# units per transfused patient	2.9	3.9	($p = 0.099$)
Postoperative cardiac events	3 (3%)	2 (3.4%)	
Discharge hemoglobin	99 ± 12.8	99 ± 7.3	

American Society of Anesthesiologists (ASA) rating of operative risk (1–2, or ≥ 3) [23], body mass index (BMI), and use of medications including iron and/or erythropoietin. Intraoperative data that were collected included anesthetic type, estimated blood loss, operative time, number of units of transfusion, preoperative and postoperative hemoglobin and hematocrit levels, procedure type, and implants used. Postoperative data that were collected included length of stay, number of blood units transfused, anticoagulant use and complications.

The ASA rating was determined by the attending anesthesiologist. For the purposes of this study, we categorized patient risk as either 1 or 2 (low risk) or 3 or greater (high risk). Operative times reflect the time from incision to wound closure. The major medical comorbidities requiring active medical treatment were recorded; specifically, a history of cardiac disease, cerebrovascular attack, and deep vein thrombosis were noted preoperatively.

The general criteria for administering a transfusion included symptomatic anemia characterized by persistent hypotension, tachycardia, dizziness, and shortness of breath, as well as asymptomatic anemia in high risk patients, as determined in conjunction with the medical service. In most cases, this involved a perioperative hemoglobin level of 90 or lower in a patient with major coronary artery disease or with advanced age. Therefore, multiple variables were taken into consideration before administering a blood transfusion. Transfusions were only administered to patients who consented to receive blood, as per local legislation.

Categorical data were assessed by chi square test, and continuous variables with t-tests. We determined differences in predictor variables for transfusion between age, BMI, gender, ASA rating, Charnley class, BUP referral, preoperative hemoglobin, revision of both acetabular and femoral components, use of tranexamic acid and operative time using logistic regression analysis (probability modeled is received transfusion = 1). The data were analyzed using SAS 9.1.3 statistical analysis software (SAS Institute Inc, Cary, NC).

Results

Despite the much higher percentage (95%) of patients not in the Blood Utilization Program with a preoperative hemoglobin level of 130 mg/dl or less, the transfusion rate and amount transfused was similar ($p = 0.4078$) to that for the patients in the Blood Utilization Program: 52% of patients in the Blood Utilization Program required a transfusion whereas 60% of patients not in the Blood Utilization Program required a transfusion. The amount of allogenic blood transfused in patients in the Blood Utilization Program was also similar ($p = 0.099$) to that for patients not in the Blood Utilization Program: 2.9 versus 3.9 units, respectively.

When all the patients who were reviewed preoperatively by the Blood Utilization Program clinic were analyzed as a group in terms of those who received a transfusion, the use of tranexamic acid was higher in the group of patients who did not receive a transfusion.

Age, gender, ferritin level, and preoperative use of iron and erythropoietin were not associated with an increased transfusion risk (Table 3). The logistic regression analysis model performed separately (adjusted for age, BMI, sex, ASA rating and Charnley class) showed that female gender, BMI, low preoperative hemoglobin, exchange of acetabular implant, increased operative time (minutes) and intraoperative use of tranexamic acid, independently predicted the need for allogenic transfusion (Table 4).

Discussion

One of the main goals of blood management for patients undergoing THA is to identify those at high risk for bleeding and to reduce the need for transfusion with allogenic blood. In this study we retrospectively reviewed revision hip arthroplasties to assess the effectiveness of the Blood Utilization Program, use of tranexamic acid and to

Table 3. Patients in the Blood Utilization Program: transfusion versus no transfusion

Variable	Received transfusion (n = 53)	Did not receive transfusion (n = 48)
Age (years)	70 ± 12	66 ± 12
Gender		
Male	27	25
Female	26	23
Ferritin level (μg/l)	152 ± 155	143 ± 92
Number of patients received tranexamic acid	15 (28%)	23 (48%)
Dose of tranexamic acid (mg)	1606 ± 1200	1771 ± 897
Dose of preoperative erythropoietin		
20000U	6	7
40000U	7	9
Number of patients received preoperative oral iron supplements	46	36

Table 4. Logistic regression analysis of predictor variables for transfusion when Blood Utilization Program is forced. (Probability modeled is Received transfusion = 1)

Variable	Odds ratio	95% CI	p-values
Age (years)	1.006	0.959–1.055	0.8124
BMI*	0.851	0.750–0.966	0.0125
Gender* (female)	0.133	0.030–0.594	0.0082
ASA 1 or 2 versus 3 or 4	0.441	0.118–1.656	0.2254
Charnley Class A or B versus BB or C	0.994	0.283–3.496	0.9929
BUP referral (no versus yes)	0.739	0.139–3.935	0.7228
Preoperative hemoglobin* (mg/ml)	0.834	0.764–0.911	< .0001
Revision of both components * (no versus yes)	0.068	0.014–0.327	0.0008
Antifibrinolytic used* (no versus yes)	7.704	1.990–29.835	0.0031
Operative time* (minutes)	1.023	1.007–1.038	0.0036

* $p < 0.05$ (statistically significant).

determine the variables associated with a higher risk of allogenic transfusion in these patients.

Our study is limited by several factors. First, patients not included in the Blood Utilization Program were admitted from the emergency room or had an urgent referral for a periprosthetic fracture or periprosthetic infection; consequently, there was no time for their preoperative assessment by the Blood Utilization Program. In contrast, all of the patients in the Blood Utilization Program were having elective surgery, and had ample time to attend the Blood Utilization Program. Therefore the non-BUP patients would not be an appropriate control group as the indications for surgery are different. We overcame this issue by performing a logistic regression analysis for all patients in this study requiring an allogenic transfusion. Second, 95% of the patients not in the Blood Utilization Program had a preoperative hemoglobin level of 130 or less, compared to only 29% of the patients in the Blood Utilization Program. Since the non-Blood Utilization Program group is dominated (95%) by patients with a preoperative hemoglobin level of 130 or less, this could contribute to the importance of preoperative hemoglobin in the logistic regression model.

To our knowledge, this is the first study in the literature that reviews a comprehensive blood management strategy in patients undergoing revision hip arthroplasty patients starting with a preoperative assessment including use of erythropoietin and hematinics, intraoperative use of tranexamic acid, cell salvage as well as postoperative use of hematinics. No single study has looked at all of these variables in any one population.

Bierbaum et al. reported a 46% rate of allogenic and autologous transfusion in a series of 9482 patients managed with total joint arthroplasty [2]. Autologous transfusion is a relatively safe and effective option for these patients, but the collection and transfusion of autologous blood carry risks including compartment syndrome, bacterial contamination, febrile nonhemolytic and septic reactions, phlebitis, and clerical error [20, 28]. Also, predonation of autologous blood has been extremely inefficient, with wastage rates ranging from 40% to 56% [3, 14]. For these reasons, autologous transfusion has been mostly abandoned at our center.

Recombinant human erythropoietin alpha is considered an effective preoperative treatment for increasing preoperative hemoglobin levels, and was administered to the patients in the Blood Utilization Program based on their preoperative hemoglobin levels and the time remaining between the Blood Utilization Program referral date and surgery date. Three major, double-blind, placebo-controlled studies involving 724 patients, with hemoglobin levels between 100 and 130, having major elective orthopaedic surgery [6, 9, 10] showed that treatment with 300 IU/kg epoetin alfa per day, for at least 14 days, beginning 10 days before surgery and continuing until the third or fourth day after surgery, decreased the number of patients requiring transfusion compared with patients given a placebo. Our patients in the Blood Utilization Program not using preoperative erythropoietin had no increased risk of transfusion.

Ho and Ismail [16] evaluated intravenous tranexamic acid in THA as well as TKA and reported it to reduce blood loss and allogenic transfusion without complications

related to the drug. Similarly, Kagoma et al. [18], based on a meta-analysis of randomized trials among patients undergoing elective THR or TKA, reported antifibrinolytic agents reduce bleeding, reduce the risk of transfusion by almost 50%, and do not appear to increase the risk of venous thromboembolism. For patients undergoing primary hip replacement, Rajesparan et al. [22] and Husted et al. [17] previously reported tranexamic acid is cost-effective in reducing blood loss and transfusion requirements. Our data support the use of tranexamic acid in patients undergoing revision hip arthroplasty.

The preoperative hemoglobin concentration is a strong predictor of perioperative transfusion and is often used to discriminate between patients at higher and lower risk for transfusion [3, 11, 24]. Several other factors reportedly influence perioperative blood loss in patients undergoing hip arthroplasty including gender, age, physical status of the patient, hypertension, body mass index, coagulation factors, type of anesthesia, and surgical procedure [1, 7, 8, 13, 19, 21, 25, 26]. Walsh et al. [27] reviewed 1035 cases of THA and reported the most important and consistent predictors of the requirement for a blood transfusion was advanced age and the use of low molecular weight heparin for DVT prophylaxis. Our data suggest that female gender, increased BMI, low preoperative hemoglobin, no intraoperative use of tranexamic acid, revision of acetabular implant, and increased operative time independently increased the need for transfusion.

Garvin et al. [12] reported total blood loss was greatest for femoral revision than for acetabular revision in 147 patients undergoing revision THA. Zarin et al. [29] reviewed the records of 126 patients undergoing revision THA and found the greatest blood loss occurred when both components were revised, while the blood loss when only one component was revised was not different between femoral component revision and acetabular revision. Our data show a higher risk for transfusion when the socket is revised.

Our data suggest referral to our center's Blood Utilization Program did not reduce the transfusion rate or transfusion amount. However, in patients referred to the Blood Utilization Program, intraoperative use of tranexamic acid was associated with reduced transfusions; the use of preoperative erythropoietin did not influence transfusion rates nor did the use of preoperative oral iron supplements. Therefore to further increase the relevance of the blood utilization program, the guidelines for patients undergoing revision hip arthroplasty need to be redefined. Also, the use of preoperative erythropoietin in these patients needs further research.

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