The benefit of early identification of anemia preoperatively in patients undergoing hip and knee joint arthroplasty

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KEYWORDS
Anemia; Blood conservation; Transfusion risks; Preoperative; Iron sucrose; Erythropoietin; Early CBC testing; Iron deficiency anemia

Abstract
Aim: The primary objective of this study was to establish the frequency of preoperative anemia (Hb < 130 g/L) in patients undergoing hip and knee arthroplasty. The secondary objective was to improve anemia optimization by identifying anemia earlier in the preoperative phase.

Methods: The study was a prospective analysis of preoperative patients undergoing joint arthroplasty. A CBC was done at the first clinic visit (as opposed to the usual second visit). Patients were asked about any history of anemia. A ferritin was added if there was a history of anemia. Anemic patients were referred to the blood conservation clinic for treatment of anemia.

Results: 782 patients were seen during the nine month study period. 365 patients were enrolled. 65% were female. The incidence of anemia was 21%. 68 patients had ferritins measured: 10 patients (15%) had iron deficiency (ferritin <30 µg/L). Overall, the transfusion rate for all procedures during the study period was 3.6% (52/1439 cases) compared to 5.1% (75/1463 cases) in the previous year.

Conclusions: Anemia is common in patients undergoing hip and knee replacement surgery. Early identification of preoperative anemia allows more time for hemoglobin optimization and may contribute to fewer transfusions perioperatively.
Editor comments: Blood loss during major elective orthopaedic surgery can be substantial. Traditionally the effects of this on recovery have been ameliorated by the administration of allogeneic blood transfusion in the early postoperative period. Careful thought is now being given to ways to avoid this risky and expensive practice. This includes a better understanding of the patient’s haemoglobin at a timely point pre-operatively to enable alternative measures to be considered and put into place. This study provides an important example of an approach to better preparation of the patient which results in a reduction in need for transfusion. JS-T

**Introduction**

For many decades fairly liberal transfusion practice was the standard of care for anemic patients in the majority of hospitals throughout the world — despite a lack of evidence showing benefit. This practice was allowed to continue because blood transfusion can be life-saving in bleeding patients and there were few studies showing that transfusions caused harm.

However, in the last decade many studies have reported adverse outcomes associated with transfusion, especially when given at the most vulnerable time — during or immediately post surgical interventions. (Marik and Corwin, 2008; Bernard et al., 2009). Blood transfusion is also associated with known risks such as transfusion related acute lung injury (risk 1 in 10,000), bacterial sepsis (risk 1 in 10,000) and circulatory overload (risk 1 in 700) (Callum et al., 2011) which are far greater than the current estimated risks of transfusion transmitted viral infections, (e.g. Hepatitis B risk 1 in 1.7 million; Hepatitis C risk 1 in 6.7 million; HIV risk 1 in 8 million) (O’Brien et al., 2012), which is often voiced as the biggest fear in the minds of patients. Transfusion is also associated with increased financial costs. The estimated cost of transfusion for a single unit of red blood cells when all activities associated with transfusion are included is $760 (Shander et al., 2010).

The biggest independent predictor of whether a patient will require a transfusion during their perioperative course is their preoperative hemoglobin level. (Faris et al., 1999; Freedman et al., 2008) In fact, recent reports estimate that approximately one third of orthopedic patients undergoing hip and knee surgery are anemic preoperatively as defined by a hemoglobin level of less than 130 g/L (Goodnough et al., 2011).

At our centre surgical candidates are seen at the Holland Centre Hip and Knee Arthritis Program-Assessment Centre (HKAP-AC) more than six weeks prior to surgery. The purpose of this study was to determine if adding a routine complete blood count (CBC) at the HKAP-AC visit, rather than waiting until the preoperative clinic visit at 2–3 weeks prior to surgery, could detect anemia earlier and allow more time for anemia optimization. The primary research question was to determine the frequency of anemia in preoperative patients undergoing hip or knee total joint replacement at our centre. The secondary research questions were to determine how often anemia was due to iron deficiency and whether increased anemia identification at an earlier preoperative time point could lead to increased referrals to the blood conservation clinic (BCC) and decreased transfusion rates compared to a similar time period prior to the change.

**Methods**

This was a prospective observational study conducted between April 2011 and January 2012 in patients presenting to their first visit to the Holland Centre HKAP-AC. All patients being assessed for hip or knee joint replacement surgery (whether single, bilateral or revision procedure) who provided informed consent were eligible to be included. The study was approved by the Sunnybrook Health Sciences Centre Research Ethics Board.

Patients present to the HKAP-AC to be assessed for readiness for surgery by a physiotherapist and a nurse typically 6–12 weeks prior to surgery. The process requires all patients to complete a questionnaire documenting their general health at the first visit to the HKAP-AC. This includes a question on whether the patient had a history of anemia. However, prior to April 2011 anemia was not routinely addressed or managed until the second patient visit at the Preoperative Orientation Program Visit (POP) where the first preoperative CBC was drawn. The POP visit typically occurs 2–3 weeks before the surgical date. All patients undergoing revision hip or bilateral hip or bilateral knee replacement surgeries are routinely referred to the blood conservation clinic regardless of hemoglobin level.

In this study anemia assessment was moved earlier to the HKAP-AC visit and performed by the nurse. If the patient was deemed to be ready for
The benefit of early identification of anemia preoperatively in patients undergoing hip surgery referral, the nurse additionally requested a CBC to be done on the same day. If the patient indicated a history of anemia on the general health questionnaire, a sample was also drawn for ferritin. All patients were given an oral iron information pamphlet, with suggestions to start oral iron 4–6 weeks preoperatively. If patients had anemia (defined as hemoglobin <130 g/L), they were referred to the BCC. The blood conservation nurse then contacted the patients directly to arrange for further testing or anemia management. The timing of this patient contact by BCC was dependent on the degree of anemia as well as time to surgery. Blood conservation interventions typically included intravenous iron and erythropoietin as well as encouraging oral iron supplementation.

The primary outcome was the frequency of anemia in patients undergoing hip or knee arthroplasty. Patients were defined as having anemia if the hemoglobin was less than 130 g/L, regardless of gender. The secondary outcome was the frequency of iron deficiency anemia. Patients were defined as having iron deficiency if the ferritin was less than 30 mcg/L. (Goodnough et al., 2011). Iron indices were not routinely done at this first visit due to financial constraints; thus the definition of iron deficiency was strict and may have underestimated the true frequency of iron deficiency.

Other secondary outcomes included the number of referrals to BCC, the number of blood conservation interventions (e.g. intravenous iron and erythropoietin) and transfusion rates. These were determined for all patients (both enrolled and not enrolled) during the study period compared to a historical cohort of patients during the same time period one year prior. With respect to transfusion, institutional red blood cell transfusion guidelines recommend transfusion of one unit at a time for non-urgent inpatient transfusions. The recommended transfusion threshold is hemoglobin < 70 g/L. If symptoms are present then a higher hemoglobin threshold may be used for transfusion based on clinical judgment. The transfusion guidelines did not change during the study compared to the year prior. Tranexamic acid (an antifibrinolytic agent which has been shown to decrease perioperative blood loss) was not routinely used during the periods of interest.

Statistical analysis

The sample size was based on determining the frequency of anemia in this population. Based on recent literature, it was estimated that approximately 30% of patients have preoperative anemia (as defined by a hemoglobin < 130 g/L). Using the Exact Clopper Pearson analysis it was determined that to produce a two-sided 95% confidence interval with a width equal to 10% 341 patients would be required in the study.

It was expected that the HKAP-AC captures approximately 90% of all patients undergoing hip or knee joint surgery and 3 months was estimated to complete the project. However, during the study period only 50% of patients booked for surgery were being seen in the HKAP-AC. During the study period of April 18 2011 to January 18 2012 there were 1439 surgical patients but only 782 patients were assessed through the HKAP-AC. The reasons for the lower than expected assessment by the HKAP-AC included patients being seen at external clinics, referrals directly to the surgeon’s office and patients undergoing revision surgery procedures who were not being assessed again at the HKAP-AC. Therefore the study was extended until 341 patients were enrolled.

For the secondary outcomes of referrals to blood conservation, number of blood conservation interventions and transfusion rates, these were calculated for all patients (enrolled and not enrolled) that underwent hip or knee arthroplasty during the study period of Apr 18 2011 to Jan 18 2012. These rates were then compared to historical rates collected in a retrospective audit of all hip and knee arthroplasty patients who had surgery at the Holland Centre for the same time period one year prior.

Results

Between April 2011 and January 2012 1439 patients underwent total hip or knee arthroplasty at the Holland Centre. 782 patients were assessed through the HKAP-AC. Only 476 patients were approached due to the limited availability of staff to enroll patients. One hundred and eleven patients declined to participate because of issues with time and transportation constraints and not wanting to wait for lab work to be done at that initial visit. Thus, 365 patients consented to enrollment in the study.

Seventy-seven patients were found to have a hemoglobin less than 130 g/L for an overall frequency of anemia of 21% (95% confidence interval CI), 17–25%). On the general health questionnaire 68 patients (19%) indicated a history of anemia of which 28 (41%) were found to have preoperative anemia with a hemoglobin less than 130 g/L. In the 297 patients who did not indicate a history of...
anemia 49 (17%) were anemic. Ferritin testing was performed on the 68 patients who indicated a history of anemia. Ten patients (15%) were found to have iron deficiency.

Comparing the study period with a similar period one year prior (Table 1) blood conservation referrals increased by 83% (from 77 to 141). Most patients referred to BCC were contacted and the use of oral iron was reinforced. Blood conservation interventions (including intravenous iron and erythropoietin) increased (from 14 to 27). The rate of intervention was low because some patients were already referred according to the usual protocol for bilateral or revision cases and others were not anemic and therefore did not require a blood conservation intervention. Some referrals were patients inquiring about autologous blood donation and some no longer had anemia by the time BCC contacted the patient, possibly due to the effects of oral iron therapy that had been initiated for a few months prior (although the percentage of these is not certain). The average hemoglobin rise in patients who went to surgery within 90 days of the HKAP-AC visit and showed any increase in hemoglobin, possibly attributable to the oral iron supplementation recommendations was 6.7 g/L.

Transfusion rates during the study period were 3.6% compared to 5.1% one year prior. Overall 131 RBC units were transfused compared to 196 units in the year prior. There was no difference in the number of transfused patients who were anemic preoperatively (55% during this study compared to 52% one year prior) (Table 1).

Discussion

In a population of patients undergoing preoperative assessment for total hip and knee joint arthroplasty we found an overall frequency of anemia of 21%. This is quite similar to other studies (Spahn, 2010; Goodnough et al., 2011) in the orthopedic population. The frequency of anemia increased to 41% in patients endorsing a history of anemia although was still significant at 17% in those without a history of anemia. This demonstrates that although the history is helpful there is still a significant proportion of patients that have anemia preoperatively and anemia assessment using a complete blood count in all patients will yield a higher rate of detection than selective screening based on history alone.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Comparison of study period compared to historical cohort.</th>
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<tbody>
<tr>
<td>Result</td>
<td>Enrolled Patients</td>
</tr>
<tr>
<td>Number of Hips and Knee surgeries</td>
<td>365 cases (65% female)</td>
</tr>
<tr>
<td>Number of Referrals to BCC (Percentage of patients)</td>
<td>45 (12.3%)</td>
</tr>
<tr>
<td>Number of pts who received erythropoietin and/or intravenous iron as recommended by BCC</td>
<td>7</td>
</tr>
<tr>
<td>Number transfused despite erythropoietin and/or intravenous iron (percentage of patients treated with erythropoietin and/or intravenous iron)</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>Number of patients transfused (%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Number of RBC Units transfused (average number of units per patient transfused)</td>
<td>6 (1.5 units per transfused patient)</td>
</tr>
<tr>
<td>% of transfused patients that were anemic preop (Hb &lt; 130 g/L) (average preoperative Hb g/L of transfused patients)</td>
<td>25%</td>
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</table>

*~50% of patients went through the HKAP-AC (including 365 patients enrolled in the study).*
In patients who endorsed anemia the rate of iron deficiency anemia was 15%. Again this is quite similar to other studies (Goodnough et al., 2011). This is likely to be an underestimate since we used a strict definition of ferritin <30 mcg/L and only tested those who had a history of anemia. We also did not consider definitions of iron deficiency that included higher ferritins and transferrin saturations of less than 20% as testing for serum iron indices were not routinely included in the initial assessment due to resource limitations.

With earlier assessment of the CBC during the perioperative phase blood conservation referrals and interventions increased. However, the increase did not seem to be simply additive. As a result of the ongoing study there was increased awareness about blood conservation and we feel that patients who may have been missed previously were also referred because blood conservation was at the forefront of the team’s mind during the study. During the study period and historical cohort period there were no other changes in clinical practice.

Finally, out of the patients referred within the study the rate of transfusion was lower than in all patients undergoing surgery during the study period. There was also a decrease in the number of units received per patient transfused in the study patients compared to the larger group of all patients during the same time period (1.5 vs. 2.5 units per transfused patient). This was unexpected as these patients who had anemia at the outset would be at greatest risk for receiving a transfusion. Overall, decreases in transfusion rates (3.6% vs. 5.1%) and number of units transfused (131 units vs. 196 units) were also observed in the study period compared to a historical cohort.

Although a direct link between earlier anemia assessment and perioperative transfusion cannot be made from this study, an associated decrease in perioperative transfusion was observed. The risk associated with blood transfusion is present with each and every unit of blood transfused. At an estimated cost of approximately $760 per unit of transfused blood (Shander et al., 2010), the decrease in 65 units translated into a cost savings of $49,400 over the 9 month study. This saving would well offset the $9000 cost of an additional CBC ($6 per test) done earlier in the preoperative phase in all patients (1439 patients) during the study period. Additional savings from earlier anemia assessment would also be introduced since there would be additional time for the effect of less expensive interventions such as oral iron supplementation alone and/or diagnosis of underlying anemia without having to use more costly blood conservation interventions such as intravenous iron and erythropoietin.

Limitations of the study include the possibility of selection bias where only 365 of 1439 patients during the study period were included. However, these patients are typically presenting for the first time to the Holland Centre. Patients already assessed through the HKAP-AC may bypass the clinic visit as they have been previously assessed. We also acknowledge that we used a strict definition of iron deficiency and did not assess serum iron indices in all patients. However, this would if anything underestimate the frequency of iron deficiency anemia. Finally, we did not specifically assess compliance of oral iron supplementation and therefore cannot determine the precise effect of oral iron on preoperative anemia treatment.

Conclusions

The multidisciplinary effort in preoperative anemia screening and management of the team involved with the orthopedic surgical patient at the Holland Centre shows that a proactive, consistent approach to anemia identification and treatment can yield many benefits for both the patient and the institution. It is hoped that these results may lead to discussion amongst surgical teams that may lead to incorporating early CBC assessment as the standard of care, thereby allowing more patients to benefit from hemoglobin optimization preoperatively, which may lead to further improvements in surgical outcomes.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Ethical Approval

This practice based research project was approved by the Sunnybrook Health Sciences Centre Research Ethics Board. This REB application included details on obtaining appropriate consent procedures, appropriate storage of patient data and the need for patient identifiers to be removed from records.

Funding Source

The funding for this project was provided in full from a grant received from the Practice Based
Research (PBR) Council of Sunnybrook Health Sciences Centre. The PBR Council had no role in the study design, collection, analysis or interpretation of data, in writing of the manuscript or in the decision to submit the manuscript for publication.

Acknowledgments

We would like to acknowledge Susan Clark, preoperative clinic nurse at the Holland Centre for helping to enrol patients and Dr. Sue Belo from the Department of Anesthesia and Dr. Marciano Reis for their input into the project. We would like to thank Alex Kiss for his assistance with statistical analysis. Finally, we would like to acknowledge the Ontario Transfusion Coordinators (ONTraC) Program for funding of the blood conservation nurse position at Sunnybrook Health Sciences Centre. The funding for this project was provided in full from a grant received from the Practice Based Research (PBR) Council of Sunnybrook Health Sciences Centre.

References


