Effect of Perioperative Intravenous Iron Administration on Transfusion Requirements in Patients Undergoing Unilateral Total Knee Arthroplasty

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Introduction

Recent growth of the elderly population has caused an increased incidence of degenerative joint diseases, thereby rendering joint replacement arthroplasty a common procedure. Joint replacement surgeries are usually accompanied by a considerable amount of blood loss. For example, according to unilateral total knee arthroplasty (TKA) research, perioperative blood loss can reach up to 2000 mL.(1-4) Transfusion of allogeneic blood is frequently required, especially for patients with elevated age and comorbidities, due to lessened tolerance for decreased oxygen transport.

Concerns about potential complications of allogeneic transfusion, along with a severe shortage of blood products and desire to reduce medical costs, have facilitated various blood-saving strategies in these patients.(5-12) Some investigations demonstrated that preoperative or postoperative administration of intravenous (IV) iron can reduce the demand for allogeneic transfusion after hip surgery.(13-16)

Some investigations have demonstrated that perioperative administration of IV iron and erythropoietin along with strict criteria for transfusion can reduce the requirements for allogeneic transfusion after TKA.(17-19)

The purpose of this study was to evaluate the effect of perioperative administration of IV iron alone on the transfusion requirements in patients undergoing unilateral TKA.

Methods

After obtaining approval from the Institutional Review Board of our hospital and written informed consent, we enrolled 64 patients with ASA physical status 1 or 2 who were scheduled for elective unilateral TKA (iron group). Patients with hematological or coagulation disorders, hepatic or renal diseases, known infection or malignancy, and those under anticoagulant therapy were not included. Patients with a preoperative hemoglobin (Hb) level of greater than 14 g/dL were also excluded.
Sixteen of these 32 patients received 400 mg of IV iron sucrose (Venoferrum®, Vifor, Switzerland). It was divided into 4 doses, with each 100 mg dose being given 48 hours prior to surgery, 24 hours before surgery, just prior to surgery, and on the first postoperative day. The other 16 patients were admitted to the hospital on the day before surgery and received only 3 doses (300 mg total) of IV iron sucrose, which were administered on the day of admission, just prior to surgery, and the first postoperative day. A previous series of 32 patients who had undergone unilateral TKA without IV iron served as the control group. These patients satisfied the same inclusion criteria as the iron group. No other blood saving method was utilized for these patients.

According to the hospital’s protocol, patients were provided with standardized antibiotic and antithrombotic prophylaxis and IV patient-controlled analgesia postoperatively. All of the surgical procedures were performed by the same surgical team using the same implant with all components being cemented. A pneumatic tourniquet was used during the procedure and was deflated after wound closure. Three closed suction drains (two inside the joint and one subcutaneously) were placed intraoperatively and were removed on the second postoperative day. After surgery, patients stayed in the post-anesthesia care unit (PACU) for about an hour and received oxygen via facial mask (5 L/min).

Allogeneic transfusion was indicated when Hb level fell below 10 g/dL. Patients were also transfused if they presented with the clinical symptoms or signs of acute anemia, such as hypotension, tachycardia, tachypnea, dizziness, or fatigue. In such cases, they received the packed RBC units (320 mL) one by one until the symptoms or signs disappeared. This protocol was equally applied in the operating room, the PACU, and the ward.

The analyzed variables included: patients’ age and gender; height and weight; anesthetic risk according to ASA classification; type and duration of anesthesia; adverse reaction to IV iron; operative and postoperative blood loss; Hb levels determined at preoperative assessment, immediately after surgery, on the first, second, and seventh postoperative days and at discharge; transfusion rate (% of transfused patients); transfusion index (units transfused per patient); and length of hospital stay (LOS).

Data were expressed as a percentage (%) or as the mean ± standard deviation. Pearson’s chi-square test or Fisher’s exact test was used for comparison of qualitative variables, and Student’s t-test was used for comparison of quantitative variables. For repeated measures, comparisons were carried out with the repeated-measures ANOVA. All statistical calculations were performed with SPSS for Windows version 18 (SPSS Inc. Chicago, IL, USA), and a p-value of less than 0.05 was accepted as an indication of statistical significance.

Results

There were no statistically significant differences between groups with respect to patients’ age, gender distribution, height, weight, ASA classification, type and duration of anesthesia, operative and postoperative blood loss, preoperative Hb levels, or LOS (Table 1). No adverse reactions to IV iron sucrose such as phlebitis, abdominal pain, fever, headache, or anaphylaxis were observed.

Although no statistically meaningful difference in the allogeneic transfusion rate was noticed (91% in the control group vs. 81% in the iron group, P=0.064), the transfusion index of the control group was significantly higher compared with the iron group (1.8±1.1 units/patient vs. 1.3±0.8 units/patient, P<0.05). No significant differences were observed between the two
Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=32)</th>
<th>Iron group (n=32)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.0±6.0</td>
<td>70.0±5.3</td>
<td>0.982</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>0/32</td>
<td>0/32</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>152.0±5.6</td>
<td>151.3±5.1</td>
<td>0.631</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59.6±7.4</td>
<td>59.6±8.5</td>
<td>0.984</td>
</tr>
<tr>
<td>ASA classification</td>
<td></td>
<td></td>
<td>0.313</td>
</tr>
<tr>
<td>1</td>
<td>0 (0)</td>
<td>1 (3.1)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>32 (100)</td>
<td>31 (96.9)</td>
<td></td>
</tr>
<tr>
<td>Anesthesia type (Spinal or CSE/general)</td>
<td>29/3</td>
<td>31/1</td>
<td>0.312</td>
</tr>
<tr>
<td>Anesthesia time (min)</td>
<td>171.4±27.5</td>
<td>159.4±23.4</td>
<td>0.064</td>
</tr>
</tbody>
</table>

Values are presented as mean±SD or number of patients.

Table 2. Clinical Data of 64 Patients Undergoing Unilateral Total Knee Arthroplasty

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=32)</th>
<th>Iron group (n=32)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss (ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraoperative</td>
<td>278.1±64.7</td>
<td>296.9±121.1</td>
<td>0.443</td>
</tr>
<tr>
<td>Postoperative</td>
<td>1045.6±362.5</td>
<td>1049.9±483.0</td>
<td>0.968</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>12.0±0.9</td>
<td>12.0±0.8</td>
<td>0.965</td>
</tr>
<tr>
<td>Immediately postoperative</td>
<td>10.0±1.0</td>
<td>10.5±1.0</td>
<td>0.098</td>
</tr>
<tr>
<td>POD #1</td>
<td>10.7±0.9</td>
<td>10.5±1.4</td>
<td>0.508</td>
</tr>
<tr>
<td>POD #2</td>
<td>10.1±0.9</td>
<td>10.2±1.1</td>
<td>0.591</td>
</tr>
<tr>
<td>POD #7</td>
<td>10.5±0.8</td>
<td>10.8±0.9</td>
<td>0.200</td>
</tr>
<tr>
<td>At discharge</td>
<td>10.9±0.9</td>
<td>11.7±0.9</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Transfusion rate (%)</td>
<td>91</td>
<td>81</td>
<td>0.064</td>
</tr>
<tr>
<td>Transfusion index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(units / patient)</td>
<td>1.8±1.1</td>
<td>1.3±0.8</td>
<td>0.031*</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>14.2±1.2</td>
<td>14.2±1.1</td>
<td>0.933</td>
</tr>
</tbody>
</table>

POD #1, #2, #7 = first, second, seventh postoperative day

Values are mean±SD or incidence (percentage).

*P<0.05 compared to control group

groups with respect to Hb levels measured immediately after surgery and on the first, second, and seventh postoperative days. The Hb level at discharge, however, was significantly lower in the control group than in the iron group (10.9±0.9 g/dL vs. 11.7±0.9 g/dL, P<0.001) (Table 2).

Discussion

The risks associated with allogeneic transfusion include allergic, hemolytic, or febrile reactions, disease transmission, transfusion-related acute lung injury, immunomodulation, and increased incidence of postoperative bacterial infections.(11,12) Moreover, allogeneic blood is becoming more expensive, as there is an insufficient supply of blood products these days. In patients undergoing joint replacement surgery, numerous methods of blood conservation have been proposed. These methods include correction of underlying anemia with synthetic erythropoietin and iron supplementation, preoperative autologous blood donation, hypotensive anesthesia, acute normovolemic hemodilution, use of antifibrinolytics or blood substitutes, modification of surgical techniques, and perioperative blood salvage.
We did not include the administration of erythropoietin in our blood-saving protocol because its use in orthopedic surgery did not prove to be cost-effective despite it having been proved to decrease the incidence of perioperative transfusion. However, it was not useful in improving other clinical outcomes such as patient survival, quality of life, or time to mobilization.(20-22)

In Korea, the price of erythropoietin is about $60 per 10,000 IU vial. If patients are expected to receive 40,000 IU of erythropoietin as in the reports cited above (17,18) they would have to pay more than $240. This charge is not covered by health insurance unless they are hemodialysis patients suffering from chronic renal failure or cancer patients undergoing chemotherapy. We also did not impose a strict restriction on transfusion. If the patients given IV iron had received allogeneic blood when their Hb levels fell below 8 g/dL, as in the aforementioned articles,(17,18) their transfusion rate would have further decreased. This study, however, is focused exclusively on the efficacy of IV iron, not in combination with erythropoietin. In addition, the surgeon in our institution did not want to restrict transfusion because he believed the benefits of allogeneic transfusion were well beyond its risks for elderly patients. Therefore, we applied the same transfusion criteria (Hb less than 10 g/dL) to the patients receiving IV iron as those who had not received it.

Although there was no statistically significant difference in the transfusion rate between the groups, the transfusion index in patients of the control group was higher. The patients receiving IV iron required 0.6 units less blood than those who had not received the therapy, and the Hb levels at discharge (measured two weeks after admission on average) were significantly higher in patients of the iron group. This result is worth emphasizing because the preoperative Hb level and blood loss were not significantly different between the groups, and the patients with IV iron therapy received less allogeneic blood.

Further randomized controlled trials of intravenous iron are define whether it should be used as a first line treatment to reduce allogeneic red blood cell transfusions in patients in hospital.(16)

The role of IV iron after major surgery is well-established. The humoral mediators produced by the systemic inflammatory response suppress the production and action of erythropoietin and cause a functional iron deficiency (FID) status. This is not corrected by oral iron due to decreased intestinal absorption of iron. (23-26) IV iron can be useful in treating the post-operative FID state, because its erythropoietic effect is 4.5 to 5.5 times more potent than that of the basal state and lasts 710 days, after which the iron is sequestered by the reticuloendothelial system.(27) Since the Hb (or hematocrit) level is to be expected to increase two weeks after administration of oral or IV iron, the higher Hb level of the iron group at discharge appears reasonable.

There are some limitations in this study. First, a shockingly high transfusion rate in both groups deserves criticism. The percentage of transfused patients is much higher than that of other research dealing with TKA patients.(1-4,17,18) It can be explained partly by the fact that we initially excluded the patients with Hb higher than 14 g/dL who are less likely to require transfusion. The primary factor resulting in this high transfusion rate, however, seems to be unnecessary transfusion. Many elderly people feel that the generalized weakness they experience postoperatively stems from the lack of blood, and some of them even request blood transfusion. In addition, we did not strictly limit transfusion because the subjective symptoms such as weakness or fatigue were not easily differentiated from the symptoms of true anemia. The second limitation of
this study is that we did not compare complication rates such as mortality rates or postoperative infection rates between groups.

In conclusion, perioperative supplementation of IV iron can be an inexpensive, effective, and relatively safe method to reduce the requirements for allogeneic blood transfusion in unilateral TKA patients. Appropriate transfusion guidelines can help achieve this goal more efficiently. A larger, randomized controlled trial may be needed to verify this conclusion.

Abstract

Purpose: Total knee arthroplasty (TKA) is associated with a considerable amount of blood loss and frequently entails allogeneic transfusion. This study was designed to evaluate the effect of perioperative intravenous iron therapy on the transfusion requirements inpatients undergoing unilateral TKA.

Methods: Sixty-four patients classified as ASA physical status 1 or 2 scheduled for elective unilateral TKA were studied. Thirty-two patients scheduled for unilateral TKA were given 300 or 400 mg of intravenous iron sucrose perioperatively (iron group). A previous series of 32 patients who had undergone the same surgery without intravenous iron served as the control group. Allogeneic transfusion was indicated when the hemoglobin (Hb) level fell below 10 g/dL or patients became symptomatic of acute anemia.

Results: Although no statistically meaningful difference in the allogeneic transfusion rate was noticed, the transfusion index in the iron group was lower than in the control group (1.3 vs. 1.8 units/patient, P<0.05). Hb levels measured at discharge were significantly higher in the iron group compared with the control group (11.7 vs. 10.9 g/dL, P<0.001).

Conclusion: Perioperative administration of intravenous iron is a safe and effective method of reducing allogeneic blood transfusion in TKA patients.

Key Words: Arthroplasty, Blood transfusion, Intravenous, Iron, Knee

References


