EXPERT ANALYSIS

patients with chronic medical diseases such as uremia, multiple factors impair the enteral bioavailability of iron, such as bacterial overgrowth, chronic GI bleeding, platelet dysfunction, use of antiplatelets, frequent phlebotomy, proteinuria and increased iron utilization (use of erythropoietin-stimulating agents). In addition, other factors may impair iron absorption, such as celiac disease, whose prevalence is increasing given a higher index of detection (17, 18).

IS INTRAVENOUS IRON A SAFE MEDICATION? WHAT EVIDENCE SUPPORTS ITS USE?

Multiple studies have been done in surgical patients, including cardiac, gynecologic, orthopedic and colorectal surgery. Most are observational studies, and there are few randomized controlled trials. On average, an administration of an IV iron dose of 1000 mg raises the hemoglobin by approximately 2.0 g/dL and even resolves the anemia in up to 58% of cases. The transfusion rate is decreased by 66% and the infection rate by 55% (19-23).

Oral versus parenteral iron administration has been compared in gynecologic patients, and patients who received IV iron sucrose had an increase in hemoglobin up to 3.0 g/dL after four weeks, compared with 0.8 g/dL in patients taking oral iron. In addition, in the IV iron group, the target hemoglobin was achieved in 76% of the patients, compared with only 11.5% of the patients taking oral iron (24, 25).

The Network for Advancement of Transfusion Alternatives (NATA), a European organization focused on blood management, proposes using preoperative IV iron in patients with ferritin less than 100 ng/mL, transferrin saturation less than 20%, or expected blood loss above 1500 mL. The cutoff limit to avoid further IV iron administration is when ferritin levels are above 300 ng/ml and transferrin saturation is above 50%, or when there is acute infection (26).

ARE INTRAVENOUS IRON PREPARATIONS SAFE?

The administration of iron requires its incorporation into a carbohydrate shield that can stabilize it and favor its absorption and incorporation into the reticuloendothelial system. Initial IV iron preparations, which were made using high-molecular-weight dextran, were associated with presumed anaphylactic reactions; this delayed widespread use until recently (27).

The development of newer non-dextran IV iron preparations in the past 20 years has increased use of parenteral iron. The current most common preparations are ferric gluconate and iron sucrose. Patients who had reactions with ferric gluconate have not had elevation in tryptase levels, which rules out an anaphylactic reaction (28).

The most commonly used preparations can be seen in Table 2 below.

The most common adverse reactions associated with newer parenteral preparations are related to transient capillary leak syndrome (nausea, hypotension, tachycardia, chest pain, dyspnea and edema). However, these reactions are dose dependent and will rarely occur with the currently dispensed parenteral iron dosage (ferric gluconate, 125 mg/d; iron sucrose, 200 mg/d).

From 2001 to 2003, the FDA has documented 30 million doses of IV iron. Eleven people who received a dose have died, and there have been 1,141 total adverse effects (most commonly anaphylactoid-type reactions, which are generally dose dependent). The rate of adverse effect is as follows (14, 31):

- iron sucrose, 0.6 per million doses
- ferric gluconate, 0.9 per million doses
- low-molecular-weight dextran, 3.3 per million doses
- high-molecular-weight dextran, 11.3 per million doses

WHAT IS THE ECONOMIC IMPACT OF USING INTRAVENOUS IRON COMPARED WITH BLOOD TRANSFUSIONS?

In general, when we calculate the deficit of iron in an average patient with hemoglobin of around 10 to 11 g/dL, the iron deficit is approximately 1 to 1.5 g. This is the rationale to supplement a whole gram of iron preoperatively, which generally elevates the hemoglobin by around 2 g/dL.

Based on this dose, the cost of IV iron versus blood (with 1 g of iron) is as follows:

- iron dextran, approximately $377/g
- iron gluconate, approximately $688/g

Table 2. Parenteral iron preparations*

<table>
<thead>
<tr>
<th>Name</th>
<th>Molecular weight, kD</th>
<th>Anaphylaxis</th>
<th>Test dose required</th>
<th>Iron, mg/mL</th>
<th>Max. daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextran</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-molecular-weight</td>
<td>265</td>
<td>Yes</td>
<td>Yes</td>
<td>50</td>
<td>1 g</td>
</tr>
<tr>
<td>(Dexferrum©)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-molecular-weight</td>
<td>165</td>
<td>Yes</td>
<td>Yes</td>
<td>50</td>
<td>1 g</td>
</tr>
<tr>
<td>(Infed©)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferric gluconate (Ferrlecit©)</td>
<td>&lt;50</td>
<td>No</td>
<td>No</td>
<td>12.5</td>
<td>125 mg</td>
</tr>
<tr>
<td>Iron sucrose (Venofer©)</td>
<td>30–100</td>
<td>No</td>
<td>No</td>
<td>20</td>
<td>200 mg</td>
</tr>
</tbody>
</table>

*Based on references 29 and 30.