Transfusion and Iron Overload: Where Are the Risks?

Table 2. Iron overload state

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum ferritin (µg/l)</td>
<td>&lt;300</td>
<td>&gt;1000 -</td>
<td>&lt;2500</td>
<td>&gt;2500</td>
</tr>
<tr>
<td>Transferrin Saturation (%)</td>
<td>20-50</td>
<td>&gt;50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LPI (µM)</td>
<td>0 – 0.4</td>
<td>&gt;0.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LIC (mg Fe/g dw)</td>
<td>&lt;1.8</td>
<td>3 - 7</td>
<td>&gt;7</td>
<td>&gt;15</td>
</tr>
<tr>
<td>Cardiac MRI T2* (msec)</td>
<td>&gt;20</td>
<td>14 - 20</td>
<td>8 - 14</td>
<td>&lt;8</td>
</tr>
</tbody>
</table>

Dw, dry weight; LIC, liver iron concentration; LPI, labile plasma iron; MRI, magnetic resonance imaging

Figure 9. Serum ferritin levels in 6 patients with HbSS disease, transfusion-dependent and treated by erythrocytapheresis.

(Fig 8C), with as a consequence an increase of hepcidin in the post transfusion period (Fig 8G) and this explains the stability of ferritin levels (Fig 8E).

Erythrocytapheresis in case of iron overload in Sickle cell anemia combines phlebotomy with transfusion. In fact, reduction of HbS concentration to 25-30% allows to « pump » iron from the iron stores of the patient, by producing new Hb S and this up to 50-55%, value when a new erythrocytapheresis will be done (in general every 4 to 8 weeks).

The main indications in sickle cell anemia are CV A (cerebrovascular accidents), acute chest syndrome, pulmonary hypertension. This therapeutic strategy is very effective against iron overload in this setting (Figure 9). In our hands it leads to iron deficiency anemia! However, the principal obstacle for a routine use is the vein access to perform the procedure.18-21

Treatment of iron overload in patients with Thalassemia

(Fig 8C), with as a consequence an increase of hepcidin in the post transfusion period (Fig 8G) and this explains the stability of ferritin levels (Fig 8E).

In these patients it is possible that chelation treatment by improving ineffective erythropoiesis, improves survival.21 Chelation should also start in patients with MDS candidates for allogeneic HSCT.

Concerning choice of chelator, the most frequently used is deferasirox in its new formulation FCT (film-coated tablet)22 and in the following dosages:

→15mg/kg (FCT) if transfusion needs are <2 Units/month;

→20mg/kg (FCT) if transfusion needs are intermediates

→25-30mg/kg (FCT) if transfusion needs are 2 or more units/month.5

Treatment of iron overload in patients with Thalassemia

The following Table 2 gives thresholds values to evaluate iron overload in patients with thalassemia.1,10

In thalassemia chelation should start at mild iron overload state. It is considered effective if the patients stays at this state and does not progress to moderate or severe iron overloaded state (Table 2). However, if this is the case then intensive iron chelation is recommended (see below).

Intensive iron chelation

Is indicated in thalassemic children (patients) with moderate or severe iron overload, leading to heart failure. In the literature we find many such cases successfully treated with intensive iron chelation.24 This is also valid for similar situations in patients with MDS.25

The applied regimen is deferoxamine (DFO) 30-50mg/kg/d 5x/week associated to deferasirox 15-20mg/kg/d or to deferriprone 50-75mg/kg/d divided in 3 doses.

The evaluation of treatment is done by measuring T2*, ferritin levels and pro-BNT levels and by performing cardiac ultrasounds.25,26