Intravenous Iron Supplementation for the Treatment of Anemia in Pre-Dialyzed Chronic Renal Failure Patients

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Intravenous iron supplementation is known as efficient for the treatment of anemia in chronic hemodialyzed patients, especially in those treated with erythropoietin (1,2). The role of iron supplementation in pre-dialyzed chronic renal failure (CRF) patients is much less clear.

The PRE-dialysis survey on anemia management (PRE-SAM) revealed that few pre-dialysis patients (32%) met the European Best Practice Guidelines target for hemoglobin concentration, despite regular nephrology care (3). Data from Romanian Renal Registry showed that 89% of patients starting renal replacement therapy in Romania had lower hemoglobin levels than recommended (4).

Most pre-dialyzed patients (94%) have absent iron staining on bone marrow examination (5).

Several reports suggested that intravenous iron corrects iron deficiency, augments response to erythropoietin and permits treatment without Epo in a significant number of patients with CRF and renal anemia (6).

The objective of our study was to evaluate the effects of one-year intravenous iron supplementation in pre-dialyzed CRF patients without erythropoietin treatment.

40 patients with moderate CRF [24 males, 16 females, mean age 55.5 (33-78) years, creatinine clearance 23.4±9.4 mL/min], who remained anemic despite previous oral iron supplementation were enrolled. Their renal function was stable within the 30 days period before inclusion. The arterial blood pressure was well controlled with calcium channel blockers, beta-blockers and/or angiotensin-converting enzyme inhibitors.

Patients with previous erythropoietin treatment, with laboratory signs of iron overload, those with gastro-intestinal bleeding, with significant weight loss or with evidence of folic acid and/or vitamin B12 deficiency were excluded.

Intravenous iron was administered monthly as Iron (III)-Hydroxide Sucrose complex in a total dose of 1600 mg elemental iron.

The primary parameters of the study were the hematological response (hemoglobin, hematocrit), the iron status (serum iron, TIBC, transferrin saturation, serum ferritin), the renal function (serum creatinine, creatinine clearance) and the blood pressure.

The pre-study and post-treatment values at 3, 6 and 9 months have been processed with descriptive methods (i.e. median, average and standard deviation). t-Student test and ANOVA were used to compare results.

36 patients completed 9 months of study. The results are presented in the table.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>0</th>
<th>3rd month</th>
<th>6th month</th>
<th>9th month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/dL)</td>
<td>9.7±1.1</td>
<td>10.5±1.0*</td>
<td>10.9±1.2*</td>
<td>11.2±0.9*</td>
</tr>
<tr>
<td>Serum iron (µg/dL)</td>
<td>73.9±17.2</td>
<td>74.8±13.8</td>
<td>84.2±9.4*</td>
<td>97.8±13.5*</td>
</tr>
<tr>
<td>Transferrin saturation (mg/dL)</td>
<td>21.6±2.6</td>
<td>34.9±5.8*</td>
<td>26.8±5.6*</td>
<td>27.8±4.4*</td>
</tr>
<tr>
<td>Serum ferritin (µg/L)</td>
<td>95.4±123.9</td>
<td>190.5±127.2*</td>
<td>240.8±156.1*</td>
<td>270.1±173.4*</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>3.7±0.8</td>
<td>3.7±0.7</td>
<td>3.7±0.9</td>
<td>3.7±1.0</td>
</tr>
<tr>
<td>Creatinine clearance (mL/min)</td>
<td>23.4±9.4</td>
<td>25.2±7.3</td>
<td>25.4±8.2</td>
<td>26.1±6.3</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>140±32</td>
<td>140±19</td>
<td>138±22</td>
<td>139±23</td>
</tr>
<tr>
<td>Diastolic pressure (mmHg)</td>
<td>82±20</td>
<td>80±12</td>
<td>81±14</td>
<td>80±18</td>
</tr>
</tbody>
</table>

* - statistically significant

After 9 months of treatment, intravenous iron supplementation was associated with a significant improvement of hematological status, as hemoglobin and hematocrit significantly increased. Transferrin saturation and serum ferritin also significantly increased, without reaching the upper limits of target iron status (50% for transferrin saturation and 600µg/L for serum ferritin (7)).

There was no decrease in renal function as described by serum creatinine and creatinine clearance. The arterial blood pressure remained well controlled. No other side effects were noted during the study period.

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Our study shows that intravenous iron therapy in pre-dialyzed patients untreated with erythropoietin seems to improve the anemia, avoiding the necessity of erythropoietin or blood transfusions. Intravenous iron supplementation appears to be safe and effective for the treatment of anemia in CRF pre-dialyzed patients.

This conclusion sustaines that the benefits of intravenous iron far outweigh any theoretical risk; the safety in administration is remarkably good when given in pharmacological doses.

Correction of anemia results in improvement of cardiac function. Amelioration of hematological status and of cardiac function reduces the rate of decline of glomerular filtration rate, postponing the renal replacement therapy and improves the outcome in dialysis (5), as it is well known that the fate of the dialysis patient is cast in the pre-dialysis period.

References

7. Aronoff GR. Hot Topics: Current controversies in iron management, ASN Satellite Symposium, 2002