THE EFFECT OF HAEMODIALYSIS ON PLASMA ERYTHROPOIETIN LEVELS AND PLASMA IRON TRANSPORT IN CHRONIC RENAL FAILURE

Robert Brown*

Reduction in the rate of red cell production is a fundamental feature of the anaemia associated with chronic renal failure\(^1\). The pathogenesis is not fully understood there being evidence for at least two mechanisms namely, 'toxic' suppression of bone marrow activity\(^2\) and deficiency of the erythropoietic hormone, erythropoietin\(^3,4\).

Kurtides et al\(^5\) reported increase in plasma iron transport rate (P.I.T.R.) and red cell incorporation of radio-iron in 5 out of 6 patients following haemodialysis. These changes which imply an improvement in erythropoiesis were noted within 24 hours of dialysis, suggesting that removal of some 'toxic' influence was responsible. The possibility of an increase in plasma erythropoietin activity after dialysis, however, was not tested.

METHODS

In the present study plasma erythropoietin, plasma iron transport rate, red cell mass and the absolute reticulocyte count were measured before and 12-24 hours after haemodialysis in 6 patients with chronic renal failure. Each patient was undergoing the first dialysis in a program in which this was repeated at 3 day intervals. A Kolff twin coil artificial kidney was used and dialysis was continued for 6-12 hours. Standard radio-iron and chromium techniques were employed with a pulse height analyser in the scaler circuit to discriminate between the two isotopes. Plasma iron transport rate is a sensitive index of erythroid activity in the bone marrow\(^6\). Changes in the metabolic pool of iron may influence it but this is unlikely to have occurred in the short period of the present investigation.

Erythropoietin was assayed by the method of Cotes and Bangham\(^7\) using hypoxia-induced polycythaemic mice. The test plasma was given in two equal intraperitoneal injections and the response measured in terms of the uptake into the mouse red cells of radio-iron 20 hours after intravenous injection. Each assay included a standard erythropoietin (M.R.C. Standard 'B'). Two dose levels of test plasma and standard erythropoietin were used so that log. dose - response lines could be constructed. Individual points represent the mean of the response in 5 animals. Spuriously positive results due to non-specific stimulation of red-cell iron incorporation are avoided by this method because erythropoietin produces a regression line with a specific slope. Thus detectable quantities in the test plasma would produce a line parallel to that for the erythropoietin standard whereas non-specific stimulants would not. Furthermore it is the most sensitive assay available at present.

*The Royal Victoria Infirmary, Newcastle upon Tyne.
This work was supported by grants from the United Newcastle upon Tyne Hospitals and the Newcastle Kidney Fund.
RESULTS

Results of the plasma iron transport rate, red cell mass, reticulocyte counts, plasma iron and blood urea before and after dialysis are shown in the table. Pre-dialysis plasma erythropoietin levels in Figure 1 and post-dialysis levels in Figure 2.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>J.C.K.</td>
<td>351</td>
<td>910</td>
<td>3630</td>
<td>63</td>
<td>38</td>
<td>69,000</td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>1113</td>
<td>2963</td>
<td>74</td>
<td>29</td>
<td>24,000</td>
</tr>
<tr>
<td>V.M.F.</td>
<td>270</td>
<td>878</td>
<td>3142</td>
<td>170</td>
<td>25.6</td>
<td>9,600</td>
</tr>
<tr>
<td></td>
<td>56</td>
<td>1285</td>
<td>2645</td>
<td>123</td>
<td>27.1</td>
<td>7,200</td>
</tr>
<tr>
<td>I.T.</td>
<td>325</td>
<td>850</td>
<td>3400</td>
<td>68</td>
<td>39.8</td>
<td>52,000</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>1242</td>
<td>3033</td>
<td>110</td>
<td>92</td>
<td>52,000</td>
</tr>
<tr>
<td>K.B.</td>
<td>488</td>
<td>865</td>
<td>4135</td>
<td>169</td>
<td>16.6</td>
<td>22,000</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>1155</td>
<td>4125</td>
<td>60</td>
<td>13.4</td>
<td>24,000</td>
</tr>
<tr>
<td>N.B.C.</td>
<td>460</td>
<td>560</td>
<td>2520</td>
<td>68</td>
<td>5.6</td>
<td>14,000</td>
</tr>
<tr>
<td></td>
<td>152</td>
<td>1076</td>
<td>2504</td>
<td>84</td>
<td>6.3</td>
<td>19,000</td>
</tr>
<tr>
<td>J.G.</td>
<td>492</td>
<td>1046</td>
<td>3533</td>
<td>184</td>
<td>21.6</td>
<td>25,000</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>1315</td>
<td>3845</td>
<td>83</td>
<td>18.4</td>
<td>16,800</td>
</tr>
</tbody>
</table>

In 5 of the 6 patients blood urea fell considerably during the dialysis in the other patient (N.B.C.) the fall was less marked. During the dialysis procedure each patient was given a blood transfusion of one to two pints whole blood and this is reflected in the increased red cell mass after dialysis.

Plasma iron transport rate increased in 3 patients and decreased in the other 3. This measurement is subject to an error of +/- 15% hence the changes noted in 5 patients are not significant. In one patient (I.T.) there is a doubling of the plasma iron transport rate after haemodialysis.

There is no correlation between the direction of the changes in plasma iron transport rate with the percentage fall in blood urea, change in red cell mass or plasma iron.

No significant change in reticulocyte counts occurred and the plasma iron levels fell in 3 and rose in 3.

COMMENTS

The patient in whom a large rise in plasma iron transport rate occurred is the only one of the group with polycystic kidneys but the situation is complicated by the presence of pyelonephritis which may have become active at the time of the estimation. Whatever the cause of the increase in plasma iron transport rate there was no detectable change in plasma erythropoietin.
In 5 of the present patients haemodialysis had no significant immediate
effect on erythroid activity in the marrow. In contrast, in the series of
Kurtides et al(1) the changes suggest improved erythropoietic activity after
dialysis. Berry et al(9) have recently reported a similar study in 4 patients
undergoing peritoneal dialysis. Three of these showed post-dialysis increase
in plasma iron transport rate and red cell iron incorporation but there was
no increase in erythropoietin levels after dialysis.

The present series differs from the others in having a large increase
in post-dialysis red cell mass. This may explain the difference in the plas-
ma iron transport rate findings. Penington(8) suggests the low plasma
erthropoietin in renal failure is due to lowered threshold for its secretion
rather than inability to produce it. If this were so an increase in red cell
mass might reduce erythropoietin secretion and consequently the tendency
to increased erythropoiesis following dialysis. There is no evidence from
the present erythropoietin assays to support this concept but the techniques
may not be sufficiently sensitive to detect such changes.

The findings in the other series indicate erythropoiesis may be
temporarily improved by dialysis. This is probably due to the removal of
'toxic' factors but the present investigation suggests this tendency is in-
hibited by blood transfusion hence the possibility that erythropoietin is
also involved cannot be excluded.

REFERENCES

   15, 511.
   med., 52, 1201.
   Blood, 12, 409.
The figures show the log. dose-response lines for pre and post-dialysis plasma samples together with that for standard 'B' erythropoietin. Plasma dosage is in ml and the erythropoietin in M.R.C. units.