IRON RESPONSIVE ANAEMIA IN REPEATED DIALYSIS TREATMENT WITHOUT ROUTINE BLOOD TRANSFUSION

F. K. WRIGHT, H. J. GOLDSMITH and S. M. HALL

Liverpool Regional Urological Centre, Sefton General Hospital, Liverpool, United Kingdom

Introduction

A policy of liberal transfusion in patients on maintenance dialysis is associated with the risk of viral hepatitis amongst both patients and staff (Friedman and Thompson, 1966; Jones et al., 1967; Ringertz and Nyström, 1967). We therefore believe that blood transfusion should be avoided if possible. Verroust et al. (1967) and Crockett et al. (1967) have reported their experience of dialysis without routine transfusion. We confirm that transfusion is only rarely required in Kiil dialysis. Comty et al. (1966) first described the value of iron in this situation. Table 1 summarises our experience.

<table>
<thead>
<tr>
<th>TABLE 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfusion experience in R.D.T.</td>
</tr>
<tr>
<td>(Liverpool Regional Urological Centre)</td>
</tr>
<tr>
<td>1966</td>
</tr>
<tr>
<td>Average units of blood/patient/month</td>
</tr>
<tr>
<td>Average pre-dialysis haemoglobin (g/100 ml)</td>
</tr>
</tbody>
</table>

TRANSFUSION EXPERIENCE

In 1966, 6 patients were dialysed with a total treatment experience of just under 5 years. 238 units of blood were given. The average pre-dialysis haemoglobin was 6.4 g/100 ml. During 1967 we acquired a total experience of 10 years 2 months with 15 patients. Twenty-seven units were given to 6 patients, once for melaena from a duodenal ulcer, twice for shunt haemorrhage, once for accidental haemolysis, and single units for severe anaemia on 5 occasions in 3 patients. The overall rate of transfusion fell to 0.22 unit/patient/month. The average pre-dialysis haemoglobin remained unaltered from the previous year. In the first 5 months of 1968 one unit was given for anaemia to a new and one to an established patient. During this period average haemoglobin levels have risen to 7.5 g/100 ml. The previously described temporary fall in haemoglobin shortly after the commencement of transfusionless dialysis was observed (Verroust et al., 1967; Crockett et al., 1967).

In the long term only one (female) patient from the transfusion era continues to require blood occasionally, when her haemoglobin falls below 6.0 g/100 ml. Dialysis is biochemically adequate in this patient and we do not know the reason for her recurrent anaemia.

In the first quarter of 1968 we lost 3 patients from myocardial infarction, pericardial tamponade and tricuspid endocarditis, respectively. Only the last of these would have been given blood in the transfusion era.
OBSERVATIONS

Since initiating a non-transfusion policy we have observed that a super-added iron deficiency, or perhaps more accurately an ‘iron responsive’ anaemia, may develop in these cases which may easily be overlooked in patients already anaemic from chronic renal failure. This possibility was suspected from serial measurements of serum iron and confirmed by the haematological response to a single 1 gram dose of elemental iron, as iron dextran complex (Imferon).

RESULTS

All investigations were carried out in the hospital laboratory. No morphological evidence of iron deficiency was detected in any peripheral blood films. The bone marrow was examined on 12 occasions, always before iron treatment was given, and in most instances before maintenance dialysis was commenced. Marrow morphology was normal, except in one patient with micro-normoblasts. Normal or increased amounts of extracellular iron were present in 11 out of 12 marrows. Sideroblasts were seen once only, in the marrow of a patient with a normal serum iron.

Estimates of serum iron, total iron binding capacity (T.I.B.C.) and percentage saturation were made 3 monthly (normal serum iron 55–135 μg/100 ml, T.I.B.C. 270–410 μg/100 ml, saturation 15–40%; Ramsay’s method, 1957). In 1967 of the 11 patients with normal or increased marrow iron, 7 had serum iron levels below our normal range. In only one of these was there clinical evidence of infection. Of 31 three monthly estimates of serum iron 11 were subnormal (range 25–54 μg/100 ml), and 4 levels were between 55–58 μg/100 ml. T.I.B.C. was within the normal range in 20 out of 29 estimates, lowered 8 times and raised once (range 175–475 μg/100 ml). The percentage saturation was below normal limits in 5 out of 29 estimates. Low serum iron levels were recorded despite intravenous iron having been given 4 months previously in some cases. Whenever a low or borderline serum iron was found 1 gram of iron as Imferon, diluted in 500 ml of saline, was given over 4 hours, during dialysis, into the arterial line. No early or late reactions to the infusion were observed. All patients during this period were receiving monthly supplements of 15 mg folic acid intravenously.

Taking the maximum haemoglobin recorded, a mean rise of 2.4 g haemoglobin/100 ml developed within 4–6 weeks on 10 occasions in 1967. Recent blood loss complicated the picture when iron was given in 5 other instances. The subsequent empirical use of iron in 2 patients

![Graph]

**Fig. 1.** Response of haemoglobin level to 1 g of iron in 12 patients.
with normal serum iron levels was accompanied by a rise of less than 0.6 g/100 ml of haemoglobin. The results are shown in Figure 1.

Only 2 of 15 patients studied in 1967 and the first 5 months of 1968 failed to develop a low serum iron level, and a serial fall was observed in 6 patients. Good responses to iron therapy were recorded in the presence of plentiful extracellular iron in the marrow. For example, one patient with abundant extracellular iron in the marrow (due to 19 units of blood given in 1966), serum iron of 25 μg/100 ml, T.I.B.C. of 368 μg/100 ml and a saturation of 7% had an increase in haemoglobin concentration of 3 g within 6 weeks, following iron. No evidence of infection was present. Modest reticulocyte responses were generally seen between 6–12 days after the iron, reaching 7% on one occasion. Following parenteral iron therapy, serum levels were again subnormal after 4 months in 4 patients, and in 6 months in 2 patients, whilst 2 patients retained normal levels for longer than 6 months. In 4 patients the picture was clouded by blood transfusion. A recently accepted patient developed a low serum iron within 3 months of starting dialysis. Once regular monitoring of serum iron levels was under way, the response to a second single infusion was less dramatic, but a rise of haemoglobin exceeding 1 g/100 ml was seen on 4 occasions.

In patients who are inevitably anaemic the recognition of associated and treatable ‘iron deficient erythropoiesis’ (Bainton and Finch, 1964) is particularly important. Only one of our patients had no stainable extracellular iron in the marrow. The absence of typical morphological changes in the peripheral blood film is known not to exclude early iron deficiency anaemia (Bainton and Finch, 1964) and should not therefore be relied on to exclude the need for additional iron in this group.

OTHER OBSERVATIONS

Factors other than the use of iron have facilitated a policy of non-transfusion. Table II shows how the introduction of low volume Kil dialysers reduced blood loss in the dialyzer.

<table>
<thead>
<tr>
<th>TABLE II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Residual blood loss with 2 types of Kil dialysers using 2 wash-out methods</strong></td>
</tr>
<tr>
<td>Type of Kil</td>
</tr>
<tr>
<td>--------------</td>
</tr>
<tr>
<td>Air wash-out</td>
</tr>
<tr>
<td>Saline wash-out</td>
</tr>
</tbody>
</table>

Figures in brackets represent the number of estimations.

The best results, averaging 9 ml of residual blood, were obtained with Watson–Marlow or Dylade low volume dialysers and wash-outs with 800 ml of saline. Following 2 episodes of suspected air embolism we no longer consider air wash-outs safe, and now use 1 litre of 5% dextrose.

Our hospital patients during 1967 were losing approximately 120 ml of blood to the laboratory each month. Home patients, being more established and less accessible, had laboratory losses of 40 ml monthly. With blood losses in the dialyser this represents a total annual iron loss of 500–700 mg, equivalent to 2–3 times the normal menstrual loss. This does not take into account blood losses from shunts, menstruation and research projects. With increasing experience, we have found that laboratory blood losses can be cut drastically. With monthly home haemoglobin checks, using a Sahli apparatus, routine laboratory tests may in future be required only every 3 months, provided satisfactory shunt flows are maintained.

No significant movement of iron across the dialysing membrane was demonstrated by Czaczkes et al. (1967), but with approximately 13,000 litres of blood being dialysed annually
against 40,000 litres of dialysing fluid, immeasurable losses or gains of iron might add up to significant quantities in the course of time.

The better health of patients dialysed 3 times weekly is generally accepted. This allows a higher protein and dietary iron intake. Circumstances forced one home dialysis patient into twice weekly dialysis with a resultant fall of haemoglobin from 8.1 g/100 ml to 5.5 g/100 ml, within a period of 6 weeks. Occult under-dialysis will result from shunt flow deterioration. By measuring the shunt blood flow once weekly, using the timed passage of a 1 ml air bubble over 1 metre of tubing, with a simple board, elective recannulation can be planned when the blood flow no longer reaches a pre-determined level, and before clotting has occurred. Dialysis will thus be improved and the useful life of the cannulated vessels prolonged.

![Fig. 2](image)

*Summary and conclusions*

Our investigations show that when transfusion is not resorted to, significant improvements in the haemoglobin level may be obtained with parenteral iron in patients with depressed serum iron levels. This will occur in the absence of morphological evidence of iron deficiency in the peripheral blood film, and in the presence of ample iron stores in the marrow. In the presence of these iron stores, the anaemia must result from inadequate availability and/or utilisation of iron by the erythron. The situation is similar to the iron deficient erythropoiesis described by Bainton and Finch (1964) in association with inflammation and malignancy. Regular parenteral iron will prevent the development of low serum iron levels, and in turn the development of the iron responsive anaemia described, but iron overload might ensue in the long run, as with transfusion. Preliminary observations suggest that smaller blood losses will, by husbanding the pool of iron present in the blood, reduce the requirements of parenteral iron.

In conclusion, we confirm that maintenance dialysis without routine transfusion is possible. The risk of viral hepatitis in dialysis units would greatly diminish if this policy were followed generally. The recognition that an iron responsive anaemia may exist or develop in patients undergoing maintenance dialysis without routine transfusion, is one of several considerations which make such a policy possible.

**ACKNOWLEDGEMENTS**

Dr. E. H. Moorhouse kindly reported on the bone marrow specimens. F. K. Wright was supported by the Merseyside Association for Kidney Research.

**REFERENCES**


IRON RESPONSIVE ANAEMIA IN REPEATED DIALYSIS TREATMENT


