

INTRAMUSCULAR VERSUS ORAL IRON SUPPLEMENTATION IN PATIENTS ON RENAL REPLACEMENT THERAPY RECEIVING ERYTHROPOIETIN

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ABSTRACT: Anaemia in patients on renal replacement therapy is a common problem and response to treatment with erythropoietin may be limited by functional iron deficiency. We recently studied prospectively for 22 weeks the effect of iron supplementation via intramuscular and oral vs intramuscular vs oral routes in 16 patients on chronic haemodialysis with renal anaemia treated with erythropoietin injections. The rise in haemoglobin was significant in all patients except those on intramuscular iron only. This study supports unconfirmed observations that oral iron supplementation may be effective in patients with renal anaemia associated with functional iron deficiency. (JUMMEC 1999; 2: 110-112)

KEYWORDS: Renal, Anaemia, Erythropoietin, Iron deficiency, Oral, Parenteral.

Introduction

Anaemia in patients on renal replacement therapy is a common problem (1). The causes of renal anaemia are multi-factorial, one of the most important of which is the relative deficiency of the hormone erythropoietin or reduced sensitivity to its actions (2). The introduction of erythropoietin in the 1980's have revolutionized the management of renal anaemia in these cases with the vast majority responding well to erythropoietin replacement therapy (3, 4). However, there still remains a small proportion of patients who fail to respond to erythropoietin, and iron deficiency whether absolute or functional, remains a major cause (3, 5). Patients started on erythropoietin may develop iron deficiency due to the increased demand by erythroid cells in the marrow outstripping supply. Studies on iron supplementation in these patients (6-8) suggest that parenteral iron may be superior to oral iron in maintaining iron stores (6, 7) but this has yet to be confirmed. In this study, we compared the effects of oral versus intramuscular iron in patients starting erythropoietin to determine the optimum route of iron replacement therapy.

Subjects and methods

All patients stable on renal replacement therapy for a period of at least 3 months with Hb < 10 g/dl and not on treatment with erythropoietin were eligible for this study. Patients with inadequate iron stores with serum ferritin < 100 mg/ml, elevated C reactive protein, upper gastrointestinal bleeding, iPTH >20 times normal and

allergy to iron were excluded. Fifteen consecutive patients, 14 on Continuous Ambulatory Peritoneal Dialysis (CAPD), and one on haemodialysis were identified and enrolled into the study. There were no significant difference in haemoglobin, ferritin and transferrin saturation levels among the three groups at entry into the study. Patient demographics are summarised in Table 1.

Patients were randomised to 3 groups to receive oral iron (Ferrous fumarate 200 mg TDS) and/or intramuscular iron (Ferrum 200 mg monthly, Housmann Laboratories Inc, Switzerland). Group A patients were given oral and intramuscular iron, Group B patients were given intramuscular iron only, whilst Group C patients were given oral iron only. All patients were also started on erythropoietin 2000iu twice a week which was continued throughout the duration of the study. All three groups were followed-up for a period of 22 weeks. Haemoglobin levels were measured once every two weeks, whilst transferrin saturation and ferritin levels were measured once every four weeks. Results are expressed as mean \pm SD. Statistical analysis was performed using the student's t test.

Results

All subjects tolerated intramuscular and oral iron well. There were no reported problems with local reactions

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Table 1. Patient demographics

	Group A	Group B	Group C
No of patients	5	6	4
Age (years)	43.2 ± 12.8	43.8 ± 12.0	36.5 ± 15.5
Transferin saturation (%)	37.6 ± 14.2	31.4 ± 12.1	36.8 ± 12.5
Serum ferritin (mg/ml)	338.0 ± 140.5	320.8 ± 312.3	489.2 ± 268.2
Haemoglobin (g/dl)	7.8 ± 1.2	8.0 ± 1.3	7.5 ± 1.0

Group A, oral + i.m. iron; Group B, i.m. iron only; Group C, oral iron only.

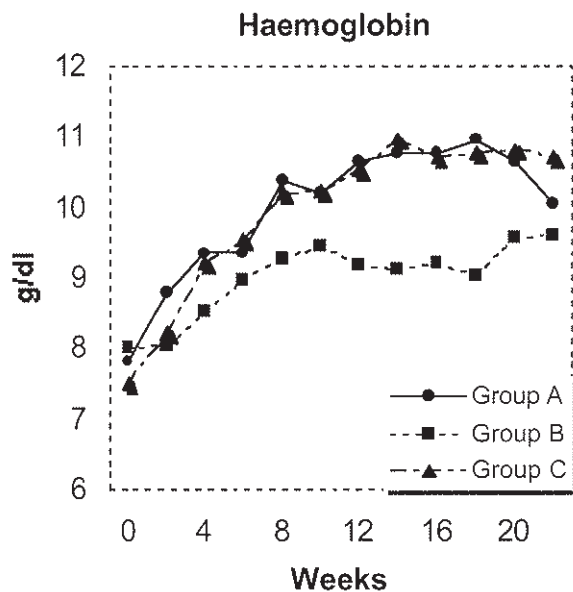


Fig. 1. Changes in haemoglobin concentration in patients receiving oral + i.m. iron (Group A), i.m. iron (Group B) and oral iron only (Group C). For Groups A and C, $p < 0.05$ compared to baseline.

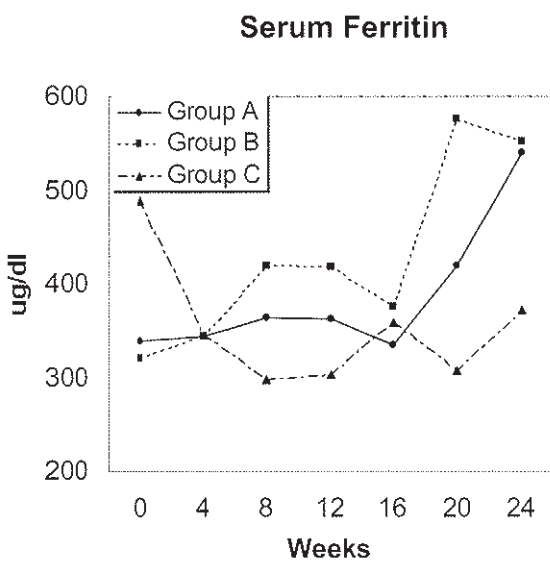


Fig. 2. Changes in serum ferritin concentration in patients receiving oral + i.m. iron (Group A), i.m. iron (Group B), oral iron only (Group C). There was no statistical significant changes in ferritin levels in all 3 groups.

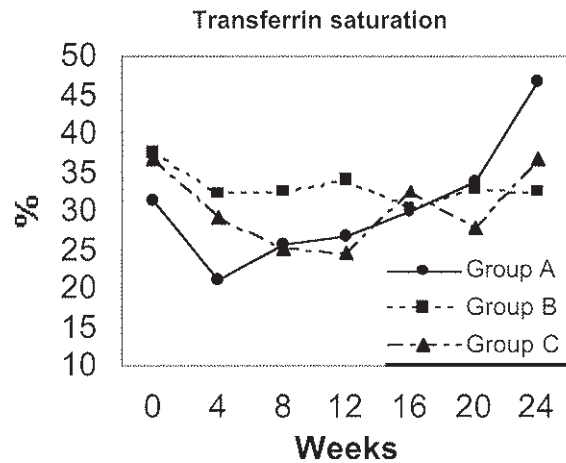


Fig. 3. Changes in percentage transferrin saturation in patients receiving oral + i.m. iron (Group A), i.m. iron (Group B) and oral iron (Group C). There was no statistical significant changes in transferrin saturation levels in all 3 groups.

after injection as has been previously described (9). The dosage of erythropoietin was unchanged in all patients except for one patient from Group A, where the dosage was reduced to 2000iu/week after two months. All three groups showed a rise in haemoglobin but it was significant only in Groups A and C (Fig 1). There was no significant drop in the ferritin and transferrin saturation levels in all three groups (Fig 2,3).

Discussion

Patients on renal replacement therapy are at increased risk of iron deficiency (9). This could be due to increased external iron losses in dialysis filters, bloodlines, frequent blood sampling or occult gastrointestinal blood loss. In addition, in end stage renal failure (ESRF) there is evidence for sequestration of iron in storage tissues with decreased availability to erythropoietic cells resulting in functional iron deficiency (5) Iron supplements are therefore frequently needed to maintain iron status in patients with ESRF especially those receiving erythropoietin. Intravenous iron has been reported to be superior to oral iron in maintenance of iron stores (7) and oral iron may indeed be no better than placebo in maintaining serum ferritin levels. This has yet to be confirmed and in our study we have demonstrated in our small series of patients that oral

iron can be used successfully to maintain iron status in patients on renal replacement therapy receiving erythropoietin. This was also demonstrated by Wingard *et al* (8) where hematocrit levels were found to be stable after 6 months of oral iron therapy. Surprisingly, the results with intramuscular compared to oral iron supplementation was poor. This observation has to be interpreted with caution due to the small number of patients involved and limited duration of follow-up. If true, it is possible that the poor response to intramuscular iron supplementation could be due to a combination of reasons including the dosage used in this study and variable absorption after injection. Finally, we have demonstrated in this study that oral iron is an effective route for iron replacement therapy in patients on chronic dialysis receiving erythropoietin. However the efficacy of oral iron supplementation compared to parenteral iron supplementation remains to be determined with larger scale studies with longer duration of follow-up.

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