BJ
BANTAO Journal

BANTAO Journal 2008; 6 (1): 31–33

Orginal Article

Intravenous Iron Therapy in Treatment of Anaemia in Dialysis Patients

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Abstract

Background. One of main causes of anaemia in patients with chronic renal insufficiency in its terminal phase is the iron deficiency. The aim of the present study is to examine the importance of intravenous iron supplementation in correction of anaemia per se.
Methods. The study group consisted of fifteen patients, which were divided into two groups. In the first three months, the experimental group (ten patients) received preparations of intravenous iron, in addition to oral iron preparations. The control group (five patients) received only a therapy of oral iron preparations. During the next four months, both groups were given erythropoietin □, in addition to intravenous iron preparations in the experimental group and oral iron preparationsin the control group.
Results. In the first part of the study, haemoglobin level increased in the experimental group by 9.12%, while in the control group it increased by 2.55%. With the addition of erythropoietin (the second part of the study) in the first eight weeks an increase in haemoglobin level was noticed in both groups, but it was statistically significant only in the experimental group. From eight weeks until the end of the fourth month, haemoglobin level increased in the experimental group, while in the control group it stagnated. On the other hand, serum iron and transferrin saturation levels decreased considerably when erythropoietin was introduced in the control group. In the experimental group values remained at approximately the same level.
Conclusions. Giving iron is often enough, on its own, to increase haemoglobin level. Erythropoietin therapy achieves much better results in combination with intravenous iron, compared to oral preparations.

Keywords: anaemia; erythropoietin; haemoglobin; iron therapy

Introduction

Anaemia in patients with chronic renal insufficiency is a serous problem, because it has a significant effect on the quality of life and survival of these patients [1]. Iron deficiency is undoubtedly one of the most important factors in the origin of this anaemia, its continuation and its further progression [2]. There are many reasons why iron deficiency occurs in dialysis: abnormal iron absorption (low intake, metabolism disorders in intestines and/or high ferritin level – feedback mechanism), external blood loss (up to 6 litres per year), functional iron deficiency and increased needs in patients on erythropoietin therapy [3]. During erythropoietin therapy, in about 50% of patients an iron deficiency occurs in cases iron is not adequately compensated [4]. It might be explained through an increase in haemoglobin concentration by 10 g/L which requires about 150 mg of iron from body iron stores [5]. For this reason, it is very important that when treating anaemia with erythropoietin iron stores and iron consumption are monitored, and at the same time iron levels maintained and compensated. Most often used tests for diagnosis of iron deficiency in patients with chronic renal insufficiency are tests for determining serum ferritin and transferrin saturation [6]. In kidney patients the aim is to have serum ferritin higher than 100 μg/L and transferrin saturation higher than 20% [4,5,7]. However, during erythropoietin therapy, the targeted values for serum ferritin are 200-500 μg/L and for transferrin saturation 30-40% [8]. In haemodialysis patients, in which anaemia is pronounced and blood loss bigger (compared to pre-dialysis patients, transplant patients and patients on peritoneal dialysis), it is recommended to administer intravenous iron, especially if the patient receives erythropoietin [8,9,10].
The aim of the present study is to examine the importance of intravenous iron supplementation in haemodialysis patients with iron deficiency, as well as in patients receiving erythropoietin preparations.

Patients and methods

Patients were divided into two groups: an experimental group and a control group. Iron deficiency in patients in the experimental group was verified through the following parameters: serum iron, transferrin saturation and ferritin. The control group consisted of patients with normal iron stores. Haemoglobin level in patients in both groups was below 80 mg/L (Table 1). The patients were chosen so that both groups are uniform in respect of age, basic kidney disease and the duration of dialysis.

Table 1. Mean age and values of some laboratory and biochemical parameters of the patients at the beginning of the study

	Experimental group	Control group
Average age (years)	62.9±14.1	57.8±12.2
Haemoglobin (g/L)	75.7	76.4
Serum iron (μmol/L)	11.35	16.78
Transferrin sat. (%)	25.5	39.0
Ferritin (μg/L)	88	147

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The patients were followed in two phases. In the first phase we measured the increase in iron levels during the three-month intravenous iron therapy. Both groups received oral iron preparations (Ferrous sulphate with 105 mg of elemental iron) two times a day, but in addition to this, the experimental group received intravenous iron (Na-Ferri III gluconium with 62.5 mg of elemental iron) two times per week after haemodialysis, while the control group did not. Both groups did not receive erythropoietin preparations.
In the second phase we followed the increase in haemoglobin levels during the four-month long therapy with subcutaneous erythropoietin preparations (3 x 2000 i.u. per week). The control group continued receiving intravenous iron two times per week after haemodialysis, and the control group only oral preparations.
Haemoglobin level in the first part of our research was measured at six-week intervals, and in the second part, with the introduction of erythropoietin, haemoglobin was measured at four-week intervals. Serum iron and transferrin saturation were measured at the beginning of the first phase, at the beginning of the second phase and at the end of the study. Serum ferritin was measured at the beginning and at the end of the study.
For statistical analysis, statistical software Minitab 13.1 was used. The following descriptive statistics were calculated for data: mean, median and standard deviation. For establishing statistical significance of results a T-test was performed.

Results

In the first phase of our study (visits 1-3), after six weeks a significant change in haemoglobin values was not observed in either group, but after twelve weeks statistically significant increase was measured in the experimental group ($p<0.01$). After twelve weeks of therapy, haemoglobin increased by 7.6 g/L (9.12%) in the experimental group, while in the control group the increase was 2.0 g/L (2.55%).
In the second phase (visits 4-7), in the first eight weeks after the introduction of erythropoietin β, an increase in haemoglobin level was observed in both groups, but it was statistically significant in experimental group only ($p<0.01$). Further, between 8th and 16th week, haemoglobin level increased in the experimental group only, while in the control group it stagnated (Table 2).

Table 2. Increase in haemoglobin levels during erythropoietin therapy

	Experimental group HGB (g/L)	Control group HGB (g/L)
Beg. EPO therapy – 3rd visit	83.3	78.4
4 week – 4th visit	88.9	85.0
8 weeks – 5th visit	98.8	90.6
12 weeks – 6th visit	104.5	90.4
16 weeks – 7th visit	107.9	92.6

From the beginning of our study, the overall increase in the haemoglobin level was 32.2 g/L in the experimental group, and 16.2 g/L in the control group (Figure 1).

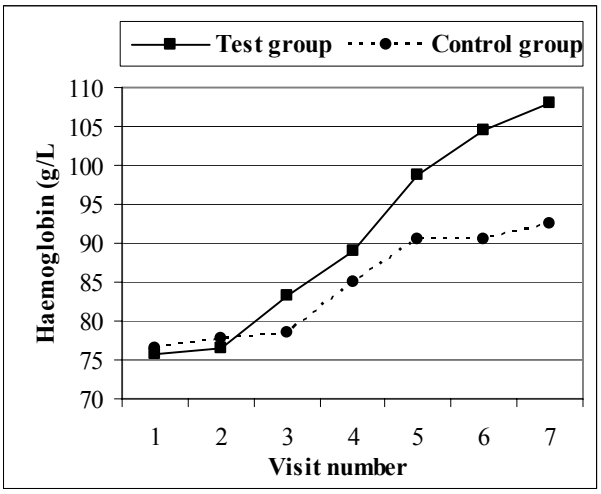

Fig. 1. Haemoglobin increase during the study

On the other hand, serum iron, serum ferritin and transferrin saturation levels decreased considerably when erythropoietin was introduced in the control group (on oral Fe preparations), while in the experimental group (on intravenous iron) values remained at approximately the same level (Figures 2 and 3).

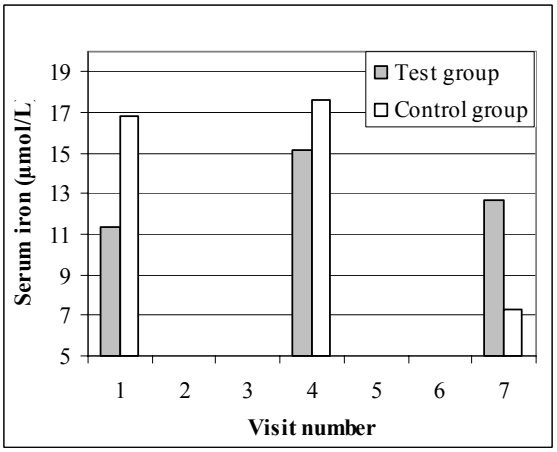

Fig. 2. Serum iron during the study

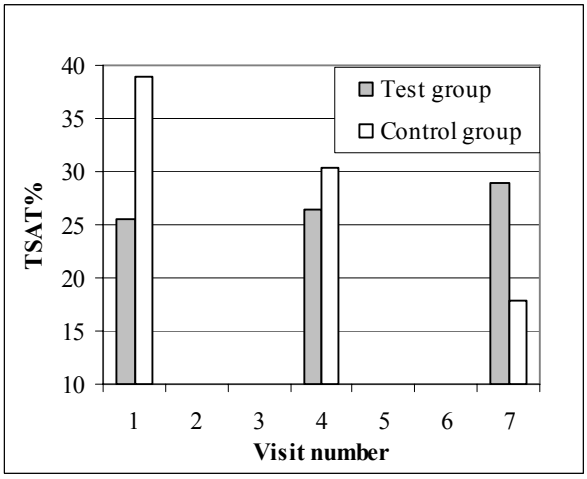

Fig. 3. Transferrin saturation during the study

Discussion

In the first phase of our study, by administering intravenous iron preparations, we increased considerably haemoglobin

levels in the experimental group only. Taking into account that iron deficiency was already present in patients in this group, with this therapy we partially replenished iron stores and eliminated on of the causes of this type of anaemia [3]. This resulted in an increase in haemoglobin level in the experimental group. On the other hand, in the control group on oral preparations we maintained iron at approximately the same level as at the beginning of the study. However, since no iron deficiency existed in this group, anaemia could not have been corrected significantly, because other factors were probably crucial in its development, not iron deficiency [3].

In the second phase of our study, in the first two months, a statistically significant increase in haemoglobin was measured in both patient groups. Namely, in the beginning, both groups had normal iron stores, and thus an adequate response to erythropoietin therapy. In the following two months, an increase in haemoglobin level was noted in the experimental group only. This could be explained by the fact that with administration of erythropoietin preparations iron stores are depleted quickly, if they are not compensated adequately [4,5]. This was the case with our control group, where oral iron therapy was not enough to complement erythropoietin therapy. In this group, iron deficiency was the main cause of the suboptimal response to erythropoietin therapy [11]. On the other hand, in the experimental group, the use of intravenous iron preparations during erythropoietin therapy was enough to keep iron stores stable [9]. Hence, that may explain why the response to erythropoietin therapy was adequate, e.g. followed by an adequate increase in haemoglobin.

Conclusions

Our results have shown that much better effects can be achieved by giving iron preparations intravenously, in comparison to oral preparations. Giving iron (especially intravenous preparations) is often enough, on its own, to increase haemoglobin levels. Erythropoietin therapy achieves much better results in combination with intravenous iron, compared to oral preparations, because intravenous therapy more efficiently replenishes and maintains iron stores. That is the reason why in the phase of correction of anaemia, during the erythropoietin treatment, intravenous iron therapy is inevitable. We conclude that intravenous iron therapy in dialysis patients is compulsory, while in pre-dialysis patients, transplant patients and peritoneum dialysis patients intravenous iron should be given in combination with oral preparations where indicated.

Conflict of interest statement. None declared.

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