INTRAVENOUS IRON THERAPY CAN BE A SECOND CHOICE OF TREATMENT IN HEMODIALYSIS PATIENTS WITH IRON DEFICIENCY ANAEMIA WHO FAIL TO MAINTAIN THE TARGET HEMOGLOBIN AFTER ORAL IRON THERAPY

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OBJECTIVES

We have previously reported that oral iron therapy (OIT) is beneficial in hemodialysis (HD) patients with iron deficiency anemia (IDA) and that hepcidin and ferritin predict OIT response (*Nutrients* **2015**, *7*, 103-18). However, it is not established whether intravenous iron therapy (IIT) is beneficial for improving hemoglobin (Hb) or maintaining the target Hb (tHb; 11~12 g/dL) in HD patients with IDA who are resistant to OIT. This prospective study was undertaken to address the issue.

METHODS

Inclusion criteria was IDA (Hb < 12 g/dL and ferritin < 100 ng/mL). Exclusion criteria were inflammation (CRP > 8.0mg/L), cancer, or poor adherence. There were 90 consecutive HD patients, and 51 patients (20 females, mean age; 63.4 years, and HD duration; 8.3 years) fulfilled the criteria and were enrolled. Iron therapy was withheld >3 months before the study. All received a continuous erythropoietin receptor activator (CERA) during the study. To determine the benefit of OIT, all patients received oral ferrous fumarate (50 mg/day, 12 weeks). If the patients respond to 3 months of OIT, OIT was continued for another 3 months. If the patients failed to respond to 3 month of OIT, OIT was switched to IIT (saccharated ferric oxide: 40mg/week x 9 times) for another 3 months (Figure 1). Patients showing the change in Hb (ΔHb) of >2 g/dL above baseline and/or maintaining the tHB were considered responders, whereas those with a smaller or no change in Hb and failure to maintain tHb were considered non-responders. We also determined whether hepcidin and ferritin predict the response to iron therapy. Serum hepcidin-25, as measured by LC-MS/MS method, ferritin, Hb and CERA dose were measured at 0, 3 and 6 months after therapy.

RESULTS

Thirty-nine patients (77%) responded to OIT (OIT-responsive group) (Figure 1). In these patients, mean Hb levels at the start of OIT were 9.9±1.1 g/dl, and ΔHb at 3 and 6 months after OIT were 1.7±0.6 g/dL, and 2.7±1.9 g/dL (Figure 2). In OIT-responsive group, Hb was maintained well at the end of the study (12.6±1.2g/dL), and thus the CERA dose could be reduced. Twelve patients (IIT group) failed to response to 3 months of OIT (Hb at the start of OIT; 9.2±1.1 vs. 9.8±0.8 g/dL at 3 months after OIT). Thus, OIT was replaced by IIT for another 3 months (Figure 2). In IIT group, 7 patients (58%、IIT-responders) responded and 5 (IIT-nonrespsonders) failed to respond to 3 months of IIT (Figure 3). In the IIT-responders, mean Hb levels at the start of OIT were 8.8±1.1 g/dL; ΔHb at 3 month after OIT, 1.1±1.3 g/dL, and ΔHb after 3 months of IIT, 1.7±0.5 g/dL. In the IIT-nonresponders, mean Hb levels at the start of OIT were 9.7±0.6 g/dL; ΔHb at 3 month after OIT,
-0.1±1.0 g/dL, and ΔHb after 3 months of IIT, -0.1±0.9 g/dL (Figure 3). The ΔHb was higher in the OIT-responsive group (2.7±1.9 g/dL, p=0.008) than in the responders of the IIT group (1.7±0.5 g/dL). Serum levels of hepcidin-25 and ferritin at the start of the study were similar between the OIT-responsive and the IIT groups. In the IIT group, ΔHb after IIT negatively correlated with hepcidin-25 (r=-0.741, p=0.009) and ferritin (r=-0.699, p=0.011) (Figure 4). Hepcidin-25 positively correlated with ferritin (r=0.869, p=0.0002). Serum ferritin levels at the end of the study were higher in the IIT-non responders (133.3±110.3 ng/mL) than in the IIT-responders (63.2±31.1 ng/mL, p<0.05) and the OIT-responsive group (44.4±24.4 ng/mL, p<0.01) (Figure 5).

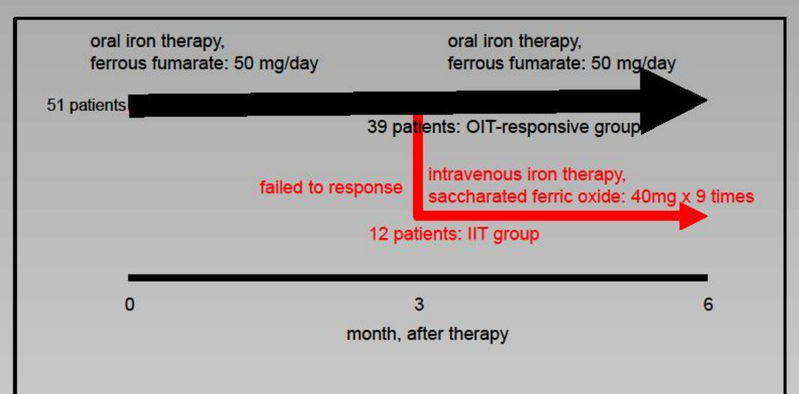

Figure 1. The protocol of this prospective study & number of patients

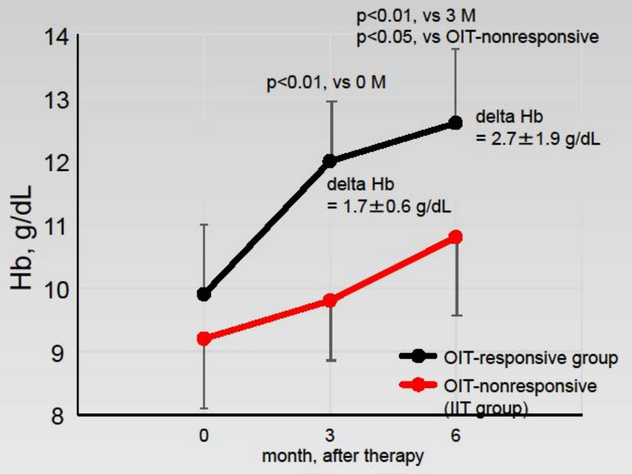

Figure 2. Change of Hb in OIT-responsive group and OIT-nonresponsive group during the iron therapy

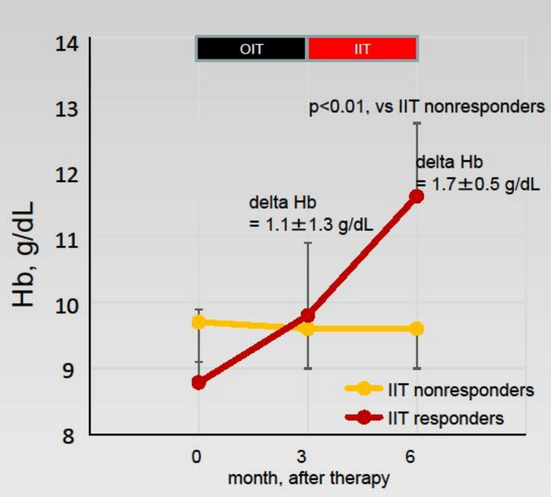

Figure 3. Change of Hb in IIT group before and after the intravenous iron therapy

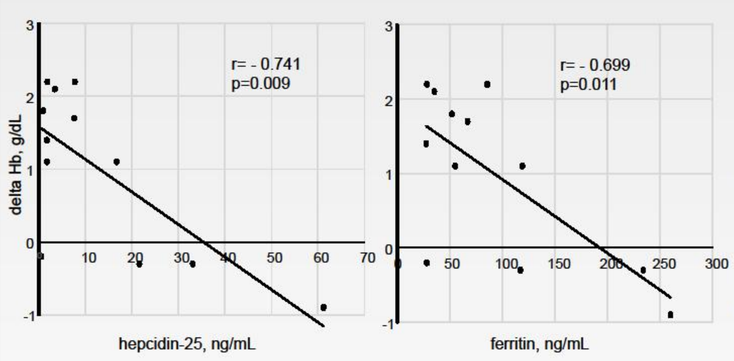

Figure 4. Correlation of delta Hb with hepcidin-25 and ferritin in IIT group

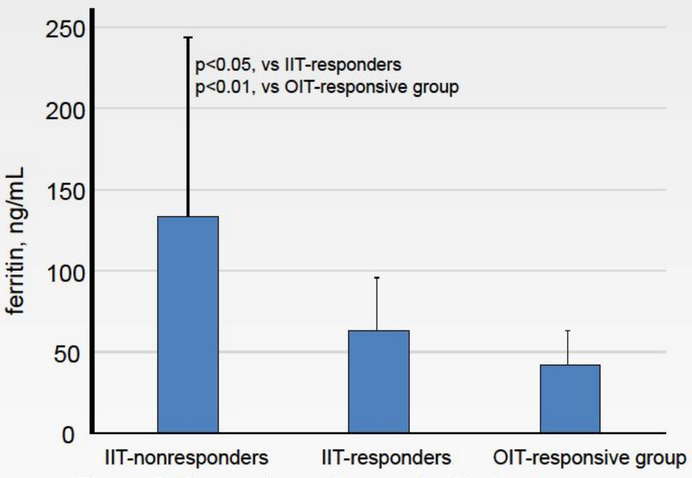

Figure 5. Comparison of serum ferritin levels between three groups at the end of the study

CONCLUSIONS

These data suggest that OIT has a benefit for improving Hb and maintaining tHb and that IIT can be a second choice of treatment when HD patients are resistant to OIT. The study also confirmed our previous finding that hepcidin-25 and ferritin can predict the response to ITT.

REFERENCES:

Takasawa K, Takaeda C, Maeda T, Ueda N: Hepcidin-25, mean corpuscular volume, and ferritin as predictors of response to oral iron supplementation in hemodialysis patients. *Nutrients* 2015;7:103-18.

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