

Combined chelation therapy with deferiprone and desferrioxamine in ironoverloaded β -thalassemia patients

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Letter to the editor:

Dear Editor-in-Chief,

We shortly report our results of combined iron chelation therapy with deferiprone (DFP) and desferrioxamine (DFX) versus chelation therapy with DFP alone, in iron overloaded β -thalassemia patients.

Desferrioxamine has been a life saving iron chelator for thousands of patients in the last 40 years. However, less than 10% of the patients requiring iron chelation therapy worldwide are able to receive DFX because of its high cost and many of them, especially teenagers, find difficulty in complying with daily subcutaneous administration.^{1,2} The only clinically available oral iron chelator is deferiprone (1,2-dimethyl-3-hydroxy-pyrid-4-one), which has so far been taken by over 6000 patients worldwide with very promising results.²

The purpose of this study was to test the efficacy and safety of DFP alone or in combination with DFX for the treatment of secondary haemosiderosis in patients with β -thalassemia.

Patients and Methods

Forty-three homozygous β -thalassemia patients were studied, 39 with thalassemia major and 4 with thalassemia intermedia. All the patients received regular blood transfusions with an average pre-transfusion hemoglobin of 9,5 gr/dL. Eighteen children and adults (mean age: 21,62 years) started 2 years ago iron chelation therapy with deferiprone (FerriproxR, Apotex Europe Ltd., Leeds, UK) at a dose of 75 mg/Kg/d, while 25 (mean age: 18,8 years) started combination therapy with DFP and DFX using doses of 75 mg/Kg/d and 40 mg/Kg/d, 3 days per week accordingly. Inclusion criteria for DFP therapy were bad compliance with novel chelation therapy and serum ferritin levels above 2000 μ g/L for the last 2 years. During therapy, hematological evaluation included, hemoglobin, haematocrit, WBC count, absolute neutrophil count and platelet count measurements every 10 days. Serum ferritin levels, liver and renal function were controlled bimonthly and 24hour urinary iron excretion (UIE) was controlled biannually.

Statistical analysis was carried out using the student's t-test for paired samples. The study was approved by the Scientific Committee of the Hospital and a written consent was given by all patients aged >18 years and parents of patients aged <18 years old.

Results

There was a statistically significant reduction of serum ferritin values in both groups. In the monotherapy group, serum ferritin levels were reduced from 3003,22 \pm 820,93 to 1870,94 \pm 1001,79 μ g/L (p <0,0001, Table 1). In the combination therapy group they were reduced from 2628,00 \pm 526,87 to 1844,28 \pm 611,26 μ g/L (p <0,0001, table 2). Patients in monotherapy group started chelation therapy with higher mean serum ferritin levels than patients in combination therapy group, but the difference between the two groups was not significant (p >0,05). The mean urinary iron excretion in the DFP group was 18,57 \pm 13,18 mg/24hours, while in the DFP+DFX group it was significantly higher, 34,31 \pm 18,14 mg/24 hours

Table 1. Serum ferritin values before and after therapy with deferiprone (duration of therapy: 21,68 \pm 1,12 months).

(p <0,0001). Compliance to therapy in both groups was very good (85-90%) and significant impact on the quality of life was mentioned by everyone. The most serious adverse drug reaction was agranulocytosis, which was observed in 2 patients. Other adverse effects that observed were neutropenia in 4 patients, gastrointestinal problems in 4, joint pains in 2, hypertransaminasemia in 4 and body weight increase in 6 patients. Seven patients discontinued therapy in total, 2 with agranulocytosis, 2 with neutropenia and 3 mainly for personal reasons.

Comments

Deferiprone has been shown in many studies to cause negative iron balance and to deplete iron from tissue compartments of iron loaded patients. Recent evidence suggests that combination of the two iron chelators (DFX plus DFP) have been shown to produce additive and synergistic effects.³⁻⁶ The results of this study confirms that either DFP or combination therapy may lead to a negative iron balance in transfusion dependant β -thalassemia patients, as assessed by serum ferritin levels and UIE over a 24-h period. They also suggests that combination therapy, comparing to DFP monotherapy, may lead to a significantly higher UIE over a 24-h period in these patients. Various side-effects in our population studied were similar to those reported from several studies.^{1,6} Serious adverse effects that noticed in the first year of the study were not increased with long-term therapy as well as with new patients started oral chelation therapy. Long-term DFP treatment is generally well tolerated and it appears that the frequency of adverse events is lower than previously assumed. For the first time it is feasible to design chelating regimens that suit the personal needs of each individual patient.

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