CLINICAL STUDY

Experience with Combination Therapy of Deferiprone and Desferrioxamine in β-Thalassemia Major Patients with Iron Overload at Maternity and Children Hospital, Al Madinah Al Munawarah, Saudi Arabia

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Abstract

Objective

Describe our experience with combination therapy of Deferiprone (DFP) and Desferrioxamine (DFO) in treating β-Thalassemia Major patients with severe iron overload in Al Madinah Al Munawarah, Saudi Arabia and to determine any adverse events of treatment.

Methods

Twenty eight patients with β-Thalassemia major between the ages of 8 - 27 (mean 15.5 ± 4.6 years SD) were enrolled into a prospective open label one year study from January 1st 2006 to December 31st 2006, at Al Madinah Maternity & Children's Hospital (Al Madinah Hereditary Blood Diseases Center). Participants were followed regularly at Al Madinah Hereditary Blood Diseases Center for at least 6 years prior to their enrolment in the study. The inclusion criteria were all patients who are transfusion dependent Thalassemia Major with an age of more than 8 years and serum ferretin levels > 3000 ng/L which were progressively increasing despite receiving chelating therapy with subcutaneous Desferrioxamine for at least 5 years prior to study. The doses used for Deferiprone was 75mg/kg while the dose of Desferrioxamine was 40- 50mg/kg/day. Serum ferretin and other laboratory investigations were monitored every 3 weeks and adverse events of both drugs were assessed regularly along with patients' compliance.

Results

There was no significant reduction of serum ferretin from baseline and by the end of the study period and no serious adverse events were observed.

Conclusion

Deferiprone is a safe drug, however it did not reduce the serum ferretin from the base line, but it maintained the iron balance despite chronic transfusion in patients with β-Thalassemia major when used in combination with Desferrioxamine.

Key words: β-Thalassemia, Deferiprone, Desferrioxamine, iron overload.

Journal of Taibah University Medical Sciences 2010; 5(1): 27 - 35

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Introduction

β- Thalassemia is a hereditary blood disease characterized by the absence or reduction in the synthesis of β-globins chains of the normal hemoglobin resulting in an imbalance between -and β chain and consequent ineffective erythropoeisis and hemolysis[1, 2]. The historical name of Cooley Anemia is the homozygous form of this disease. β- Thalassemia is endemic in all Arab countries and particularly among the Mediterranean population.

The molecular basis of β- Thalassemia in various Arab Countries reveals the presence of 52 mutations[3], which are mostly of Mediterranean and Asian origin. In Saudi Arabia 14 mutation were Identified and the commonest of which is IVS-1-110 (G—A), codon 39 (C-T) and IVS 11-1 (G—A)[4-7].

This study was conducted in Al Madinah and the estimated gene frequency of β-Thalassemia turned out to be 0.1 %[8].

Al Madinah Hereditary Blood Diseases Center was established in 1992 at Al Madinah Maternity and Children Hospital. It serves Thalassemia patients including adults in Al Madinah Region. The center provides comprehensive management that includes regular blood transfusion at 2-4 weeks intervals with regular use of Desferrioxamine (DFO).

The total of currently followed Thalassemia patients being at the center is 80. The research team first published a report on Thalassemia from Al Madinah region in 2003[9].

Since 1980s Desferrioxamine was the only Iron chelator used as subcutaneous infusion. The major disadvantage to this mode of therapy is its route of administration. Desferrioxamine is given subcutaneously with a special pump for 8-12 hrs everyday for at least 5 days a week placing considerable burden on the social and psychological life of the patients and their families.

Deferiprone (DFP) was the first oral Iron chelator to be licensed for use in India in 1995 and was granted in European license in 2000 under special conditions. It achieved full license in Europe in 2002, and was approved as a second line drug for patients who are unable to use DFO or on whom DFO therapy had proven ineffective.

Some studies[10-12] have shown the effectiveness of DFP alone as an oral chelator but a combination therapy with DFO and DEP has shown to be more effective in reducing serum ferritin[13-15] .

Deferiprone was introduced to the Ministry of Health in Saudi Arabia in 2005 and has been used in the Thalassemia center since then. Many centers however had concerns about its safety; hence its use was not universally taken up in Saudi Arabia.

The aim of this study was to describe the experience with DFP in combination with DFO in the treatment of iron overload in β-Thalassemia patients, and to determine its safety.

Material and Methods

This is a prospective open label 1 year study of combined therapy with Deferiprone and Desferrioxamine in β thalassemic patients with iron overload.

Twenty eight patients with β-Thalassemia major were enrolled into the study over one year from January 1st 2006 to December 31st 2006, at Al Madinah Maternity & Children's Hospital (Al Madinah Hereditary Blood Diseases Center). The age ranges were 8-27 years with mean ±SD, (15 ± 4. 60) all patients were followed regularly at the Thalassemia center for at least 6 years.

Diagnosis of β-Thalassemia major was based on the clinical history of pallor, jaundice and hepatosplenomegaly with hemoglobin electrophoresis showing high HbF values (95-98%), raised HbA2 (3.5-5%) on cellulose acetate medium at alkaline PH 8.4 (Helena laboratories, 1530 Lindbergh Drive, Beaumont Texas, USA).

All patients were on chronic blood transfusion regimen receiving 10-15 ml/kg of packed red blood cells every 2-4 weeks. They had been receiving DFO (Desferal, Novartis Inc, Basel, Switzerland) at a daily dose of 40 – 50 mg/kg / day by subcutaneous infusion pump over 8-12 h for