IRON METABOLISM

The Egyptian experience with oral iron chelators

AMAL EL BESHLAWY

Hematology Department, Pediatric Hospital, Cairo University, Egypt

Abstract

As no physiological mechanism exist for excreting transfusional iron overload in thalassemia, chelation therapy is the mandatory way to remove iron to prevent end organ damage and prolong survival. Desferoxamine (DFO) has been the major iron chelating agent used extensively worldwide for more than three decades for treatment of transfusional iron overload. However compliance has been a major obstacle in achieving an optimal therapeutic results. During the last 20 years the search for an affective oral iron chelators alternatives to Sc. DFO has been intensive. Different compounds have been studied, most of them although effective in animals have shown unacceptable toxicity with the exception of Deferiprone (L1) and ICL670.

Keywords: Thalassemia, Egypt, iron chelators

Experience on Deferiprone (L1)

Since January 2002, 108 transfusion dependant thalassemia patients (mean age 13.7 years) have been recruited to a Randomized Open – Label Phase III study with L1 and or DFO. This to evaluate the efficiency and safety of L1 single and combined with DFO by measuring the levels of serum ferritin (SF), Urine iron excretion (UIE) and liver iron content (LIC) at base line, after 3 mo. (n=44) and 12 mo. (n=66). Secondary end point included liver iron score (LIS), liver and heart function, compliance, tolerance and toxicity of the treatment regimens. Patients were classified into three arms; Arm A received L1+DFO, Arm B and Arm C received L1 or DFO as monotherapy respectively. Drug regimen: for L1 daily dose of 60 to 75 mg/kg Bw for Arm A & B. The dose of DFO was 23 to 50 mg/kg Bw for 2 days in Arm A and for 5 days in Arm C. Patients evaluation included complete blood count weekly for the first two months of treatment, there after fortnightly. In All Arms SF decreased significantly after 3 and 12 months of treatment in 100% in Arm A & C and in 86% in Arm B (P =0.001 & 0.02 & 0.04 respectively). The highest UIE was in week one and 12 in all arms. A synergistic or even additive effect could be observed in Arm A as the UIE was clearly higher during the days of combination treatment if compared with the UIE when L1 is given solely. A significant decrease in the LIC was observed in all Arms, however the LIS was more Significant in Arm A (P=0.009 vs. P=0.67). A significant improvement in the diastolic function of the heart was observed in all arms after treatment. The liver function test (ALT) increased after 3 months of treatment in 46% in Arm A, 73.3% in Arm B and 50% in Arm C. Most of the patients with increasing ALT were hepatitis C positive cases. Arthropathy was more marked in patients in Arm B (38%) and neutropenic episodes were observed in two cases one in Arm A and another in Arm B. Agranulocytosis (ANC <200/mm³) was detected in one case in Arm B, for whom we stopped the treatment.

Experience on ICL 670

It is a tridentate oral Iron Chelator given once daily. Forty three patients with a median age of 12 years were recruited sequentially since May 2004 for an open label multicenter trial on efficiency and safety of long term treatment with ICL 670 in beta thalassemia with transfusional iron overload. Patients received the treatment in a daily dose of 20 mg /Kg Bw based on their LIC at base line. Preliminary results revealed appreciable lowering of serum ferritin in most of patients (>67%). All patients tolerate the drug satisfactory with few treatable side effects in the form of vomiting and skin rashes. From theses studies it seems that the combined therapy L1+DFO is the most effective in lowering the SF, LIC and increasing
the UIE. Close monitoring of liver enzymes and neutrophilic count is recommended for patients receiving L-1, especially in hepatitis C positive cases.

Preliminary results of ICL670 were convenient being well tolerated and effective once daily oral iron chelator.