

COMPARISON OF DEFERASIROX, DEFERIPRONE, AND DESFERIOXAMINE EFFECTIVENESS ON MYOCARDIAL IRON CONCENTRATIONS AND BIVENTRICULAR FUNCTION BY QUANTITATIVE MR IN BETA-THALASSEMIA MAJOR

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Background

Despite dramatic gains in life expectancy in the desferrioxamine era for thalassemia major patients, the leading cause of death for this young adults population remains iron-induced heart failure. For this reason, strategies to reduce heart disease by improving chelation regimens has of the highest priority in this phase. These strategies include development of novel oral iron chelators to improve compliance. Oral deferiprone was proved more effective than subcutaneous desferrioxamine in removing cardiac iron. The novel oral one-daily chelator deferasirox has been recently commercially available but its long-term efficacy on myocardial iron concentrations and cardiac function is unknown.

Aims

To compare in thalassemia major patients the effectiveness of deferasirox, deferiprone and desferrioxamine on myocardial and liver iron concentrations and bi-ventricular function by quantitative magnetic-resonance imaging (MRI).

GLOBAL HEART T2* (ms)

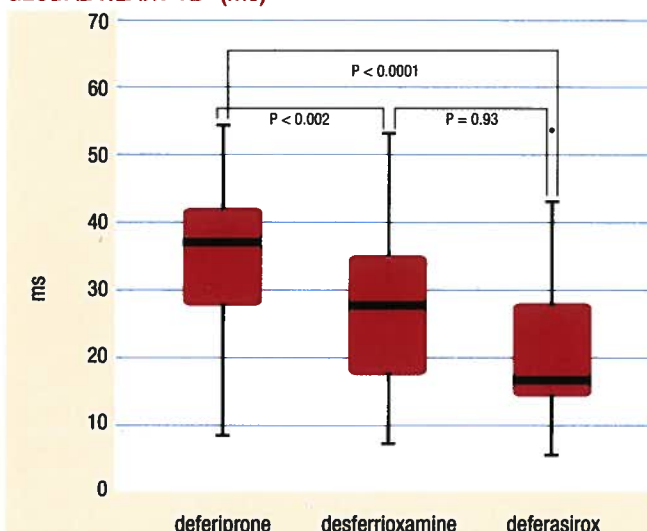


Figure 1

Methods

Among the 550 thalassemic subjects enrolled in the MIOT (Myocardial Iron Overload in Thalassemia) network between September 2006 and September 2007, we selected patients receiving one chelator alone for longer than 1 year. MIOT is an Italian network of 6 MR sites where the cardiac and liver iron status is assessed by validated and homogeneous standard procedures.

We identified 3 groups of patients: 24 treated with deferasirox, 42 treated with deferiprone and 89 treated with desferrioxamine. The 3 groups were matched for gender, Hb pre-transfusion levels, age of starting chelation, and good compliance to the treatment. The deferasirox group was significantly younger (26 ± 7 years) than the deferiprone- (32 ± 9 years) and desferrioxamine group (33 ± 8 years) ($p=0.0001$) and showed significantly higher mean serum ferritin levels (2516 ± 2106 ng/mL) than the deferiprone- (1493 ± 1651 ng/mL) and the desferrioxamine group (987 ± 915 ng/mL) ($p=0.0001$). Myocardial iron concentrations and distribution were measured by MRI T2* multislice multiecho technique. Biventricular function parameters were quantitatively evaluated by cine-dynamic MRI images. Liver iron concentrations were measured by MR T2* multiecho technique. Written informed consent was obtained from all subjects.

Results

The global heart T2* value was significantly higher in the deferiprone group (34 ± 11 ms) versus the deferasirox (21 ± 12 ms) and the desferrioxamine group (27 ± 11 ms) ($p=0.0001$). The T2* in the mid ventricular septum was significantly higher in the deferiprone (36 ± 12 ms) versus the deferasirox (20 ± 12 ms) and the desferrioxamine group (28 ± 13 ms) ($p=0.0001$). The number of segments with normal T2* value was significantly higher in the deferiprone and the desferrioxamine group versus the deferasirox group (14 ± 2 versus 11 ± 6 versus 7 ± 7 segments; $p=0.0001$). Among the biventricular function parameters, we found higher left ventricular ejection fractions in the deferiprone and the desferrioxamine group versus the deferasirox group (64 ± 7 versus 62 ± 6 versus $58 \pm 7\%$; $p=0.005$). Liver T2* values were significantly higher in the desferrioxamine group versus the deferiprone - and the deferasirox group (10 ± 9 versus 6 ± 6 versus 5 ± 5 segments; $p=0.002$).

Summary and conclusions

Oral deferiprone seems to be more effective than oral deferasirox and subcutaneous desferrioxamine in removal of myocardial iron with concordant positive effect on left global systolic function.