

# Efficacy of oral iron chelators as a single agent or in combination in beta thalassemia major

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# Introduction

- Standard supportive therapy in beta thalassemia major patients is regular blood transfusion
- This leads to secondary hemochromatosis
- Iron chelation therapy should be started when serum ferritin rises more than 1000 ng/ml
- For last 40 years deferioxamine has proven to be safe and effective but compliance remains the main issue

# Introduction

- Currently two oral iron chelators deferiprone and deferasirox are licensed and in use for treatment
- Different studies have proven the effectiveness of deferioxamine in combination with deferiprone
- But there is no published data on the effectiveness of both oral iron chelators if given in combination

# Hypothesis

- We hypothesize that combination of deferiprone & deferasirox is superior to deferiprone or deferasirox alone in  $\beta$ -thalassemia major

# Objective

- To assess the efficacy of deferiprone & deferasirox combination vs deferiprone or deferasirox alone in b-thalassemia major
- To document the renal, hepatic and bone marrow toxicity

# Patients and methods

- Experimental study
- At National institute of blood diseases and bone marrow transplant, Karachi
- Duration of study – 1 year (Jan 2008-Jan 2009)

# Patients and methods

- **Inclusion criteria**

- Patients of BTM on regular blood transfusion
- Serum ferritin >1000ng/ml
- Age > 2years

- **Exclusion criteria**

- Poor compliance
- Hypersensitivity to any of the study drugs

# Patients and Methods

- Deferiprone was given to those patients who were non complaint to deferioxamine (75mg/kg/d in 3 divided doses)
- Patients who could not tolerate deferiprone were offered deferasirox (30mg/kg x OD)
- Heavily iron loaded patients (s. ferritin >3000 ng/ml) were advised combination of the two oral chelators

# Monitoring

- Patients taking deferiprone were monitored for ANC every 2 weeks
- Serum ferritin, SGPT and creatinine were done at baseline, then at 6 months or if indicated in between
- Medicine was discontinued if enzymes raised to twice the level of baseline

# Patients and methods

- Statistical analysis done by SPSS 17
- ANOVA test was applied for calculating mean, standard deviation, and difference in values
- Value  $<0.05$  was considered significant

# Results

Drug	Age mean/range	M : F	Mean no of Tx/yr	HCV positive	Mean duration of drug exposure (days)
Deferasirox	10.5 (3-20)	9:5	15.8	3	214
Deferiprone	10 (4-22)	8:10	14.3	0	366
Combination	10.4 (4-18)	7:3	15.5	1	185

n= 42

<b>Parameter/ Drug</b>	<b>Baseline (Pre) (mean ±SD)</b>	<b>Post (mean ±SD)</b>	<b>P Value for change from baseline</b>	<b>P-value for difference between groups</b>
<b>Ferritin ng/ml</b>				
Desferasirox	4585.5±4181.5	4428.1±3262.0	0.45	0.384
Deferiprone	3226.2±1554.8	3189.9±1882.8	0.69	
combined	3523.6±1564.9	4260.8±3564.3	0.91	
<b>SGPT U/L</b>				
Desferasirox	76.8±48.33	58.5±35.5	0.99	0.970
Deferiprone	75.6±33.7	64.0±40.4	0.04	
combined	67.0±30.90	67.1±20.0	0.31	
<b>Creatinine mg/dl</b>				
Desferasirox	0.6±0.13	0.5±0.17	0.32	0.361
Deferiprone	0.5±0.14	0.5±0.11	0.09	
combined	0.5±0.24	0.5±0.20	0.05	
<b>ANC x 10<sup>9</sup>/L</b>				
Desferasirox	4.5±2.0	4.5±2.1	0.20	0.278
Deferiprone	4.1±2.7	4.4±1.7	0.83	
combined	3.0±1.1	3.6±1.5	0.66	

# Conclusion

- Our study showed that both the oral chelators are equally effective in reducing iron overload as monitored by serum ferritin
- They also appear safe as monitored by renal and liver functions
- Serum ferritin remained stable throughout the study period in all the three groups
- Further studies on large number of patients and longer follow up are needed to assess the efficacy of combined oral iron chelators