

ABSTRACT

Introduction: Thalassemia is an autosomal recessive disorder of defective B chain production leading to ineffective erythropoiesis. Hence, these children require regular blood transfusions to survive. Iron overload has deleterious effect on various organs hence it becomes very necessary to chelate the excess iron from body as human body has no means of

excreting iron. In earlier days deferoxamine was treatment of choice, now we have better oral iron chelators namely Deferasirox and Deferiprone. **Aims and Objectives:** To compare the efficacy of oral iron chelators – Deferasirox and Deferiprone in reducing serum ferritin levels and to compare their side effect profile.

Material and methods: The study was prospective stratified randomized comparative study conducted at Shadan Hospital, studied for 1 year. 41 children were selected for the study based on inclusion and exclusion criteria. These children have received 10 – 15 ml/kg of packed red blood cells every 5 weeks. These 41 children were divided in to two groups.

Group 1 and 19 children who received Deferasirox and group II had 22 children who received Deferiprone. Three children in Deferiprone group dropped from study because of severe arthralgia and 19 remained at the end of study

KEYWORDS:

Intervention

Group I received 20mg/kg/day once a day dose of Deferasirox and Group II received [4]mg/kg/day thrice a day dose of Deferiprone for a period of one year, their laboratory parameters were followed up.

Results:

Baseline ferritin levels were statistically similar in both the groups with group I having 3261 + 2613 ng/ml and group II with 4109 + 3153 ng/ml, p value was 0.372. The study showed that both drugs are equally effective in reducing serum ferritin levels. Mean baseline ferritin in Deferasirox group was 3261 + 2613 ng/ml, dropped to 15[12] + 766 ng/ml at end of study (with p value of 0.011). The median percentage of fall of ferritin observed was 4817%. Mean baseline ferritin in Deferiprone group was 4109 + 3153 ng/ml and at the end of study it dropped to 1743 + 1138 ng/ml with significant p value of 0.0040 (<0.01). The percentage fall from baseline was median of 55.61%. When these drugs are compared we did not find and statistically significant difference. In both the groups, patients with baseline ferritin levels of >4000 ng/ml and in patients with baseline ferritin of 2000 - 4000 ng/ml had statistically significant fall in serum ferritin levels and in patients with baseline ferritin levels of <2000 ng/ml there was no statistical fall in serum ferritin levels and levels were maintained at steady state.

Both drugs did not have significant deleterious effects on neutrophil counts, liver and renal functions. Arthralgia was major side side effect of Deferiprone, developed in 41% patients. Three children had severe arthralgia because of which drug was stopped and switched over to Deferasirox. Nausea and vomiting were common in both the groups.

RESULTS

This study was prospective stratified randomized comparative study conducted for period of 1 year from February 2011 to January 2012 at Thalassemia Day Care Center of Shadan Institute.

Study Design:

Comparative two group randomized clinical study of 41 patients with 19 patients in group I (Deferasirox) and 22 patients in Group II (Deferiprone) was undertaken to compare the effectiveness of these drugs in reducing serum ferritin levels and to compare their side effects. At the end of study period all 19 children remained in group I and there were three dropouts in group II, hence the remaining 19 were considered in analysis of drug effectiveness.

Table 1. Age distribution of patients studied

Age in years	Group I		Group II	
	No.	%	No.	%
1-5	13	68.42	04	21.05
6-10	05	26.31	12	63.12
>10	01	5.27	03	15.[9]
Total	19	100	19	100
Mean <u>+</u> SD	5.23 <u>+</u> 2.76		7.26 <u>+</u> 2.42	
Median	4		7	

Table 2: Gender distribution of patients studied

Gender	Group I		Group II	
	No.	%	No.	%
Male	11	57.[15]	11	57.[15]
Female	08	42.11	08	42.11
Total	19	100.0	19	100.0

Samples are gender matched.

Table 3: comparison of study variables in two groups of patients studied

Variables	Group I	Group II	P value
No of transfusion before chelation(- median)	21	29	NA
Volume of blood before chelation in ml	3600 <u>+</u> 2010	47[13] <u>+</u> 1[6]3	0.0627

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chelation 3261±2613 4109±3153 0.3727	Ferritin before chelation	3261 <u>+</u> 2613	4109 <u>+</u> 3153	0.3727
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Both groups are comparable with respect to number of transfusion received before chelation and baseline ferritin values.

Table 4: Comparison of number and volume of transfusion received during the study period

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Variables	Group I	Group II	P Value
No of transfu- sions during chelation	10.68 <u>+</u> 2.1	11.42 <u>+</u> 2.11	o.2[11]8
Volume of blood during chelation (ml)	2163 <u>+</u> 645	2560 <u>+</u> 646	0.0661

Both groups are comparable with respect to number and volume of blood received during study period.

Table 5: Comparison of ferritin levels in 3 monthly intervals in two groups of patients studied

Ferritin levels	Group I	Group II	P Value
Initial	3261 <u>+</u> 2613	4109 <u>+</u> 3153	0.3727
3 months	23[17] <u>+</u> 15[15]	3439 <u>+</u> 2[5]4	0.1616
6 months	20[14] <u>+</u> 1536	2352 <u>+</u> 1269	0.511
9 months	1811 <u>+</u> 1155	2161 <u>+</u> 1324	0.3[17]0
12 months	15[12] <u>+</u> 766	1743 <u>+</u> 1138	0.6209
P value (from baseline to end value)	0.0110	0.0040	

We observed fall in serum ferritin levels in both groups, but no statistically significant difference between the two drugs studied.

Table 6: Percentage of fall in ferritin between to drugs

	Deferasirox	Deferiprone	P Value
% fall in Serum ferritin	40.64 <u>+</u> 24.4	50.57 <u>+</u> 22.03	0.20

Percentage of fall of ferritin from baseline is comparable in two groups.

Table 7: Deferasirox Group: changes in ferritin values in each subgroup (grouped according to baseline ferritin levels)

Ferritin (ng/ ml)	>4000	2000-4000	<1999
Number (N=)	5	7	7
Baseline ferritin	6252 <u>+</u> 3551	2[17]7 <u>+</u> 765	1469 <u>+</u> 397
3 months	41[3] <u>+</u> 2053	2254 <u>+[</u> 3]1	1257 <u>+</u> 310
6 months	3497 <u>+</u> 2356	1[11]5 <u>+</u> [8]4	1314 <u>+</u> 536
9 months	2[8]0±1816	16[8] <u>+</u> 609	1219 <u>+</u> 397
12 months	2425 <u>+[</u> 20]3	1361 <u>+</u> 423	1211 <u>+</u> 421
P value (baseline to end value)		0.0005	0.261
Percent- age of fall % (from baseline)	58.8 <u>+</u> 6.48	51.43 <u>+</u> 18.6	16.[14] <u>+</u> 18.53

Observed significant fall in serum ferritin in group with baseline ferritin of 200 ng/ml or more.

Ferritin (ng/ml)	>4000	2000-4000	<1999
Number (N=)	6	9	4
Baseline ferritin	[5]62 <u>+</u> 3349	27[13] <u>+</u> 411	1606 <u>+</u> 4[15]
3 months	6437 <u>+</u> 32[14]	2411 <u>+</u> 429	1254 <u>+</u> 3[9]
6 months	3445 <u>+</u> 1[7]6	2033 <u>+</u> 319	1430 <u>+</u> 362
9 months	3473 <u>+</u> 16[14]	1[3]7 <u>+</u> 265	11[18] <u>+</u> 541
12 months	2[7]6 <u>+</u> 1401	13[8] <u>+</u> 5[4]	960 <u>+</u> 3[17]
P Value (baseline to end value)	0.0074	<0.0001	0.0[10]6
Percentage of fall % (from baseline)	62.63 <u>+</u> 13.3	48.3 <u>+</u> 23.05	37.59 <u>+</u> 25.[10]

Observed significant fall in serum ferritin in group with baseline ferritin of 2000 ng/ml or more.

Table 8: Comparison of neutrophil count in 3 monthly intervals in two groups of patients studied

Neutrophil count per mm ³	Group I	Group II	P value
Initial	4281 <u>+</u> 2211	30[9] <u>+</u> 1517	0.060
3 months	3[13]4 <u>+</u> 1568	3730 <u>+</u> 1272	0.[4][5]
6 months	4361 <u>+</u> 1[19]2	38[13] <u>+</u> 1222	0.3721
9 months	4334 <u>+</u> 1325	3[9]6 <u>+</u> 1625	0.3074
P value (from baseline to end value)	0.[18]9	0.148	

Mean neutrophil counts comparable in both groups.

SGOT levels	Group I	Group II	P value
Initial	56 <u>+</u> 22.9	42.15 <u>+</u> 26.56	0.0[19]7
3 month	[5].52 <u>+[</u> 17].64	43.57 <u>+</u> 23.3	0.1263
9 months	76.[15] <u>+</u> [4].38	60.[20] <u>+</u> 33.36	0.4046
P value (from baseline to end value)	0.2554	0.0627	

SGOT levels were comparable in both groups

Table 9: Comparison of SGPT levels in 3 monthly intervals in two groups of patients studied

SGPT levels	Group I	Group II	P value
Initial	58.78 <u>+</u> 28.48	55.2 <u>+</u> 29.[14]	0.[2]76
3 months	81.57 <u>+</u> 106.42	49.21 <u>+</u> 32.21	0.2127
9 months	[16].57 <u>+</u> [13].18	1 <u>+</u> 40.19	0.2[17]6
P value (from baseline to end value)	0.1395	0.3112	

SGPT levels were comparable in both groups.

Table 10: Comparison of calcium levels in 3 monthly intervals in two groups of patients studied

Calcium levels	Group I	Group II	P value
Initial	8.[14] <u>+</u> 1.02	9.27 <u>+</u> 0.9[11]	0.23[10]
3 months	9.09 <u>+</u> 0.[10]7	9.14 <u>+</u> 0.[16]5	0.[12]14
6 months	9.08 <u>+</u> 1.25	9.68 <u>+</u> 0.[17]	0.1000
9 month	9.37 <u>+</u> 0.[12]	9.5 <u>+</u> 0.645	0.600
P value (from baseline to end value)	0.1181	0.4001	

No fall in serum calcium levels in both the groups.

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Table 11: Comparison of phosphorous levels in 3 monthly intervals in two groups of patients studied

Phosphorous levels	Group I	Group II	P value
Initial	4.5 <u>+</u> 0.97	4.33 <u>+</u> 1.06	0.60[18]
3 months	4.5 <u>+</u> 0.[12]	3.98 <u>+</u> 0.6[19]	0.0501
6 months	4.2 <u>+</u> 0.1	4.27 <u>+</u> 0.[13]6	0.7[9]6
9 months	4.[12] <u>+</u> 1.18	4.32 <u>+</u> 0.734	0.09[15]
P value (from baseline to end value)	0.3111	0.9732	

No fall in serum phosphorous levels in both the groups.

Table 12: Comparison of alkaline phosphatase levels in3 monthly intervals in two groups of patients studied

ALP levels	Group I	Group II	P value
Initial	219 <u>+</u> [8].98	213 <u>+</u> 58.51	0.[6][8]
3 months	224 <u>+</u> [17].[20]	205 <u>+</u> 49.68	0.4333
6 months	216 <u>+[</u> 2].64	197 <u>+</u> 45.45	0.3307
9 months	211 <u>+</u> 52.28	205 <u>+</u> 68.4	0.7630
P value (from baseline to end value)	0.[3]43	0.[2]07	

No increase in alkaline phospatase levels in both the groups.

Table 13: Comparison of urea levels in 3 monthly intervals in two groups of patients studied

Urea levels	Group I	Group II	P value
Initial	21 <u>+</u> 7.39	33.38 <u>+</u> 11.35	0.44[13]
3 months	35.[18] <u>+</u> 9. [18]	29.73 <u>+</u> 10.33	0.017
6 months	33 <u>+</u> 8.73	27.13 <u>+</u> 8.14	0.0512
9 months	31.8 <u>+</u> 7.56	28.22 <u>+</u> 8.28	0.1725
P value (from baseline to end value)	0.7434	0.1181	

Blood urea levels were comparable in both the groups.

Table 14: Comparison of creatinine levels in 3 monthly intervals in two groups of patients studied

Creatinine levels	Group I	Group II	P value
Initial	0.62 <u>+</u> 0.21	0.61 <u>+</u> 0.20	0.[14]14
3 months	0.61 <u>+</u> 0.19	0.68 <u>+</u> 0.19	0.2636
6 months	0.1 <u>+</u> 0.22	0.64 <u>+</u> 0.18	0.64[9]
9 months	0.58 <u>+</u> 0.18	0.63 <u>+</u> 0.18	0.3976
P value (from baseline to end value)	0.5324	0.7478	

Serum creatinine levels were comparable in both the groups.

Table 15: Distribution of adverse effects in two groups of patients studied

	Group I n=19		Group II n=22(19+3)	
Adverse effects	No.	%	No.	%
Nil	12	63.1	7	31.8
Present	7	36.8	15	68.2
Arthralgia	1	5.2	9	40.9
Pain abdomen	0	0	1	4.5
Nausea & vomiting	6	31.5	6	27.2
Rash	0	0	0	0

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DISCUSSION

The primary study outcome was to measure and compare the fall in serum ferritin levels between the two the study groups.the secondary outcome measures were to compare the side effect profiles assessed by patient's signs and symptoms of side effects and by laboratory measures among the two groups p values < 0.05 were considered as statistically significant.

Age groups studied:

Study included 38 paediatric thalassemia children. The children were assigned in to two groups by random method; children were alternatively allotted group I or group II. Group I had children with mean age of 5.23+2.76 years and group II had children with mean age of 7.26+2.42 years. The Deferiprone group (group II) had higher mean age group because 4 children in that group had thalassemia intermedia. Matching the age group was not at verv significant factor affecting the study results, as the main study is to find out the efficacy of the chelators to reduce the serum ferritin levels. Largest ever investigation conducted for an iron chelator was EPIC study by Cappellini et al with 1744 patients included patients aged 2-[15] years.¹⁵¹ Gender distribution in our study was exactly similar.

Mean volume of transfusions received in group I was 3600+2010 ml and 47[13]+1[6]3 ml in group II with no statistical significance between two groups. Baseline ferritin levels were statistically similar in both the groups with group I having 3261+2613ng/ml and group II with 4109+3153 ng/ml, p value was 0.372. This was important so as to compare the effect of these drugs on serial serum ferritin levels, which was our main outcome measure.

Number of transfusion received during the 1 year study period was comparable in two groups, Group I received 10.68+2.1 times and group II received 11.42+2.11 times. Volume of blood received during study period was also similar in both the groups, group I has received 2163+645 ml of packed cell and group II has received 2560+646 ml, which was statistically similar. Hence, both groups are matched to study the study the efficacy of these chelators to reduce ferritin levels.

All children of group I received Deferasirox at dose of 20 mg/kg/day once a day dosage. Children of group II received [4]mg/kg/day in three divided doses of Deferiprone. The dosages of these drugs used were similar in many other studies mentioned below.

Efficacy in reducing serum ferritin

Baseline ferritin levels were recorded and te same were repeated for every child in both the groups every three months, and levels were noted.

Deferasirox (group I): Mean baseline ferritin in this group was 3261+2613 ng/ml, with the therapy we observed fall in mean serum ferritin levels tested at serial intervals.at the end of 1 year the mean serum ferritin level dropped to 15[12]+766 ng/ml with p value of 0.011 (<0.05) which is statistically significant, indicating the efficacy of Deferasirox in reducing the serum ferritin in transfused thalassemic children. The median percentage of fall of ferritin observed is 48.17%. This result was comparable with many other studies on Deferasirox.

Rashid Merchant et al from Dr. Balabhai Nanavati Hospital, Mumbai studied 30 thalassemia patients of mean age 15.7+6.8 years, who were given Deferasirox at doseof 20-35 mg/kg/day for 18 months. He noticed statistically significant decrease in serum ferritin values form baseline of 3[11]9.8+16[16].7 ng/ml to 26[19].4+1[9]1.5 at end of study and percentage of fall was 30.2% which was comparable to our study.^[6]

Anil Pathare et al studied 19 heavily iron-overloaded patients. Deferasirox was given over an 18-month period. He noticed reduction in median serum ferritin from a baseline of 5497 to 4235 ng/mL (p=0.001). He also noted good cardiac chelation property of Deferasirox.^[7]

Cappellini et al in EPIC study studied 1744 patients, who were given Deferasirox at dose of 10-30 mg/kg/day for 52 weeks, showed a significant reduction in serum ferritin from baseline of 3135 (-264 ng/mL; p<0.0001) in > 20 mg/kg dosage group, also observed significant fall in LIC.^[5]

Mohammad Ali Molavi et al investigated [7] patients aged 3 to 31 years were studied, for period of 1 year. He observed that serum ferritin decreased from 20[20].4+[6]6.96 to 1578.73+7[10].6 (p<0.05).^[4]

Similarly Ali Taher et al noted median serum ferritin levels were maintained around baseline levels (1[18]1 ng/mL) in the LIC <7 mg Fe/g dw cohort and decreased significantly in the LIC >7 mg Fe/g dw cohort (362l ng/mL at baseline to 2398 ng/mL after 2 years of therapy). ^[8]

Deferiprone (group II): Mean baseline ferritin in this group was 4109+3153 ng/ml and at the end of study it dropped to 1743+1138 ng/ml with significant p value of 0.0040 (<0.01).The percentage fall from baseline was median of 55.61%.

The results indicate the Deferiprone is good iron chelator.

Panigrahi et al from Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India studied 110 patients with mean age of 17 years, given the drug for 72 months and observed significant fall in ferritin levels.^[9]

El Alfy and colleagues reviewed its use in 100 children (mean age 5.1+2.4 years) with thalasseimia or sickle cell disease. At the end of the 6 month treatment period there was a significant drop in mean serum ferritin levels from 2532+1463 ng/ml to 2176+1144 ng/ml (P<0.05).¹¹⁰ Similar results were reported in another trial by Won et al who reported that mean serum ferritin levels decreased from a mean of 417+1130 ng/ml at baseline to 3363+1149 ng/ml following median treatment duration of 11.4 months.^{[111}

Hoffbrand et al and Cohen et al noted no significant change in overall mean serum ferritin levels achieved in up to 1 year of treatment.^{[12],[13]} The reasons for those study results are not known.

Similarly Ceci et al in 2002 studied 532 patients who received [4] mg/kg per day of Deferiprone and analysed the serum ferritin levels in 151 patients who completed 3 years of therapy with no missing measurements. The mean serum ferritin level declined from 25[6] ng/ml at baseline to 2320 ng/ml at 3 years (p value of 0.01). Patients with initial serum ferritin levels higher than 4000 ng/ml showed a significant decline in ferritin level consistently overtime.^[14]

Comparison between the two drugs

Comparing the baseline ferritin levels and ferritin levels at regular intervals, we did not find statistically significant difference between these two drugs in reducing serum ferritin levels. Percentage of fall of serum ferritin in group I was 40.64+24.4 (mean), which was comparable to percentage of fall of 50.57+22.03 (mean) of group II, with p value of 0.20.

In EPIC study, total 1[4] (10.0%) patients had two consecutive serum creatinine of more than 33% above baseline. 11 (0.6%)cases of drug-related proteinuria and there was one case of acute renal failure. 13 (0.7%) patients experienced two consecutive increases in ALT over ten times the upper limit of normal.^[5]

Wood et al studied 27 children and noticed 3 children having creatinine twice the baseline value, 1 child had renal failure and 2 children had ten time raise in SGPT levels.^[15]

Cappellini MD et al and Elliott Vichinsky et al noted > 35% patients having creatinine of twice the baseline levels.^{[16],[17]}

Studies	Raise in Serum cre- atinine (2 x baseline)	Renal failure	SGPT (10 x ULN) (ULN-up- per limit of normal)	ANC <1500/ mm ³ (absolute neutrophil count)
Present study	1(5.26%)	0(0%)	1(5.26%)	0(0%)
EPIC study ^[5]	1[4](10%)	0(0%)	13 (0.7%)	0(0%)
Cappellini MD et al ^[16]	112(38%)	0(0%)	2 (0.7%)	0(0%)
Ali Taher et al ^[8]	9(3.8%)	0(0%)	13 (5.5%)	0(0%)

Elliott Vichinsky et al ^[17]	48(36.4%)	0(0%)	5 (3.8%)	0(0%)
Wood et al ^[15]	3(11.1%)	1(3.7%)	2 (7.4%)	0(0%)

Deferiprone

Many studies have noted cases of neutropenia and agranulocytosis, we may need to follow up these children to observe possibilities of children developing neutropenia.

Cohen et al studied 1[13] patients and noted that in all patients the mean ALT (SGPT) was significantly higher than the baseline. ALT levels greater than twice the upper limit of the reference range were present in 43 patients. Agranulocytosis occurred in 1 out of 1[13] patients, neutropenia occurred in 9 (43%) Patients.^[13]

Caterina Borgna-Pignam noted out of 157 patients, neutropenia in 5% patients, agranulocytosis in 0.63% patient, increased levels of alanine aminotransferase in 1.3% patients and worsening of renal failure 1 patient.^[3]

Table 24: Studies on Deferiprone side effects

Studies	Raise in Serum creatinine (2 x base- line)	Renal failure	SGPT 10 x ULN (ULN- upper limit of normal)	ANC <1500/ mm ³ (Absolute neutrophil count)	Agranu- locytosis ANC < 500 mm ³
Present study	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ceci et al ^[14]	0 (0%)	0 (0%)	15 (2.8%)	21 (3.9%)	5 (0.9%)
Cohen et al ^[13]	0 (0%)	0 (0%)	0 (0%)	9 (4.8%)	1 (0.53%)
Pignatti et al ^[3]	1 (0.63%)	1 (0.63%)	2 (1.27%)	8 (5%)	1 (0.63%)
Agarwal et al ¹	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hoffbrand et al ^[12]	0 (0%)	1 (1.9%)	0 (0%)	2 (5.8%)	1 (1.9%)
Pennel et al ^[2]	0 (0%)	0 (0%)	0 (0%)	1 (3.44%)	0 (0%)

Table showing Comparing the side effects of drugs

Studies with Number of subjects (n)	Raise in Serum creatinine (2 x baseline)	Renal failure	SGPT 10 x ULN (ULN- upper limit of normal)	ANC <1500/ mm ³ (Abso- lute neu- trophil count)	Agranu- locytosis ANC < 500 mm ³
Deferasirox (n=19)	1 (5.26%)	0 (0%)	1 (5.26%)	0 (0%)	0 (0%)
Deferiprone (n=19)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

In this study, we did not observe significant difference between these two drugs with respect to their effect on neutrophil counts, liver and kidney functions.

Table showing Studies on Deferasirox side effects

Studies	Pain ab- domen	Nausea	Vomit- ing	Diarrhea	Rashes	Joint Pain
Present study	0 (0%)	6 (31.5%)	6 (31.5%)	0 (0%)	0 (0%)	1 (5.2%)
EPIC study ^[5]	97 (5.6%)	135 (7.7%)	66 (3.8%)	251 (14.4%)	174 (10%)	10 (0.6%)
Capellini et al ^[18]	50 (9%)	41 (7.4%)	35 (6.3%)	28 (5%)	36 (6.5%)	0 (0%)
Ali Taher et al ^[8]	14 (6%)	17 (7.2%)	21 (8.9%)	14 (6%)	19 (8%)	0 (0%)
Elliott Vichinsky et al ^[17]	37(28%)	30 (22.7%)	28 (21.2%)	26 (19.7%)	18 (13.6%)	20(15.2%)
Wood et al ^[15]	3(11.1%)	7 (25.9%)	3(11.1%)	5 (18.5%)	5 (18.5%)	0 (0%)

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In EPIC study the most common adverse events were gastrointestinal (28%) and skin rash (10%).The most common drug-related adverse events were diarrhoea (14. 4%), skin rash (10.0%), nausea (7.7%), and arthralgia (0.6%).^[S]

Ali Taher et al noted vomiting (11%), nausea (8%), skin rash (8%), abdominal pain (6%) and diarrhoea (6%).The side effects of Deferasirox were minimal and easily manageable.^[8]

In all studies adverse effects were predominantly transient and mild to moderate in nature. Their incidence generally decreased after the first Year of Deferasirox and tolerance appeared to improve over the long term, because the proportions of patients presenting with the most common drug-related adverse effects decreased considerably after the first year of Deferasirox treatment.

Deferiprone

Agarwal et al studied 52 patients on Deferiprone and noted 20 patients having arthralgia as major side effect.¹

In another study involving 1[13] patients Cohen et al, noted raddish discoloration of the urine in 74 patients, 20 patients had had joint pain, 2 reported joint swelling and 2 reported both symptoms.^[13]

Studies	Ab- dom- inal Pain	Nausea	Vomit- ing	Diarrhea	Rashes	Joint pain
Present study n=22	1 (4.5%)	6 (27.2%)	6 (27.2%)	0 (0%)	0 (0%)	9 (40.9%)
Ceci et al ^[14]	17 (3.2%)	17 (3.2%)	17 (3.2%)	-	0 (0%)	20 (3.9%)
Cohen et al ^[13]	62 (33%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	20 (10.6%)
Pignatti et al ^[3]	2 (1.27%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	10 (6.36%)
Daar et al ^[19]	6 (6.6%)	6 (6.6%)	6 (6.6%)	0 (0%)	0 (0%)	22 (24%)
Goel et al ^[20]	2 (3.44%)	2 (3.44%)	2 (3.44%)	0 (0%)	0 (0%)	28 (48%)
Agarwal et al ¹	0 (0%)	2 (3.5%)	0 (0%)	0 (0%)	0 (0%)	20 (38.5%)
Pennel at al ^[2]	19 (66%)	19 (66%)	19 (66%)	0 (0%)	0 (0%)	8 (28%)

Table showing Comparing the side effects of Deferasirox and Deferiprone

Studies with Number of subjects (n)	Ab- dom- inal pain	Nausea	Vomiting	Diar- rhoea	Rashes	Joint Pain
Deferasirox n=19	0 (0%)	6 (31.5%)	6 (31.5%)	0 (0%)	0 (0%)	1 (5.2%)
Deferiprone n=22	1 (4.5%)	6 (27.2%)	6 (27.2%)	0 (0%)	0 (0%)	9 (40.9%)

Deferiprone has major adverse effect of causing arthralgia, and in 3 children lead to stoppage of drug. G I side effects are similar in both the groups.

CONCLUSIONS

Deferasirox and Deferiprone are orally active iron chelators, equally effective in reducing the serum ferritin levels. Rate of fall in serum ferritin levels is directly proportional to baseline ferritin levels. When the baseline ferritin levels are < 1999 ng/ml these chelators will maintain the ferritin levels at stead state.

Both the drugs studied did not have major adverse effects on renal functions, liver functions and did not cause neutropenia in any of the patients.

Arthralgia was major side effect of Deferiprone because of which drug was stopped in three children. Nausea and Vomiting were common side effects in both the drugs.

Considering the once daily dosing and favourable side effect profile, Deferasirox seems a more suitable iron chelator as compared to Deferiprone. But in order to recommend one over the other, further studies with detailed evaluation of compliance as well as side effect profile involving a larger patient population are required.

Reference

- Agarwal MB, Gupte SS, Viswanathan C. long-term assessment of efficacy and safety of L1, an oral iron chelator, in transfusion dependent thalassemia: Indian trial. British Journal of Haematology 19[18] October; [8](2): 460-466.
- [2]. Dudley J. Pennell, Vasili Berdoukas, Markissia Karagiorga. Randomized controlled trial of Deferiprone or Deferoxamine in beta-thalassemia major patients with asymptomatic myocardial siderosis. Blood 2006; 107: 3738-3744.
- [3]. Caterina Borgna-Pignatti, Maria Domenica Cappellini, Piero De Stefano. Cardiac morbidity and mortality in deferoxamine- or deferiprone-treated patients with thalassemia major. Blood. 2006; 107: 3733-3737.
- [4]. Mohammad Ali Molavi, Faegheh Jomehpoor, Abdolmajid Nazemi Gheshmi and Hakimeh S. Sajjadi. Assessment of Effectiveness and Side Effects of Osveral chelator Drug in Thalassemia Major Patients with Iron Overload. Jornal of applied Environmental and Biological Sciences 2012; 2(5): 153-156.
- [5]. Maria Domenica Cappellini, John Porter, Amal El-Beshlawy. Tailoring iron chelation by iron intake and serum ferritin: the prospective EPIC (Evaluation of Patients' Iron Chelation) study of deferasirox in 1744 patients with transfusion-dependent anemias. Haematologica 2010; 95(4): 557-566.
- [6]. Rashid Merchant, Javed Ahmed, Pradeep Krishnan, Efficacy and Safety of Deferasirox for Reducing Total Body and Cardiac Iron in Thalassemia. Indian Pediatrics 2012; 49: 281-2[11].
- [7]. Anil Pathare, Ali Taher, Shahina Daar. Deferasirox (Exjade(R)) significantly improves cardiac T2* in heavily iron- overloaded patients with B-thalassemia major. Ann Hematol 2010; [15]: 405-409.
- [8]. Ali Taher, Mohsen S. elalfy, Kusai Al Zir. Achieving treatment goals of reducing or maintaining body iron burden with deferasirox in patients with B-thalassaemia: results from the ESCALATOR study. European Journal of Haematology 2011; [13]: 349-354.
- [9]. Inusha Panigrahi, Ram K. marwaha, Rashmi R. Das. Long-term response to deferipronetherapy in Asian Indians. Ann Hematol 2010; [15]: 135-140.
- [10]. El Alfy M, Sari TT, Lee CL. The Safety, Tolerability, and Efficacy of a liquid Formulation of Deferiprone in Young Children with Transfusional Iron Overload. J Pediatr Hematol Oncol J 2010; 32(8): 601-5.
- [11]. Won SC, Han DK, Seo JJ, et al. Efficacy and Safety of Deferiprone (Ferriprox); an Oral Iron-chelating Agent in Pediatric Patients. Korean J Hematol 2010; 45; 58-61.
- [12]. Victor Hoffbrand, Faris AL-Refaie, Bernard Davis. Long-Term Trial of Deferiprone in 51 Transfusion-Dependent Iron Overloaded Patients. Blood 1998; [17]: 295-300.
- [13]. Alan R. Cohen, Renzo Galanello, Antonio Piga. Safety and effectiveness of long term therapy with the oral iron chelator deferiprone. Blood 2003; 102: 15[9]-15[13].
- [14]. Adriana Ceci, Paola Baiardi, Mariagrazia Felisi. The safety and effectiveness of deferiprone in a large-Scale, 3-Year Study in Italian patients. British Journal of Haematology 2002; 118: 330-336.
- [15]. John C. Wood, Barinder P. Kang, Alexia Thompson. The effect of deferasirox on cardiac iron in , thalassemia major impact of total body iron stores. Blood, 2010; 116(4): 537-543.
- [16]. Maria Domenica Cappellini, Alan Cohen, Antonia Piga. A phase 3 study of deferasirox (ICL10), a once-daily oral iron chelator, in patients with B-thalassemia. Blood 2006; 107: 3455-3462.
- [17]. Elliott Vichinsky, Onyinye Onyekwere, John Porter. A randomized comparison of deferasirox versus deferoxamine for the treatment of transfusional iron overload in sickle cell disease. British Journal of Haematology 2006; 136: 501-508.
- [18]. Domenica Cappellini M, Mohamed Bejaoui, Leyla Agaoglu. Iron chelation with deferasirox in adult and pediatric patients with thalassemia major: efficacy and safety during 5 years' follow-up. Blood. 2011; 118(4): 8[10]-[15]3.
- [19]. Daar S, Pathare AV. Combined therapy with desferrioxamine and deferiprone in beta thalassemia major patients with transfusional iron overload. Ann Hematol 2006; [11]: 315-319.
- [20]. Himanshu Goel, Girisha KM and Shubha R. Phadke. Long-term efficacy of oral deferiprone in management of iron overload in beta thalassemia major. Hematology 2008; 13(2): [5]-[8].