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COMPARISON OF THALASSEMIA MAJOR ADOLESCENT CASES WHEN TREATED WITH DEFERASIROX AND DEFEROXAMINE IN TERMS OF MEAN LEVEL OF FERRITIN SERUM

[1]Dr. Humble Bin Ahmed, [1]Dr. Samreen Manzoor Mehar, [2]Dr. Hafsa Rafi
[1]Nishter Hospital Multan
[2]THQ Kharian

Abstract:
Objective: *Our research was aimed at the comparison of the level of mean serum ferritin in the patients of major thalassemia after the treatment of deferoxamine and deferasirox.*
Methods: *Design of our research was randomized control which was carried out at Mayo Hospital, Lahore (Sept, 2016 to August, 2017) on 160 patients including both male and female with an age group of (1 – 14 years). All the patients were managed with blood transfusion in a year once and with a level of serum ferritin (above 1000 mcg/L). Patients were allotted randomly groups A and B respectively deferoxamine and deferasirox group. Iron profile was assessed before and after the treatment. Both groups were applied Sample T-test and paired T-test with a significant P-value as (0.05).*
Results: *Male to female proportion was respectively 96 and 64 patients with a mean age as (7.54±4.21) years. Mean age, weight, height and transfusion duration in deferasirox group was respectively (6.35±4.11 years), (18.01±6.74 kg), (102.04±19.48 cm) and (7.48±3.99 months/year). Whereas, deferoxamine group was observed respectively as (8.74±3.97 years), (20.44±6.77 kg), (102.19±20.85 cm) and (8.14±3.55 months/year). In deferasirox group patients before and after treatment level of serum ferritin was observed as (1385.73±117.01 and 1047.59 ± 117.08) mcg/L, which reduced in this group. Whereas, deferoxamine group before and after treatment level of mean serum ferritin was observed as (1362.58±134.42) and (1124.36±134.52) mcg/L, which also reduced. Before treatment there was a significant variation in the level of serum ferritin with a significant P-value as (< 0.01). There was a high and significant pre and post treatment variation in the level of serum ferritin with significant P-value as (< 0.01).*
Conclusion: *Deferasirox is one of the effective, tolerable and safe chelation therapy in order to treat major patients of thalassemia having an overload of iron overload because of the provision ability of the coverage of chelation with an additional capability of compliance improvement.*
Keywords: *Thalassemia Major, Ferritin, Chelation Therapy, Deferoxamine and Deferasirox.*

*** Corresponding author:**
Dr. Humble Bin Ahmed,
Nishter Hospital,
Multan.

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INTRODUCTION:

The cause of the thalassemia is linked with the limited and reduced hemoglobin (Hb) production in the red blood cells which is also a genetic disease. Disease is carried by parents to children (25%). Family and healthcare department faces burden of the disease in psychological and economical form [1]. Life expectancy can be restricted to (15 – 20 years) because of this disease [1]. Every year there is an addition of five thousand patients all over Pakistan is reported about thalassemia [2, 3].

Complications are attributed to blood transfusion frequency (overload of iron) as various tissues get extra accumulated by iron specifically endocrine cells, liver and heart [4]. Multiple organ failure and mortality is also reported because of the overload of iron in the absence of chelation therapy [5, 6]. In the course of regular transmission of blood with level of serum ferritin, thalassemia and increase in the concentration of liver iron which requires chelation therapy. It has been observed in various research studies that in the management of iron chelation therapy iron associated complications are reduced which improves survival chances and life quality [7].

A dose which is standard is helpful for the removal of excessive iron in (8 – 12 hours) duration within five to seven days as the plasma half-life is short [8]. A daily dose of deferasirox can be acceptably used till sixteen hours for the maintenance of drug plasma level [9]. Mean change in the level of serum ferritin in deferoxamine group was reported as (337±0); whereas, in another research on deferasirox it was observed as (235±44.39) [10, 11].

Deferasirox is pain free because of its regular dose and oral route; it is effective and less time consuming than deferoxamine. Longer half-life of deferasirox is also reported in various other research studies [12]. Our research was aimed at the comparison of the level of mean serum ferritin in the patients of major thalassemia after the treatment of deferoxamine and deferasirox.

PATIENTS AND METHODS:

Design of our research was randomized control which was carried out at Mayo Hospital, Lahore (Sept, 2016 to August, 2017) on 160 patients including both male and female with an age group of (1 – 14 years). All the patients were managed with blood transfusion in a year once and with a level of serum ferritin (above 1000 mcg/L). Patients were allotted randomly groups A and B respectively deferoxamine and deferasirox group. Iron profile was assessed before and after the treatment. Mean change in the level of serum ferritin in deferoxamine group was reported as (337±0); whereas, in another research on deferasirox it was observed as (235±44.39) [10, 11].

We did not include all the cases with anemia other than thalassemia, iron intake cases, allergic cases and iron cheating agents use with thalassemic complications.

Data entry and analysis was carried out through SPSS software. Quantitative variables were expressed in mean and SD values and qualitative variables were expressed in the percentage and frequency. Both groups were applied Sample T-test and paired T-test with a significant P-value as (0.05).

RESULTS:

Male to female proportion was respectively 96 and 64 patients with a mean age as (7.54±4.21) years. Mean age, weight, height and transfusion duration in deferasirox group was respectively (6.35±4.11 years), (18.01±6.74 kg), (102.04±19.48 cm) and (7.48±3.99 months/year). Whereas, deferoxamine group was observed respectively as (8.74±3.97 years), (20.44±6.77 kg), (102.19±20.85 cm) and (8.14±3.55 months/year). In deferasirox group patients before and after treatment level of serum ferritin was observed as (1385.73±117.01 and 1047.59 ± 117.08) mcg/L, which reduced in this group. Whereas, deferoxamine group before and after treatment level of mean serum ferritin was observed as (1362.58±134.42) and (1124.36±134.52) mcg/L, which also reduced. Before treatment there was a significant variation in the level of serum ferritin with a significant P-value as (< 0.01). There was a high and significant pre and post treatment variation in the level of serum ferritin with significant P-value as (< 0.01). Table I, II & III show detailed outcomes with respective figures.

Table – I. Mean difference of serum ferritin level (ng/ml) pre- and post-treatment in deferasirox group

Variables		Number	Paired Difference		T	df	P-Value
			Mean	SD			
Gender	**Male**	54	338.074	1.33	1868.393	53	0.001
	Female	26	338.269	1.079	1598.299	25	0.001
Age Group	**Under 7**	52	338.173	1.294	1884.036	51	0.001
	Above 7	28	33.071	1.184	1510.76	27	0.001
Weight	**Under 19**	52	338.115	1.263	1931.016	51	0.001
	Above 19	28	338.179	1.249	1432.994	27	0.001
Height	**Under 105 cm**	50	338.12	1.256	1903.796	49	0.001
	Above 105cm	30	338.167	1.262	1468	29	0.001
Transfusion Duration	**Under 7**	47	338	1.234	1878.432	46	0.001
	Above 7	33	338.333	1.267	1534.536	32	0.001

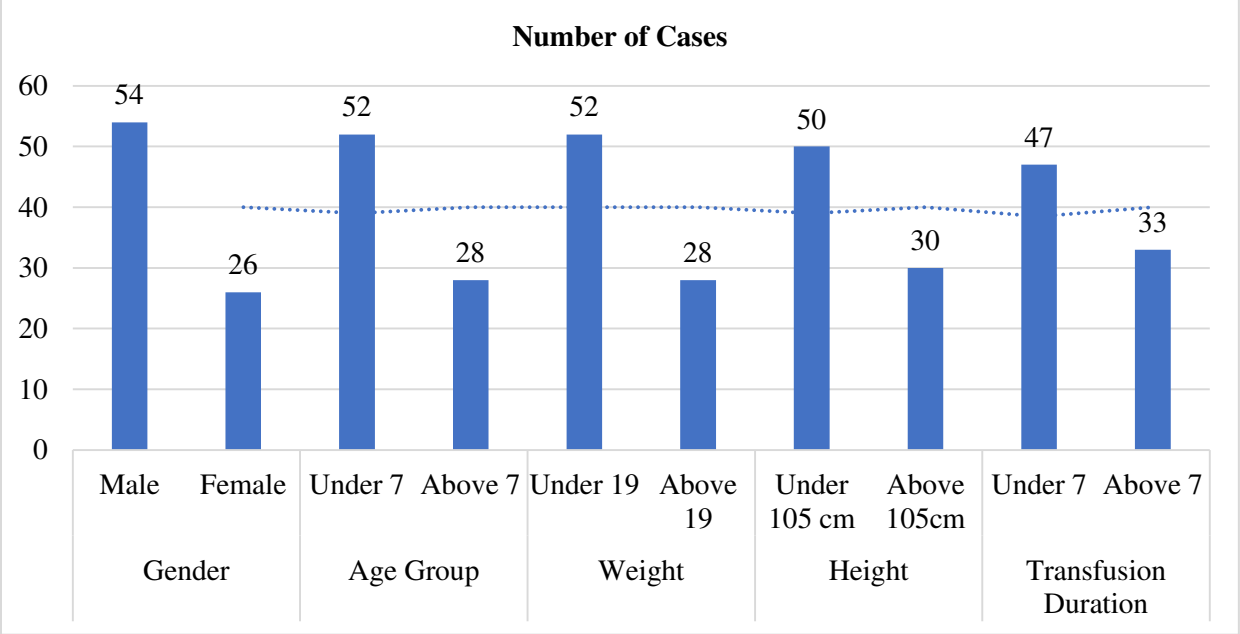


Table – II. Mean difference of serum ferritin level (ng/ml) pre- and post-treatment in deferoxamine group

Variables		Number	Paired Difference		T	df	P-Value
			Mean	SD			
Gender	**Male**	42	238.333	0.928	1663.83	41	0.001
	Female	38	238.079	0.941	1559.627	37	0.001
Age Group	**Under 7**	37	238.162	0.958	1512.482	36	0.001
	Above 7	43	238.256	0.928	1683.185	42	0.001
Weight	**Under 19**	28	238.357	0.911	1383.848	27	0.001
	Above 19	52	238.135	0.95	1807	51	0.001
Height	**Under 105 cm**	26	238.308	0.884	1374.515	25	0.001
	Above 105cm	54	238.167	0.966	1801.978	53	0.001
Transfusion Duration	**Under 7**	34	238.206	1.008	1377.354	33	0.001
	Above 7	46	238.217	0.892	1810.752	45	0.001

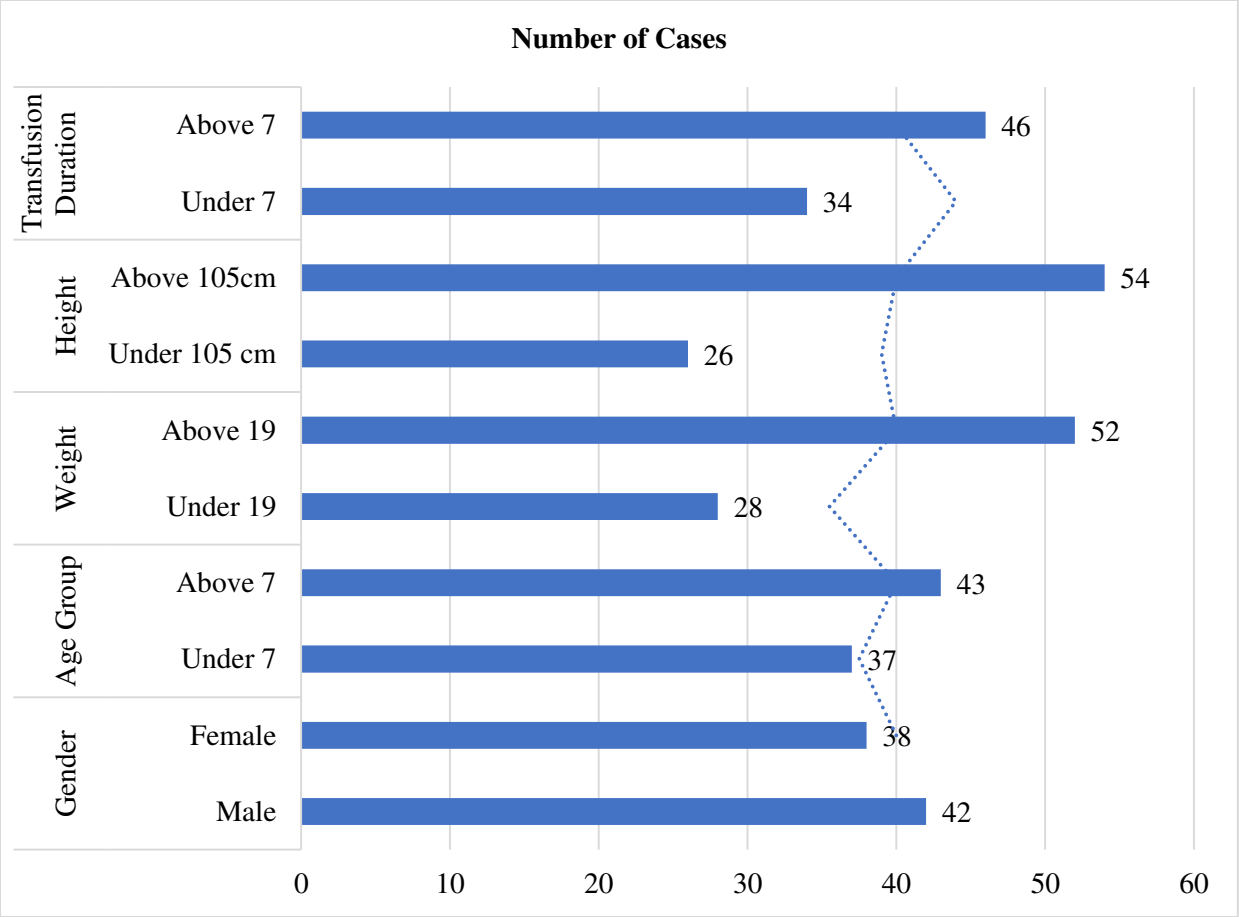
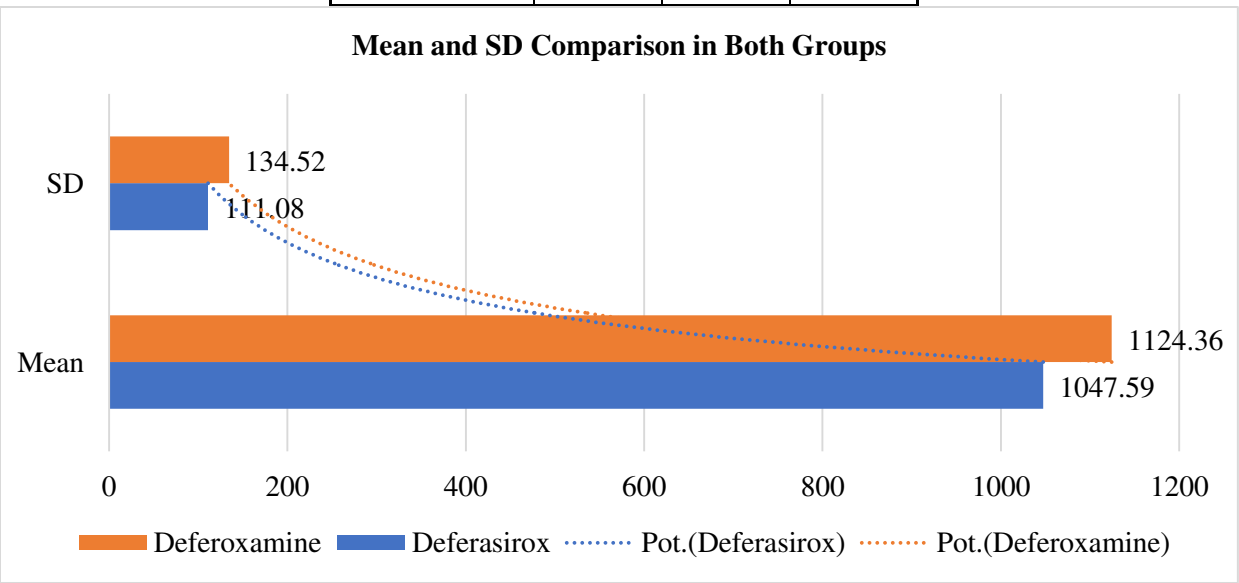


Table – III. Comparison of post-treatment mean difference of serum ferritin level (ng/ml) among deferasirox and deferoxamine groups

Group	Mean	SD	p-value
Deferasirox	1047.59	111.08	0.001
Deferoxamine	1124.36	134.52	



DISCUSSION:

Thalassemia is one of the prevalent and recognized genetic disorder of blood in Pakistan, which is also reported in more than sixty countries all over the world [1, 13,14].

As a result of multiple transfusions of blood iron overload becomes unavoidable in number of cases which makes it a second disease while the treatment of first is continued [15, 16]. Reliable indications cannot be obtained through one-time iron burden measurements. SQUID and MRI are new measurement tools for the iron overload but these facilities are scarcely used in Pakistan as it is costly and complex.

We can judge the chelation therapy importance because of the ferritin level which has an inverse association with the patient's survival [15]. For the children survival monthly chelation therapy accompanies the transfusion of blood as the annual birth blood transfusion count is (90,000 units) and deferoxamine worth is (22 million dollars) [14, 17]. Increased ferritin level is also linked with liver cirrhosis in numerous research studies [16 – 21].

There are limited clinical trials are available for the treatment of thalassemia as Iron chelation therapy is required for life-time [22]. A research analyzed 79 cases of beta-thalassemia with 46 males (58.2%) and 33 females (41.8%) with mean factor as (10.8±4.5 years) [15]. Mean level of ferritin serum was observed as (4236.5 ng/ml) that was high than the normal range as (12 – 122 ng/ml) [15, 23]. It was expected that the level of ferritin serum was low as (3319.6±1925.8 ng/ml) in chelation therapy treated patients against no intake of medicines such as (5514.8±2383.0 ng/ml) [15].

Another author reported long-term observation of the safety and efficacy about iron chelation with deferasirox in adult and pediatric thalassemia patients. In this research almost two third of the thalassemia patients [22]. Pediatric patient's growth and sexual progression in the adolescent with beta-thalassemia has a relevance with multiple factors which include toxicity of iron that may potentially lead to delay in the puberty. Its prevalence has decreased in the availability of iron chelation therapy, number of cases experience the sexual progression and growth-related complications linked with the poor deferoxamine compliance [22]. There are no adverse effects of deferasirox on the children growth which were prone to retardation of the growth because of an overload of iron in the thalassemia patients. Suitable adjustments of dose lead to decrease in the serum ferritin and LIC which highlights dose titration necessity for the negative iron balance achievement. Deferasirox, is a long-term and effective patient's iron overload because of blood transfusions in the cases of thalassemia [22].

Male were dominant over female with a mean age of (7.54±4.21) years. In deferasirox group patients before and after treatment level of serum ferritin was observed as (1385.73±117.01 and 1047.59 ± 117.08) mcg/L, which reduced in this group. Whereas, deferoxamine group before and after treatment level of mean serum ferritin was observed as (1362.58±134.42) and (1124.36±134.52) mcg/L, which also reduced. Before treatment there was a significant variation in the level of serum ferritin, which proves the effectiveness of the deferasirox than deferoxamine without any gender discrimination in the age bracket of (1 – 14 years).

CONCLUSION:

Deferasirox is tolerable, effective and safe chelation therapy for the management of major thalassemia cases having an iron overload because of the easy administration and constant coverage. Deferasirox is one of the effective, tolerable and safe chelation therapy in order to treat major patients of thalassemia having an overload of iron overload because of the provision ability of the coverage of chelation with an additional capability of compliance improvement.

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