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Iron Chelation Therapy in Beta Thalassemia

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Abstract

Background: Iron accumulation is an inevitable consequence of chronic blood transfusions and results in serious complications in the absence of chelation treatment to remove excess iron. Desferioxamine reduces morbidity and mortality although the administration schedule of slow, parentral infusions several days each week limits compliance and negatively affects long-term outcome, so different strategies have been developed to overcome these problems such as deferiprone or deferasirox alone or dual chelator therapy.

Aim of Study: Was to evaluate the effect of monotherapy and alternating therapy of iron chelators (deferioxamine, deferiprone, deferasirox) after six months of follow-up of regular administration of these iron chelators in hematology Clinic in pediatric Insurance Hospitals in Beni Suef.

Patients and Methods: This study was carried out on 120 children with beta thalassemia major in hematology Clinic in pediatric Insurance Hospitals in Benisuef. They were divided into four groups. Group A: 30 patients received oral deferiprone (DFP) at 75mg/kg/day for 4 days/week and subcutaneous desferioxamine (DFO) at 40mg/kg/day for the other 3 days/ week for 6 months. Group B: 30 patients who received oral deferiprone only at 75mg/kg/day in 3 divided doses for 6 months. Group C: 30 patients who received subcutaneous desferoxamine only at 40mg/kg/day daily for 6 months. Group D: 30 patients who received oral desferasirox at a dose of 30mg/kg/day, single dose daily, taken on an empty stomach at least 30 minutes before food for 6 months.

Results: There were highly significant reduction in serum ferritin levels and serum iron levels after chelation therapy in each studied group. There was also elevation in TIBC after chelation therapy in each studied group. The reduction of serum ferritin levels and serum iron levels and the elevation of TIBC were higher in group A (alternating) followed by group C (desferioxamine) followed by group D (deferasirox) and lastly group B (deferiprone). There was no statistically significant difference between the studied groups before and after chelation therapy. There was no significant difference as regard to urinary iron before chelation therapy in all studied group and also between the studied groups of patients after chelation therapy. But 24h urinary iron showed a significant difference in group A and insignificant difference in other groups of patients before and after chelation therapy.

Conclusion: Alternating DFO/DFP has some significant advantages over DFO monotherapy; it can keep a balanced iron load, targets different iron pools & is well accepted by the patients. This approach is more appropriate for well-chelated patients, who have difficulties in continuing DFO monotherapy.

Key Words: *Thalassermia – Haemoglobinopathy – Iron overload – Iron chelation.*

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Introduction

THALASSAEMIA is an autosomal genetic disease characterized by impaired synthesis of polypeptide chains of normal haemoglobin leading to anaemia. It remains one of the major health problems in Mediterriran [1]. In severe cases, in order to improve survival and quality of life, multiple blood transfusions are required. Iron overload is the life limiting complication commonly found in thalassaemics, which may be due to ineffective erythropoiesis, increased gastrointestinal absorption, lack of physiologic mechanism for excreting excess iron, and above all multiple blood transfusions [1].

As the body has no effective means for removing iron, the only way to remove excess iron is to use iron binders (chelators), which allow iron excretion through the urine and/or stool. As a general rule, patients should start iron chelation treatment once they have had 10-20 transfusions or when ferritin levels rise above 1000ng/ml [2].

Iron chelating agents including deferoxamine, deferiprone, and deferasirox which reduce iron overload in these patients in different degrees and therefore reduce morbidity and mortality, including cardiac complications [3].

Because of poor compliance with recommended subcutaneous regimens, the patients become massively iron overloaded and are at risk of early death, principally from cardiac complications, as the infusion can be troublesome, time consuming and painful [4]. The availability of oral iron chelators in recent years has enabled clinicians to tailor chelation therapy to the needs of the patient. Possible regimens are monotherapy with either deferiprone (DFO) or dual chelator therapy, whereby both drugs can be given on the same days (combination regimen) or on different days (alternating regimen) [5].

Patients and Methods

Study design: This study is a comparsion of iron chelators in B thalassemia major in hematology Clinic in pediatric Insurance Hospitals in Beni Suef.

Site of the study: In hematology Clinic in pediatric Insurance Hospitals in Beni Suef.

Patients: This study was done after having approval from ethical committee of research center in Beni Suef University Hospital and informed written parental consent from every case that participates in this research and was carried out on 120 children with beta thalassemia major under follow-up in in hematology Clinic in pediatric Insurance Hospitals in Benisuef. They were 68 males and 52 females with their age ranged from 4-7 years and mean age value of 5.43 ± 1.37.

Clinical assessment: Which included General examination, anthropometric measurements and abdominal examination. All patients were subjected to the following: Full history taking which included Personal history, History of present illness, Family history of any member requiring frequent blood transfusion.

Laboratory investigations: In the form of Complete blood picture, Liver function tests including AST and ALT, total and direct bilirubin. Renal function tests including Serum creatinine, Blood urea Nitrogen. Serum ferritin which was done at start of the study and after 6 months.

Urinary iron excretion for 24 hours by flame atomic absorption spectroscopy which was done at start of the study and after 6 month.

Treatment Methods:

Patients were divided into 4 groups:

- Group A: 30 patients received oral deferiprone (DFP) at 75mg/kg/day for 4 days/week and subcutaneous desferioxamine (DFO) at 40mg/kg/day for the other 3 days/week for 6 months.
- Group B: 30 patients who received oral deferiprone only at 75mg/kg/day in 3 divided doses for 6 months.
- Group C: 30 patients who received subcutaneous desferoxamine only at 40mg/kg/day daily for 6 months.
- Group D: 30 patients who received oral desferasirox at a dose of 30mg/kg/day, single dose daily, taken on an empty stomach at least 30 minutes before food for 6 months.

Results

Table (1) shows no significant difference between studied groups of patients as regard to age of blood transfusion. Also, there is a non significant difference between the studied groups of patients as regard to clinical data.

Table (1): History and clinical manifestations of studied groups at the start of the study.

Items	Group A (N=30)	Group B (N=30)	Group C (N=30)	Group D (N=30)	ANO VA	
					F	*p*
Age of 1 st transfusion (months)	5.10±1.61	5.68±1.64	5.83±0.92	4.91±0.93	2.04	0.11
Inter-transfusion interval (days)	10.93±10.96	10.60±6.67	12.07±7.19	8.60±4.47	0.52	0.66

Clinical data	A (n=30)		B (n=30)		C (n=30)		D (n=30)		Chi-square	
	No.	%	No.	%	No.	%	No.	%	X^2	*p*
Pallor	30	100	30	100	30	100	30	100	0.0	1.00
Jaundice	10	33.3	18	60	20	66.6	10	33.3	5.53	0.13
Hepatomegaly	30	100	30	100	30	100	30	100	0.0	1.00
Spleen:										
Splenomegaly	18	60	17	57	14	46	16	53.3	0.74	0.86
Splenectomy	3	10	4	13.3	5	16.7	5	16.7	1.27	0.73

Table (2): Comparison of the mean values of serum iron status before and after chelation therapy in studied groups of patients.

	Mean ±SD				ANOVA	
	Group A (N=30)	Group B (N=30)	Group C (N=30)	Group D (N=30)	F	*p*
Serum ferritin (ng/ml):						
Before	3201.22±2013.03	3030.37±1538.36	3280.88±1865.31	3140.53±1228.85	0.059	0.981
After	1669.57±790.40	2215.09±1521.65	2112.02±1440.298	2226.80±741.48	0.744	0.530
Difference	1531.65±1441.20	815.28±570.13	1168.86±816.13	913.73±742.02		
Paired t-test:						
t	4.116	4.769	5.547	54.769		
p	0.001*	<0.001*	<0.001*	<0.001*		
Serum iron (ug/dl):						
Before	298.00±102.58	278.07±139.24	271.40±142.69	282.60±89.30	0.132	0.941
After	174.85±61.52	212.73±103.21	177.73±140.92	209.00±87.21	0.576	0.633
Difference	123.15±80.97	65.33±40.44	93.67±19.15	73.60±39.53		
Paired t-test:						
t	5.891	6.257	18.945	7.210		
p	<0.001*	<0.001*	<0.001*	<0.001*		
TIBC (ug/dl):						
Before	213.47±80.36	217.20±69.32	217.67±68.48	213.67±45.04	0.017	0.997
After	303.27±97.97	264.93±75.08	286.20±95.77	267.20±74.06	0.653	0.584
Difference	89.80±60.57	47.73±17.27	68.53±59.99	53.53±53.20		
Paired t-test:						
t	5.742	10.705	4.424	3.897		
p	<0.001*	<0.001*	<0.001*	0.002*		

*Significant.

There were highly significant reduction in serum ferritin levels & serum iron levels after chelation therapy in each studied group. There was also elevation in TIBC after chelation therapy in each studied group.

There were no significant changes as regard to blood count, after chelation therapy in each studied groups and between the four studied groups before and after chelation therapy.

Table (3): Comparison of mean values of white blood cells, absolute neutrophils and platelets counts before and during 6 months of chelation therapy in studied patients.

	Mean ±SD				ANOVA	
	Group A (N=30)	Group B (N=30)	Group C (N=30)	Group D (N=30)	F	*p*
WBCs ($x10^3/mm^3$):						
Before	7.57±2.14	7.23±2.16	7.53±2.18	7.30±1.88	0.097	0.961
After	7.83±1.72	8.43±2.13	7.77±2.02	7.30±1.88	0.861	0.467
Paired t-test:						
t	0.802	1.632	0.406	0.000		
p	0.436	0.125	0.691	1.000		
ANC/mm^3:						
Before	3860.30±311.66	3937.87±323.51	3756.37±327.42	3766.80±327.56	1.055	0.375
After	3881.17±309.50	3973.47±389.85	3777.60±302.28	3758.40±328.05	1.335	0.272
Paired t-test:						
t	0.324	0.850	1.802	0.802		
p	0.751	0.409	0.093	0.436		
Platelets ($x10^3/mm^3$):						
Before	294.40±40.23	301.20±25.71	305.5±35.39	299.67±38.95	0.251	0.860
After	275.67±42.55	283.87±40.29	295.07±39.04	298.33±46.83	0.738	0.534
Paired t-test:						
t	1.190	1.574	2.030	0.087		
p	0.254	0.138	0.075	0.932		

*Significant, during 6 months of chelation therapy is the mean values of weekly done CBC parameters.

Table (4): Comparison of serum ALT, AST, creatinine and blood urea before and during 6 months of chelation therapy in studied patients.

	Mean ±SD				ANOVA	
	Group A (N=30)	Group B (N=30)	Group C (N=30)	Group D (N=30)	F	*p*
ALT (lu/l):						
Before	74.13±12.49	77.07±11.37	74.80±11.31	72.96±10.95	0.336	0.799
After	75.33±10.99	78.60±11.78	78.83±13.29	74.13±9.11	0.639	0.593
Paired t-test:						
t	0.277	0.437	0.915	0.417		
p	0.786	0.668	0.376	0.683		
AST (lu/l):						
Before	82.80±6.78	81.93±6.36	81.13±7.52	80.61±4.07	0.345	0.793
After	82.00±7.87	81.93±5.68	81.23±5.79	81.87±5.20	0.049	0.986
Paired t-test:						
t	0.396	0.474	0.040	0.736		
p	0.698	1.000	0.969	0.474		
Blood urea (mg/dl):						
Before	31.93±6.46	26.27±4.83	27.09±4.85	26.51±5.45	2.113	0.066
After	25.67±4.22	31.73±5.15	27.47±5.61	30.53±7.18	2.383	0.057
Paired t-test:						
t	2.179	2.203	0.195	1.890		
p	0.112	0.106	0.848	0.080		

*Significant, during 6 months of chelation therapy is the mean values of weekly done CBC parameters.

According to this table, there were no significant changes as regard to liver enzymes and kidney functions after chelation therapy in each studied groups and between the four studied groups before and after chelation therapy.

There were no significant differences in serum creatinine before and after chelation therapy.

Table (5): Comparison of creatinine before and during 6 months of chelation therapy in studied patients.

	Mean ±SD				ANOVA	
	Group A (N=30)	Group B (N=30)	Group C (N=30)	Group D (N=30)	F	*p*
Creatinine in (mg/dL):						
Before	0.65±0.07	0.68±0.12	0.63±0.10	0.65±0.16	3.34	0.02
After	0.63±0.09	0.65±0.12	0.61±0.14	0.69±0.13	2.56	0.064
Paired t-test:						
t	2.284	1.000	0.286	0.796		
p	0.038	0.334	0.779	0.439		

Discussion

Beta thalassemias are hereditary blood disorders caused by reduced or absent beta chains synthesis resulting in imbalanced globin chain with early destruction of RBCs and subsequent anemia [6]. Patients with thalassemia major become transfusion-dependent with excess iron deposited in major organs resulting in their damage [7]. This study was done to evaluate the effect of monotherapy and alternating therapy of iron chelators (deferioxamine, deferiprone, deferasirox) after six months of follow-up of regular administration of these iron chelators in the hematology Clinic in pediatric Insurance Hospitals in Beni Suef. In the present study, serum ferritin and iron levels were reduced after chelation therapy in all studied groups. The reduction of serum ferritin and serum iron was highest in group A (alternating) followed by group C (SC desferrioxamine) followed by group D (oral deferasirox) and finally group B (oral deferiprone). There were no statistically significant differences between the studied groups before and after chelation therapy.

The effectiveness of the alternating DFO/DFP was initially reported in Mirbehbahani et al., 2015 **[8]** in a small controlled clinical study (n=7, age 9.4±3.1 years) who used DFO/DFP regimen similar to ours without DFO monotherapy for 6 months only. Baseline serum ferritin was 5536±5220mg/dl vs. 3778±mg/dl at the end of the study. At the six month of the therapy, a non-significant decline in serum ferritin was observed (p=0.08), and a significant reduction in LIC (Liver Iron Concentration) was also determined (p=0.03).

Also our study was in agreement with Waheed who studied 60 patients, the mean serum ferritin fell dramatically from 4500±1250ng/ml at the start of the study to 1250±750ng/ml (alternate therapy group; p<0.001) at the end of the study **[9]**.

In contrary, this was not in agreement with Baksi who found more reduction in mean ferritin levels with oral deferasirox versus SC desferrioxamine with statistically significant difference **[10]**, Hoffbrand found that oral deferasirox had comparable efficacy with SC desferrioxamine **[11]**, Totadri found that oral deferiprone had comparable efficacy as SC desferrioxamine **[12]**, and Sayani found deferiprone more effective than SC desferrioxamine **[13]**.

In this study, there were no significant differences in the mean white blood cells, absolute neutrophils and platelets counts before and after chelation therapy in the studied groups. This was agreed with Song et al., 2014 **[14]**. These study found no changes in mean values of blood count after oral deferasirox or SC desferrioxamine. Arandi found no changes in blood count after SC desferrioxamine or oral deferiprone **[15]**, but this was not in agreement with Hoffbrand who found neutropenia, agranulocytosis and thrombocytopenia after deferiprone. Song found neutropenia and thrombocytopenia after deferasirox **[11]**.

In this current study, there were no significant differences in ALT and AST before and after chelation therapy in the studied groups. This is agreement with Hosen who found no differences with SC desferrioxamine **[16]** and Voskaridou found no differences with oral deferiprone **[17]** but not in agreement with Ratha who found elevation of ALT and AST after oral deferiprone and SC desferrioxamine therapy **[18]**. Grady found elevated ALT and AST with oral deferasirox **[19]**.

In this work, there were no significant differences in serum creatinine and blood urea before and after chelation therapy. This result was in agreement with Yadav who **[20]** found no affection of kidney functions after oral deferiprone or SC desferrioxamine. However, Pepe found transient increase in serum creatinine ≥30% with doses of 20mg/kg and 30mg/kg of oral deferasirox **[21]** Saliba found renal affection with oral deferiprone therapy **[22]**.

24h urinary iron shows a significant difference in group A and in significant difference in other groups of patients before and after chelation therapy. This was in agreement with Salibia who reported that 24 hour UIE (Urinary Iron Excretion) increased significantly in alternating regimen (baseline 41±2.7 to 76±4.9mg/24h at the end of the study, p<0.001). In the DFO monotherapy, 24h UIE increased insignificantly, (p=0.15) **[22]**.

Variation between the results of this study and others could be explained by different number and mean age of studied patients, different presentation of thalassemia, different duration of the studies, variation of degree of iron overload, variation in dose and compliance with iron chelating agents and variation in the methods of evaluation of iron overload in different studies.

References

1- KHOYUMTHEM P., SHARMA A.B., DEVI T.I., SINGH K.R. and SINGH A.M.: Study of Iron Status in Multi-Transfused Thalassaemic Patients in a Referral Hospital in Manipur. International Journal of Health Sciences and Research (IJHSR), 4 (5): 53-8, 2014.

2- SANDHYA RANI P., VIJAYAKUMAR S., VIJAY KUMAR G. and CHANDANA N.: Thalassemia minireview. International Journal of Pharmacology Research, Vol. 3 /Issue 2/71-79, 2013.

3- ANSARI S., AZARKEIVAN A., MIRI-ALIABAD G., et al.: Comparison of iron chelation effects of deferoxamine, deferasirox, and combination of deferoxamine and deferiprone on liver and cardiac T2* MRI in thalassemia maior. Caspian J. Intern. Med., 8 (3): 159-164, 2017.

4- MUSALLAM K.M. and TAHER A.T.: Iron chelation therapy for transfusional iron overload: A swift evolution. Hemoglobin, 35: 565-573, 2011.

5- PANIGRAHI I., MARWAHA R.K. and DAS R.R.: Long-term response to deferiprone therapy in Asian Indians. Ann. Hematol., 89: 135-140, 2010.

6- AGOUZAL M., ARFAOUIL A., QUYOUL A. and KHATTAB M.: Beta thalassemia major: The Moroccan experience-Journal of Public Health and Epidemiology, Vol. 2 (2): pp. 25-28, 2010.

7- ALGREN D.A.: Review of oral iron chelators (deferiprone and deferasirox) for the treatment of iron overload in pediatric patients, 1-22, 2010.

8- MIRBEHBAHANI N., JAHAZI A., AMLASHI H.M. and BEHNAMPOUR N.: Comparative efficacy of deferiprone, deferoxamine and combination of deferiprone and deferoxamine on serum ferritin value in beta-thalassemia

patients. Journal of Krishna Institute of Medical Sciences University, 4 (1): 70-76, 2015.

9- WAHEED N., ALI S. and BUTT M.A.: Comparison of deferiprone and deferrioxamine for the Treatment of transfusional iron overload in children with beta thalassemia major. J. Ayub Med. Coll Abbottabad, 2; 26 (3), 2014.

10- BAKSI A.J. and PENNELL D.J.: Randomized controlled trials of iron chelators for the treatment of cardiac siderosis in thalassaemia major. Front Pharmacol., 5: 217, 2014.

11- HOFFBRAND A.V., TAHER A. and CAPPELLINI M.D.: How I treat transfusional iron overload. Blood, 120 (18): 3657-3669, 2012.

12- TOTADRI S., BANSAL D., BHATIA P., ATTRI S.V., TREHAN A. and MARWAHA R.K.: The deferiprone and deferasirox combination is efficacious in iron overloaded patients with β-thalassemia major: A prospective, single center, openlabel study. Pediatr Blood Cancer, 62: 1592-6, 2015.

13- SAYANI F., WARNER M., WU J., WONG-RIEGER D., HUMPHREYS K. and ODAME I.: Guidelines for the clinical care of patients with thalassemia in Canada. Anemia Institute for Research & Education, Thalassemia Foundation of Canada, ON, Canada, 199-200, 2009.

14- SONG T.-S., HSIEH Y.-W., PENG C.-T., CHEN T.-L., LEE H.-Z., CHUNG J.-G. and HOUR M.-J.: Combined versus monotherapy or concurrent therapy for treatment of thalassaemia. In Vivo, 28: 645-649, 2014.

15- ARANDI N., HAGHPANAH S., SAFAEI S.Z. et al.: Combination therapy - deferasirox and deferoxamine - in thalassemia major patients in emerging countries with limited resources. Transfus Med., 25 (1): 8-12, 2015.

16- HOSEN M.B., KARMOKAR N.C., KARIM M.F., AL MAHMUD R. and MESBAH M.: Association of AST, ALT, ALB and Total Protein with Beta-thalassemia in Bangladeshi Population. International Journal, 3 (1): 991-995, 2015.

17- VOSKARIDOU E., KOMNINAKA V., KARAVAS A., et al.: Combination therapy of deferasirox and deferoxamine shows significant improvements in markers of iron overload in a patient with beta-thalassemia major and severe iron burden. Transfusion, 54 (3): 646-9, 2014.

18- RATHA R. and ALTAEI T.: Therapeutic Drug Monitoring of Chelating Agent Deferoxamine for β-Thalassemia Major Patients. International Journal of Clinical Medicine, 4: 331-342, 2013.

19- GRADY R.W., GALANELLO R., RANDOLPH R.E., KLEINERT D.A., DESSI C. and GIARDINA P.J.: Toward optimizing the use of deferasirox: Potential benefits of combined use with deferoxamine. Haematologica, 98 (1): 129, 2013.

20- YADAV S.P.: Combination of Oral Iron Chelators for Thalassemia. Indian Pediatrics, 53 (3): 199-200, 2016.

21- PEPE A., MELONI A., CAPRA M., CIANCIULLI P., PROSSOMARITI L., MALAVENTURA C. and MAGGIO A.: Deferasirox, deferiprone and desferrioxamine treatment in thalassemia major patients: Cardiac iron and function comparison determined by quantitative magnetic resonance imaging. Haematologica, 96 (1): 41, 2011.

22- SALIBA A.N., HARB A.R. and TAHER, A.T.: Iron chelation therapy in transfusion-dependent thalassemia patients: Current strategies and future directions. Journal of Blood Medicine, 6: 197, 2015.

العلاج بإمتزاز الحديد فى أنيميا البحر المتوسط

يعانى مرضى أنيميا البحر المتوسط من زيادة نسبة الحديد فى الجسم والذى يعد من المخاطر الهامة الناتجة من مرض أنيميا البحر المتوسط لأنه يترسب فى أعضاء جسم الإنسان مثل القلب والكلى والكبد لذا يجب إستخدام أدوية إستحلاب مثل الديسفيروكسامين والديفيربيرون والديفيرازوركس لتقليل نسبة الحديد بالدم والحد من مخاطر زيادته.

الأشخاص وطرق البحث تم إجراء البحث على مائة وعشرين طفل من الأطفال المصابين بأنيميا البحر المتوسط وتتراوح أعمارهم ما بين ٤ إلى ٧ سنة بوحدة أمراض الدم بقسم طب الأطفال بكلية الطب بمستشفى جامعة المنيا فى الفترة من نوفمبر ٢٠١٦ إلى نوفمبر ٢٠١٧.

ولقد خضع جميع أشخاص البحث للتالى : معرفة التاريخ المرضى للحالات، فحص الحالات إكلينيكيا الحالة العامة وطول القامة الوزن وفحص الكبد والطحال، إجراء الفحوصات المعملية المعتادة : صورة دم كاملة بعدد خلايا شبكية وعدد كرات الدم البيضاء والصفائح الدموية، وظائف كلى وكبد كاملة قياس نسبة الفيرتين بالدم، مستوى الحديد بالدم، القدرة الكلية للإرتباط بالحديد، قياس نسبة الحديد فى تجميع بول أربعة وعشرين ساعة.

وتم تحليل هذه النتائج إحصائياً وأثبت الآتى :

إنخفاض واضح لنسبة الفريتين والحديد بالدم وارتفا ع فى القدرة الكلية للارتباط بالحديد بالدم فى كل المجموعات بعد العلاج، وهذا يوضح دور مستقطبات الحديد فى علاج زيادة نسبة الحديد بالدم فى الأطفال المصابين بأنيميا البحر المتوسط. لا يوجد تغيير واضح فى قيم صور الدم وإنزيمات الكبد ووظائف الكلى بعد العلاج بمستقطبات الحديد. يعانى جميع الأطفال المصابين بأنيميا البحر المتوسط من شحوب ويرقان وتضخم بالكبد.

يعتبر العلاج بالتناوب الأكثر فاعلية فى علاج نسبة الحديد بالدم فى الأطفال المصابين بأنيميا البحر المتوسط يليه الديسفروكسامين تحت الجلد يليه الديفرازوريكس (إكسجاد) وأخيراً الديفريبرون ولكن دون فروق ذات دلالة إحصائية.