

Research Article

Impact of Diet Modification on Serum Ferritin Level in Thalassemia Children

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- Iron absorption

Abstract

Background and Aim: Blood transfusion is the main treatment for people who have moderate or severe thalassemias. The main side effect of transfusion therapy is that the patient develops iron overload, which lead to serious damage to the internal organs. Many foods can play an important role in decreasing iron absorption from the intestine and that could improve the prognosis of these patients. The aim of our study is to detect the effect of diet adjustment in thalassemia children, to a more iron-excreting and less iron-absorption diet, on their level of serum ferritin.

Patients and Methods: In a randomized case control study, 36 thalassemia patients presented to the hematology/oncology center at the Maternity and children Hospital (MCH) in Almadinah Almounourah, KSA in the period from January 2014 to July 2014 were observed prospectively for their serum ferritin level. The cases were asked to follow a diet that limits iron absorption and increases iron excretion.

Results: Serum ferritin level is significantly decreased in cases after 6 months of diet iron restriction more than in controls (p value =0.03).

Conclusions: Restriction of foods that contain iron and increase intake of foods that excrete iron from body can significantly decrease serum ferritin level in thalassemia children.

Recommendations: According to our results, control of diet and following food regimens that can minimize iron absorption and maximize iron excretion are of great benefit for thalassemia children and can act as an adjuvant for drug chelation therapy.

ABBREVIATIONS

RBCs: Red Blood Cells

INTRODUCTION

Thalassemia is a hereditary blood disease that causes formation of an abnormal hemoglobin and consequently excessive destruction of red blood cells (RBCs). For sever thalassemia blood transfusion is the main therapy. Transfusion therapy has many side effects of these is iron overload which can cause vital damage to body organs such as liver, heart, pancreas, thyroid, pituitary gland and other endocrine organs with multiple disabilities [1].

It is well known that blood transfusion is the main cause of iron overload in thalassemia patients but it is found that even those with thalassemia inter media, with minimal or no transfusions

have high ferritin levels. Besides, it is found that thalassemia inter media patients have high rates of iron absorption from gut that reaches 3 to 4 times those of normal person [2].

A variety of foods has the ability to decrease iron absorption from intestine and therefore can improve thalassemia patients' prognosis. These foods include; dairy foods that contain calcium; high fiber foods due to its phytate content and coffee and tea that have poly phenolic compounds. Iron binding poly phenols are common in foods and can be found in cereals, vegetables and spices [3]. Similarly, curcumin can highly change proteins involved in iron metabolism in our bodies, suggesting that curcumin can be a powerful iron chelator [4]. The effect of coffee on non-heme iron absorption is a subject of interest. It is found that a cup of coffee reduces iron absorption from a meal by 39% as compared to a 64% decrease with tea, which is a potent iron absorption inhibitor. Drinking of coffee with a meal or one hour

after meal can decrease iron absorption from 5.88% to 0.97 while no decrease in iron absorption occur when coffee is taken one hour before meal of [5]. We assume that when we modify the diet of thalassemic patient by adding foods that have iron chelating activity together with low iron diet to design a specific food regimen this will improve the prognosis and prevent thalassemic patient to suffer from iron overload complications. The aim of our study is to detect the effect of modifying the diet of thalassemic patients to a less iron containing and more body- iron excreting diet on the level of serum ferritin.

MATERIALS AND METHODS

In a randomized case control study 36 thalassemia patients presented to the hematology/oncology center at the Maternity and children Hospital (MCH) in Almadinah Almounourah, KSA in the period from January 2014 to July 2014 were observed prospectively for their serum ferritin level. The cohort of patients were randomized by taking 3 cases to 1 control so totally we had 24 cases and 8 controls as 4 patients were dropped from the study either due to failure to have their serum ferritin level or to communicate with them. Patients' consent was taken either from their parents or from patients themselves when they age more than 13 years. An ethical committee agreement was taken from the hospital where the study was done.

Inclusion criteria in our study are all thalassemia major patients presented to the hematology/oncology unit at the MCH hospital in Almadinah Almounouraha, KSA, during the period of the study that are on regular transfusion therapy for the previous year, aged more than 5 years and accepted voluntarily to participate in this study. We excluded those patients who have language barriers due to difficulty in communication with them.

An interview was made with each case and their parents where the authors explained the study and provide the parents with 3 lists; one for foods to be avoided, the other is for foods that recommended to be eaten, and a third list for a variety of different dishes for each meal Table 1. Each participant has a sheet containing his/her socio-demographic information, past history, investigation, frequency of transfusion therapy, dose of chelating agents and, for cases only, the sheet contain also a diet therapy table. Each week during 6 months follow up period the authors check the cases compliance to the recommended diet regimen through telephone calls with their parents.

Serum ferritin level is recorded at the start of our study for each participant (cases and controls) and is considered as the

baseline ferritin level. Ferritin level is evaluated after the end of the follow up period for both cases and controls.

Statistical analysis

Clinical and biological parameters were described using percentages, medians, and ranges. Groups of patients were compared using the Mann-Whitney test and Kruskal-Wallis one-way analysis of variance for continuous variables and chi-squared test for categorical data. Pre and post intervention ferritin level were compared using Wilcoxon signed-rank test. A *p-value* < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

A total of 36 thalassemic patients were treated at the hematology /oncology department at MCH and were involved as the cohort of our study. Of these, 24 were randomized as cases and followed a strict diet regimen for 6 months duration while other 8 patients were randomized as controls. Four patients were dropped out of the study because of either failure of communication or failure to follow their serum ferritin level. Of 24 cases, their median age was 10 years (range 5-20), 11 (45.8%) were boys and 13 (54.2%) were girls. The cases had a median age at diagnosis of 7 months (range 1-36). Eleven (45.8%) cases had splenectomy with a median duration science splenectomy of 24 months (range of 6- 72). Characteristics of cases and controls involved in the study are presented at Table 2. Baseline ferritin (before the start of study) had a median of 3538.5 ng/ml (range from 1484-7079) and its level after 6 months of diet control had a median of 2456.5 ng/ml (range from 1106 to 6754) in cases. In controls, the baseline ferritin had a median of 3194 ng/ml (range from 200 to 5183) and its level after 6 months had a median of 3033 ng/ml (range 2000-3873). The difference in ferritin level before and after start of the study is shown in table 2.

Baseline ferritin level showed no significant difference between control and cases, neither when cases were compared as one group (*p* = 0.34), nor when cases were classified based on patient compliance into low compliance, medium compliance, high compliance (*p* = 0.26). Table 3 shows the differences between serum ferritin before and after study in controls; whole group; and in low, medium, and high diet compliance subgroups.

Ferritin is the storage form of iron in human body. The normal serum ferritin level ranges from 12-300 ng/ml in males and 12-150 ng/ml in females. In Thalassemia children, serum ferritin level is usually used to estimate the iron overload status. Elevated serum ferritin level is usually an indicator of increase iron

Table 1: Lists of allowed or prevented foods for cases.

Foods to avoid	Appropriate Foods
Egg Yolk	Egg white
Jam	Honey
Dried fruits, Dates	Milk Products (Cheese, Cream, Yogurt, Butter)
Tomatoes, Peppers, Broccoli	Bran Bread, Cereals, Beans
Red Meat, Liver	Chicken breasts, Fish
Dark chocolate	Milk, Coffee, Tea
Green leaves (parsley, watercress, spinach)	Cabbage, Carrots, Onions

deposition in body organs. This results in many complications to thalassemia patients including, heart failure, hepatic failure, hormonal imbalance and growth failure. Iron chelating drugs have an important role to eliminate the excess ferritin levels. Similarly, control of diet through limitation of foods that contain higher levels is a way to minimize iron intake in Thalassemia patients. Recently, certain foods and beverages are found to help iron body excretion and minimize iron absorption [4-6]. This can be of a great help in thalassemia patients and can act as an adjuvant to drug chelating agents. In our study, we were advised by a clinical-nutrition specialist about the types of foods, which can help iron excretion and decrease iron absorption. We used these foods to make lists of meals to be given to families who have thalassemia children and advised them to follow this diet regimen for a period of 6 months. Our results (Table 3) showed that within the 24 cases, who are thalassemia children followed a specific diet regimen, which help excretion of iron and minimize iron absorption for a period of 6 months; the serum ferritin level is significantly (p value = 0.002) decreased. While in controls (thalassemia children without diet control) the serum ferritin

level is not significantly decreased (p value = 0.37). As shown in table 2 the change in serum ferritin when compared between the cases and control groups was significant (p= 0.03). The cases group showed a decline in ferritin level. These results are concomitant with the results of another study [7], which proved that many foods can interfere with iron absorption from gut, and decrease the serum ferritin level. Our study proved that this can also occur in thalassemic children.

Our study showed also that there is only significant difference in serum ferritin level before and after the study in cases with high diet compliance but there is no significant difference in serum ferritin level in between low and medium diet compliance cases, which indicate the significance of compliance in decreasing the serum ferritin level using diet control. On the other hand, an effect of diet regimen might have been masked due to the small numbers in the low and medium compliance subgroups. There was no significant difference between the baseline serum ferritin level between cases and control (p value = 0.34), supporting the conclusion that the effect seen after the study was not due to different levels of starting ferritin levels.

Table 2: Characteristics of cases and controls involved in the study.

	Cases N=24	Controls N=8	p value
Age (years)	10 (5-20)	12 (8-15)	0.7
Age at Diagnosis (months)	7 (1 - 36)	12(3-24)	0.6
Male: Female	1-12	1.7-1	0.7
Socioeconomic level			
low	15 (62.5%)	4 (50%)	0.6
middle	5 (20.8%)	3 (37.5%)	
high	4 (16.7%)	1 (12.5%)	
Other siblings with Thalassemia	20 (83.3%)	7(87.5%)	0.8
Splenectomy	11 (45.8%)	1 (12.5%)	0.09
Duration since splenectomy (months)	24 (6-72)	72	
On Chelating agents	24 (100%)	8 (100%)	
Number of blood units transfused during study	1.5 (1-2)	1.5 (1-2)	
Chelating Agents Compliance			
low	0	0	0.1
medium	3 (12.5%)	3 (37.5%)	
high	21 (87.5%)	5 (62.5%)	
Diet Compliance			
low	4 (16.7%)	n/a*	
medium	9 (37.5%)	n/a	
high	11 (45.8%)	n/a	
Difference in ferritin level**	-510 (2447 to -4736)	240 (1839 to -1310)	0.03

Values are presented as median (range) and numbers (Percent %).

*n/a: not applicable.

**Difference in ferritin level= ferritin level after the end of the follow up period - baseline ferritin level before the start of the study

Table 3: Ferritin level before and after the start of our study.

	Ferritin level before the start of study	Ferritin level after 6 months	p value
Cases totally (n=24)	3538.5 (1484-7079)	2456.5 (1106- 6754)	0.002
Low compliance cases (n=4)	5070 (2309-7079)	2388.5 (1956- 6462)	0.14
Medium compliance cases (n= 9)	3221 (1484-5160)	2352 (1229- 5443)	0.11
High compliance cases (n= 11)	4142 (1649-6754)	2883 (1106- 6754)	0.01
Controls (n=9)	3194 (200-5138)	3033 (2000- 3873)	0.37

Values are presented as median and range.

Pre and post intervention ferritin level were compared using Wilcoxon signed-rank test.

The median of serum ferritin levels in the control group before and after intervention were comparable with no significant change in a period of 6 months. This can draw attention to the fact that drug chelation therapy alone can maintain to a limited extent serum ferritin level from marked increase in thalassemia patients but does not cause it to decline, while the association between drug chelation and diet regimen as happened in the cases included in our study may cause ferritin level to head towards declining under chelation therapy. This may prove the role of diet regimen as an adjuvant therapy for drug chelation in thalassemia patients.

CONCLUSIONS

Limitations of foods that contain iron and increase intake of foods that excrete iron from body can significantly decrease serum ferritin level in thalassemia children and can act as an adjuvant to the chelating agents.

LIMITATIONS OF OUR STUDY

Small number of cases and controls are the main limitation of our study. Besides, short follow up period is another issue. We may have more significant results with prolonged study period.

RECOMMENDATIONS OF OUR STUDY

According to our results, control of diet and following food regimens that can minimize iron absorption and maximize iron excretion are of great benefit for thalassemia children and can act as an adjuvant for drug chelation therapy.

FUTURE WORK

A larger multi-centric randomized case-control study including most of hematology centers in the province of Almadinah Almounourah, KSA, is planned to be done for better analysis of data and explaining of the effect of diet control on the serum ferritin level in thalassemia children.

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