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Determining the Change of Hormonal and Biochemical Parameters in the Thalassemia Major Patients Over 3 Years

Mohammad-Reza Mohajeri-Tehrani [1], Mobina Ostadi [2], Hadis Gerami [3], Bagher Larijani [4], *Zohreh Hamidi [5]

[1] MD, Prof, Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

[2] BS, Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

[3] MSc, Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

[4] MD, Prof, Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

[5] MD MPH, Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Background: Endocrinopathies are common complications in Thalassemia Major (TM) patients. They are important as secular trends of complications in childhood as a critical period for growth and development. The present study, then, aimed to investigate these complications in children and young adults.

Methods: 34 TM patients, with the mean age of 19 ± 6 y/o, entered this study. Female to male ratio was 21/13. Their medical history was obtained by review of medical records. Data about FBS, AST, ALT, TG, cholesterol, and ferritin, TSH, LH and FSH was collected. Due to the lack of normality of some continuous variables, an appropriate transformation method was implemented to convert them to normal distribution. Repeated measure ANOVA was used to assess change of outcomes across time. Correlations between different parameters were also calculated.

Results: After 3 years, only FBS changed significantly in comparison to phase 1 and 2 results (P-value=0.028). Ferritin in the first phase significantly correlated with ALT (P-value = 0.021), in the second phase with AST (P-value=0.029) and ALT (P-value=0.002) and in the third phase with FSH, LH and TG (P-value=0.047, 0.020, 0,027, respectively). In the first phase AST correlated with TG and cholesterol (P-value=0.015, 0.001, respectively) and ALT with cholesterol (P-value <0.001). ALT correlated with TG in the second phase (P-value=0.040). ALT and AST correlated with cholesterol in the third phase (P-value=0.002, 0.007, respectively).

Conclusion: Hormonal parameters do not show significant change during a 3 years period in TM patients.

Key Words: Biochemistry, Cohort, Endocrinopathies, Hormones, Thalassemia.

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Corresponding Author:

Zohreh Hamidi, MD MPH, Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran. Email: zohreh.hamidi@gmail.com

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1- INTRODUCTION

Thalassemias as the most prevalent monogenic disorders worldwide are a group of congenital diseases that their most common feature is anemia. Disturbances of genesis of beta-globin chains of hemoglobin lead to beta-thalassemia major with features of erythropoiesis and hemolysis; so chronic transfusions are vital for them (1).

Hypertransfusion leads to iron overload, a malicious event that negatively affects multiple systems including the endocrine system. Duration of transfusion therapy is the most important factor in endocrine malfunction (2). Ferritin is a standard criterion for iron overload. Due to its importance, many studies have investigated the correlation between it and endocrinopathies (3) (4).

About endocrine complications, hypogonadotropic hypogonadism is found to be the most prevalent, as high as 42% in one study (5), and 44–65% in another study (6).

Impaired glucose metabolism is also another complication with a differently reported prevalence. Cario et al, acclaimed the prevalence of 5% for diabetes and 27% for IGT (7**).** Data from Italy showed the prevalence rate of diabetes to be 5–17% (6).

Hypothyroidism is also a common finding in thalassemia major, reported to be as high as 21% (8**).** Our studies in Iran showed the prevalence of hypogonadotropic hypogonadism, hypothyroidism, impaired fasting glucose and diabetes as 10%, 10%, 10% and 7%, respectively (9) (10). As patients get older, endocrinopathies become more prevalent. Age of 10 has been reported as the age that at least one endocrinopathy appears. (6).

Although there is a bulk of studies about the prevalence of endocrine disorders and the cut-off age of their incidence (11), little is known about their secular trend. One study on adults, with the mean age of 40 y/o, reported changes of endocrine disorders in 5 years (6).

But we didn't find such a study in regard to children and young adults. As childhood is a critical period for growth and development, we tried to find the secular trends of these disorders in children and young adults.

2- METHODS

2-1. Study protocol

Major beta-thalassemia patients, 34 cases with the mean age of 19 ± 6 y/o (10-34 years), entered this study. Female to male ratio was 21/13. Their medical history was obtained by review of medical records. Information about biochemistry and hormonal blood evaluation including FBS, AST, ALT, TG, cholesterol, ferritin, thyroid-stimulating hormone (TSH), luteinizing hormone (LH) and follicle-stimulating hormone (FSH), was entered in the data sheet.

2-2. Statistical Analyses

Continuous variables were summarized as means, SDs, and ranges. Categorical variables were summarized as simple percentages. Normal distribution of continuous variables was assessed using the Shapiro-Wilk test. Due to the lack of normality of distribution in some continuous variables, appropriate transformation method was used to convert them to normal distribution. Repeated measure ANOVA was used to assess change of outcomes across time. Correlation tests were also applied for finding the relations between different parameters. SPSS was used for analyses and all p-values were two sided with the level of significance set at <0.05.

3- RESULT

After 3 years, only FBS changed significantly in comparison to phase 1 and

2 results (P-value=0.028). The differences between changes of parameters between the first and second phase and also between phase 2 and phase 3 were not significant. Ferritin in the first phase significantly correlated with ALT (P-value=0.021). In the second phase, it correlated with AST (P-value=0.029) and ALT (P-value=0.002). In the third phase, it significantly correlated with FSH, LH and TG (P-value=0.047, 0.020, 0,027, respectively). ALT and AST showed significant correlations with TG and cholesterol in different phases. In the first phase, AST correlated with TG and cholesterol (P-value=0.015, 0.001, respectively) and ALT with cholesterol (P-value<0.001). ALT correlated with TG in the second phase (P-value=0.040). ALT and AST correlated with cholesterol, in the third phase (P-value=0.002, 0.007, respectively). **Table 1** shows other characteristics of the parameters.

Table-1: Some characteristics of the parameters

Quantity / Parameters	First phase	Changes between phase 1 and 2	Changes between phase 2 and 3
FSH	5.221 ± 5.1	-0.108 ± 4.3	-0.160 ± 2.6
LH	4.435 ± 4.2	-0.321 ± 3.8	0.012 ± 5.6
TSH	2.597 ± 1.2	1.387 ± 6.8	-1.086 ± 6.2
FBS	95.529 ± 7.9	0.181 ± 13.1	12.062 ± 36.1
AST	38.636 ± 23.9	-3.825 ± 21.2	2.553 ± 27.0
ALT	41.787 ± 38.3	-4.183 ± 28.8	2.156 ± 40.6
TG	122.935 ± 61.5	11.392 ± 50.2	-15.032 ± 64.3
Cholesterol	101.937 ± 20.7	6.866 ± 28.0	1.656 ± 26.6

4- DISCUSSION

In our study hormonal and biochemical parameters, except FBS, didn't show significant changes in 3 years. A study in adults with the mean age of 40 y/o reported changes in the prevalence of endocrine disorders in 5 years (6)**.** In their patients on deferasirox, cases of endocrinopathies decreased. The significant changes in many of the parameters in our study may be due to the younger age of our patients and shorter duration of the study. However, FBS increased significantly in the third phase. In the same line, there are studies that show that the mean age of patients in impaired glucose metabolism group is lower than the mean age of patients with hypothyroidism and hypogonadism. This might mean that FBS needs a shorter duration to be affected by thalassemia disease (12) (13) (14) (15).

Other than AST and ALT that are hepatic parameters, ferritin was only related to FSH, LH and TG in the third phase. This is in conflict with the findings of some other studies (3) (4).

and in agreement with other ones (16) (17). However ferritin is not only a marker of iron overload but also is a marker of inflammatory status. Thus, ferritin is not a gold standard for measuring iron overload (18).

ALT and AST, as other parameters for liver iron overload showed significant relationships only with TG and cholesterol. Before this, there were studies showing that TG and cholesterol are elevated in non-alcoholic fatty liver disease (NAFLD) and AST and ALT are also raised in NAFLD (19) (20).

The fact that in our study, the parameters which are signs of iron overload generally showed no significant relationship with

many investigated parameters may be attributed to the low sample size of our study. In addition, we did not measure iron overload by liver biopsy, or MRI or superconductive quantum interference device (SQUID).

4-1. Limitations of the study

The main limitation of our study is the low sample size and the use of medical records of patients instead performing measurements during the study. However, our study consists of three phases, and so, changes are measured in an additional phase between the first and the last phase.

5- CONCLUSION

Hormonal parameters do not show significant changes during a 3 years period in transfusion dependent thalassemia patients.

6- ETHICAL CONSIDERATIONS

The procedures were approved by the ethics committee of the Endocrinology and Metabolism Research Institute of Tehran University of Medical Sciences (EMRI of TUM) and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

7- CONFLICT OF INTEREST

None.

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