Iron Overload Complication in Thalassemia Patients

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Abstract

Thalassemia is an inherited disorder. All the types of thalassemia that require continuous blood transfusion, lead to increase of absorption of iron, which will lead to iron overload eventually. The precipitation of iron will affect many organs in the human body, and can be measured by S- ferritin.

In this study, patients with all kinds of thalassemia that require multiple blood transfusion, have been evaluated for the level of ferritin and iron overload as well as other complications such as liver diseases, heart diseases, bone disorders, and hormone disorders. One-hundred patients have been selected randomly with different ages to evaluate the serum ferritin, calcium level, liver enzymes, and Hb by use enzyme linked assay. This study confirms the use of chelation therapy to remove the iron overload.

Keywords*: iron overload, thalassemia, GPT GOT , hormone disorder*

Introduction

Hemoglobin, which is a red pigment that gives the RBCs their color, is presented around the RBCs. This pigment has the ability to transport loaded oxygen from the lung to other cells of body tissues and carries carbon dioxide from tissues toward lung [(1)]. The globulin, which is the proteinaceous subunit of the hemoglobin, contains two kinds of chains; alpha and beta. These two chains are in association with the hem group that contains the iron atoms in form of Fe2+. Despite the fact that the two chains are required for normal oxygen transportation, the alpha chain is expressed before birth, however,the beta chain does not and its expression is delayed for few months after birth. The synthesis of hemoglobin is controlled by specific genes in DNA. There are four genes control alpha chain expression whereas there are two genes control the beta chain expression [(2)].

The normal value of serum ferritin (a protein that stores iron in the body) is160-180 mg/dl and the daily requirement is deferent from man and woman. In the adult man (19 years and older) the value is about 8mg/dl,whereas this valuein the pregnant female may reach up to 27mg/dl. However, this value is only about18mg/dl in non-pregnant women.

Many food sources are rich in iron especially animal products such as meat, liver, fish, and chicken. The non-hem sources such as plant iron.

We need to examine hemoglobin (HB test) in many cases such as the state of anemia (hemoglobin deficiency) and the iron overload which leads to hemochromatosis. Generally, the determination of the level of iron is carried out at the morning because during this period, the level of iron is in the maximum. Usually, the measurement of the level of iron, which represents the iron binding with transferrin, the total iron binding capacity, the ability of iron of binding with transferrin (T1BC) and the amount of iron. The mean the amount of iron that binds with transferrin is (400-250) mg/dl and transferrin saturation is (10%-50%) in men and (15%-50%) women ferritin. This gives the mostindicators to the level of iron normally[(3)].

Heamatochromatosis means the accumulation of iron more than the normal value, which is genetic disorder, and may be resulted from the repetitive blood transfusion such as in thalassemia.

The symptoms and signs of Hematochromatosis are the change in the skin color into dark color, jaundice due to elevated bilirubin which gives yellowish of color of the skin, and painful joints that occurs due to iron precipitation in different organs of the body such that occurs in thalassemia.

Finally the iron overload (Haemotochromatosis), which occurs as a result of repeated transfusion of blood to the patient of thalassemia represents one huge

problem to these patients because the human body does not have the ability to eliminate the excess iron, therefore, patients with thalassemia suffers from many disorders and disease and discoloration of patient such as liver disease,diabetes, heart abnormalities, disease Ferro protein disease, and decrease the secretion of hormones [(4)]

Continuous blood transfusion to the patient with thalassemia the main reason of iron overload which precipitate in the deferent organ and tissue and cause many deferent problems, to prevent happen iron over load use long term of chelation treatment to prevent (indochrinopathies and cardiomyopathy) [(5)]

Material and Method

About100 patients of thalassemia, who are all suffering from iron overload, have been selected randomly regardless of gender, age, and social background at the Center of Thalassemia in Kut province. by drawing venous blood from the patients ,preserving their blood by cooling using the refrigerator not long to make the tests like s-calcium ,s-ferritin and the other tests in table (2),and the instruments use in the tests , the electrophoresis and spectrophotometer, all the tests carried out in labs of kut centerof thalassemia treatment

Statistical Analyses

The data statistically analyzed by using spss-18 and sample t-test statistical program and the result of analyzing find the parameter report and the control and p-value for every parameter report p-value 0.05 or less consider significant.

Findings

The results showed that most of the patients were at the ages of youth and childhoods. Most of the sampled patients were from relative parents who were with different education levels; however, most of the parents were non-educated (Table 1). Most of the families were having one patient with the average value to the serum ferritin was about 4316 ng/ml. Deferoxamine, which is used as chelating factor to prevent overload of iron, is only used in patients who are less than 18year of age. To diagnose thalassemic patients, electrophoresis method is used routinely in order to differentiate between the normal hemoglobin and defected hemoglobin. This testcould differentiate the patients withthalassemia according to the particle size of the hemoglobin and electrical charge of these particles. All other parameters measure with colorimetric method which the concentration proportion with depth of color includes the serum Ca^{2+}, serum ferritin, serum GOT, serum GPT, serum Urea,and serum Creatinin .

Table1. Classification of the thalassemia patients according to age, gender, and relativity.

	Classes of age	frequency	Ra
Age	< 1	1	1%
	1 - 5	15	15%
	6 - 15	46	46%
	16 - 25	26	26%
	26 - 50	10	10%
	50 <	2	2%
	Total	100	100%
	Mean	10.75	
Gender	male	54	54%
	Female	46	46%
	Total	100	100%
Relationship	Non relatives	11	11%
	relatives	89	89%
	Total	100	100%

Cont... **Table1. Classification of the thalassemia patients according to age, gender, and relativity.**

Number of families with more than one patient	1	74	74%
	2	20	20%
	3	5	5%
	4	1	1%
	Total	100	100%
Types of disease	Major thalassemia	66	66%
	trait	23	23%
	minor		
	sickle	3	3%
	Thalassemia and sickle	2	2%
	other	6	6%
	Total	100	100%

In this study 100 patients with thalassemia have been selected randomly during 2018. Their ages were from one month to 30 years. However, only few were at 51 years of age and most of them were less than 30 years. The number of male and female was nearly equal, The table also shows the presence or absence of more than one patient in the same family and the frequency of the complicating disease (Table 1). Most of patients were taking chelating factor Deferasirox.

Table 2. Differences in some serum parameters between patients with thalassemia and healthy looking people.

variable	**N**	**Patient gm/dl**	**df**	**control**	**P- value**
Ca mg/dl	100	8.9970± .80722	99	10	0.000 S
S ferritin ng/dl	100	4316.1800±311.32261	99	150±80	0.000 S
GOTIU/Ll	100	38.9740± 3.00802	99	28±4	0.000 S
GPTIU/L	100	46.4200±5.00630	99	30±5	0.000 S
S-Bilirubin mg/dl	100	0.90.5±0.5		0.7±0.3	0.00s
B urea mg/dl	100	27.2500±1.59964	99	30	0.089 NS
S creatinin mg/dl	100	0.3630±.01186	99	0.4	0.070 NS
HB g/dl	100	8.92±0.8		13. ±0.6	0.00 s
Iron ng/dl	100	250±70	99	75±15	0.00s

Table 2 shows the differencesin value of some parameters between the patients' serum and the apparently healthy individuals. The value of the serum ferritin was highly elevated in patient than in control (4316± 311.22 ng/dl, whereas the normal 150± 80 ng/dl). No bilirubin was detected more than normal (no jaundice). In addition, enzymes of liver were also with high reading level than to the normal GOT and GPT as reported. The HB less than to the normal especial before transfusion HB=8.92±8 when the control equal13±0.6

.so can see the deference and the anemia that the patient suffering as a result of decrease of HB.

Discussion

From the data parameters changing than to the normal as a result of elevated ferritin in blood,and this could be attributed to the precipitation of iron on deferent glands and organs. The free iron found in the blood is highly toxic to cells in the body. On the other hand, iron in serum bind with transferring , however, some of iron may present as non-binding iron especially when the concentration of iron exceeds the iron binding capacity of blood. There are a number of mechanisms to protect against the toxicity of free iron, which binds iron to various parts of the tissues. ferritin appear in the blood although its role is unknown thalassemic patients need blood transfusion continually causing excess load of iron in human body. These patients not have any physiological method to remove excess load of iron. Non transferrin iron binds easily to translated with calcium canal to the liver (hepatocyte),heart (cardiac myocytes),and the other endocrine glands. The accumulation of iron in these organs leads to multiple complications. The most important complication of iron over load is the siderosis of heart, which may lead to heart failure, and considered as main reason of death. In addition, liver dysfunction could be observed for the same reason. Reports indicated that 25%of cardiac siderosis affect the patient of thalassemia in South East Asia and affecting 15 -20 % in Middle East [6].

From the data in (Table1), we found that the level of calcium was less than normal in the patients because of the precipitation of iron on and in the parathyroid gland, which will reduce the secretion of parathyroid hormone. This hormone is the main factor that controls the level of calcium and phosphorus ion iron over load [7]. This occurs in large numberof patient of thalassemia as a result of increase absorption of iron in gastrointestinal tract and multiple transfusion of blood and inappropriate iron chelation therapy and this will lead to accumulation of iron in liver, endocrine glands, and heart eventually [8,9].

In our study, we found that the level of ferritin was 4316 gm/dl and this value is about eight fold higher than normal (Table 2), which lead to precipitate iron in liver and injury and fibrosis. Therefore, the levels of the transaminase enzymes s-GOT and GPT were highly elevated in comparison to the normal (s-GOT 39IU/L and S-GPT 46 IU/L, respectively) [10,11.12].

Liver is the main organ to metabolism and for storage iron, hence, highly affected by the toxicity of iron. When iron accumulates in liver, it may cause lipid peroxidation may and may lead to hepatocyte necrosis and apoptosis. The end results for this pathway is hepatic fibrogenesis, which affectsthe collagen production and lead to fibrosis [13,14]. As mentioned above, the complication of iron over load include heart disease(heart failure due to cardiac siderosis), chronic anemia,liver disease liver injury, liver fibroses, and as result viral hepatitis,hypogonadisim, and bone disease. Our results indicated the absence of any effect of the iron overload on kidney and the parameters limited the health of renal function s-urea, and s-creatinin found in normal value as indicate in table (2).

Conflict of Interest: Non

Source of Findings: Self findings.

Ethical Clearance: Non

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