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"Clinical Evaluation of Alpha-Lipoic Acid For Controlling Iron Overload-Induced Hepatotoxicity and Oxidative Stress In Beta Thalassemia Major Patients"

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WE AIM at assessing the impact of α-lipoic acid (ALA) supplementation on the oxidative stress markers, Hb-derivatives, erythrocytes' hemolysis, and liver function of β-thalassemia major (β-TM) patients. We studied 10 β-TM patients who were assessed by evaluation of serum ferritin, plasma malondialdehyde (MDA), erythrocytes' hemolysis, serum alanine transaminase (ALT) and aspartate transaminase (AST) activities, methemalbumin (Mha), oxyhemoglobin (HbO_2), total bilirubin (TB), and haemoglobin (Hb) derivatives following 3 and 6 months of supplementation with 300–600 mg/day of ALA according to age. 12 healthy volunteers of the same age and sex were examined at baseline only and did not receive ALA. We detected a significant decrease in serum ferritin levels, plasma lipid peroxidation (MDA), and serum oxyhemoglobin concentrations ($p<0.05$) after 6 months of treatment with ALA, which suggests a reduction in iron overload and oxidative stress. This decrease in oxidative damage can account for the decrease in the percentage of erythrocytes' hemolysis ($p<0.0005$), liver enzyme activity of ALT and AST by ($p<0.05$) and ($p<0.005$) after 3 and 6 months of treatment with ALA, respectively, indicating liver function improvement, which was confirmed by decreasing serum TB concentration ($p<0.054$) after 6 months of supplementation. However, there was an insignificant effect of ALA on the levels of Hb-derivatives. Still, a 7.54% increase in total blood Hb-concentration indicates improvement of anemia after 3 months of ALA supplementation. Those results highly support the clinical usage of ALA in supplementing the treatment of β-TM patients to alleviate the severity of symptoms resulting from iron overload and oxidative stress.

Keywords: Malondialdehyde: MDA; (β-TM) Beta Thalassemia Major Patients, oxyhemoglobin :HbO2; α-lipoic acid (ALA) ; total bilirubin:TB

Introduction

The adverse biological effects of oxygen free radicals are known as oxidative stress, which is brought on by an imbalance between the production and removal of reactive oxygen species (ROS) in cells and has been connected to the etiology of several diseases [1]. Therefore, using antioxidant supplements to reduce oxidative stress may have clinical advantages. Alpha lipoic acid is one of the antioxidants that is universally acknowledged since it maintains protective properties in both its reduced and oxidized states [2].

Adult hemoglobin, a molecule responsible for oxygen transport, consists of four structural subunits: two alpha (α-) and two beta (β-) globin chains. Alteration in the patterns of these chains can result in severe medical conditions. β -thalassemia is one of these diseases, which is a widespread genetic disorder brought on by abnormalities in the beta-globin gene that lead to decreased synthesis of beta-globin, which consequent buildup of unpaired α- globin chains. This excessive alpha-globin chains is the main factor causing cellular oxidative damage in thalassemia. The free unpaired α-globin chains aggregate inside a cell, causing the destruction of red blood cells (RBCs). The distortion of hemoglobin produces heme and iron, which stimulate the generation of ROS [3].

Thalassemia is widespread worldwide. In Egypt, β-thalassemia is the most frequent cause of persistent hemolytic anemia. β -Thalassemia can be divided into three categories: beta thalassemia major, beta thalassemia intermedia, and beta thalassemia minor. β -Thalassemia major (β-TM) is the most severe form, requiring long term blood transfusion for survival. Although iron chelation has led to an improved survival outcome in β-TM, hemosiderosis (the buildup of iron in tissues) and iron overload are frequent negative side effects of blood transfusion [4].

As a result of iron overload, major organs, including the endocrine system, spleen, heart myocardium, and liver, became deposited with iron. There are complications as a result, such as cardiomyopathy, liver disease, diabetes mellitus, growth retardation, and delayed puberty [5]. Iron is a redox active element that, through the Fenton reaction, produces OH radicals, which can significantly worsen oxidative stress [6]

Hence, using antioxidant supplements to reduce oxidative stress may have clinical advantages. In this context, alpha lipoic acid (ALA) endogenously synthesized in both plants and animals. It has received increased attention due to its antioxidant action. ALA, often known as Thioctic acid, is an antioxidant that is soluble in both fat and water and also serves as a cofactor for a number of distinct mitochondrial processes. ALA is transformed into dihydrolipoic acid following its absorption into cells and tissues and it has metal chelating characteristics that reduce the generation of ROS [7]

Malondialdehyde (MDA), the result of lipid peroxidation, acts as a sensitive indicator of tissue damage and oxidative stress [8]. Prior studies in animal models have shown that ALA supplementation resulted in the reduction of MDA level [9, 10]

Several theories concerning how ALA exerts cellular antioxidant effect are through; inducing the transcription of endogenous antioxidants or enzymes with antioxidant activity or by promoting their absorption [2]. Also, several studies have shown that ALA can recycle ascorbic acid, glutathione, and α-tocopherol while reducing MDA [11, 12] , as well as lower osteoprotegrin, a novel cardiovascular disease risk factor, in thalassemia patients [13].

Desouky et al. [3] reported antioxidant characteristics of ex vivo administration of

α-lipoic acid in reducing the harm exerted by ROS on β -Thalassemia major patients. In 2021, Sharifi-Zahabi et al. [14] reported decrease in MDA and ferritin concentrations as oxidative markers following ALA supplementation in β-Thalassemia major patients . However, they did not study the effect of ALA supplementation on liver function, erythrocytes and/or hemoglobin level within their study group. Herein, we aim at studying the effect of α-lipoic acid on oxidative stress, liver function, hemoglobin, and erythrocytes in a group of β-thalassemia major patients.

Materials and methods

Patients

Following obtaining the approval of the National Research Centre Research Ethics committee and signing informed consents by the patients or their parents, ten β-thalassemia major patients (7 males and 3 females with ages 9 to 22 years) receiving regular blood transfusion and chelation therapy were recruited from the Hereditary Blood Disorders Clinic (HBD), National Research Centre, Egypt. Twelve age and sex matched healthy individuals (8 males and 4 females with ages 9 to 22 years) who were not exposed to smoking, malnutrition, chronic illnesses, or any other source of oxidative stress, were included as a control group. Patients with history of chronic renal failure, other hematologic diseases, chronic infections, and/or receiving antioxidant or herbal medications were excluded.

Study group received oral α-lipoic acid (Thiotex) in a dose of 300 mg/day in patients aged ≤ 14 years and 600 mg/day in patients more than 14 years for 6 months. Beta-thalassemic patients received α-lipoic acid therapy as soon as the first transfusion was given. Three 5 ml venous blood samples were collected from each patient: the first sample prior to the beginning of the ALA administration then the second and third samples 3 and 6 months following the ALA usage.

Sampling

Three sampling sessions are scheduled for each patient; 5 mL venous blood were collected in one heparinized tube and one tube without anticoagulant from the patients, prior to their scheduled blood transfusion, as well as from the healthy volunteers.

The heparinized blood sample tube was used for hemoglobin derivatives determination and erythrocytes hemolysis test. Heparinized blood samples were centrifuged for 10 minutes at 3000

rpm to separate the plasma, which was then used to measure malondialdehyde (MDA). Un-heparinized blood samples were centrifuged for 15 minutes at 3000 rpm followed by measuring total bilirubin, oxyhemoglobin, and methemalbumin, ferritin content, and the activity of the liver enzymes in the serum.

Determination of Biochemical Parameters

The enzyme-linked immunosorbent assay [ELISA] method was used to quantify serum ferritin using the DiaMetra kit (Via Pozzuuolo, Italy). Aspartate transaminase [AST] and alanine transaminase [ALT] activities were measured following Reitman and Frankel [15]. The malondialdehyde [MDA] level was determined through Satoh's protocol [16].

Determination of Erythrocytes hemolysis

The amount of hemoglobin (Hb) released from the cells in relation to the total amount of cellular Hb content was measured to estimate the percentages of hemolysis. 40 μL of the whole blood were hemolyzed by adding 5 mL of ice-cold distilled water (pH=7.3). To get rid of lipid aggregates and erythrocyte ghosts, this hemolysate was next centrifuged at 10,000 rpm for 10 min. Then 40 μL of whole blood was added to 5 mL of phosphate buffered saline (PBS). This mixture was incubated in a refrigerator at 4 °C for 14 days.

The proportion of hemolysis was determined using the following equation:

$$H\% = \frac{A_{Sample}}{A_{100\%Hemolysis}} \times 100 \qquad (1)$$

where A_{Sample} is the absorbance of the Hb in the supernatant made by centrifuging a mixture of 40 μL of whole blood and 5 mL of PBS at 3000 rpm for 10 minutes. $A_{100\%Hemolysis}$ is the absorbance of the Hb solution after complete hemolysis. At 522 nm, which is the isobestic point for oxyHb and metHb, the absorbance of these solutions was measured. All absorbance measurements were made at room temperature.

Determination of hemoglobin derivatives

By using a multi-component spectrophotometric method based on 4-absorbance measurements at wavelengths of 500, 569, 577, and 620 nm, respectively, the levels of Hb-derivatives [sulfohemoglobin (SHb), methemoglobin (metHb),

carboxyhemoglobin (HbCO), and oxyhemoglobin (oxyHb)] as well as the total blood Hb concentration of healthy subjects, whose blood contains 99% adult hemoglobin (HbA), were determined following the method in Attia et al. [17]

While the levels of Hb-derivatives in β-thalassemic major patients, whose blood contains a high percentage of fetal Hb (HbF) [18] were calculated from these 4 absorbance, by matrix calculation, taking into account the fraction of HbF besides HbA during the calculation of Hb-derivatives, since the millimolar absorptivities are different for HbA and HbF as described in Zijlstra et al. [19]. The mathematical formalism of healthy subjects and the details, including formulas, are presented in Attia *et al.* [20].

In the case of β-thalassemic subjects, containing high levels of HbF, the levels of the Hb-derivatives, present in a purified (non-turbid) aqueous Hb solution, were calculated from the 4 absorbances at 500, 568, 578 and 620nm, by matrix-calculation, using the millimolar absorptivities, determined by Zijlstra *et al.* [19] .

$$A^\lambda = \sum_{i=1}^{4} \varepsilon^\lambda_{i,HbA/HbF} C_i l \qquad (2)$$

The absorptivity of a corresponding derivative as measured for the HbA/HbF mixture is given by:
$$\varepsilon^\lambda_{HbA/HbF} = F_{HbF} \times \varepsilon^\lambda_{HbF} + (1 - F_{HbF}) \times \varepsilon^\lambda_{HbA} \qquad (3)$$

where, $\varepsilon^\lambda_{HbF}$ is the absorptivity of a derivative of HbF at wavelength λ and $\varepsilon^\lambda_{HbA}$ is the absorptivity of the corresponding derivative of HbA. F_{HbF} is the fraction of HbF and "1-F_{HbF}" is the fraction of adult hemoglobin (HbA).

Determination of total bilirubin, oxyhemoglobin and methemalbumin in human sera

The total bilirubin (TB), oxyhemoglobin (HbO2), and methemalbumin (Mha) in human sera were determined by the multi-component spectrophotometric method described in Attia et al. [21].

Data analysis

The data were presented as the mean±standard deviation (SD) values. One-way analysis of variance (ANOVA) was carried out, and the statistical comparisons among the groups were performed with post hoc and the least significant difference (LSD) tests using statistical programmes (Statistical Package for the Social Sciences, version 14 [SPSS Inc., Chicago, IL]). P<0.05 was considered statistically significant.

Based on the advanced database (Clipper)

language, a Clipper compiler and PLINKER [22] computer programs were developed that allow calculation of the percentages and various hemoglobin derivative concentrations as well as the total hemoglobin concentration in human blood. The software is characterized by simplicity, speed, and high accuracy.

Results

Obtained studied participants' data are presented as mean percentage values before and after 3 and 6 months of lipoic acid therapy in tables 1 and 2 and figures 1- 6 representing different parameters of interest.

Figure 1 shows the histogram of mean values of the lipid peroxidation product (MDA) concentration in the plasma of healthy subjects and β-TM patients before and after lipoic acid therapy for 3 and 6 months, respectively.

The results showed higher basal values of plasma MDA concentration in β-TM patients before therapy when compared to controls (P<0.0005). An insignificant decrease in plasma MDA concentration in β-TM patients after lipoic acid therapy for 3 months was observed when compared to those values before treatment. A significant decrease in plasma MDA concentration in β-TM patients after lipoic acid therapy for 6 months was observed when compared to those values before treatment (P<0.05).

Figure 2 shows the histogram of mean values of the serum ferritin concentration of healthy subjects and β-TM patients before and after lipoic acid therapy for 3 and 6 months, respectively. A marked increase in serum ferritin concentration of β-TM patients before therapy of the mean value (4338.8

μg/L) when compared to those of healthy controls (250 μg/L) was observed. A marked decrease in serum ferritin concentrations of β-TM patients after lipoic acid therapy for 3 and 6 months, of mean values (3515.7 μg/L) and (3011.1 μg/L), respectively, when compared to its value in β-TM patients before therapy (4338.8 μg/L), was observed.

Figure 3 shows the histogram of mean values of the serum ALT activity of healthy subjects and β-TM patients before and after lipoic acid therapy for 3 and 6 months, respectively. The results showed higher basal values of serum ALT in β-TM patients before therapy when compared to controls (P<0.005). A marked and significant decrease (p<0.05 and p<0.005) in serum ALT activity of β-TM patients after lipoic acid therapy for 3 and 6 months, respectively, of mean values (32.5 IU/L) and (27.3 IU/L), when compared to its value in β-TM patients before therapy (61 IU/L), was observed.

Figure 4 shows the histogram of mean values of the serum AST activity of healthy subjects and β-TM patients before and after lipoic acid therapy for 3 and 6 months, respectively. A marked and significant increase (p<0.005) in serum AST activity of β-TM patients before therapy of the mean value (59.9 IU/L) when compared to those of healthy controls (19.25 IU/L) was observed. A marked and significant decrease (p<0.05 and p<0.005) in serum AST activity of β-TM patients after lipoic acid therapy for 3 and 6 months, respectively, of mean values (33.9 IU/L) and (28.9 IU/L), when compared to its value in β-TM patients before therapy (59.9 IU/L), was observed.

Figure 5 shows the histogram of mean values of the percentage hemolysis of healthy subjects and β-TM patients before and after lipoic acid
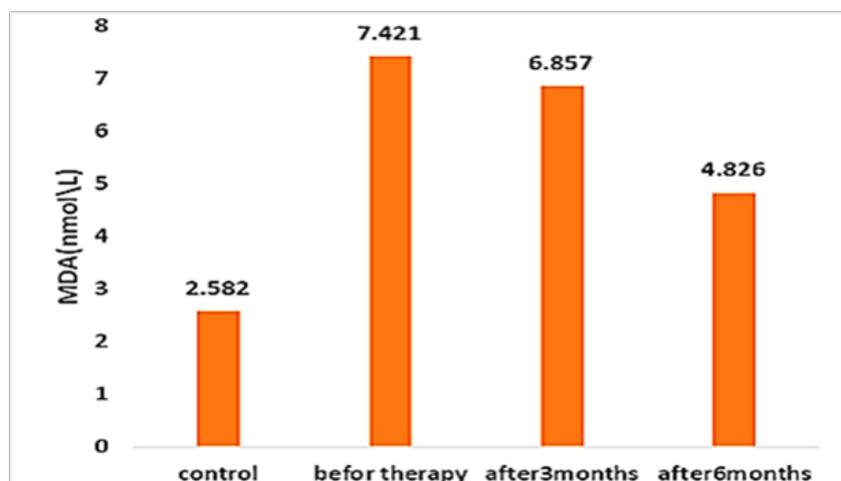

Fig. 1. Plasma malondialdehyde (MDA) concentration of β-TM patients before and after lipoic acid therapy as compared to healthy controls.
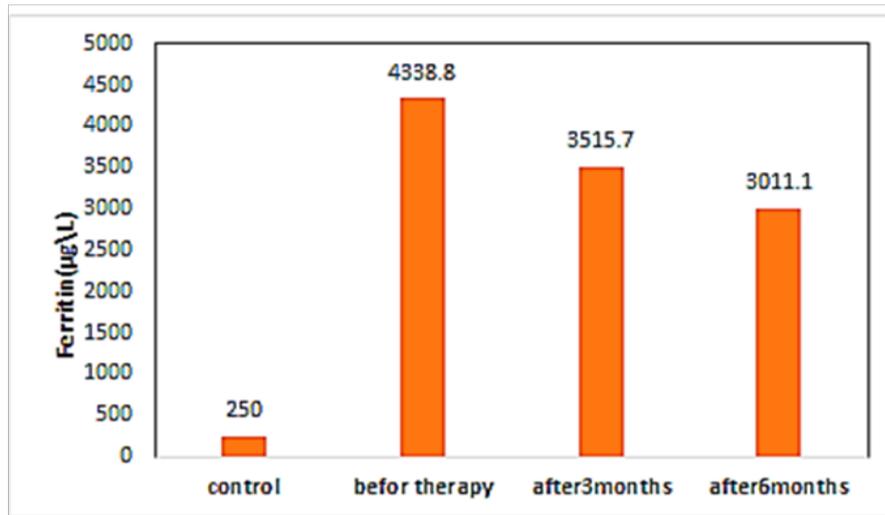
Fig. 2. Serum ferritin concentration of β-TM patients before and after lipoic acid therapy as compared to healthy controls.
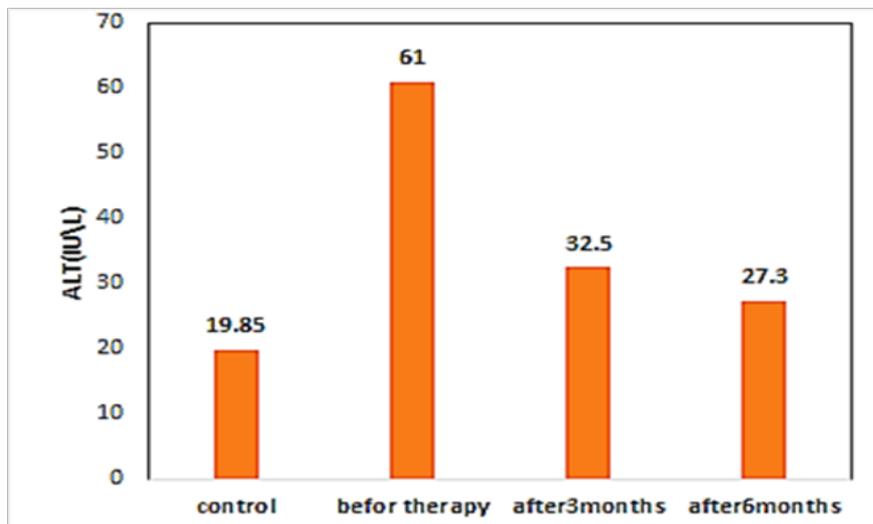

Fig. 3. Activity of serum ALT of β-TM patients before and after lipoic acid treatment compared with healthy controls

therapy for 3 and 6 months, respectively. The results showed higher basal values of percentage hemolysis in β-TM patients before therapy, when compared to controls (P<0.0005). A highly significant decrease in percentage of hemolysis in β-TM patients after lipoic acid therapy for 3 and 6 months was observed when compared to those values before treatment (P<0.0005).

Figure 6 shows the histogram of mean values of the total Hb concentration in the blood of healthy subjects and β-TM patients before and after lipoic acid therapy for 3 and 6 months, respectively. A significantly lower value of total Hb in thalassemic patients, as compared to controls, was observed (p<0.0005). The total Hb concentration of β-TM patients before therapy of mean value (9.5072) increases by 0.717 g to be 10.2246 g/dL after 3 months of lipoic acid therapy.

Table 1 shows the mean ±SD values of serum methemalbumin (Mha), oxyhemoglobin (HbO2) and total bilirubin (TB) of healthy subjects and β-TM patients before and after lipoic acid therapy for 3 and 6 months, respectively. The results showed higher basal values of serum Mha, HbO2 and TB concentrations in β-TM patients before therapy, when compared to controls (P<0.005). Insignificant changes in serum Mha and TB concentrations in β-TM patients after lipoic acid therapy for 3 and 6 months were observed when compared to those values before treatment. A significant decrease in serum HbO2 concentration in β-TM patients after lipoic acid therapy for 6 months was observed, when compared to those values before treatment (P<0.05).

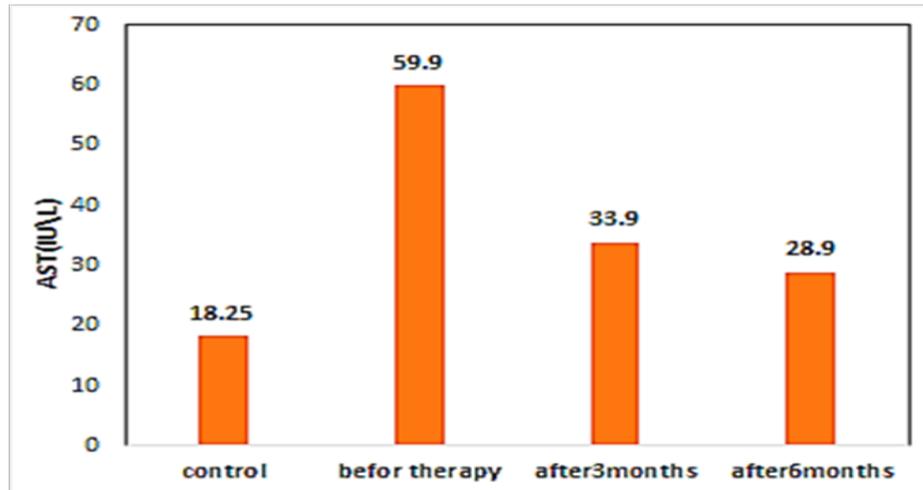Table 2 shows the mean ±SD values of the

Fig. 4. Activity of serum AST of β-TM patients before and after lipoic acid treatment compared with healthy controls
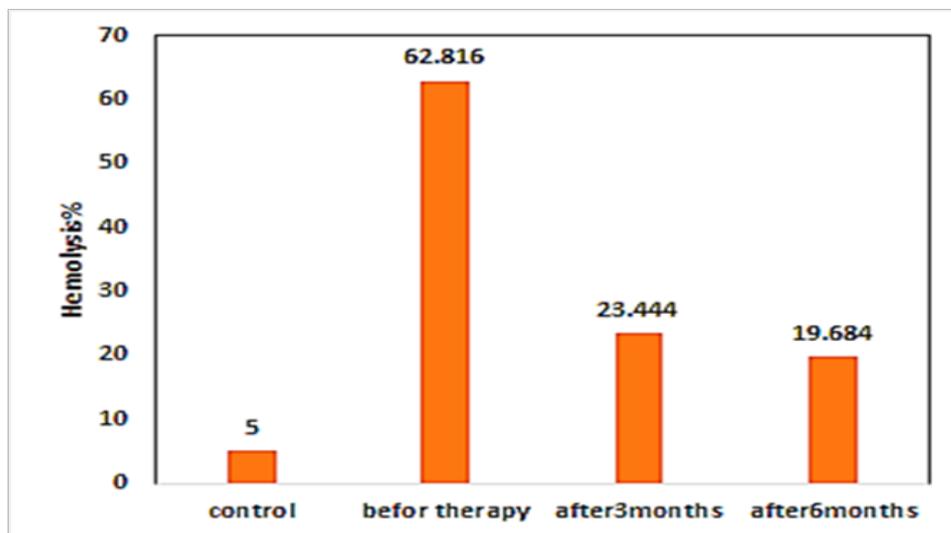

Fig. 5. Percentage hemolysis of erythrocytes after incubation at 4ºC for 14 days of β-TM patients before and after lipoic acid therapy as compared to healthy controls.
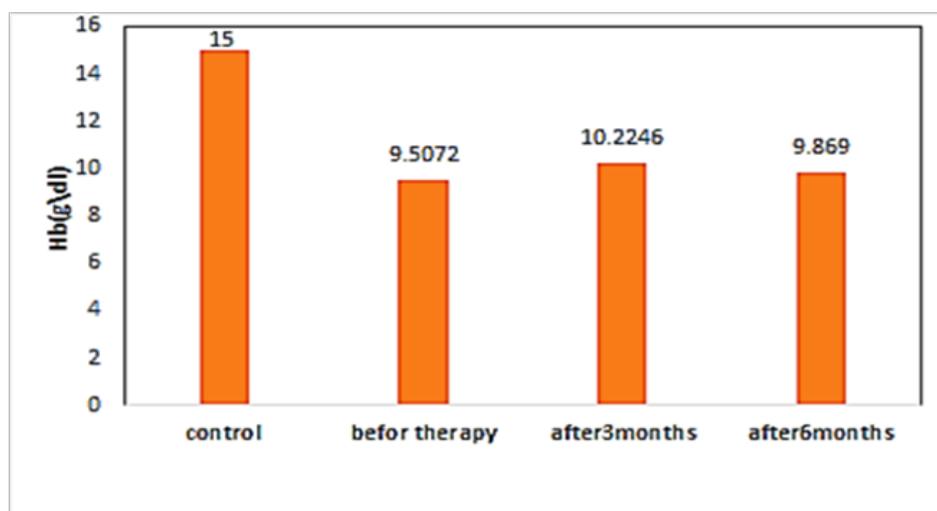

Fig. 6. Concentration of whole blood hemoglobin of β-TM patients before and after lipoic acid therapy as compared to healthy controls.

percentage values of sulfhemoglobin (SHb), methemoglobin (metHb), and carboxyhemoglobin (HbCO) in healthy subjects and β-TM patients before and after 3 and 6 months of lipoic acid therapy, respectively. The results showed higher basal values of SHb (%) in β-TM patients before therapy when compared to controls (P<0.05). The results also showed higher mean values of SHb% in β-TM patients after therapy with lipoic acid for 3 and 6 months when compared to controls (0.0005). The results also showed higher basal values of metHb% and HbCO% in β-TM patients before therapy when compared to controls (P<0.0005). Insignificant changes in the mean percentage values of SHb, metHb, and HbCO of β-TM patients after therapy for 3 and 6 months were observed when compared to thalassemic patients before treatment.

Discussion

The aim of the current study was to assess the influence of α-lipoic acid (ALA) supplementation on alleviating the oxidative stress and iron overload in β-Thalassemia major patients through measuring several findings before and after ALA administration. Reviewing the literature, our study is the second in vivo study of ALA for the control of oxidative damage and iron overload in β- TM following that by Sharifi-Zahabi et al.[14].

Our cohort of β- TM patients suffered iron overload as evaluated by high ferritin levels (mean value 4338.8 µg/L) which markedly decreased following using α-Lipoic acid, indicating an effective role of ALA in iron overload management. Sharifi-Zahabi et al., in their study in 2021, reached the same conclusion [14], confirming ALA supplementation may attenuate iron overload, decreasing serum ferritin in β- TM. However, Hosseinpour et al. [23], reported that ALA supplementation could not alter serum ferritin in their study of a cohort of obese patients, this controversy in outcome of ALA supplementation might be attributed to variations in patients' characteristics and ferritin level, which was at lower baseline, suggesting that ALA could work better in patients with higher serum ferritin levels.

The dithiol molecule ALA, after being absorbed by cells, is often converted to dihydrolipoic acid (DHLA). Both compounds are naturally existing, low molecular weight molecules extremely potent

TABLE 1. Serum methemalbumin (Mha), oxyhemoglobin (HbO2) and total bilirubin (TB) of beta-thalassemia patients before and after lipoic acid treatment compared with healthy controls.

Serum pigment	Healthy Controls (N=12) (Mean±SD)	B-Thalassemic Patients (N=10)		
		Before treatment (Mean±SD)	After 3 months of treatment (Mean±SD)	After 6 months of treatment (Mean±SD)
Mha (µmol/L)	5.983±1.834	39.04±15.504 (**)	53.079±21.908 (**)	31.487±14.40 (**)
HbO2	2.069±1.024	32.189±27.825 (**)	22.461±35.222 (*)	8.211±13.29 (***)
TB (mg/dL)	0.621±0.215	2.090±1.103 (**)	2.224±0.884 (**)	1.879±0.794 (**)

Values are given as mean ±SD.
*Significantly different from control, P<0.05.
** Significantly different from control, P<0.005
*** Significantly different from beta-thalassemic group before treatment, P<0.05.

TABLE 2. The mean percentage values of sulfhemoglobin (SHb), methemoglobin (metHb), carboxyhemoglobin (HbCO) and active hemoglobin in the HbO2 form in healthy subjects and β-TM patients before and after 3 and 6 months of lipoic acid therapy, respectively.

Hb derivative	Healthy Controls (N=8) (Mean±SD)	B-Thalassemic Patients (N=10)		
		Before treatment (Mean±SD)	After 3 months treatment (Mean±SD)	After 6 months treatment (Mean±SD)
SHb (%)	0.3583±0.0830	0.5451±0.404 (*)	0.9593±0.1695 (**)	0.8633±0.3096 (**)
metHb (%)	0.4898±0.3200	4.7675±1.748 (**)	5.6968±1.3271 (**)	5.3161±1.0981 (**)
HbCO (%)	1.0737±0.2301	4.3834±0.293 (**)	4.4004±0.7282 (**)	4.7032±0.5352 (**)

Values are given as mean ±SD.

*Significantly different from control, P<0.05.

** Significantly different from control, P<0.0005.

as antioxidants that are effective in both aqueous and lipid domains, hence regarded as good therapeutic antioxidants. They have the ability to quench free radicals, chelate iron, and regenerate other antioxidants, including glutathione, vitamin E, and ascorbic acid. The effect of iron chelation is to lower the buildup of free iron in the body, which can lessen oxidative stress. Together with its chelating effects, DHLA can remove iron from ferritin to lower ferritin iron levels [24].

Bilirubin is a breakdown product of hemoglobin's heme and its level is increased with excess red blood cells destruction. Before ALA administration, β- TM patients had high serum total bilirubin level (average 2.090 mg/dL), as a result of increased hemolysis and impaired liver function. Six months following using ALA, the level of total bilirubin decreased by 10.09% in β-TM relative to before treatment, indicating enhancement in liver function. This result is in agreement with Dissayabutra et al. [25], who reported that vitamin C and E supplementation in β- TM patients, significantly increased the

plasma levels of vitamins with a mild decrease in total bilirubin. They concluded that vitamin supplementation improves antioxidant status and enhances liver function. In the present study, the activities of the liver enzymes alanine transaminase (ALT) and aspartate transaminase (AST) were 3.073 and 3.28 times, respectively, that is higher than healthy controls similar to Nafady et al. [26], who reported abnormal ALT and AST levels associated with higher ferritin due to iron overload in β-thalassemia patients. An enhancement in liver function and decreased levels of liver enzymes (ALT) and (AST) by 50% each, in the sera of β-TM patients after α-Lipoic acid treatment relative to before treatment is in agreement with Attia et al. [27], reporting on improved activities of liver enzymes after six months of treatment with vitamins E, C, and A, compared to their activities before treatment.

Similar to previous reports [28, 29], MDA as a good indicator of oxidative damage was significantly increased (2.874 times greater than in healthy controls) in our studied cohort of β-TM

patients. We report a significant reduction in MDA level in twenty percent of patients following three months of α-lipoic acid administration also, MDA showed a highly significant response after therapy for six months; where 30% of studied patients achieved normal MDA values. Our results are consistent with those of Sharifi-Zahabi et al. [14], who suggested ALA supplementation might reduce the level of MDA.

The high oxidative stress may lead to high lipid peroxidation in the erythrocytes of β-thalassemic patients, which is accompanied by a higher rate of destruction of cell membranes and therefore can account for the high rate of hemolysis in β-thalassemic erythrocytes. In the present study, the extent of hemolysis of erythrocytes in β-thalassemic patients before treatment with ALA was markedly higher than that of controls, whereas, a highly significant decrease in hemolysis after treatment with ALA was observed. Our study agrees with Desouky et al. [30] reporting a hemolysis rate of β-thalassemic RBCs around twice that of normal RBCs.

Assessment of hemoglobin level of studied patients after three and six months of α-lipoic acid treatment revealed marked increase throughout treatment compared to before treatment where the Hb level in β-thalassemia patients improved markedly (7.542% and 3.808%) after three and six months of α-lipoic acid administration respectively. Our results support the findings of Das et al.,2004 [31], reporting that four weeks of vitamin E treatment considerably improved the Hb level in β-thalassemia patients compared to the level in the untreated participants. However, even with vitamin E treatment, the Hb levels in thalassemic individuals never return to normal ranges, which is again in agreement with our findings.

Since the inactive components of Hb (MetHb and HbCO) cannot transport oxygen, the net concentration of the functionally active Hb (HbO_2) is an indicator of the actual degree of anemia. The increase in MetHb% and HbCO%, together with the increase in hemolysis rate, may explain the decrease in HbO_2 concentration in β-TM prior to therapy. Insignificant changes in the mean percentage values of SHb, metHb, and HbCO of β-TM patients after therapy for 3 and 6 months were observed.

In this hemolytic anemia, the hemin groups are released from erythrocytes as breakdown products of hemoglobin and bind with plasma albumin, forming methemalbumin (Mha). While, Mha increases significantly in β-TM as a hemolytic anemia, α-lipoic acid has no effect on its concentration.

In β-thalassemia, the high hemolysis rate can explain the high concentration of serum HbO_2 .The improvement of erythrocyte hemolysis after six months of the antioxidant α-lipoic acid treatment can explain the associated decrement of serum HbO_2 concentration .

Conclusions

In conclusion, our study is the second in vivo assessment of ALA. We conclude that the treatment of β-thalassemia major patients with α-lipoic acid improves their oxidant status and saves their organs from the damage resulting from iron overload, a result of continuous blood transfusions, which leads to more free radicals that cause organ dysfunction. Also, treatment with α-lipoic acid enhances the liver functions and reduces the percentage of hemolysis of erythrocytes, therefore improving the total Hb concentration. This new insight should encourage medical professionals to use alpha-lipoic acid in diseases affecting liver in which oxidative stress is implicated.

Declaration of competing interest
The authors affirm that their publishing of this paper does not include any conflicts of interest.

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تقييم سريري لحمض ألفا-ليبويك للتحكم في سمية الكبد والإجهاد التأكسدي الناجم عن تراكم الحديد في مرضى الثلاسيميا البيتا الشديدة.

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نحن نهدف إلى تقييم تأثير مكملات حمض ألفا ليبويك ALA)على علامات الإجهاد التأكسدي ومشتقات الهيموغلوبين وانحلال الدم في كريات الدم الحمراء ووظيفة الكبد لمرضى الثلاسيميا الكبرى β-TM)). درسنا ١٠ مرضى β-TM الذين تم تقييمهم من خلال تحليل مستويات مصل الفيريتين ، مالونديالديهايد في البلازما (MDA))، انحلال كرات الدم الحمراء ، وأنشطة ألانين ترانسامينيز (ALT))وأنشطة أسبارتيت ترانسامينيز (AST)) ،ميتهيمالبومين (Mha))، أوكسي هيموغلوبين (HbO2))، إجمالي مشتقات البيليروبين (TB والهيموجلوبين (Hb)بعد ٣ و ٦ أشهر من المكملات ALA بمعدل ٣٠٠-٦٠٠ مجم / يوم وفقا للعمر. تم تقييم ١٢ من الأشخاص الأصحاء متطابقي العمر والجنس في البداية فقط ولم يتلقوا ALA. اكتشفنا انخفاضًا في مستوى الفيريتين في الدم وبيروكسيد الدهون في البلازما (MDA) وتركيز أوكسي هيموجلوبين في المصل p 0.05<)) بعد ٦ أشهر من العلاج بحمض ألفا ليبويك . مما يشير إلى انخفاض الحمل الزائد للحديد والضغط التأكسدي. يمكن أن يؤدي هذا الانخفاض في الضرر التأكسدي إلى انخفاض النسبة المئوية لانحلال كريات الدم الحمراء (p<0.0005)) ، ونشاط إنزيم الكبد مثل نشاط ALT و AST بمقدار p <0.05)) و (p<0.005))بعد ٣ أشهر و ٦ أشهر من العلاج بحمض ألفا ليبويك على التوالي. تشير هذه التأثيرات على إنزيمات الكبد إلى تحسن في وظائف الكبد ، وهو ما أكده أيضًا الانخفاض في تركيز البيليروبين الكلي في الدم (p <0.054) بعد ٦ أشهر من المكملات بحمض ألفا ليبويك. ومع ذلك ، كان هناك تأثير ضئيل لحمض ألفا ليبويك على مستويات مشتقات الهيموغلوبين. ومع ذلك ، تشير الزيادة بنسبة ٧,٥٤٪ في إجمالي تركيز الهيموغلوبين في الدم (p<0.056)) إلى تحسن فقر الدم بعد ٣ أشهر من مكملات حمض ألفا ليبويك.

تدعم هذه النتائج بشدة الاستخدام السريري لـ ALA في تكملة علاج مرضى β-TM للتخفيف من حدة الأعراض الناتجة عن الحمل الزائد للحديد والإجهاد التأكسدي.