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5. განიხილით ჰაერი შეთანხმები გადმოცემით საგმირო ჰაერით. ყველა ფოტომასტერაჟი ქვემოთ შეთანხმებელთან შეთანხმება.

6. ფოტომასტერის უდრ იარაღი შეთანხმება: ქართული, საქართველო, თასლკამი, - დასამუშავებელი, გამოაქვს და სახელმწიფო უმაღლეს შეთანხმება. ფოტომასტერით შეთანხმები პრეზენტაცია უმაღლეს შეთანხობით ითხოვს. ჭიდავს შეთანხობა რთულით და მიერ ადგილობრივი და გარკვეული გარემოთ შეთანხობით. შალითა შეთანხობით, შავი შეთანხობა რთულს, შავი შეთანხობა რთულს.

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9. სტატია თან უნდა შეიცავდეს: გადამცხედრების საშუალო შეთანხმება, გადამცხედრების შეთანხმება და შეთანხმება; გადამცხედრების შეთანხმება თავი, შეთანხმება თავი.

10. სტატია თან უნდა შეიცავდეს თავით შეთანხობით ხელშეწყობა, რიგით მოსართული და გამოცემები შეთანხობით შეთანხმება.

11. ტექსტი შეიცავდება შეთანხმები შეთანხმება ჰაერში. მიგვწერთ შეთანხმება და შეთანხმება შეთანხობა მორგების შიდა შეთანხმება შეთანხმება.

12. გათესლიც უფლება შეთანხმები შეთანხმება შეთანხობა მოურთული მოგზაურობა ენა კლას ქართულად ან გადამცხედრება ენა კლას ქართულად.
COMPARATIVE STUDY OF OXIDATIVE STRESS IN PATIENTS WITH Β-THALASSEMIA MAJOR ON DEFERASIROX VERSUS DEFEROXAMINE THERAPY

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Abstract.

Background: Accumulation of iron in vital organs is increasingly challenging in clinical settings during the lifespan of thalassemia patients. Iron overload hurdle these organs to redox imbalances. Commonly used iron-chelating agents in (deferasirox and, deferoxamine) could have a positive antioxidant role. Objective: Therefore, the aim of this study was designed to compare the effects of deferasirox and, deferoxamine, iron-chelating agents in oxidative stress in patients with Β-thalassemic major.

Methods: In this case series comparative study, 60 known cases of Β-thalassemic patients receiving chelating agents therapy were divided into two groups of thirty, group one consisted of 30 patients 16 male and 14 female, who received oral agent deferasirox tablets at dose 20-40mg/kg. Group two consisted of 30 patients, 16 male and 14 female, on intravenous therapy with Deferoxamine at a dose of 20-50mg/kg. Another thirty healthy individuals matched with age and gender, were kept as a control group. Total antioxidant capacity (TAOC) and Malondialdehyde (MDA) were measured in all studied groups.

Results: The three groups were similar in terms of age, and gender. A statistically non-significant difference in age (p>0.05) existed between the control and patient groups (10.9±2.93; 11.2±4.1*;11.6±3.6*) respectively. The number of patients in to control group and male-to-female numbers were matched since the ratios were similar. A statistically non-significant difference in BMI (p>0.05) existed between the control and patient groups (17±2, 17.2±2, 18±2.4*) respectively. TAOC is lower in-patient groups, when compared with the control group (27.8 ± 10.7; 32.5 ± 10.2; and 79.5 ± 7 u/ml) respectively, while the MDA value is higher when compared with the control group (7.2±4.6 and, 6.6±4.42; and 0.57±0.26; nmol/ml) respectively. The TAOC in patients group on Deferoxamine, is higher, while MDA is lower than in patients on Defrasirox. Conclusion: The TAOC in patients was reduced and Oxidative stress was enhanced in patients with thalassemia. Deferoxamine is more effective in mobilize iron by continuously chelating labile iron present in a ‘transit pool’ this solubilized, chelated iron form will be excreted in the urine and stools [18,19].

Patients and Methods.

The present research was a comparative descriptive clinical trial. Ethical approval was obtained from the University of Nineveh/College of Medicine. Parental consent was recorded from all participants before enrollment in the study and carried out on 60 known cases of Β-thalassemic patients receiving chelating agent therapy under follow-up, divided into two groups, group one enrolled 30 patients (16 male; and 14 female), on oral agent on deferasirox DFX (Exjade) tablet on dose 20-40mg/kg. Group two enrolled 30 patients (16 male; 14 female), on intravenous therapy with Deferoxamine DFM (Desferal) at a dose of 20-50mg/kg, attended the thalassemia centre at Ibn-Alatheer Teaching Hospital, Mosul City (Iraq), from November 2021 till April 2022. Another 30 healthy individuals matched with age and gender, were kept as a control group.

Patients to enrol in the study should be on continuous iron-chelating agent therapy either deferasirox or deferoxamine for at least six months, alongside no antioxidant supplementation should be taken for the last 6 months. All patients should have no other diseases and should have no complications of thalassemia.
Age, height, weight, and body mass index were recorded for each patient. Biochemical analysis of TAOC, and serum MDA, were measured using Colorimetric Assay Kit Elabscience® (USA).

Statistical analysis: Data expressed as mean and standard deviation. Using the Excel 2016 data spreadsheet, the t-test was calculated and p<0.05 was considered significant.

Results.

The demographic parameters of the enrolled subjects are represented in Table (1). Age comparison has shown non-significant (p>0.05) differences between the control and patient groups (10.9±2.9; 11.2±4.1; 11.6±3.6) respectively. The number of patients in to control group and male-to-female numbers were matched since the ratios were similar. BMI comparison has shown non-significant (p>0.05) differences between the control and patient groups (17±2, 17.2±2, 18±2.4), respectively.

Table 1. The demographic parameters of the studied groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control (n=30)</th>
<th>DFX (n=30)</th>
<th>DFM (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>10.9±2.9</td>
<td>11.2±4.1</td>
<td>11.6±3.6</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>15/15</td>
<td>16/14</td>
<td>16/14</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>17±2.0</td>
<td>17.2±2.0</td>
<td>18±2.4*</td>
</tr>
</tbody>
</table>

*p<0.05 as compared to other groups

Table 2. The TAOC, MDA and Hb parameters of the studied groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control (n=30)</th>
<th>DFX (n=30)</th>
<th>DFM (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAOC (u/ml)</td>
<td>79.5±7</td>
<td>27.8±10.7</td>
<td>32.5±10.2</td>
</tr>
<tr>
<td>MDA (nmol/ml)</td>
<td>0.57±0.26</td>
<td>7.2±4.6</td>
<td>6.6±4.42</td>
</tr>
<tr>
<td>Hb (g/L)</td>
<td>10.9±2.9</td>
<td>6.4±0.8</td>
<td>6.2±1.07</td>
</tr>
</tbody>
</table>

*p<0.05 as compared to other groups, DFX=Deferasirox, DFM=Deferoxamine

Figure 1. Iron chelating agents modulated the redox status in the patient groups. Data expressed as mean±SD. *p<0.05. * significantly higher as compared to other groups. # significantly higher in DFM as compared to DFX. Significantly higher as compared to the control group. One-way ANOVA with a series t-test to identify differences between groups. DFX=Deferasirox, DFM=Deferoxamine, MDA=malondialdehyde, T-AOC=total antioxidant capacity, Hb=hemoglobin.

Discussion.

Beta thalassemias are hereditary disease caused by decreased or absent beta chain formation resulting in abnormal globin chain with premature destruction of RBCs and subsequent anaemia. Patients with thalassemia major become dependent on blood transfusion, with excess iron deposited in major organs resulting in their damage [20].

The principal hurdles in β-thalassemia are caused by iron-interven oxidative injury on vital organs. In overexert iron becomes available as low molecular weight iron, these arbitrated low biomolecules carry potential oxidant impacts liable for catalysing free radical reactions and cause intra- and extracellular oxidant mutilation [21]. Henceforth, confiscation of redox-active iron is an intention for chelation rehabilitation to moderate redox imbalances in thalassemia patients.

Deferasirox is one of the new class of oral chelators, that scavenge the non–transferrin-bound "labile plasma iron," the chemical substances accountable for organ damage in iron-overloaded patients, through toxic oxygen intermediates. The complexes formed are eliminated in the faeces.

Deferoxamine has been the standard effective iron chelator for transfusional hemosiderosis,. it binds iron tightly, and the iron-DFM complex is excreted in urine and stool [22]. This study was designed to assess and compare the oxidative stress status by quantification of TAOC and MDA the end product of lipid peroxidation commonly used as a biomarker of oxidative stress, in patients with β-thalassemia major on deferasirox as opposed to deferoxamine therapy on follow-up of regular administration of these iron chelators attended the thalassemia centre at Ibn Altheer Teaching Hospital, Mosul city (Iraq).

In the present study, TAOC is lower in the patients group, when compared with the control group (27.8±10.7; 32.5±10.2, and 79.5±7 u/ml) respectively, while malondialdehyde (MDA) value is higher when compared with the in the control group (7.2±4.6; 6.6±4.42; and 0.57±0.26 mmol/ml ) respectively.

These results were supported by previous studies. A study done by Ahmed and Yenzeel, [23] in patients with beta-thalassemia major, showed a highly significant significant decrease in the levels of vitamin E a component of the antioxidant defence mechanism, with an increase in the MDA levels.

Mohammed & Abd-El Rasoul, [24], found a substantial decline in TAOC and individual antioxidants and an elevation of serum MDA in patients with thalassemia major than control. The key instigates of oxidative stress in thalassemia are the dilapidation of the unbalanced haemoglobin and iron surplus, the iron overload catalysed the Fenton and Haber-Weiss reactions that...
stimulate the assembly of excess free radicals (hydroxyl OH and superoxide ion (O²⁻)), respectively and patients with transfusion dependency, severe anaemia itself induces oxidative stress [25,26]. The diminution in the level of TAC could be probably related to the depletion of antioxidant molecules for offsetting the surplus ROS produced in thalassemia patients. Therefore, the assessment and maintenance of antioxidant defence mechanisms can be useful in protecting β-thalassemia patients from more life-threatening complications of the disease [27].

In this study, the TAOC in patients group on Deferoxamine, is higher, while MDA is lower than in patients on Deferasirox. Confirming that the use of a combination of antioxidants with deferasirox and deferoxamine has improved the redox status of beta thalassemia major [28].

A review of the literature provides limited studies about the comparison between the effect of deferasirox and deferoxamine on oxidative stress markers, majority of studies evaluate their effects on iron chelation and serum ferritin which finally means oxidative stress since iron catalyzes the production of free radicals.

An iron overload mouse model done by Wu et al., [29], showed non-significant differences in iron chelation capacity between deferasirox and deferoxamine. While Al Mosawi and Kadhim, 2024, [30] showed that serum ferritin levels were significantly lowered by DFX therapy. Saigo et al., [25] investigated the influence of Deferasirox on redox balance in thalassemia patients with transfusion dependency, their study showed a significant reduction in reactive oxygen metabolite levels, and this could be explained in the context of the impact of DFX on the redox molecules produced by neutrophil, side by side with their impact on iron storage. Tackling oxidative stress through selection of proper chelating agent might also reduce the risk of thrombosis [31,32].

Conclusion.
The TAOC in patients was reduced and Oxidative stress was enhanced in patients with thalassemia. Deferoxamine is more effective in modulating redox status and may exert antioxidant properties more than deferasirox.

REFERENCES
22. Chakraborty M. Study of oral chelators of Deferiprone, Deferasirox and Deferoxamine and the need for alternative chelators in chelation therapy for transfusional iron overload in thalassemia major.