OXIDANT-ANTIOXIDANT SYSTEM AND LYMPHOCYTE DNA DAMAGE IN BETA THALASSEMIA CHILDREN

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Objectives
Thalassemia is an autosomal recessively inherited hemoglobinopathy which basically characterised by ineffective erythropoesis, hemolysis and anemia. Metabolic disorders, iron overload, chronic hypoxia and cell damage are added to these findings. Oxidative stress is recently being investigated in β-thalassemia major (TM) patients as well as in cardiovascular diseases, cancer, renal diseases, infection and neurological diseases. Oxidative stress develops as a result of imbalance between formation and neutralisation of pro-oxidants. Pro-oxidant / antioxidant equilibrium disorders may cause oxidative stress and DNA damage in cellular structures.

The aim of this study was to detect and correlate iron overload with the oxidant / antioxidant status and DNA damage in transfusion dependent β – TM patients.

Methods
The patient group was constituted from 83 patients with transfusion dependent β-TM whose mean age was 7.34±4.21 years. 40 sex and age-matched children with non-anemia, served as control group. The damage of mononuclear DNA were assessed with comet assay method and total oxidant status (TOS) and total antioxidant capacity (TAC) measurement by using Erel’s methods (1).

Results
In the β-TM patients, mean DNA damage level was 10.65±6.58 AU, mean TOS level was 15.98±9.44 (μmol H2O2/Eqv./L), mean TAK level was 1.62±0.27 (mmol Trolax Eqv./L), mean Oxidative Stres Index (OSI) level was 11.11±8.42 AU and mean lipid hydroperoxide (LOOH) level was 5.44±1.80 (μmol H2O2/Eqv./L) detected. In control group, mean DNA damage level was 1.45±2.02 AU, mean TOS level was 7.18±3.46 AU and mean LOOH level was 2.44±0.66 (μmol H2O2/Eqv./L) detected. When compared to the controls, DNA damage was detected to be increased in β-TM patients (p<0.001) (Table 1). When oxidant-antioxidant system were evaluated, while TOS, OSI and LOOH levels were significantly increased, TAC levels were decreased in β-TM patients compared to controls (p<0.001; p<0.001; p<0.001 and p<0.01 respectively). There was a statistically significant positive correlation between serum ferritin levels and DNA damage, TOS, OSI and LOOH; however a negative correlation was observed between serum ferritin and TAC levels in the β-TM patients. TOS, OSI and LOOH levels were positively correlated with ALT, however a negative correlation was observed between TAC and ALT levels in the β-TM patients. Serum AST and ALT levels were detected to have a statistically significant positive correlation with transfusion years in the β-TM patients. In the β-TM patients the DNA damage was detected to have a statistically significant positive correlation with TOS, OSI, LOOH, AST and ALT respectively; however a negative correlation was observed between DNA damage and TAC levels (Figure 1,2,3).

Table 1. Comparison of DNA damage and oxidative stress parameters of the subjects in the β-TM and control group

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Patient (n=83)</th>
<th>Control (n=40)</th>
<th>Statistic</th>
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</thead>
<tbody>
<tr>
<td>DNA damage (Arbitrary Units)</td>
<td>10.65±6.58</td>
<td>1.45±2.02</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TOS (μmol H2O2 Eqv./L)</td>
<td>15.98±9.44</td>
<td>7.18±3.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OSI (Arbitrary Unit)</td>
<td>11.11±8.42</td>
<td>4.66±3.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LOOH (μmol H2O2 Eqv./L)</td>
<td>5.44±1.80</td>
<td>2.44±0.66</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: Despite the recent improvements in longevity of patients with thalassemia with appropriate blood transfusions, iron-dependent organ toxicity and oxidative damage remain critical prognostic factors in these patients (2-7). In this study, oxidant/antioxidant system and possible DNA damage were investigated in patients with transfusion-dependent β-TM. The association between detected changes and iron load was studied. These analyses demonstrated an increased oxidative stress index and a marked DNA damage in patients with β-TM. DNA damage may be decreased by reducing iron overload and oxidant level on one hand and increasing antioxidant capacity on the other. The combination of effective iron-chelatory agents with natural or synthetic antioxidants can be very helpful in the clinical practice and in decrease of the oxidant stress and DNA damage of patients with β-TM.

References