Malondialdehyde and sulfhydryl groups as biomarkers of oxidative stress in patients with systemic lupus erythematosus

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ABSTRACT
Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown origin associated with oxidative stress. The present study aimed to investigate the presence of oxidative stress in patients with newly diagnosed SLE. SLE patients (n = 36) and control subjects (n = 28) were enrolled in this study. Blood samples were used for malondialdehyde (MDA), sulfhydryl groups (SH) and uric acid determination. MDA levels (µmol/L) were higher in patients (3.9 ± 2.6) than in control subjects (1.6 ± 2.6). SH were significantly lower in SLE patients. The findings suggest that MDA can be a good marker of oxidative stress in SLE.

Keywords: oxidative stress, antioxidants, lupus erythematosus systemic, uric acid.

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before taking part in the study and were submitted to a standardized questionnaire for demographic factors.

The venous blood collection (10 mL) from each participant was done with an evacuated tube system (BD Vacutainer® System) and centrifuged (800 g, 15 min). Serum was used for determining biochemical and immunological markers.

MDA was determined by High Performance Liquid Chromatography (HPLC); chromatograms were monitored at 532 nm and the sample concentration was determined in µmol/L. Uric acid was measured using Cobas Mira® spectrophotometric analyzer (Roche Instruments Inc.), with commercially available kits (Labtest, Minas Gerais, Brazil). SH groups were determined by the Ellmans method, modified by Hu et al. The results were expressed as means ± standard deviation (SD). Student’s t-distribution was used to compare mean values. Pearson’s and Spearman’s correlations were applied to correlate the parameters with SLEDAI. P < 0.05 was considered to be statistically significant.

General and demographic characteristics of SLE patients and healthy controls are presented in Table 1. There was also no difference between duration, criteria number, and activity of the disease and oxidative stress (P > 0.05).

Lupus is characterized by direct aggression of autoantibodies and complement-fixing immune complex deposition that result in tissues’ damage associated to oxidative stress. Waszczykowska et al. suggested that intracellular free radicals are capable of inducing cytokine synthesis that participate and modulate inflammatory responses with the creation of superoxide radicals.

Oxidative stress, measured by MDA levels, was found increased in 78.9% (n = 30) of SLE patients, while only 21.1% (n = 8) of normal controls presented that increase (OR = 12.5; 95% CI 3.7–41.5). As shown in Table 2, MDA levels were found to be significantly increased in SLE patients compared to normal controls. No significant difference was found between MDA levels and the duration of the disease or comorbidities. Increased level of MDA in the serum and in the erythrocytes was reported in SLE patients. Wang et al. and Shah et al. associated stronger oxidative stress response with higher SLEDAI scores, similar to the previous report of Tewthanom et al. However, we have not identified, in our study, the association of MDA or SH levels with SLEDAI scores. The high levels of MDA in SLE patients indicate that the lipid cell membrane was attacked and that MDA can be a good marker of oxidative stress in this disease.

There was no significant change in serum levels of uric acid in SLE patients compared to normal controls (4.1 ± 1.5 and 3.8 ± 0.9 mg/dL, respectively). No correlation was found between the serum levels of this compound and disease activity. Deminice et al. associated uric acid as an oxidative stress biomarker response to an acute session of hypertrophy-resistance traditional interval training and circuit training. Ikeda et al., however, could not make the same association when oxidative stress was observed in patients with progressive amyotrophic lateral sclerosis. Although uric acid is consider an important antioxidant and its serum levels were expected to be lower in SLE patients than in normal controls, our study could not associate this substance as a secure biomarker of oxidative stress either.

Morgan et al. showed that markers of protein oxidation correlate with worsening disease status in SLE. In our study, SH group levels were found to be significantly decreased in SLE patients compared to normal controls (260.2 ± 182.7 versus 339.4 ± 104.3 µmol/L), similar to the report of Zhang et al. This supports the role of oxidative stress in the pathogenesis of SLE.

We concluded that SLE patients present increases in oxidative stress. However, this response is not correlated to the disease activity or its duration. MDA and SH group levels can be used as biomarkers to measure oxidative stress in SLE patients, whereas uric acid cannot be used for the same purpose. Further studies on oxidative stress and SLE are still necessary to improve our understanding of the disease pathogenesis.

Table 1
General and demographic characteristics of systemic lupus erythematosus patients and healthy controls

<table>
<thead>
<tr>
<th>General data</th>
<th>SLE (n = 36)</th>
<th>Control (n = 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>28.2 ± 13</td>
<td>27.9 ± 9.9</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>33 (91.6%)</td>
<td>28 (100%)</td>
</tr>
<tr>
<td>ACR number</td>
<td>5.3 ± 1.1</td>
<td>NA</td>
</tr>
<tr>
<td>DT (month)</td>
<td>5.9 ± 3.5</td>
<td>NA</td>
</tr>
<tr>
<td>SLEDAI number</td>
<td>10.3 ± 6.6</td>
<td>NA</td>
</tr>
</tbody>
</table>

SLE: systemic lupus erythematosus; ACR: American College of Rheumatology; DT: disease time; NA: not applicable.

Values are expressed as mean ± SD.

Table 2
Comparison between oxidant and antioxidant parameters in patients with systemic lupus erythematosus and healthy controls

<table>
<thead>
<tr>
<th>Mean</th>
<th>SLE (n = 36)</th>
<th>Control (n = 28)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA (µmol/L)</td>
<td>3.9 ± 2.6</td>
<td>1.6 ± 2.6</td>
<td>0.001</td>
</tr>
<tr>
<td>SH group (µmol/L)</td>
<td>260.2 ± 182.7</td>
<td>339.4 ± 104.3</td>
<td>0.04</td>
</tr>
<tr>
<td>Uric acid (mg/dL)</td>
<td>4.1 ± 1.5</td>
<td>3.8 ± 0.9</td>
<td>0.48</td>
</tr>
</tbody>
</table>

SLE: systemic lupus erythematosus; MDA: malondialdehyde; SH: sulfhydryl.

Values are expressed as mean ± SD and the differences were considered significant when P < 0.05.
REFERENCES


