The role of oxidants and antioxidants in chronic tonsillitis and adenoid hypertrophy in children

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Received 26 September 2003; received in revised form 5 April 2004; accepted 6 April 2004

KEYWORDS
Tonsil; Adenoids; Oxidative stress; Antioxidants

Summary Objective: To determine the possible role of oxidants and antioxidants in the pathogenesis of chronic tonsillitis (CT) and adenoid hypertrophy (AH) in children. Methods: Randomized, prospective, controlled. The study group was made up of children with chronic tonsillitis and adenoid hypertrophy who are to undergo tonsillectomy and adenoidectomy. The control group was constructed with otherwise healthy children with normal ENT examination. The blood levels of antioxidants (retinol, ɑ-carotene, ɑ-tocopherol, laycopene, ascorbic acid, superoxide dismutase, glutathione peroxidase, GSH) and peroxidation products (malondialdehyde) were determined before and 1 month after the operation in the study group and once only in the control group. These antioxidants and peroxidation products were also measured in the tonsil and adenoid tissue that were obtained during operation. Results: In the study group, the blood levels of antioxidants and oxidant before and after the operation were significantly different when compared to the control group (P < 0.05). In the study group, the blood antioxidant levels increased and oxidant level decreased significantly after the operation (P < 0.05). These levels after the operation never reached those of the control group. Conclusions: Oxidants and antioxidants played a significant role in the pathogenesis of chronic tonsillitis and adenoid hypertrophy in children. These children are under significant oxidative stress. Tonsillectomy and adenoidectomy significantly decreased the oxidative stress in these patients, but could not normalize it completely. Further studies are necessary to evaluate their possible therapeutic role in preventing recurrent tonsillitis and treating postoperative patients to help normalize their blood levels of antioxidants.

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1. Introduction

Chronic tonsillitis (CT) with or without adenoid hypertrophy (AH) is a very frequently encountered disease in children. It leads to recurrent attacks of throat pain, fever, dysphagia, and malaise. It causes frequent absenteeism from school. It is among the most common causes of obstructive sleep apnea syndrome in children. It has a negative impact on sleep quality and school success of young children. The nutrition, growth, development and social lives of children are influenced negatively by this disease. Antibiotics and various adjunctive drugs used to treat this disease lead to many side effects in children. The economic burden of medical and surgical treatment of this disease is tremendous.
A free radical can be defined as any species containing one or more unpaired electrons. Since these molecules are highly reactive they can cause tissue damage especially in cell membranes by reacting with cellular lipids, proteins, nucleotides and carbohydrates. Under normal circumstances, the potential damaging effects of these free radicals are limited by a number of antioxidants in body. In addition to the antioxidant enzymes, namely catalase, superoxide dismutase, glutathione peroxidase and glucose-6-phosphate dehydrogenase, the blood and some other tissues contain non-enzymatic antioxidants, namely \( \alpha \)-tocopherol, \( \beta \)-carotene, retinol, and ascorbic acid, among others. Antioxidants within cells, cell membranes, and extracellular fluids can be up-regulated and mobilized to neutralize excessive and inappropriate free radical formation. Within strategy to maintain redox balance against oxidant conditions, blood has a central role because it transports and redistributes antioxidants to every part of the body [1].

Oxidation products are produced within the cell during various cellular reactions. Chemical substances, drugs, radiation, oxygen, cellular aging, and phagocytes lead to production of oxidants. These molecules must be neutralized by antioxidants; otherwise, oxidants react with cellular proteins and nucleic acids to eliminate their actions. As a result cellular injury and death is possible. This cellular injury may lead to various diseases. Antioxidants are known to counteract the destructive effects of oxidants at cellular level and also play a significant role in treatment of oxidant related diseases.

The oxidation products are produced during inflammation and are involved in the tissue injury due to this inflammation. The antioxidants play role in neutralizing the destruction by these oxidation products. Since CT and AH is a chronic inflammatory disease in the oro- and nasopharynx, there is a significant possibility that the balance between oxidation products and antioxidants is involved in the appearance and the chronicity of this disease in the pharynx. However, the role of oxidants and antioxidants in the pathogenesis of CT and AH is not well defined.

There are a few studies on the role of oxidants and antioxidants in CT and AH in the medical literature. However, these studies measured only few parameters. In this study we investigated nine different parameters in blood, tonsil and adenoid tissue to determine whether antioxidants are associated with CT and AH under the view of the recent literature.

2. Methods

This study was done in the tertiary referral center during summer months of 2001. Institutional ethic committee approval was obtained. Informed consent was obtained from the parents of all children.

The control group was made up of 23 otherwise healthy children without any complaint in the head and neck region, without any infection and any other systemic disease. The study group consisted of 38 patients who were planned to undergo tonsillectomy with adenoidectomy with a diagnosis of CT and AH. The patients were 2–14-year-old children without any systemic disease and without any history of operation to the tonsils and adenoids.

CT and AH was diagnosed by history, ENT examination and endoscopic examination. Frequent attacks of tonsillitis and adenoiditis, respiratory obstruction by enlarged tonsils and adenoids, chronically inflamed tonsils and adenoids with white debris coming from the crypts of tonsils were accepted as indications for tonsillectomy and adenoidectomy. The operation was carried out under general anesthesia.

In addition to the routine preoperative blood tests in the study group, 8 cc of blood was obtained from the patients before the operation. The blood was stored at \(-70^\circ C\) after separating serum from the cells (1500 rpm; 10–15 min). Tonsillectomy and adenoidectomy specimens were also stored at \(-70^\circ C\). One month after the operation another blood specimen was obtained from the study group and stored in a similar manner. Blood was obtained from the control group just once.

The following antioxidants were determined in the sera of the children in the study and control group: retinol, \( \beta \)-carotene, \( \alpha \)-tocopherol, laycopene, and ascorbic acid. In their plasma, superoxide dismutase (SOD) activity, glutathione peroxidase activity and reduced glutathione (GSH) were also obtained as antioxidants. As a peroxidation product malondialdehyde-thiobarbituric acid (MDA) combination was determined in the plasma. The same measurements were also done in the tonsil and adenoid tissue. However, ascorbic acid level was found too low to be measured in the adenoid tissue.

The biochemical measurements were carried out in the laboratory at the Department of Nutrition and Dietetics. Retinol, \( \beta \)-carotene, \( \alpha \)-tocopherol, and laycopene measurements in the sera were performed using high-pressure liquid chromatography (HPLC). HPLC was also used to measure peroxidation product malondialdehyde-thiobarbituric acid combination in the plasma. Serum ascor-
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were expressed as 'laycopene, ascorbic acid, and reduced glutathione
malondialdehyde-TBA level as 'dase and superoxide dismutase level as 'U/ml',
were expressed as 'laycopene, ascorbic acid, and reduced glutathione
levels of retinol,
H9252
8700.
carried out spectrophotometrically with Unicam
H9250
H9251
H9262

\[1\]. Plasma glutathione peroxidase activity
was determined by following the changes in
H9251
H9252
NADPH with Unicam 8700 at 340nm after stimula-
tion with hydrogen peroxide. Plasma reduced gluta-
thione and superoxide dismutase analyses were
carried out spectrophotometrically with Unicam
H9270.

Blood levels of retinol, β-carotene, α-tocopherol, laycopene, ascorbic acid, and reduced glutathione
were expressed as 'μmol/l'; glutathione peroxi-
dase and superoxide dismutase level as 'U/ml',
malondialdehyde-TBA level as 'μmol/ml'. Tissue
levels of retinol, β-carotene, α-tocopherol, lay-
copene, ascorbic acid, and reduced glutathione
were expressed as 'μmol/g'; glutathione peroxi-
dase and superoxide dismutase level as 'U/mg',
and MDA level as 'μmol/mg'.

Tonsil and adenoid tissues were initially homog-
enized using IKA T-25 homogenization apparatus;
afterwards, the antioxidants and oxidation prod-
ucts were measured using the methods mentioned
above.

After the operation the patients were regularly
followed. One month postoperatively the same
amount of blood was withdrawn from the patients
and the antioxidants and oxidation products were
measured as mentioned.

It was not ethically acceptable to create a control
group for the tonsillar tissue measurements in order
to statistically compare these values with any cor-
responding value. Antioxidant and oxidation prod-
uct levels in the adenoid tissues of patients with
CT and AH were compared with those of the pa-
tients with otitis media with effusion (OME) who
underwent bilateral ventilation tube insertion and
adenoidectomy. These values were obtained in the
study performed in a similar manner on patients
with OME.

The antioxidant and oxidation product levels in
preoperative and postoperative blood were statisti-
cally compared with each other and with those of
the control group using Student’s t-test. The sta-
tistical analyses of our study were done using SPSS
H9262
H9262
H9262
H9262
H9262
H9262
H9262

1055

3. Results
The study group was made up of 14 girls and 24 boys
with a mean age of 6.7 years. The control group
consisted of 14 girls and nine boys with a mean age
of 7.1 years. The differences between sex distribu-
tions and mean ages of both groups were statisti-
cally insignificant (P > 0.05).

The preoperative and postoperative blood levels
of antioxidants and oxidation products of the study

group were given in Table 1. The differences be-
tween preoperative and postoperative blood levels
were statistically significant for all materials tested
(Student’s t-test for dependent samples, P < 0.05).
The mean blood levels of antioxidants and oxidation
products of the control group were given in Table 2.
The differences between preoperative blood lev-
els of the study group and those of the control
group were statistically significant for all materials

tested (Student’s t-test for independent samples,
P < 0.05) (Table 3).

The differences between postoperative blood
levels of the study group and those of the control
group were statistically significant for all materials
tested (Student’s t-test for independent samples,
P < 0.05), except MDA (P > 0.05) (Table 4).

Antioxidant and oxidation product levels in the
tonsillar tissues of patients with CT and AH who un-
derwent tonsillectomy and adenoidectomy opera-
tion were shown in Table 5.

Antioxidant and oxidation product levels in the
adenoid tissues of patients with CT and AH who
underwent tonsillectomy and adenoidectomy opera-
tion were compared with those of the OME
patients who underwent adenoidectomy and ven-
tilation tube insertion. The differences were found
to be statistically insignificant for all materials
tested (Table 6, Student’s t-test for independent
samples, P > 0.05).

4. Discussion

Attacks of acute tonsillitis and adenoiditis and
tonsillar and adenoid hypertrophy are among
the important health problems in preschool- and
school-aged children. The social and physical mor-
bidity they cause is significant. If they do not re-
spond to medical treatment and disturb the life of
the patient significantly, the treatment of choice
is surgery. Despite the frequency of these diseases
and the significant morbidity they cause their
pathogenesis is not exactly known [2,3].

During chronic inflammatory processes antioxi-
dants decrease slowly when the level of oxidative
stress they can neutralize is exceeded. Low antiox-
idant levels may be the result of chronic diseases.
Free radical damage to the membrane lipids of
leucocytes leads to increased permeability, and
therefore decreases their immune function. DNA
damage by free radicals decreases synthesis of cer-
tain critical factors by leucocytes and decreases
reproductive capacity of leucocytes. Low antioxidant levels in blood may predispose children to frequent upper respiratory infections by negatively influencing their immune system.

Finding antioxidants and oxidation products in tonsil and adenoid tissues of patients with chronic adenotonsillitis indicates their association with this disease.

The levels of antioxidants and oxidants in adenoid tissue of patients with otitis media with effusion and chronic tonsillitis were found similar in our study. This indicates a similar pathogenesis of adenoiditis in both clinical conditions. We may also speculate that almost identical inflammation takes place in adenoid tissue in OME and chronic tonsillitis, and that this inflammation produces oxidation products and uses up the antioxidants in adenoid tissue. It is not exactly clear yet, why some of these children develop OME and some only adenoiditis.

Shukla et al. [4] determined that in adolescents with chronic tonsillitis the postoperative blood levels of MDA decreased and those of SOD and catalase increased. Our results are parallel to their findings. In our patients with chronic tonsillitis, high blood level of oxidation product (MDA) decreased and low blood levels of antioxidants increased postoperatively.

Westerveld et al. [5] found lower levels of glutathione and uric acid in the sinus mucosa of patients with sinusitis when compared to healthy subjects. This result indicates inflammatory consumption of antioxidants in sinus mucosa.

In patients with CT who developed complications or who had severe attacks were shown to have lower blood levels of Vitamins B and C than healthy people. These patients also had decreased activity of cellular immune system and leukocyte chemotaxis [6].

Our results showed that the decreased preoperative blood levels of antioxidant vitamins and enzymes significantly increased postoperatively, and that increased preoperative blood level of oxidation product MDA significantly decreased post-
Oxidants and antioxidants in chronic tonsillitis and adenoid hypertrophy in children

Table 3

<table>
<thead>
<tr>
<th>Preoperative blood</th>
<th>Study group</th>
<th>Control group</th>
<th>P</th>
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<tbody>
<tr>
<td>Retinol</td>
<td>1.60 ± 0.09</td>
<td>1.85 ± 0.10</td>
<td>0.0001</td>
</tr>
<tr>
<td>a-Tocopherol</td>
<td>23.08 ± 0.40</td>
<td>24.26 ± 0.60</td>
<td>0.0001</td>
</tr>
<tr>
<td>β-Carotene</td>
<td>0.30 ± 0.03</td>
<td>0.39 ± 0.03</td>
<td>0.0001</td>
</tr>
<tr>
<td>Lycopene</td>
<td>0.52 ± 0.02</td>
<td>0.72 ± 0.06</td>
<td>0.0001</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>53.14 ± 3.56</td>
<td>65.09 ± 4.71</td>
<td>0.0001</td>
</tr>
<tr>
<td>GSH</td>
<td>4.58 ± 0.17</td>
<td>5.93 ± 0.30</td>
<td>0.0001</td>
</tr>
<tr>
<td>Glutathione peroxidase</td>
<td>40.16 ± 2.52</td>
<td>51.85 ± 6.78</td>
<td>0.0001</td>
</tr>
<tr>
<td>Superoxide dismutase</td>
<td>936.98 ± 99.63</td>
<td>1115.79 ± 193.39</td>
<td>0.0001</td>
</tr>
<tr>
<td>MDA</td>
<td>12.68 ± 1.10</td>
<td>11.31 ± 2.37</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Student’s t-test for independent samples, \( P < 0.05 \), mean ± standard deviation.

Table 4

<table>
<thead>
<tr>
<th>Postoperative blood</th>
<th>Study group</th>
<th>Control group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinol</td>
<td>1.70 ± 0.04</td>
<td>1.85 ± 0.10</td>
<td>0.0001</td>
</tr>
<tr>
<td>a-Tocopherol</td>
<td>23.73 ± 0.34</td>
<td>24.26 ± 0.60</td>
<td>0.0001</td>
</tr>
<tr>
<td>β-Carotene</td>
<td>0.34 ± 0.02</td>
<td>0.39 ± 0.03</td>
<td>0.0001</td>
</tr>
<tr>
<td>Lycopene</td>
<td>0.60 ± 0.03</td>
<td>0.72 ± 0.06</td>
<td>0.0001</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>59.97 ± 3.18</td>
<td>65.09 ± 4.71</td>
<td>0.0001</td>
</tr>
<tr>
<td>GSH</td>
<td>5.17 ± 0.20</td>
<td>5.93 ± 0.30</td>
<td>0.0001</td>
</tr>
<tr>
<td>Glutathione peroxidase</td>
<td>48.66 ± 3.56</td>
<td>51.85 ± 6.78</td>
<td>0.045</td>
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<tr>
<td>Superoxide dismutase</td>
<td>1021.78 ± 108.46</td>
<td>1115.79 ± 193.39</td>
<td>0.05</td>
</tr>
<tr>
<td>MDA</td>
<td>11.87 ± 1.02</td>
<td>11.31 ± 2.37</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Student’s t-test for independent samples, \( P < 0.05 \), mean ± standard deviation.

Operatively. However, these levels never reached those of the control group. The oxidative stress in the tonsillar tissue obviously affected the whole body. We may conclude that antioxidant capacity of the study group increased but not normalized 1 month after the operation and that the oxidative stress decreased but still continued. The noxious effects to whole body of the oxidative stress also decreased. Probably 1 month was not long enough for the oxidative stress or antioxidant capacity to normalize. Nevertheless, significant postoperative improvement in the oxidative stress indicated that the operation was helpful in this respect. Tonsillectomy and adenoidectomy removed microbrial sources in these children and thus, decreased general oxidative stress. These operations also might have supported the immune system of these children.

Özdemir et al. [7] found decreased tonsillar blood flow in patients with CT and increased blood flow in hypertrophic tonsils. Our results demonstrated lower tonsillar levels of antioxidants taken in diet (vitamins) and higher tonsillar levels of locally produced antioxidants (SOD, glutathione peroxidase and GSH) and oxidation product MDA compared to their blood levels. These findings indicate either that antioxidants in the blood reached tonsils less due to decreased blood supply or that they were consumed locally due to inflammation, or that more antioxidants and lipid oxidation products were produced locally due to inflammation and pooled in tonsillar tissue due to decreased blood supply of tonsils.

As a conclusion, low blood and tissue levels of antioxidants and high blood and tissue level of oxi-
The comparison of antioxidant and oxidation product levels in the adenoid tissues of patients with CT and AH with those of the OME patients

<table>
<thead>
<tr>
<th>Adenoid tissue</th>
<th>Group</th>
<th>Mean ± standard deviation</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinol</td>
<td>Tonsil</td>
<td>0.24 ± 0.03</td>
<td>0.73</td>
<td>0.467</td>
</tr>
<tr>
<td></td>
<td>OME</td>
<td>0.25 ± 0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>α-Tocopherol</td>
<td>Tonsil</td>
<td>4.54 ± 1.24</td>
<td>0.59</td>
<td>0.557</td>
</tr>
<tr>
<td></td>
<td>OME</td>
<td>4.77 ± 1.79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Carotene</td>
<td>Tonsil</td>
<td>0.06 ± 0.01</td>
<td>0.06</td>
<td>0.899</td>
</tr>
<tr>
<td></td>
<td>OME</td>
<td>0.06 ± 0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lycopene</td>
<td>Tonsil</td>
<td>0.09 ± 0.01</td>
<td>1.04</td>
<td>0.302</td>
</tr>
<tr>
<td></td>
<td>OME</td>
<td>0.09 ± 0.01</td>
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<td></td>
</tr>
<tr>
<td>GSH</td>
<td>Tonsil</td>
<td>0.75 ± 0.19</td>
<td>1.98</td>
<td>0.053</td>
</tr>
<tr>
<td></td>
<td>OME</td>
<td>0.87 ± 0.26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glutathione peroxidase</td>
<td>Tonsil</td>
<td>9.06 ± 2.39</td>
<td>0.50</td>
<td>0.618</td>
</tr>
<tr>
<td></td>
<td>OME</td>
<td>9.36 ± 1.90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOD</td>
<td>Tonsil</td>
<td>456.02 ± 135.62</td>
<td>0.94</td>
<td>0.351</td>
</tr>
<tr>
<td></td>
<td>OME</td>
<td>497.64 ± 210.62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDA</td>
<td>Tonsil</td>
<td>3.85 ± 0.25</td>
<td>0.12</td>
<td>0.904</td>
</tr>
<tr>
<td></td>
<td>OME</td>
<td>3.86 ± 0.39</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

dation product in patients with CT and AH, and the tendency of blood levels to normalize after surgery indicate that they are involved in the pathogenesis of CT and AH. Further studies are necessary to evaluate their possible therapeutic role in preventing recurrent tonsillitis and treating postoperative patients to help normalize their blood levels of antioxidants.

Acknowledgements

This work was partially supported by Grants from the Hacettepe University Scientific Research Fund (01 402 01 002 and 01 402 01 004).

References