NON-INVASIVE MONITORING FOR LOCAL IMMUNE AND ANTIOXIDANT RESISTANCE IN PATIENTS WITH ISCHEMIC HEART DISEASE AND TYPE 2 DIABETES


Kuban State Medical University, Krasnodar, Russian Federation

The item offers a view at the changes taking place in the immunologic responsiveness and the indices for the pro-oxidant–anti-oxidant system in the blood and in the oral liquid in case of T2D and IHD. There has been a significant IgA increase detected in the oral cavity in cases of T2D coming along with IHD (2.1 times), and IgM – at T2D (4 times). An imbalance has been found in the pro-oxidant–anti-oxidant system, accompanied by an increase in products of oxidative modification of biomolecules and decreased activity of catalase and superoxide dismutase in blood and oral liquid, especially in case of T2D comorbid with IHD. There has been significant correlation links established between the indices of immunologic responsiveness and the enzymes of anti-radical protection in blood and in oral liquid, as well as direct reliable correlation links between clinical indices for periodontal status and the indicators of non-specific protection in the oral cavity (r=±0.76–0.99).

Key words: oral liquid, diabetes mellitus, ischemic heart disease, immunoglobulin, superoxide dismutase
Material and Methods. The biological material used for the study included blood and oral liquid in patients with T2D (Group 1, n=25), average duration of disease 8.9±1.1 yrs, mean age 60.3±2.9 yrs, IHD (Group 2, n=25), average duration of disease 9.3±0.9 yrs, mean age 77.4±2.0) and cases of IHD along with T2D (Group 3, n=25), average duration of diseases 14.1±1.3 yrs, mean age 65.9±2.1), while the control group included 25 people (Group 4, mean age 64.7±11.5 yrs). The selection and check-up of the patients was carried out on the premises of the Cardiology Ward of Prof. Krasovitov Regional Clinical Hospital № 1, Cardiocrinology Ward of Prof. Ochapovsky Regional Clinical Hospital, Regional Counseling Polyclinic, Polyclinic № 7 of City of Krasnodar.

The status of the periodontal tissues was evaluated using clinical indices, which was done in order to improve the general reliability of the findings [4]. The periodontal status was scored in points employing the Periodontal disease index of Russell (PI – A. Russell, 1956) and the papillary marginal alveolar index (PMA, %), where the gum around each tooth is stained following Schiller-Pisarev’s test.

The activity levels for anti-radical enzymes of the first-line protection (SOD) was detected based on the SOD capacity to inhibit quercetin auto-oxidation due to dismutation of superoxide anion radical that develops at quercetin oxidation in the presence of N,N,N₁,N₁-te-tramethylenediamine under aerobic conditions [8]. The SOD specific activity was expressed in standard units in relation to 1g protein of oral liquid or hemoglobin. The catalase (CAT) activity was detected via the peroxidation of TBA-reactive products (TBA-RP) per 1 L of oral liquid or blood plasma [6].

The evaluation of the major Ig’s in blood serum was performed with variation statistics methods employing the Student’s t-test. The difference was considered statistically meaningful at p<0.05. Pearson’s coefficient (r) was used to evaluate the correlation interconnections of certain parameters under study.

Results and Discussion. The study has shown that the patients with IHD and T2D revealed prominent changes in the clinical indices reflecting the periodontal status (Table). There were prominent inflammation-dystrophic processes identified. The PI, which allows detecting the prevalence and the intensity of gum tissue lesion proved rather high in Group 3 and was above that of Group 1 by 4.9 %, Group 2 – by 67.9 %, while exceeding the control Group’s (4) indices 18.4 times (p<0.05). The PMA index was basically no different in Groups 1 and 3, yet exceeded the same index of Group 2 by 11.6 %, and was significantly above that in the control Group.

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The evaluation of the major Ig’s in blood serum showed the presence of the most prominent changes in the IgA concentration, which was significantly above the control level in all the clinical groups with a maximum level (2.8 times, p<0.05) registered in the patients of Group 3 whereas the minimal increase (1.7 times, p<0.05) was detected in Group 2. Study of the oral liquid showed lack of prominent changes in the IgG levels. Locally, the most significant changes are related to IgM, the levels of which were significantly above the control indices: in Group 1 – 4 times; in Group 3 –3.6 times, and in Group 2 –3 times, and was in significant correlation with the clinical indices of the periodontal status: rlgM[PM(A),PI] = 0.99*, 0.98*, respectively (“*”p<0.05). The levels of IgA and M correlated in the blood and in the oral liquid of the patients from the groups under study: r(lgA)= 0.76, r(lgM)= 0.50, which proves that oral liquid can be reasonably used to evaluate the immune disbalance at such nosologies.

When studying the AOS indices in blood there was detected a decrease in the activity of the major anti-radical protection enzymes: the CAT activity was reduced in Group 1 – by 41.6 % (p<0.05), Group 2 – by 30.6 % (p<0.05), Group 3 – by 49.5 % (p<0.05). This means a higher risk of hydrogen peroxide change to a toxic free hydroxyl radical, which can initiate peroxide modification of biomolecules followed by cytology. During that, even more prominent was the reduction in the SOD activity, which dropped in all the experimental groups as well, and which serves proof to disturbed deactivation of superoxide anion radical, whilst the latter is one of the key oxi-dation factors. The oral liquid also revealed some reduction in the CAT and SOD activity, yet to a lower degree compared to the blood of the patients who went through the check-up, which is indicative of the oral cavity having its internal local AOS that allows autonomous regulation of FRO intensity through anti-radical enzymes.

### Table 1

<table>
<thead>
<tr>
<th>Index</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>sIgA</td>
<td>0.26±0.04</td>
<td>0.19±0.03</td>
<td>0.35±0.05*</td>
<td>0.17±0.02</td>
</tr>
<tr>
<td>IgM</td>
<td>0.012±0.001*</td>
<td>0.009±0.001*</td>
<td>0.011±0.001*</td>
<td>0.003±0.001*</td>
</tr>
<tr>
<td>IgG</td>
<td>0.20±0.02</td>
<td>0.20±0.02</td>
<td>0.20±0.01</td>
<td>0.19±0.01</td>
</tr>
<tr>
<td>Lactoferin</td>
<td>1675.29±123.12*</td>
<td>1741.06±109.43*</td>
<td>1868.58±98.32*</td>
<td>1410.75±98.43</td>
</tr>
<tr>
<td>SOD</td>
<td>13.48±0.45*</td>
<td>15.98±0.71*</td>
<td>12.19±0.52*</td>
<td>23.36±1.43</td>
</tr>
<tr>
<td>CAT</td>
<td>41.67±0.92*</td>
<td>50.72±1.06*</td>
<td>32.86±0.93*</td>
<td>65.29±1.51</td>
</tr>
<tr>
<td>TBA-RP</td>
<td>1.93±0.07*</td>
<td>1.09±0.10*</td>
<td>2.71±0.14*</td>
<td>0.62±0.08</td>
</tr>
</tbody>
</table>

* p<0.05 compared with the indices in the control Group 4.
The study revealed the highest reverse correlation between the clinical indices and the activity of the anti-radical enzymes of the first (SOD) and the second (CAT) lines of protection: r_{SOD/(PMA, PI)} = –0.97* and –0.99* respectively (p<0.05), r_{CAT/(PMA, PI)} = –0.89* and –0.97* respectively (p<0.05). The obtained outcomes indicate the leading role of the enzymes in regulating the utilization of active oxygen forms both in implementing local protection mechanisms at OS that prevent delayed complications following IHD and Type 2 diabetes, and in maintaining the auxiliary reactions in the local immunity.

Increased lactoferrin levels were less prominent in the oral cavity compared to their fluctuations in blood in cases of IHD and T2D. The nature of the changes taking place in the lactoferrin in the oral liquid of patients from the clinical groups generally indicates excessive production of superoxide anion radical at inflammatory lesion of periodont under reduced activity of SOD in the oral liquid and the clinical value of the reactive oxygen species involvement in the development of delayed dental complications in patients with IHD and Type 2 diabetes.

Conclusions. Disturbed local production of humoral protection factors at IHD and T2D at the local and the systemic levels are mostly due to prominent increase in the production of IgA and IgM in the oral liquid, while their study revealed a reliable direct correlation with similar indices in blood and the clinical indices for the periodontal status.

The development of imbalance in the functioning of pro-oxidant–anti-oxidant system linked with reduced activity in the AOS enzyme chain in oral liquid and in blood (SOD, CAT) results in significant OS, leads to lesion in the periodontal tissues, and points at need for measures aimed at improving anti-oxidant potential in the oral liquid.

The changes of certain indices registered in the oral liquid in some cases (IgM, sIgA, LF, SOD) is of higher diagnostic importance in case of IHD and Type 2 diabetes than detecting similar values in blood, which allows conducting non-invasive monitoring and evaluating the efficiency of the respective therapeutic measures in the outpatient setting.

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References