Levels of Insulin, IL-6 and CRP in Patients with Unstable Angina

Stężenie insuliny, IL-6 i CRP u pacjentów chorych na niestabilną dławicą piersiową

Abstract

Background. Unstable angina is a condition in which your heart doesn’t get enough blood flow and oxygen. It may lead to a heart attack. Insulin resistance is typically defined as decreased sensitivity or responsiveness to metabolic actions of insulin, such as insulin-mediated glucose disposal in skeletal muscle and adipose tissue and inhibition of hepatic glucose production. Crosstalk between inflammatory signaling pathways and insulin signaling pathways causes metabolic insulin resistance and endothelial dysfunction.

Objectives. The present study aimed to evaluate the serum levels of pro-inflammatory cytokines and insulin in unstable angina patients.

Material and Methods. The study included 50 patients with unstable angina divided into a female group which contained 16 female patients with an age range of 35–73 years, and a male group which contained 34 male patients with an age range of 40–72 years. Control groups contained forty healthy individuals divided into a female group which contained 16 healthy females with an age range of 35–73 years, and a male group which contained 24 males with an age range of 42–72 years. ELISA kits were used to measure insulin, IL-6 and CRP. The kits were imported from Biological Company in the United States of America.

Result. The levels of insulin and IL-6 were considerably elevated throughout (p < 0.001), an optimistic relationship concerning insulin with CRP and IL-6 in unstable angina patients.

Conclusions. There was increase in the level of insulin regarding patients with unsteady angina as a result of insulin resistance that was caused by the elevated level of proinflammatory cytokine (IL-6) (Adv Clin Exp Med 2013, 22, 5, 655–658).

Key words: insulin, CRP, IL-6, unstable angina.

Słowa kluczowe: insulina, CRP, IL-6, niestabilna dławica piersiowa.
inhibition of hepatic glucose production. Crosstalk between inflammatory signaling pathways and insulin signaling pathways causes metabolic insulin resistance and endothelial dysfunction [3]. Insulin resistance plays a major pathophysiological role in type 2 diabetes and is tightly associated with major public health problems including obesity, hypertension, coronary artery disease, dyslipidemia, and a cluster of metabolic and cardiovascular abnormalities that define the metabolic syndrome [4]. The metabolic syndrome is a pro-inflammatory state because it is associated with elevations in the levels of IL-6, C-reactive, plasminogen activator inhibitor-1 and protein fibrinogen, all of which promote the development of atherosclerotic cardiovascular disease [5].

IL-6 could be considered the most significant intermediate of temperature rising in the body serious phase response. IL-6 initiates dynamism utilization in the fatty tissues and muscles which results in fever. The secretion of IL-6 could be achieved by macrophages as a response to certain bacteriological molecules denoted as PAMPs (Pathogen Associated Molecular Patterns). The PAMPs binds to extremely significant collections of recognition particles of the distinctive immune system named PRRs (Pattern Recognition Receptors) containing TLRs (Toll-Like Receptors). TLRs exist in compartments inside the cells and also on the surface of the cells to initiate intercellular signaling to proactively increase the production of cytokine.

IL-6 is vital for the growing of hybridomas, which is also found in several additional duplicating media like briclane. Adipocytes also produce IL-6 and it is believed to be the cause of overweight persons that have greater endogenous amounts of CPR. Pedersen BK, during his study in 2009, mentioned that intranasal controlled IL-6 displayed improvement of sleep-associated alliance with emotion reminiscences [6]. C-reactive protein plays a biological role in binding phosphocholine, which could be found on the dying or dead cell surfaces (and some sorts of microbes) in order to stimulate the immune system. The liver is responsible for the synthesis of C-Reactive protein [7].

Material and Methods

This study was conducted between February 2010 and May 2011. This study included fifty male patients with unstable angina who were known to the Cardiac Care Unit (CCU) at Ibn Al-Betaar hospital in Baghdad, Iraq. Patients included in this study ranged 35–73 years old. After a thorough examination, samples of blood were collected from the patients, on the first day of admission. Any patients that had diabetes mellitus were excluded. Forty age, sex and BMI matched, seemingly healthy persons, were involved in this study as a control group.

Blood Collection and Laboratory Analysis

Five milliliters of intravenous blood were taken from each control and patient. These samples were taken from fasting persons (at least 10 hours) between 8 a.m. and 9 a.m., the samples transported to plain tubes to determine insulin, CRP and IL-6. Leaving the blood non-heparinized in the tubes to be clotted. After that and in order to separate the serum, centrifugation of the sample was conducted for 5 min (4000 RPM). 1.0 mL was taken into strongly closed Eppendorf tubes and kept at ≈-20°C until examined. To omit kidney diseases, urea and creatinine were analyzed in each serum sample. IL-6, CRP and insulin were determined by using ELISA kits.

Statistical Analysis

Statistical analysis was done by statisticians using SPSS 15.01 Statistical Set for Social Sciences and also Excel 2003. The statistics investigation was done with a self-determining sample t-test for tables with means and standard deviations. \( p \) value of \( \leq 0.05 \) was used as the level of impact. The relationship constant used to find the connection among the calculated markers used a Pearson correlation. Data for the experimental and test results was expressed as mean and standard error.

Results

Serum levels of insulin, CRP and IL-6 were compared between the studied groups as in Table 1. The patients with unstable angina were found to have significantly greater serum of insulin, IL-6 and CRP with \( (p < 0.001) \).

Discussion

The results in Table 1 show there was significant elevation in the level of insulin in patients with unstable angina. This increase may be due to physiological response to a narrowing in vessel diameter because insulin can act as a vasodilator [8]. Also, the increasing level the proinflammatory markers (IL-6 and CRP), as seen in Table 1, may lead to insulin resistance as a response to the decrease in insulin activity \( \beta \)-cell increase insulin secretion.

Recently, a relationship was reported between overweight, irritation, infection and cardiac actions, which now seems well proven.
The latest studies regarding inflammation show a significant association of heart disease and overweight [9, 10].

In serious inflammatory situations, cytokines recruit and organize the inflammatory reaction that comprises growing the hepatic production of acute phase reactants, including CRP. In the absence of active diseases, the plasma quantities of C-reactive protein were small, but this quantity could be raised 1000 times in patients with a provocative response. Moreover being a marker of infection, C-reactive protein can have pro-inflammatory properties as it can initiate the immune system [11].

Chronic contact to IL-6 harms insulin indication in adipocytes and hepatocytes by exciting the suppressor of cytokine signing. Serious IL-6 levels raise insulin sensitivity in muscle. The action of IL-6 on glucose homoeostasis is complicated.

In 2011, Atsushi and his co-workers reported that HbA1c reduced symptoms in patients suffering from diabetes with rheumatoid arthritis (RA) who were treated with a civilized anti-IL-6 antibody [9].

C-reactive protein quantities were reliably found to be elevated over the growing levels of overweight. Also, this study showed an important relationship concerning cardiovascular danger aspects and the likelihood of having raised CRP. This agreed with the latest findings that overweight is in part an inflammatory disorder. C-reactive protein is one of the strongest markers of metabolic danger, and furthermore, may contribute directly in the wall of the arterial cell mechanisms which leads to atherosclerotic lesions and cardiac actions. There is growing recognition that coronary heart disease (CHD) has an inflammatory component [12].

C-reactive protein (CRP) is an inflammatory marker formed and secreted by the liver under the stimulus of cytokines such as tumor necrosis factor-α and interleukins 1 and 6. Numerous studies have confirmed raised levels of CRP and IL-6 among both types of the insulin resistance.

<p>| Table 1. The comparison between groups for (insulin, glucose IL-6 and CRP) in the studied groups |</p>
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Female patients Mean ± SD No. = 16</th>
<th>Female Control Mean ± SD No. = 16</th>
<th>P-value</th>
<th>Male Patient Mean ± SD No. = 24</th>
<th>Male Control Mean ± SD No. = 34</th>
<th>P-value</th>
<th>Total Patients Mean ± SD No. = 50</th>
<th>Total Control Mean ± SD No.40</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin ulU/mL</td>
<td>69.45 ± 12.08</td>
<td>27.71 ± 4.05</td>
<td>&lt; 0.001**</td>
<td>70.19 ± 10.37</td>
<td>33.48 ± 5.89</td>
<td>&lt; 0.001**</td>
<td>69.72 ± 10.99</td>
<td>31.77 ± 4.66</td>
<td>&lt; 0.001**</td>
</tr>
<tr>
<td>Glucose mg/dL</td>
<td>126.56 ± 22.51</td>
<td>84.71 ± 12.07</td>
<td>&lt; 0.001**</td>
<td>137.85 ± 23.48</td>
<td>87.59 ± 10.09</td>
<td>&lt; 0.001**</td>
<td>133.61 ± 21.99</td>
<td>85.55 ± 10.09</td>
<td>&lt; 0.001**</td>
</tr>
<tr>
<td>IL-6 Pg/mL</td>
<td>109.51 ± 21.32</td>
<td>35.76 ± 5.16</td>
<td>&lt; 0.001**</td>
<td>111.27 ± 17.15</td>
<td>34.97 ± 7.82</td>
<td>&lt; 0.001**</td>
<td>110.01 ± 15.03</td>
<td>34.88 ± 10.13</td>
<td>&lt; 0.001**</td>
</tr>
<tr>
<td>CRP mg/L</td>
<td>24.89 ± 6.75</td>
<td>15.99 ± 5.09</td>
<td>&lt; 0.001**</td>
<td>22.07 ± 5.18</td>
<td>11.28 ± 4.33</td>
<td>&lt; 0.001**</td>
<td>23.57 ± 3.14</td>
<td>13.24 ± 2.16</td>
<td>&lt; 0.001**</td>
</tr>
</tbody>
</table>

** – highly significant.

| Table 2. The correlation (r) between insulin with (CRP and IL-6) for the studied groups |
| Parameters | Female Patients No. = 16 (r) | Female Control No. = 16 (r) | Male Patients No. = 24 (r) | Male Control No. = 34 (r) | Total Patients No. = 50 (r) | Total Control No. = 40 (r) |
| IL-6 Pg/mL | 0.416* 0.219 | 0.411* 0.309 | 0.481* 0.397 |
| CRP mg/L | 0.496* 0.381 | 0.429* 0.311 | 0.442* 0.391 |

* – highly significant with p < 0.001.
Shahedi and his co-workers, in 2011, showed that the CRP as a proinflammatory cytokine was considerably greater in diabetic patients compared to ordinary people. Also, they proved that C-reactive protein correlated extremely well with insulin resistance in these patients [13]. The authors concluded there was increase in the level of insulin in patients with unstable angina as a result of insulin resistance, which was caused by elevated levels of pro-inflammatory cytokine (IL-6).

References

Address for correspondence:
Isam Hussain T. Al-Karkhi
College of Dentistry
University of Baghdad
Baghdad Bab Al Mozam
Baghdad
Iraq
Tel.: 00 96 479 036 124 11
E-mail: isamhtk@hotmail.com

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