The Relationship Between The Surgical Stress Associated with Total Hip Arthroplasty and DNA Oxidative Damage

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Introduction

The aim of the present study was to investigate whether 8OHdG (8-hydroxy-2'-deoxyguanosine), which thus indicates DNA oxidative damage, can be used as a parameter to assess surgical stress. Surgical stress involves complex interrelationship of physical stress and mental factors. The results of the reaction to surgical stress can elicit a characteristic response involving increased circulating concentrations of stress hormones (such as cortisol and catecholamines), the synthesis and release of various humoral mediators (such as proinflammatory cytokines), the induction of synthesis and the release of acute-phase proteins (such as C-reactive protein (CRP)), and it may also induce various metabolic changes (such as lipolysis or hyperglycemia). Cytokines and the acute-phase responses play an important role in controlling the immune system. Proinflammatory cytokines, such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8), are all considered to be important mediators of the pathological changes associated with surgery. These cytokines are upregulated after surgical stress to maintain homeostasis; however, an impaired balance of these cytokines can lead to the development of either systemic inflammatory response syndrome (SIRS) or compensatory anti-inflammatory response syndrome (CARS), thus occasionally resulting in multiple-organ failure. However, orthopaedic surgery is generally associated with less surgical stress than abdominal and cardiac surgeries, and SIRS or CARS are very rare after orthopaedic surgery. Therefore, one should be cautious when attempting to estimate the surgical stress associated with orthopaedic surgery by IL-6.

8-hydroxy-2'-deoxyguanosine (8OHdG) which is oxidized from 2'-deoxyguanosine (dG) is an excellent marker of oxidative DNA damage and the 8OHdG/dG ratio in the cell and the tissue is a critical marker of DNA damage, thus resulting in mutagenesis (G-C → T-T; A transversion), carcinogenesis, apoptosis, etc. Therefore, the 8OHdG and 8OHdG/dG ratio has recently gained much attention because of its mutagenic potential, influence on cancer, geriatric disease, mental health, and so on. Because the 8OHdG and 8OHdG/dG ratio can increase in response to both physical and mental stress, it may therefore be potentially useful as an index for surgical stress in orthopaedic surgery. This study investigated the level of 8OHdG and the 8OHdG/dG ratio before and after total hip arthroplasty (THA).

Materials and Methods

In this study any patients with inflammatory arthritis, systemic inflammatory or autoimmune disorders or a history of any type of cancer or chronic illness were excluded and the remaining 10 female patients were thus evaluated. The mean age was 63 years old. The surgical indication for each patient was osteoarthritis of the hip. All of the subjects gave their informed consent and agreed to participate in this study. The anesthesia team was not involved in this study, however, all patients were administered spinal anesthesia. During surgery, each patient had an indwelling urinary catheter inserted which was removed on the second postoperative day. All operations were performed by the senior author using a cementless femoral component (a PerFix-HA modular component, K Yaşargil, Japan) and an AMS-HA acetabular shell with AMS liner. Under spinal anesthesia, the posterolateral approach was selected in all cases. Before wound closure, a 1/8-inch silk suture was used with vacuum suction was inserted, which was removed on the second postoperative day. All patients were given similar postoperative pain regimens. Following surgery, postoperative pain was controlled by the administration of Flurbiprofen axetil, diclofenac sodium and loxoprofen sodium, which were selected by the physician in charge. To measure the CRP levels, blood samples were taken before surgery then at appropriate points at 24 hours thereafter for routine monitoring in accordance with the critical path established at this institution, no additional blood samples were taken for this study. To measure the IL-6 level, 8OHdG level and dG level in the blood samples were spun in a centrifuge for 5 minutes at 3500 rpm to separate the serum. The supernatant was stored at -25°C until a sample analysis was performed. The concentration of IL-6, 8OHdG and dG samples then were determined using commercially available enzyme-linked immunosorbent assays (ELISA). The 8OHdG/dG ratio was calculated based on the results.

All numerical data were expressed as the mean ± standard deviation. Statistical significance was set at p < 0.05 using paired t-test.

Results

No anesthetic or surgical complications were observed including pneumonia, atelectasis, urinary tract infection, thromboembolic events and wound infections. The mean surgical time and total blood loss were 31 ± 4 minutes and 747 ± 212 g. The CRP levels before surgery and the first day after the surgery were 0.1 ± 0.0 mg/dl and 2.7 ± 2.1 mg/dl (p<0.01), respectively. The IL-6 levels before surgery and the first day after the surgery were 4.3 ± 1.9 pg/ml and 57.3 ± 20.1 pg/ml (p<0.01), respectively. The 8OHdG levels before surgery and the first day after the surgery were 1.0 ± 0.2 ng/ml and 4.9 ± 0.7 ng/ml (p<0.01), respectively. The dG levels before surgery and the first day after the surgery were 31.8 ± 11.8 ng/ml and 48.9 ± 15.1 ng/ml (p<0.01), respectively. The 8OHdG/dG levels before surgery and the first day after the surgery were 3.5 ± 1.2 % and 10.7 ± 0.2 % (p<0.01), respectively. (Table)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before THA (mean ± SD)</th>
<th>After THA (24 hours) (mean ± SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP (mg/dl)</td>
<td>0.1 (0.0)</td>
<td>2.7 (2.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>4.3 (1.9)</td>
<td>57.3 (20.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>8OHdG (ng/ml)</td>
<td>1.0 (0.2)</td>
<td>4.9 (0.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>dG (ng/ml)</td>
<td>31.8 (11.8)</td>
<td>48.9 (15.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>8OHdG/dG (%)</td>
<td>3.5 (1.2)</td>
<td>10.7 (0.2)</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

Table Parameters in before and after THA.

Discussion

This is the first study to evaluate surgical stress using the 8OHdG and 8OHdG/dG ratio. The 8OHdG and the 8OHdG/dG ratio, was found to be significantly different before and after THA. Moreover, these indexes responded immediately to the surgical stress of THA. In view of how these indexes are affected by physical and mental stress, the 8OHdG and 8OHdG/dG ratio therefore seems to be a good parameter for monitoring surgical stress in orthopaedic surgery.

References