The immunological response toward botulinum toxin in individuals with facial rejuvenation

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Abstract
The study was conducted in the cities of Tikrit and Kirkuk for the period from December 2016 to February 2017. The study included 60 people who had previously had facial procedures, both male and female, aged between 15 and 50 years to determine the levels of interleukin 2, interleukin 6 and interleukin 8 in individuals with facial rejuvenation by botulinum toxin. The study included those who did not suffer from chronic diseases, immunodeficiency or hypersensitivity for any reason. The study also included 40 healthy and healthy people from all diseases from blood donors and the same age group of the person in question. The study included all information from people in the study, such as age, sex, marital status, smoking, family members, living conditions and concomitant diseases. All people undergoing cosmetic surgery were Botox injectors. The study involved taking 3 ml of blood where the serum was isolated and saved for detection and measurement of levels of interleukin 2, interleukin 6 and interleukin 8 by ELISA technique. The current study showed 50% of each of males and females of patients under butux were within 25-34 years. In this study serum interleukin-2, IL-6 and IL-8 were significantly elevated in cases as compared with control ones (P<0.05), (IL-2: 26.13±2.8 versus 17.11±1.7 pg ml), (IL-6: 31.71±3.1 versus 14.74±3.5 pg ml) and (IL-8: 20.77±4.1 versus 16.38±3.9 pg ml). In comparison between males and females regarding the immune response toward botulinum toxin, the study indicated that interleukin-2, IL-6 and IL-8 were significantly elevated in females as compared with males cases (P<0.05), (IL-2: 28.13±3.1 versus 20.11±2.6 pg ml), (IL-6: 33.91±2.8 versus 26.81±3.8 pg ml) and (IL-8: 24.93±3.8 versus 20.77±3.3 pg ml). It was concluded that IL-2, IL-6 and IL-8 were elevated in facial rejuvenation persons with botulinum toxin especially in females ones

Keyword: Interleukin; IL-6; Botulinum; facial rejuvenation; Plastic surgery

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Introduction
Botulinum toxin (BoNT) is a proteinaceous exotoxin that is produced in the growth and reproduction of anaerobic Clostridium botulinum, a gram-positive and spore-shaped rod bacterium (1). BoNT, as a neurotoxin, is the strongest biotoxin among all known natural and synthetic toxins. Investigations have demonstrated that BoNT could affect the cholinergic motor nerve endings to disturb the release of acetylcholine via the antagonism of calcium ions, thus inhibiting shrink of muscle fibers, causing flaccid paralysis of muscles and developing temporary denervation (2, 21). Botulinum toxin’s most common cosmetic application is in the treatment of upper facial rhytides and dynamic lines, namely glabellar lines, horizontal forehead wrinkles, and crow’s feet (3). In the lower face, the use of botulinum toxin was initially controversial because results were considered unpredictable. While the demarcation between the upper and lower face is somewhat arbitrary, the utility of botulinum toxin in the lower face is becoming increasingly apparent (4, 20). However, the medical literature on the use of botulinum toxin in the lower face and neck is sparse with most publications limited to clinician experiences only. Despite the centrality of the hypothesis, divergent frequencies of neutralizing antibodies have been reported in nonresponders (5). One group reported that 33% of secondary nonresponders had neutralizing antibodies detectable by mouse lethality assays, 4 whereas others, using a mouse diaphragm paralyzation technique, detected neutralizing antibodies in 100% of nonresponders. This reflects differences in the antibody detection technique and illustrates the importance of using objective standardized clinical criteria to identify those who are true secondary non-responders (6). Antibody formation may occur in response to botulinum toxin injections. As the protein load in current preparations is lower than in earlier formulations (prior to 1998), immunological responses with antibody formation have decreased. Nonetheless, immunogenic responses may still occur in the modern formulations, particularly when large doses of botulinum toxin are utilized (most frequently in therapeutic, noncosmetic applications) (7). The overall risk of antibody formation may be minimized by using low
doses with the longest feasible interval between injections (8). So the aim of this study was to determine the levels of interleukin 2, interleukin 6 and interleukin 8 in individuals with facial rejuvenation by botulinum toxin.

**Material and method**

The study was conducted in the cities of Tikrit and Kirkuk for the period from December 2016 to February 2017. The study included 60 people who had previously had facial procedures, both male and female, aged between 15 and 50 years. The study included those who did not suffer from chronic diseases, immunodeficiency or hypersensitivity for any reason. The study also included 40 healthy and healthy people from all diseases from blood donors and the same age group of the person in question. The study included all information from people in the study, such as age, sex, marital status, smoking, family members, living conditions and concomitant diseases. All people undergoing cosmetic surgery were Botox injectors. The study involved taking 3 ml of blood where the serum was isolated and saved for detection and measurement of levels of interleukin 2, interleukin 6 and interleukin 8 by ELISA technique.

**Finding**

The current study showed 50% of each of males and females of patients under Botox were within 25-34 years, (Table: 1).

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>15-24</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>25-34</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>35-50</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>40</td>
</tr>
</tbody>
</table>

In this study serum interleukin-2, IL-6 and IL-8 were significantly elevated in cases as compared with control ones (P<0.05), (IL-2: 26.13±2.8 versus 17.11±1.7 pg ml), (IL-6: 31.71±3.1 versus 14.74±3.5 pg ml) and (IL-8: 20.77±4.1 versus 16.38±3.9 pg ml), (Table: 2).

<table>
<thead>
<tr>
<th>Interleukins</th>
<th>Patients (No. 60)</th>
<th>Control (No. 40)</th>
<th>P. Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-2 (pg/ml)</td>
<td>26.13±2.8</td>
<td>17.11±1.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>31.71±3.1</td>
<td>14.74±3.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IL-8 (pg/ml)</td>
<td>20.77±4.1</td>
<td>16.38±3.9</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

In comparison between males and females regarding the immune response toward botulinum toxin, the study indicated that interleukin-2, IL-6, and IL-8 were significantly elevated in females as compared with males cases (P<0.05), (IL-2: 28.13±3.1 versus 20.11±2.6 pg ml), (IL-6: 33.91±2.8 versus 26.81±3.8 pg ml) and (IL-8: 24.93±3.8 versus 20.77±3.3 pg ml), (Table: 2).

<table>
<thead>
<tr>
<th>Interleukins</th>
<th>Females (No. 40)</th>
<th>Males (No. 20)</th>
<th>P. Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-2 (pg/ml)</td>
<td>28.13±3.1</td>
<td>20.11±2.6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>33.91±2.8</td>
<td>26.81±3.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IL-8 (pg/ml)</td>
<td>24.93±3.8</td>
<td>20.77±3.3</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

**Discussion**

As shown in the study, most of the people who underwent cosmetic surgery after Botox were within the age group 25-34 years. This finding is consistent with the results of previous studies. A previous study found that middle-aged young people were the most visited by plastic surgery clinics (7). Another study showed that the age above 25 years are the most vulnerable to cosmetics because of the requirements of modern life as well as the increase of cosmetic clinics and the development of cosmetic procedures in the world, and social media has actually contributed in

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increasing the number of visitors to these clinics. In the case study, the results showed that the level of interleukins in the study was high in people who had previously had Botox injections in their faces for any reason compared to people who did not have those operations. In light of these findings, a recent study revealed that levels of immune media such as cytokines were relatively high in people undergoing Botox injections (10). Various studies conducted in separate cities in various international cities have shown that there is a strong correlation between the exposure of people who have injected Botox to allergies and the high level of antibodies to toxins as well as the high level of many interleukins such as 6 and 8 (11-13). In a parallel and cross-sectional study that included immunosassay assessment in people injecting bacterial toxins into their skin, another recent study showed that the level of interleukin-2 was significantly higher in patients compared to the control group (13). It is worth mentioning that they are sick because it is not often that the people who perform these operations are healthy because the injection of antibacterial toxins from the body is a source in stimulating the body to produce antibodies and equivalent to toxins as well as the production of many immune media (14-16). Other studies have shown that women are more likely to have elevated immunoglobulin than men, which is consistent with our findings, which found that the level of interleukins was higher in women than in men (17-19). In conclusion, it was concluded that IL-2, IL-6 and IL-8 were elevated in facial rejuvenation persons with botulinum toxin, especially in females ones.

Conflict of interest: None
Source of findings: Self
Ethical clearance: This research was carried out with the patient’s verbal and analytical approval before the sample was taken. According to this approval, all the samples were collected and the tests were carried out. A copy of the results of the tests was then given to the patients.

References.
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