BACKGROUND – The current methods of treating muscle spasticity are not fully desirable. The present study was conducted to assess the effect of botulinum toxin type A (BTA) on spastic hemiplegia due to cerebrovascular accident as a therapeutic modality.

METHODS – Thirty-eight patients with a history of stroke who signed an informed consent were treated with BTA within a year (mid-2001 to mid-2002) in Azzahra Hospital, Isfahan, Iran. Five-hundred units of botulinum toxin type A was injected into the flexor carpi ulnaris, flexor carpi radialis, flexor digitorum profundus, and biceps brachii muscles. The injections were repeated 2 – 4 times for some patients at three-month intervals. The level of spasticity was assessed before injection, based on Ashworth scale. Response to treatment was evaluated according to the Global Assessment table. The range of motion of the wrist and elbow joints as well as patients’ satisfaction with the treatment were evaluated before and after the intervention. Wilcoxon test was used to compare the data before and after the intervention. SPSS 9 software (SPSS Co, Chicago, IL, USA) was used to analyze the data.

RESULTS – Mild to moderate reduction in spasticity was observed in the hands of 13 (34.2%) and arms of 14 (35.55%) patients following injections. This reduction in spasticity was temporary, lasting for two to three months. Patients with severe reduction of range of motion prior to treatment experienced more satisfactory improvement than those with mild to moderate reduction in range of motion. Improvement in the range of motion of the wrist joint corresponded to that of the elbow. Sixty percent of the patients reported “moderate” to “good” improvement in their conditions.

CONCLUSION – Injection of botulinum toxin type A can temporarily reduce limb spasticity after stroke and improve the range of motion of involved joints, bringing about patients’ satisfaction. However, the effect of botulinum toxin type A on the underlying etiology of disability is open to question.

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KEYWORDS • botulinum toxins • cerebrovascular accident • hemiplegia • spasticity

INTRODUCTION

Severe upper limb hypertonia is a common complaint of stroke patients. Few (less than 5%) of these patients regain satisfactory upper limb function. The prognosis for restoration of healthy function to the paralyzed limb is usually poor three months after the stroke. Although muscle weakness and loss of manual dexterity are the principal causes of functional motor disability in these patients, muscle spasticity remains an equally important concern. Muscle spasticity can interfere with voluntary motor movement in stroke patients, resulting in loss of their ability to perform daily functions such as dressing and cleaning. Muscle pain is sometimes an accompanying condition. The current methods of treating muscle spasticity are not fully satisfactory. Antispasmodic agents may interfere with the function of normal muscles due to their nonselective effect leading to patient’s reduced...
Antispasmodic Effect of BTA on Spastic Hemiplegia due to CVA

ability to sit and rise normally. Development of tolerance gradually shrinks the duration of drug effectiveness, necessitating increased dosage. Topical injection of phenol or alcohol induces chemical neurolysis, however, it often results in dysesthesia and loss of skin sensation. Moreover, repetitive injections of these agents tend to result in their reduced effectiveness.

In recent years, botulinum toxin type A (BTA) has been advocated as an effective antispasmodic agent. BTA injections are now used in the treatment of a wide range of neurological disorders including dystonias, spasticity due to stroke, head trauma, and multiple sclerosis. Instituting BTA injections for treating upper limb spasticity has several advantages, namely the speed and simplicity of injections for ambulatory patients and dispensing with the need for anesthesia. Furthermore, BTA injections are not accompanied by loss of skin sensation or dysesthesia. BTA curbs the release of acetylcholine-containing vesicles at the site of neuromuscular synapses, hence, preventing depolarization of the postsynaptic membrane.

BTA was used for the first time by Das and Park for treatment of spasticity. The results of using BTA in treatment of upper limb spastic paralysis in stroke patients were released in 1993. Further weakening of muscles injected with BTA, topical reactions, temporary duration of effect, and most importantly, development of tolerance subsequent to formation of antitoxin antibodies in the body are among the side effects of this agent. The present study was conducted to evaluate the efficacy of BTA injections in the treatment of upper limb spasticity in stroke patients.

Patients and Methods

Thirty-eight patients with spastic hemiplegia due to cerebrovascular accident (CVA) were selected to enter the study within a year (mid-2001 to mid-2002). All cases including 20 men and 18 women were among the patients who were referred to Azzahra Hospital, Isfahan, Iran. The patients were selected using randomized convenient method. The included patients were those with a history of stroke more than 9 months prior to the study who had never received BTA injections or oral antispasmodic agents. Patients whose upper limb and joints had been fixed in an abnormal posture due to hyperspasticity were excluded from the study. The patients were examined prior to BTA injection by a neurologist who assessed the severity of arm and hand spasticity according to Ashworth scale (Table 1).

Five-hundred vials of BTA having the brand name of Dysport (IPSEN, England) were used in the study. BTA injections were performed separately into superficial and deep muscles of the arm and forearm. The patients were examined within 2 weeks and 1, 2, and 3 months after the injections. Reduction in muscle pain and spasticity as well as improved range of motion (ROM) of the elbow and wrist joints constituted the main criteria for assessing improvement upon successive examinations. The Global Assessment (GA) table was used to score improvement (Table 2). The degree of satisfaction of the patients with changes in their limb function was also recorded. Ten patients received injections twice while another five received three or more injections. The patients were followed up over a period of nine months. Findings regarding the efficacy of BTA in reducing spasticity were statistically analyzed. All patients signed an informed consent prior to entering the study. Wilcoxon test was used to compare the data before and after the intervention and SPSS 9 software (SPSS Co, Chicago, IL, USA) was employed to analyze the data.

Results

Thirty-eight stroke patients were involved in this study (20 men and 18 women). The patients had a mean age of 49 years (age range: 13 – 73 years).

Table 1. Muscle tone assessed by Ashworth scale.

<table>
<thead>
<tr>
<th>Muscle tone</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No increase (mild resistance to passive movements within normal ROM)</td>
<td>0</td>
</tr>
<tr>
<td>Notable increase within normal ROM (passive limb movement is possible)</td>
<td>1</td>
</tr>
<tr>
<td>Severe increase (passive limb movement is difficult)</td>
<td>2</td>
</tr>
<tr>
<td>Limb rigidity during flexion and extension, accompanied by deformity</td>
<td>3</td>
</tr>
</tbody>
</table>

ROM = range of motion.

Table 2. Global Assessment (GA) of spasticity after BTA injection.

<table>
<thead>
<tr>
<th>Increase or decrease of spasticity</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very severe increase of spasticity</td>
<td>4</td>
</tr>
<tr>
<td>Severe increase of spasticity</td>
<td>3</td>
</tr>
<tr>
<td>Moderate increase of spasticity</td>
<td>2</td>
</tr>
<tr>
<td>Mild increase of spasticity</td>
<td>1</td>
</tr>
<tr>
<td>No change of spasticity</td>
<td>0</td>
</tr>
<tr>
<td>Mild decrease of spasticity</td>
<td>1</td>
</tr>
<tr>
<td>Moderate decrease of spasticity</td>
<td>2</td>
</tr>
<tr>
<td>Severe decrease of spasticity</td>
<td>3</td>
</tr>
<tr>
<td>Very severe decrease of spasticity (nearly normal)</td>
<td>4</td>
</tr>
</tbody>
</table>
1. Changes in the forearm and brachial muscle tone were assessed according to the GA table following BTA injection at the elbow and wrist. Following the first injection, mild reduction of the wrist and elbow spasticity (GA = 1) was observed in 14 (36.8%) and 18 (47.4%) patients, respectively. Moderate reductions of the wrist and elbow spasticity (GA = 2) was seen in 12 (31.6%) and 9 (23.7%) patients, respectively (Figure 1).

2. Moderate reduction of ROM improved, decreasing from 19 (~49%) before, to 14 (~36%) after the injections. More strikingly, the most severe reduction of ROM improved, dropping from 13 (~33%) to 2 (~5%). BTA seems to exert its best antispasmodic effects when reduction of ROM is most severe. Wilcoxon test revealed a meaningful difference in respect of ROM improvement before and after the injections ($p < 0.0001$).

3. Patient’s satisfaction with improvement of the hand function and finger extension expressed as “moderate” or “good” was seen in more than 23 (60%) of the patients (Figure 2). BTA injections did not seem to produce any serious side effects. Transient skin rashes were rarely seen following the injections. One of the patients who was under treatment with warfarin at the same time developed hematoma at the site of injection due to uncontrolled international normalized ratio (INR).

**Discussion**

This study was conducted to assess the effect of BTA injections in resolving upper limb spasticity in stroke patients. An injection of 500 U of BTA seems to produce beneficial effects. It is likely that higher doses will bring about further benefits. Nevertheless, an injection dose higher than 1,000-1,500 U leads to muscle weakness in the affected limb. In a study conducted by Bakheit et al, the patients were divided into three groups receiving 500, 1,000, and 1,500 U of BTA (Dysport). The patients who received high doses of BTA experienced remarkable improvement, however, muscle weakness developed in the patients who received 1,500 U of BTA resulting in decreased active ROM.

Although an increase in the number of injections is accompanied by further reduction in spasticity, five patients in this study experienced more improvement after the second injection but not after subsequent ones. This can be accounted for by production of anti-BTA antibody in the recipients. The patients who received injections at the intervals less than three months and those who continued to undergo occupational and physical therapy displayed better results. The patients were followed up for a period of at least 9 months. Later assessments indicated that reduced spasticity, increased ROM, and satisfaction with treatment were temporary in most patients, often lasting for two to three months after which the patients experienced a return to previous condition. Verifying the results of previous trials, this study demonstrates that BTA can temporarily reduce the upper limb hyperspasticity in stroke patients (for 3 – 4 months, at the longest). In a study conducted by Hesse et al, electrical...

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**Figure 1.** Changes in the elbow and wrist spasticity according to the Global Assessment table.

**Figure 2.** Patient's satisfaction with improvement of hand function and finger extension.
stimulation intensified the effect of BTA in treating chronic spasticity of the upper limb flexor muscles following stroke. Likewise, the patients undergoing physical therapy in this study experienced more benefits. Although various controlled trials have demonstrated that BTA can reduce hand and arm spasticity following stroke, its effectiveness in reducing patient disability and career burden is open to question. BTA seems to exert its best antispasmodic effects when reduction of ROM is most severe.

References