Long-Term Botulinum Toxin Treatment of Cranial Dystonia

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Abstract

We report the results of an open trial of botulinum toxin (Botox) in the treatment of 46 patients with cranial dystonia (38 patients with blepharospasm and 8 patients with Meige syndrome). The average age of the patients was 55.8 years, and duration of symptoms was 10.6 years. The blepharospasm involuntary movement (BIM) scale was used to assess clinical severity at baseline before BoNT/A injections and at two follow up visits after 6 and 12 weeks covering one BoNT/A treatment period with maximum effect size at the first follow up. The average latency from injection to response was 6.8 days, and the average duration of maximum improvement was 10.5 weeks. Local complications, lasting an average of 20.6 days noted in three patients, consisting of ptosis. Botulinum toxin treatment led to a significant improvement of clinical scale assessed with the blepharospasm involuntary scale (BIM). The results of this study indicate, that botulinum toxin injection is safe and effective for the long-term management of focal cranial dystonia.

Keywords: blepharospasm, Meige syndrome, botulinum toxin, blepharospasm involuntary movement scale

Blepharospasm, repetitive involuntary sustained contraction of orbicular oculi, is one of the most frequent types of idiopathic adult onset focal dystonia. As a result of increased publicity and general awareness of this disabling condition, more and more patients are being recognised throughout the world. Several open label and double blind studies have shown the efficacy of botulinum toxin treatment on this condition. In placebo controlled studies, BoNT/A provided efficient reduction of the increased muscle tone in dystonia. (1-2). Jankovic et al also showed long term clinical efficacy of BoNT/A injections over at least five treatment sessions in patients with blepharospasm and cervical dystonia. (3). This study was performed to assess the effects of botulinum toxin treatment on cranial dystonia with the blepharospasm involuntary movement (BIM) scale, and define which subgroups of patients (blepharospasm and Meige syndrom) are likely to gain the greatest benefit.

Patients and Methods

As clinical experience had shown that patients just starting on BoNT/A often report an initial dramatic treatment effect compared with follow up injection, only patients with long term BoNT/A treatment were selected to avoid possible confounding of our results.

46 patients (31 women and 15 men) with cranial dystonia (38 patients with blepharospasm and 8 patients with Meige syndrome) were studied after we obtained informed consent. Their diagnosis had been established in accordance with common diagnostic criteria. (4). Their mean age at onset was 55.8 (range 26-84) years and the mean duration of symptoms was 10.6 years. Dosage and injection sites of BoNT/A were individualized according to the distribution and degree of dystonic muscle activity. Botox (Allergan Inc, Irvine, CA, USA) was applied in 34 patients and 12 patients received Dysport (Speywood Biopharm Ltd, Wrexham, UK;)

In each patients, the disease severity was assessed by the blepharospasm involuntary movement (BIM) scale at three time point covering one BoNT/A treatment period: first at the baseline assessment before the BoNT/A injection and at two follow up visits reflecting the presumed time of the maximal BoNT/A effect in the first (interval from baseline to first follow up visit 5.9 weeks) and the end of the BoNT/A treatment period in the second visit (interval from first to second follow up visit 6.2 weeks). As additional sociodemographic data, after
Many patients were severely disabled before treatment. Approximately two-thirds of patients were rendered functionally blind to the extent that they were judged to require surgery or botulinum toxin injections to restore vision. Many had to give up work, or could not leave the house alone because they were "blind". Improvement appeared from 4 days to 2 weeks after injection, and reached its peak from 10 days to 3 weeks. The duration of improvement measured from its onset until the first evidence of deterioration ranged from 8 to 15 weeks. Doses for a single treatment of both eyes ranged from 0.4-2ng of neurotoxin. Side effects are described on Tab.2.

Discussion

Blepharospasm is a focal dystonia, which appears mainly in women, usually in six decade (5). Blepharospasm very often was associated with dystonia elsewhere, principally involving the cranial -cervical area (6). Oromandibular dystonia is the commonest association (Meige syndrome)(7). Most cases of cranial dystonia have no other identifiable disease.

Many drugs have been claimed to relieve muscle spasm, but there is not consistent pharmacological response (8-10). Anticholinergic drugs give probably the best chance of benefit, (11-12), but side effects are common and the response is inconsistent. Different surgical approaches were tried to relieve blepharospasm. Bilateral avulsion of facial nerves was the most successful, (13) producing initial improvement in more than 90% of the patients. Unfortunately recurrences were frequent (75%), occurring on average one year after surgery, although then not as disabling as the original illness. Muscle stripping of orbicularis oculi was initially successful in only 25% of patients so treated (14). Other surgical approaches such as alcohol injections or thermolytic lesions of facial nerves (15) produced only temporary benefit.

Injection of botulinum toxin type A into orbicularis oculi and lower face muscles, for cranial dystonia is the most effective treatment. Botulinum neurotoxin binds to peripheral motor nerve terminals and inhibits the release of acetylcholine. (16). Side effects are not common and usually local and transient.

In this open labelled prospective study, we assessed changes in two cohorts of patients with either blepharospasm or Meige syndrome over a 12week period.
BoNT/A treatment cycle. In both of over study groups limitations of physical and social functions was found. Meige syndrome cohort seemed to experience a higher degree of disability, than patients with blepharospasm, which was expressed by blepharospasm disability scale. However, the higher mean age of patients with blepharospasm has to keep in mind while interpreting these results.

Our data demonstrate a significant temporary improvement in clinical scale (BIM) in both types of focal dystonia after BoNT/A treatment. Side effects in our trial including partial ptosis, facial weakness, were most likely the result of using a relatively high dose of toxin. Nevertheless botulinum toxin injections are so far the best therapeutic measure that can be offered to patients with disabling cranial dystonia.

<table>
<thead>
<tr>
<th>cranial dystonia (n=46)</th>
<th>age (y)</th>
<th>sex</th>
<th>disease duration (y)</th>
<th>BoNT/A duration (y)</th>
<th>Baseline BIM scale</th>
<th>First follow up BIM scale</th>
<th>Second follow up BIM scale</th>
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<tbody>
<tr>
<td>blefarospasm (n=38)</td>
<td>68,7*</td>
<td>10M/28F</td>
<td>6,8</td>
<td>3,6</td>
<td>7,4**</td>
<td>4,7**†</td>
<td>6,1**</td>
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<tr>
<td>Meige syndrome (n=8)</td>
<td>61,4</td>
<td>5M/3F</td>
<td>10,6</td>
<td>3,9</td>
<td>12,6**</td>
<td>9,4**††</td>
<td>10,8**</td>
</tr>
</tbody>
</table>

Tab.1 % of Georgian Pharmaceutical market

References

Длительное лечение краниальной дистонии ботулиновым токсином

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Р Е З Ю М Е

Приводятся результаты проспективного исследования лечения ботулиновым токсином 46 больных краниальной дистонией (38 пациентов с блефароспазмом и 8 - "Meige" синдромом). Средний возраст пациентов составлял 55,8 лет, продолжительность симптомов болезни -10,6 лет. Для оценки клинической тяжести использована шкала непроизвольных движений блефароспазма (BIM) до инъекции ботулинового токсина и затем 2 раза: через 6 и 12 недель после лечения с учетом максимальной эффективности на 6 неделе после инъекций. Средний период первых положительных клинических проявлений составлял 6-8 дней, а средний период максимальной клинической эффективности - 10,5 недель. Выявленные локальные побочные явления в виде птоза отмечались у трех пациентов в течение 20 дней. На фоне лечения ботулиновым токсином типа А, улучшились показатели клинической шкалы. Результаты исследования указывают, что инъекции ботулинового токсина являются максимально безопасными и эффективными для длительного лечения фокальных краниальных дистоний.

Ключевые слова: краниальная дистония, ботулиновый токсин типа А, шкала непроизвольных движений блефароспазма (BIM)