Botulinum injection for the management of myofascial pain in the masticatory muscles. A prospective outcome study

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Abstract

We prospectively analysed the outcome after botulinum injection in patients who did not recover after conservative measures to manage masticatory myofascial pain, and who were not willing to take low dose tricyclic antidepressants as a muscle relaxant. We prospectively 62 patients were assessed with visual analogue scores (VAS) for pain on the affected side before, and 6 weeks after botulinum injection(s) (50 units Dysport® in up to 3 sites), and measured mouth opening in mm. Of those treated 49 (79%) showed at least some improvement (pain reduced by more than 25%). Patients reported more than a 90% reduction in the VAS for 25 (30%) of the 84 sides of the face treated. Only 22 of the 62 patients had more than one course of treatment to the same side. Interincisal distance improved by a mean/median of 0.9 mm (p < 0.03) after treatment. Side effects included 3 cases of temporary weakness of a facial muscle. Ranking the VAS pain scores using the Wilcoxon test before and after injection showed a significant reduction in pain (median change −29.5, interquartile range −53 to −16, p < 0.0001).

The treatment significantly improved patients’ pain scores and the overall mean/median reduction in pain was 57%. Botulinum injection does not guarantee complete resolution of myofascial pain, but it usually has some beneficial effect in improving the symptoms, and should be considered as an alternate treatment for masticatory myofascial pain if conservative methods have failed.

Keywords: TMJ; Myofascial pain; Botulinum toxin injection; Muscles of mastication
flinching, or referred pain as the sensitised nociceptors are stimulated.\(^2\) Newer diagnostic methods include the use of magnetic resonance elastography to quantify asymmetries in muscle tone,\(^3\) and a more convenient and readily accessible technique that involves ultrasonography has shown some promise. Myofascial trigger points in two-dimensional ultrasound show as hypoechoic, elliptically shaped, focal areas of tissue that exhibit reduced amplitude with vibration sonography when compared with the surrounding muscle tissue.\(^4\)

Myofascial pain related to the TMJ is initially managed with advice, rest, use of splints, physiotherapy, and other conservative measures. Despite the success of such management, a small number of patients do not respond, and the possibility of medical treatment with low dose tricyclic medication may be considered. For various reasons some are reluctant to agree to this treatment, and botulinum toxin injection may be a useful and efficient alternative.

Botulinum toxin (a neurotoxin produced by the bacterium Clostridium botulinum) acts by irreversibly binding to the terminals of presynaptic cholinergic nerves. Once internalised, it blocks the exocytosis of acetylcholine at the neuromuscular junction, which inhibits muscular contraction. Recovery of muscular paralysis occurs when the motor nerve supplying it sprouts new axons and forms new synaptic contacts to re-establish the junction. Botulinum neurotoxin type A (BTX-A) has an effect that lasts between 3 and 5 months, and the United States Food and Drug Administration (FDA) have approved its use for the treatment of blepharospasm, primary axillary hyperhidrosis, strabismus, and cervical dystonia, but it is not licensed for the treatment of muscular spasticity (in cerebral palsy for instance) perhaps because larger doses are required than those used for the approved conditions.

Botulinum toxin causes a profound reduction in muscle tone or muscular paralysis, hence its use in myofascial pain syndrome elsewhere in the body. Botulinum injections can lead to improved blood flow to the muscle and the release of nerve fibres that were compressed by abnormally contracting muscle, both of which may contribute to the cause of pain. It can also have an immediate effect because of the direct release of endogenous endorphins from the introduction of the needle and an alteration in the balance of peripheral and central neurotransmitters. This is caused by local inhibition of pain peptides from sensory ganglions and nerve terminals, and anti-inflammatory and antiguiltyaminergic action.\(^2\)–\(^7\)

Studies have shown that 3–10% of patients develop neutralising antibodies\(^8\) with long-term adverse effects that include muscular atrophy.

We analysed outcome after treating masticatory myofascial trigger points with injections of botulinum toxin. We aimed to evaluate and to find out whether it is an effective treatment by using defined primary and secondary outcomes from a prospective study of patients with masticatory myofascial pain who failed to respond to a standard conservative regimen.

### Method

An initial retrospective review of 21 patients treated with botulinum injection suggested success in 70%. We collected prospective data from one clinician’s practice between 2005 and 2010 on patients who had had BTX-A (Dysport\(^\circledast\), Ipsen, Slough, UK) injections into the masticatory muscles (masseter, temporalis, or pterygoid) for clinically diagnosed masticatory myofascial pain. Diagnosis had been based on their history and an increase in muscle tone and stiffness with contracted muscles that contained myofascial trigger points.\(^1\)

All patients had initially had a 3-month course of conservative treatment, which included reassurance and explanation of the nature of the problem, supplemented in a written format: advice on rest, soft diet, and how to avoid opening the mouth wide; advice on the regular use of topical or systemic non-steroidal anti-inflammatory drugs such as ibuprofen, or both; and the use of a lower soft bite-raising appliance for a minimum of 8 weeks. Those who did not respond to conservative measures on subsequent review were given the following options: persevere with conservative measures; take low dose titrated tricyclic antidepressants (nortriptyline 25–75 mg once a day) to relieve muscle spasm; or have botulinum injections into the affected muscle(s).

Outcomes for injections were assessed using 10 cm visual analogue pain scores (VAS) at 0 and 6 weeks, self-reported pain at 6 weeks, a request for further treatment at 6 weeks, and measurement of mouth opening at 0 and 6 weeks.

Once patients had consented to treatment with botulinum toxin, they indicated their average pain for the previous week on a VAS sliding ruler for both sides of the face. They then had up to 50 units of Dysport\(^\circledast\) (diluted 1 ml saline/500 units) injected into clinically identifiable myofascial trigger points in the affected muscles with a maximum of 3 injections/muscle, according to the theories and clinical practice originally described by Travell and Simons.\(^9\) All patients were reviewed 6 weeks after injection and they again recorded their average pain levels for the previous week using the same VAS ruler. If free from pain they were discharged to primary care and told to return to clinic if it returned. We considered our true primary endpoint to be a reduction in pain of 75% or more. The outcome was the proportion of patients whose pain had reduced at 6-week review, which was measured by taking the difference in the two scores (VAS) as a percentage of the score before injection. Primary outcome was the proportion of patients who had a 75% reduction in pain. Secondary outcomes were the proportion of patients with a 25% reduction in pain, the proportion with increased mouth opening, and the proportion that did not respond or had worsening pain.

### Statistical methods

Non-parametric tests were used for all analyses. Correlations were described using Spearman’s correlation co-efficient. The change in pain score within muscle groups was summarised as a median change and tested using Wilcoxon’s
sign rank test. The difference between muscle groups in the median change in pain score was tested using the Mann–Whitney test. All statistical tests were two sided ($\alpha = 0.05$).

**Results**

A total of 62 patients completed the study. One patient did not attend the review after injection and was therefore not included in the analysis. The mean (SD) age was 41 (14.4) years, and 49 of the 62 (79%) patients were female (Table 1).

Of the 62 patients treated, 22 (35%) had more than one course of injections to the same side at two or more visits (median number of visits 2, range 2–5). In total 84 sides of the face were treated with first-time injections (48 courses of treatment to the left side, and 37 to the right). After the first visit mouth opening had increased in 22, reduced in 15, and not changed in 25.

Improved percentage change in pain scores using the VAS for each patient showed no real correlation with improved mouth opening on the scatter plot (Fig. 1) and was not considered significant. Spearman’s $r$ coefficient of 0.19, with the significance of a 2-tailed test of 0.62 indicates a small but insignificant positive coefficient as in the scatter plot (with the exception of a few cases in whom mouth opening was reduced). The mean (SD) interincisal distance for patients before treatment was 39.0 (7.76) mm compared with 39.9 (7.16) mm after injection, a mean/median improvement of 0.9 mm. The rank data show a significant result using a non-parametrical test (Spearman’s correlation coefficient = 0.24, df = 60, $p = 0.03$) where $n = 62$.

The distribution of muscles injected, independent of the number of injections given to each patient, showed that the most commonly injected muscle was the masseter (76%); it was occasionally injected together with the temporalis. Twenty percent of injections were into the temporalis, and 4% into the medial pterygoid. Of 47 patients (76%) who had a VAS of over 50 before treatment, 23 (49%) had a VAS of less than 25 after treatment, compared with 35/62 (56%) overall who had minimal pain scores (0–25) after the first course of treatment. The treatment significantly improved pain scores as was shown when the paired VAS (before and after injection) at 0 and 6 weeks after treatment were ranked using the Wilcoxon test (median change $-29.5$, interquartile range (IR) $-53$ to $-16, z = 6.42$) ($p < 0.0001$). Pearson’s chi-square test used to cross-tabulate the change in pain scores gave a likelihood ratio of 43.69 (chi square value 39.36).

Fig. 2 shows the distribution of pain scores before treatment (divided into four groups), and how those specific groups responded after treatment. Generally, the higher the initial score, the better the chance of a reduction in pain. One patient’s score deteriorated from 0 –25 before to 50–75 after injection for unknown reasons. A small number of patients in each of the 4 categories did not improve after treatment: 3/16 (19%) in the 76–100 category; 5/31 (16%) in the 51–75 category; and 2/12 (17%) in the 26–50 category. In the 0–25 category, one of the 3 patients had complete resolution of pain, another who was suffering from myositis ossificans deteriorated from 10 to 18, and the third deteriorated. Overall, 4 patients (6%) deteriorated after treatment, and in 5 (8%) the level of pain did not change. Of these one had myositis ossificans and another had weakness of the left zygomaticus (the

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>No. of patients</th>
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<tbody>
<tr>
<td>18–30</td>
<td>15</td>
</tr>
<tr>
<td>31–40</td>
<td>20</td>
</tr>
<tr>
<td>41–50</td>
<td>11</td>
</tr>
<tr>
<td>51–65</td>
<td>13</td>
</tr>
<tr>
<td>65+</td>
<td>3</td>
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Fig. 1. Correlation of individual patients’ change in mouth opening with a change in pain score after the first injection of botulinum. A plus change on the $x$-axis (VAS) indicates resolving pain, whereas a minus value indicates worsening pain. A plus value on the $y$-axis indicates increased mouth opening and minus values indicate reduced opening.
injection may have been too superficial). Of the 9 patients who did not improve, 4 were referred to the pain team, 3 were given tricyclic antidepressants, and 2 were booked for arthroscopy of the TMJ with suspected degeneration of the joint. None of these 9 patients were in the group of 22 that had more than one course of treatment with Dysport®.

The mean percentage reduction in pain for all sides injected was 53%, with a mean reduction of 57% in the overall pain score for each patient (Fig. 3). Of the 84 sides treated there was complete or near complete (more than 90%) resolution of pain in 25 (30%) sides.

Overall, 26 (43%) patients had an improvement in pain of more than 75%, 49 (76%) had their pain score reduced by more than 25%, and only 13 (24%) had minimal improvement or deterioration in pain.

Side effects reported included difficulty in talking and a transient inability to smile only within the first week after injection (n = 1). Also, one patient each had masseteric wasting, weakness of the left zygomaticus, and left buccal weakness. All resolved without complications.

Given the marked variation of the patients’ response to botulinum, we analysed individual influencing factors. We used the patients’ percentage change in VAS to eliminate subjective bias when judging improvement in pain scores.

Some studies imply that the masseter responds best to treatment for myofascial pain. We investigated the overall response/patient by assessing those who had a single muscle injected only and excluded combinations such as temporalis and masseter. There seems to be little difference in outcome from treating the masseter or temporalis in isolation, although there is not enough data to render this result significant regardless of the fact that both results were successful (Table 2).

There was no sign that one muscle was more successful than another, which was confirmed using a Wilcoxon test of non-parametric ranked data. Table 3 shows a similar median change within the groups, with the change in the temporalis group being only 3.5 points more than that in the masseter group. Change in the masseter compared with that in the temporalis, however, (p = 0.006 Kruskal–Wallis) rendered the temporalis more favourable statistically in terms of better outcomes when treated in isolation, because the median change for the temporalis was 31.5 (IQ range 10–52) compared with 28 (IQ range 16–53) for the masseter. More people in the masseter group seem to have had a reduction in pain after treatment, whereas in the temporalis group outcomes were better if they began in a lower pain group.

Another variable was the amount of botulinum injected into a muscle or each side, and its contribution to varying outcomes. The amount of Dysport® injected depended on the number of trigger points a patient had and may have influenced the amount of pain relief. Fig. 4 shows marked variability in outcome for all amounts of Dysport® injected. There were some poor outcomes when 250 units were injected into several muscles, and 4/7 patients (57%) showed only a 40% or less reduction in pain. Interestingly, of 18 facial sides that had injections of less than 100 units of botulinum, 7 (39%) were fully cured. The correlation with the amount of botulinum injected was therefore poor. Larger

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**Table 2** Changes related to muscle injected. Pain localised to single muscle type only.

<table>
<thead>
<tr>
<th>Muscle injected</th>
<th>Mean improvement in pain score (% VAS)</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Masseter</td>
<td>52.8</td>
<td>39</td>
</tr>
<tr>
<td>Temporalis</td>
<td>56.9</td>
<td>10</td>
</tr>
<tr>
<td>Medial pterygoid</td>
<td>91</td>
<td>2</td>
</tr>
</tbody>
</table>

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**Fig. 2.** Distribution of patients’ pain scores before treatment (split into VAS pain: 0–25, 26–50, 51–75, and 76–100). The bars show the pain scores (outcome) for each patient 6 weeks after injection.

**Fig. 3.** Manhattan graph showing the overall change in pain score for each patient after the first course of treatment with botulinum. A plus value in the y-axis indicates a reduction in pain.

**Fig. 4.** Manhattan graph showing the overall change in pain score for each patient after the first course of treatment with botulinum.
Table 3
Signed-rank skewed paired data of patients in the masseter and temporalis groups.

<table>
<thead>
<tr>
<th></th>
<th>Median IQR</th>
<th>Median change IQR</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>25 75</td>
<td>25 75</td>
<td></td>
</tr>
<tr>
<td>Masseter before</td>
<td>63 45</td>
<td>76 – – –</td>
<td>– – –</td>
</tr>
<tr>
<td>Masseter after</td>
<td>20 0 50</td>
<td>28 16 53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Temporalis before</td>
<td>67.5 57</td>
<td>76 – – –</td>
<td>– – –</td>
</tr>
<tr>
<td>Temporalis after</td>
<td>40.58 5</td>
<td>62 31.5 10 52</td>
<td>0.0059</td>
</tr>
</tbody>
</table>

Doses were often used in multiple sites, but there was an association between fewer units injected and an improvement in pain. This may be because these patients had fewer trigger points and therefore responded better to injections into individual muscles.

Discussion

Botulinum toxin injection provides a useful addition to the therapeutic armamentarium for non-responsive masticatory myofascial pain. To date all the studies we know of have been on a small scale and most report on the treatment of masticatory hyperactivity, bruxism, and TMD; few are about masticatory myofascial pain. We know of no long-term outcomes that have been published over the last 12–18 months, and there are no established protocols or guidelines for the use of botulinum toxin for the treatment of myofascial pain syndrome.

BTX-A has been shown to be more effective with fewer side effects than type B. Research has shown different patterns of pharmacophysiology, which leave no obvious conclusion. Pain may be reduced by the postulated antinociceptive effect of botulinum both peripherally and centrally, although a study by Qerama et al. showed a reduction in pain with botulinum and with saline in control groups.

The reduced interference patterns on electromyography that were seen in both groups suggested that pain was relieved by a reduction in motor endplate activity. Electromyographic activity was reduced in the saline groups, which implies that treatment with botulinum toxin is better and lasts longer. Another randomised, double blind, placebo controlled study that examined the analgesic effects of BTX-A suggested that pain had reduced after treatment because of a reduction in muscle tone and not because of an effect on the sensory nerve terminals. Therefore there was no direct analgesic effect.

Several studies show the potential benefits of botulinum injection into the trigger points associated with myofascial pain. Kotuglu et al. randomly assigned patients with myofascial facial pain into 2 groups. Electromyography of the masseter and temporalis confirmed a reduction of action potentials in the group injected with botulinum compared with the saline group. In 20 patients who were injected with 25–50 units Dysport into their masticatory muscles, pain and mouth opening improved after 4 weeks and persisted for 8 weeks with a concurrent improvement in mandibular movement. In a separate double-blind, randomised controlled trial 91% of patients with masticatory hyperactivity had a mean reduction in VAS pain of 3.2 compared with placebo.

In contrast to the above, injection with local anaesthetic or steroid have had noted benefits. A single blind study showed a 30% greater reduction in pain in 4 of 6 patients who had cervical, paraspinal, and shoulder girdle trigger points injected with botulinum compared with a saline group. Significant improvement was also shown with lidocaine and botulinum injection into a total of 87 trigger points (cervical or periscapular regions, or both) compared with...
placebo dry needling in 29 patients in a short term (4-week) study. Güı̇l et al. also found that pain control was significantly better when botulinum was injected directly into the trigger points in 25 patients compared with those who had lidocaine injected alone. Porta, however, showed better long-term pain relief with botulinum than with steroid injection into trigger points in the piriiformis, iliopsoas, or scalenus anterior muscles, although steroids controlled pain better in the short term.

In our study 13 (21%) of the 62 patients had minimal (less than 25% improvement on VAS) or no improvement in their pain scores after treatment with botulinum, and in 9 (15%), pain did not improve or was worse. There are various hypotheses for this, and it has been well documented that some patients do not respond to botulinum, or respond better to other methods. A randomised, double-blind, prospective study of 33 patients with refractory cervicothoracic paraspinal myofascial pain showed no significant benefit from botulinum injection although some patients had a more prolonged response to botulinum toxin compared with placebo; however, all groups showed some improvement. Graboski et al. compared the effect of botulinum toxin A directly with bupivacaine injections in the treatment of myofascial trigger points in the neck, shoulder girdle, hip girdle, or back, in a randomised, double blind, crossover study. Patients were injected in up to a maximum of 8 trigger points, and both agents effectively and independently reduced pain compared with the baseline (p = 0.0067). However, there was no significant difference in duration or amount of pain relief, satisfaction, or function between the groups.

It would be difficult to promote botulinum toxin as a clear and effective first line treatment. Our study has encouraging results, but only in appropriate patients or at a defined point in treatment. Cost may also be a problem and may be an influencing factor in the current economy. One paper advocates primary use of lidocaine with botulinum for refractory cases of myofascial pain if lidocaine did not produce the desired effect. Lidocaine had statistically similar results to botulinum, whereas botulinum caused less sensitivity after injection and was a much better “rescue” medication. More importantly there was a large difference in cost. The argument for using botulinum primarily is the initial cost compared with that of repeat visits for follow up, loss of clinical appointments, and the cost of alternative prescribed analgesics.

The mean/median improvement in interincisal distance in this study was 9.0 mm, and the mean/median interincisal distance before treatment was 39.0 mm. Both values are within the normal range for mouth opening and were not clinically significant, although the large sample size gives a small positive correlation. A reduction in mouth opening after treatment does not correlate with more or less pain and vice versa (Fig. 1), so treatment for masticatory myofascial pain does not necessarily improve the patients’ ability to open their mouths, although statistically, mouth opening should improve.

Varying doses and therefore volumes of fluid were given in this study, ranging from 50-150 units/muscle depending on the number and distribution of trigger points. This could have influenced the duration and amount of denervation and improvement in pain. Whilst Ferrante et al. reported no significant responses to different doses, we did not have a control group in our study; we included only patients who had been given Dysport® injections according to a subjective protocol. We found no direct correlation with the dose given, although lower doses seemed to give a slightly better outcome, possibly because fewer trigger points were being treated.

The medial pterygoid gave a far superior and predictable outcome when injected than trigger points in the masseter or temporalis. A much larger population than the 2 groups used in this study would need to be recruited to obtain a significant result. Most patients in our study presented with trigger points primarily, but not exclusively, in the masseter or temporalis, or both. The masseter was involved more than twice as often as the temporalis with equally favourable results but less significantly improved outcomes. It would be preferable to compare the muscles with equal numbers of subjects in each group.

Conclusion

Our results show the effectiveness of botulinum toxin in treating patients with masticatory myofascial pain after initial conservative treatment had failed, and they confirm previous findings in other muscle groups. To our knowledge it is the largest study to date to assess the treatment of masticatory myofascial pain, and whilst botulinum neurotoxin does not guarantee complete resolution of pain, it has shown a significant effect in improving the symptoms. The outcome is unpredictable as shown by the variability in outcomes with the total dose given. Botulinum toxin is therefore a valuable alternative second line treatment for masticatory myofascial pain when conservative measures have failed.

References


