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# Botulinum toxin in the management of myalgia in temporomandibular disorders: are all injections equal?

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**Abstract**

Botulinum toxin (BTX) is becoming widely used as an adjunct to conservative management of myalgia-predominant temporomandibular disorders (TMDs) with reports of improved quality of life. There is, however, no consensus on the optimal dosage. Based on previous studies, dose regimens vary between clinicians, and we know of no standard dose protocol for the administration of BTX for the purpose of TMD management. A survey was sent to members of the British Association of Oral and Maxillofacial Surgeons (BAOMS) Temporomandibular Joint Sub-Specialty Interest Group (TMJ SSIG) and an international mailing list of high-volume TMJ surgeons (the TMJ Internetwork) to ascertain variations in dose regimens between different clinicians. The survey found that 41 respondents offered BTX to patients. The masseter muscle group was the most commonly injected site, and the majority of respondents (34/41) used Botox® (Allergan). Brands less commonly used included Dysport® (Ipsen), and Xeomin® (Merz Pharma). Botox® doses varied between 30 and 100 units, whilst Dysport® doses ranged from 50 - 300 units/muscle. The number of injection sites/muscle also varied. This survey demonstrates the wide variation in practice amongst clinicians with respect to BTX administration. To ensure optimal dose and response titration, further studies and evidence-based research are needed to standardise its use for the treatment of TMDs.


*Keywords*: Botox; Botulinum toxin; TMJ; Temporomandibular disorder; Myofascial pain; Myalgia

## Introduction

Temporomandibular disorders (TMDs), which are some of the most common causes of orofacial pain, can be debilitating and reduce a patient's quality of life.[1] They are also known to be the second most common form of musculoskeletal pain after lower back pain.[2] TMD is an umbrella term used to describe chronic pain affecting the masticatory muscles and/or the temporomandibular joint itself. A recent systematic review suggested that 31% of adults and 11% of children suffer from TMD.[3] Its aetiology is multifactorial, with contributions to varying degrees in individual patients from trauma, inflammatory and degenerative arthritides, psychosocial factors, bruxism, and other parafunctional habits. These risk factors can act alone or in combination, and in many circumstances it can be difficult to isolate a single cause.[4] TMD can further give rise to referred pain in the head and neck due to shared nerve supplies.

Due to being multifaceted complex conditions, the chronic nature of TMDs can be a source of depression and disability.[5] TMDs may be associated with central sensitisation that results in an increased sensitivity of pain receptors in the brain. Central sensitisation is also associated with conditions such as fibromyalgia, tension-type headaches, and generalised chronic pain syndromes that may overlap with TMD.[6] The Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) classifies different conditions that encompass TMD, such as myofascial pain or myalgia, arthralgia, intra-articular disorders, and headaches.[7] The classification helps to categorise pain that is attributed to the above conditions, and also provides the clinician with screening tools that identify psychosocial factors that contribute to, and exacerbate, TMDs.

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There is, therefore, a spectrum of treatment modalities that ranges from conservative to minimally invasive techniques to major surgical interventions. Treatment options depend on the aetiological risk factor(s) that contribute to TMD and the presence of identifiable pathology (for example, degenerative changes in the joint). Ultimately the aim of TMD management is to reduce pain, increase quality of life, and improve function.[8] In general, there is a consensus stepwise approach to managing TMDs, beginning with conservative management, including patient education, physiotherapy, and analgesia.[9] Failing this, minimally invasive options are considered, such as arthrocentesis or arthroscopy for presumed or diagnosed intra-articular pathology.[10]

For patients with predominantly myofascial pain or myalgia, in whom conservative measures have failed, botulinum toxin (BTX) treatment has become popular and is regarded as effective.[7] BTX is a neurotoxin produced by *Clostridium botulinum* and is administered as an intramuscular injection. Its effect is reversible, lasting between three and six months. It is considered minimally invasive and thus, for these reasons, has become a popular choice of treatment.

Traditionally, BTX has been licensed for the treatment of movement disorders. This has now expanded to treat a range of conditions such as blepharospasm, axillary hyperhidrosis, migraines, and headaches, and to manage bladder dysfunction.[11,12] More recently its unlicensed use has been adopted to treat a range of conditions. Although the evidence has been inconsistent, studies have shown that BTX has improved quality of life and reduced pain in TMD patients who have attempted to undergo conservative treatment without any benefit.[13,14]

Currently, there is no consensus on the optimal dosage of BTX and, based on previous studies, dosing schedules vary between clinicians.[15–20] Further to this, there are currently no guidelines in the United Kingdom for the use of BTX in the management of TMD.

The aim of this survey was to explore the current practice of TMD management and the usage of BTX amongst clinicians, such as type and dose regimen, the muscle group(s) injected, and patient follow up after treatment.

## Method

A survey questionnaire was created using SurveyMonkey™. The survey was emailed by hyperlink to members of the British Association of Oral and Maxillofacial Surgeons (BAOMS) Temporomandibular Joint Sub-Specialty Interest Group (TMJ SSIG) and internationally via the TMJ Internetwork mailing list, restricted to high-volume TMJ surgeons. The survey asked members whether they provide BTX in the management of TMD, the type and dose of BTX used, and the muscle group(s) injected, including the number of injection sites/muscle group. Members were also asked whether they followed up patients and how often this was done.

## Results

There were 43 responses in total. At the time of the survey there were 105 active members of the TMJ Internetwork and 77 active members of the BAOMS TMJ SSIG. Given that there were 12 UK-based members of the TMJ Internetwork, we estimated the total number of potential respondents to be between 170 and 182 (the former assuming complete overlap in UK membership, and the latter assuming no overlap). This could yield a potential response rate of between 22.5% and 24.1%.

Of those potential respondents, 41/43 administered and/or prescribed BTX for TMDs. Thirty-nine administered BTX, and two delegated BTX injections to other staff. The main brand used was Botox® (Allergan) with 34/41 respondents using it. Eleven of 41 used Dysport® (Ipsen), and five used both Botox® and Dysport®. Xeomin® (Merz Pharma) was a choice for two.

The muscles targeted varied by respondent. The masseter was the most injected muscle group, being targeted by all 41 respondents, followed by the temporalis, which was injected by 26. Other muscles targeted included the procerus and lateral pterygoid. The dose regimen varied considerably between respondents (Tables 1–3). The number of injection sites for different muscle groups also varied (between one and five sites/muscle group) (Fig. 1).

Follow up varied with most patients seen every three to nine months. Follow up was also determined in some cases by the patient (Fig. 2). The majority of respondents provided BTX treatment indefinitely (Fig. 3).

## Discussion

The administration of BTX for TMD has been steadily increasing over the years. Although reports on its effectiveness in the treatment of TMD have been inconsistent, several primary studies have shown that it successfully reduces the pain and symptoms that contribute to TMD.[17–19,21] There is evidence to suggest that its analgesic effect extends beyond the simple neuromodulatory effect, but as yet this is incompletely understood.[10,22]

Table 1
Dose variations by respondents who use Botox® (Allergan).

| Muscle group | Botox® units | No. of respondents |
|---|---|---|
| Masseter | 10 | 1 |
| | 25 | 4 |
| | 30 | 11 |
| | 50 | 13 |
| | 75 | 2 |
| | 100 | 2 |
| Temporalis | 10 | 2 |
| | 25 | 12 |
| | 50 | 7 |
| Procerus | 10 | 2 |
| | 25 | 1 |

Table 2
Dose variations by respondents who use Dysport® (Ipsen).

| Muscle group | Dysport® units | No. of respondents |
|---|---|---|
| Masseter | 50 | 2 |
| | 75 | 1 |
| | 125 | 1 |
| | 250 | 1 |
| | 300 | 1 |
| Temporalis | 25 | 1 |
| | 30 | 1 |
| | 75 | 2 |
| | 200 | 2 |
| Procerus | 10 | 2 |
| | 25 | 1 |

Table 3
Dose variations by respondents who use Xeomin® (Merz Pharma).

| Muscle group | Xeomin® units | No. of respondents |
|---|---|---|
| Masseter | 25 | 1 |
| | 100 | 1 |
| Temporalis | 10 | 1 |
| Procerus | 10 | 1 |
| Lateral pterygoid | 10 | 1 |

This survey highlights the variation in BTX treatment doses and management amongst clinicians, and confirms that there is no clear consensus about the dose and/or brand used and the number sites injected /muscle group. A number of studies in the past have varied in the number of injection sites used in the treatment of TMD.[14] This variation has also been demonstrated by the respondents in the survey. More studies therefore are required to establish the optimum number of injection sites and muscles injected. Manufacturer's guidance suggests that multiple injection sites may allow BTX to have more uniform contact with innervated areas of the muscle.[23]

It has been established that BTX is relatively safe, with an estimated lethal dose of 3000 units.[24] There are some well-known side effects to the treatment, such as flu-like symptoms, pain, oedema, ecchymosis at the injection site, unwanted facial paralysis, and facial asymmetry.[11,12,25] Studies using BTX in the management of TMD have shown a common adverse effect of unilateral paralysis to the zygomaticus major affecting the smile symmetry.[18] This may be attributed to an increased dose and volume resulting in diffusion of the BTX into the muscle group.[26] It could perhaps be preventable in a patient who could respond to a lower dose, suggesting that adequate dose-response titration is important to reduce adverse effects. A recent study that assessed the efficacy and safety of BTX in patients suffering from myofascial pain at three different doses showed a statistically significant transient decline in masticatory performance, muscle contraction, and thickness at higher doses, but no additional therapeutic benefit.[27]

Further to this, it has been demonstrated that increased doses of BTX, particularly at the onset of treatment, can result in the production of antibodies against BTX, which subsequently cause a lack of response after initial sensitivity.[28] To avoid neutralising antibody induction, it has been suggested that BTX should be started at a low dose and adjusted to the individual.[24,28]

It must be noted that BTX products are pharmacologically unique and thus there will be variations in dose regimens that are not interchangeable.[26] The consensus is a conversion rate of Dysport® to Botox® of 3:1, however, when BTX has been used to treat movement disorders, lower conversion rates have been effective.[26]

The use of BTX in the management of TMDs was first established by Schwartz and Freund[29] but since then we know of no studies that have established effective guidelines or investigated optimal doses. This contrasts with spasticity guidelines, which have been beautifully illustrated with a user-friendly guide that takes into account the different types of BTX preparations used.[11] Thus, further research into dos-

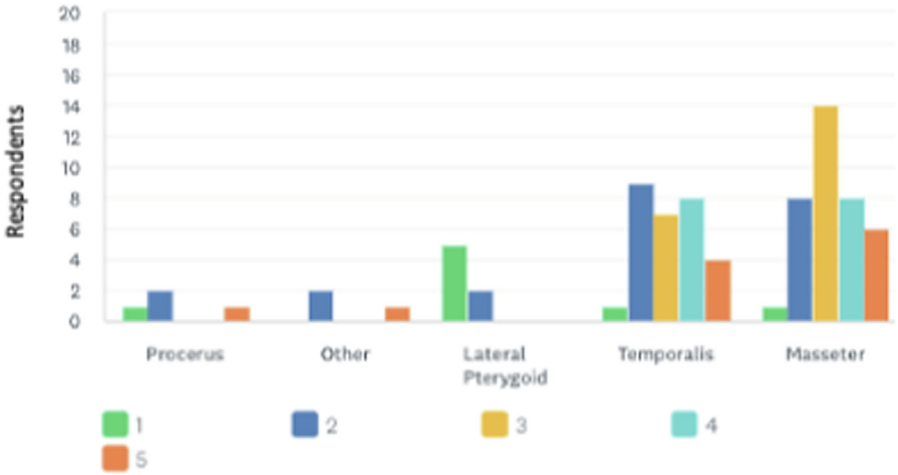


Fig. 1. Number of injection sites for different muscle groups.

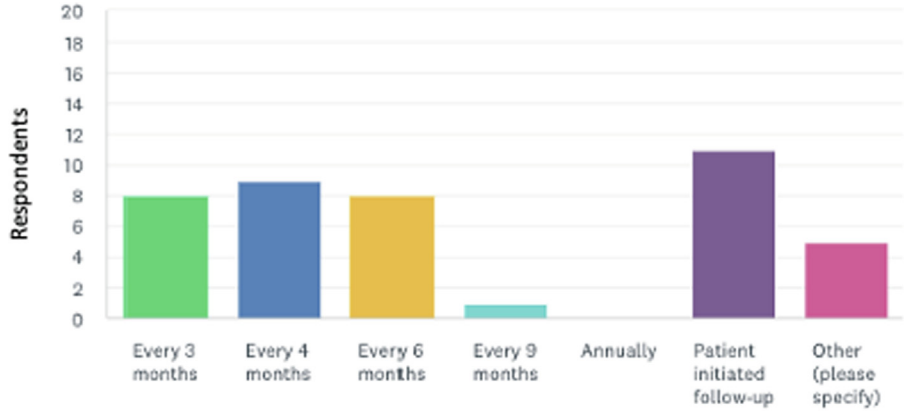


Fig. 2. Patient follow up during the course of treatment.

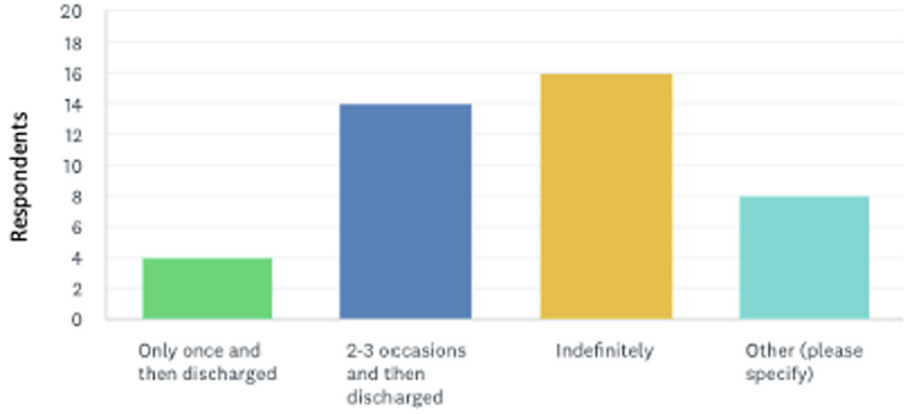


Fig. 3. The average duration of BTX treatment in patients with TMD, provided a positive response to BTX was achieved.

ing schedules will set precedents for the provision of the most effective dose with minimal adverse effects.

Considering that BTX is becoming widely available and increasingly used in the management of TMD, it is imperative that the specialty keeps up to date with evidence-based methods to provide patient care. The National Institute for Health and Care Research (NIHR) has recently invited applicants to take part in a randomised controlled trial to look at the clinical and cost-effectiveness of BTX in the management of chronic masticatory myofascial pain.[30] This would be a welcome opportunity for evidence-based research that would help to guide clinical practice and inform patient choice. Certainly, coordinating international multicentre studies via organisations such as the European Society of TMJ Surgeons (ESTMJS), the American Society of TMJ Surgeons (ASTMJS) and the BAOMS TMJ sub-specialty interest groups (SSIG) would maximise the response rates and hopefully introduce some homogeneity into the doses and methods of administration.

## Conflict of interest

There are no conflicts of interest to disclose.

## Ethics statement/confirmation of patient permission

No formal ethics approval was warranted for this study. Patients' permission was also not required.

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