Efficacy of botulinum toxins on bruxism: an evidence-based review

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The objective of this study was to assess the efficacy of botulinum toxins on bruxism. Electronic databases (PubMed, Embase and Science Citation Index), websites (Cochrane Central Register of Controlled Trials and ClinicalTrials.gov) and the literature database of SIGLE (System for Information on Grey Literature in Europe) were searched from January 1990 to April 2011 for randomised controlled trials or nonrandomised studies assessing the efficacy of botulinum toxins on bruxism. There was no language restriction. Through a predefined search strategy, we retrieved 28 studies from PubMed, 94 from Embase, 60 from the Science Citation Index, two ongoing clinical trials and two from the Cochrane Central Register of Controlled Trials. Of these, only four studies met our inclusion criteria and were finally included. Of the four included studies, two were randomised controlled trials and two were controlled before-and-after studies. These studies showed that botulinum toxin injections can reduce the frequency of bruxism events, decrease bruxism-induced pain levels and satisfy patients’ self-assessment with regard to the effectiveness of botulinum toxins on bruxism. In comparison with oral splint, botulinum toxins are equally effective on bruxism. Furthermore, botulinum toxin injections at a dosage of <100 U are safe for otherwise healthy patients. Botulinum toxin injections are effective on bruxism and are safe to use. Therefore, they can be used clinically for otherwise healthy patients with bruxism.

Key words: Botulinum toxins, bruxism, systematic review, tooth clenching, tooth grinding

INTRODUCTION

Bruxism, a diurnal or nocturnal parafunctional activity that includes tooth clenching or grinding, can result in several orofacial lesions, such as tooth wear, periodontal lesions, temporomandibular joint disorders and muscle pain. Although several therapeutic modalities have been employed, including oral splint, medications and behavioral approaches, none has been reported to be fully effective. Thus, it is of paramount importance to find a more effective therapeutic modality. Recent advances have shown that bruxism is caused by centrally mediated high levels of motor activity in the jaw muscles, indicating that reductions in this activity may be helpful. Botulinum toxins, proteases that block the release of acetylcholine, can ultimately inhibit muscle contraction, rendering them applicable to bruxism. However, the efficacy of botulinum toxins on bruxism has not been demonstrated. Thus, we conducted a systematic review of randomised controlled trials and nonrandomised studies assessing the efficacy of botulinum toxins on bruxism.

METHODS

Inclusion criteria for the studies

Types of study

Studies that reported the treatment effects of botulinum toxins on bruxism were included, mainly randomised controlled clinical trials and nonrandomised studies. Studies in which bruxism was induced by other disorders, e.g. brain injury and medications, or complicated by other unrelated systemic diseases, e.g. Huntington’s disease, were excluded. Moreover, studies in which therapy aimed at the treatment of other diseases was used were also excluded.

Types of participant

The participants in the studies suffered from bruxism and were over the age of 18 years.

*These authors contributed equally to this article.
Types of intervention

The test interventions were botulinum toxin injections and the control interventions were either placebo or other interventional procedures, e.g. oral splint.

Study identification

We searched the electronic databases of PubMed, Embase and Science Citation Index, websites of the Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov, and the literature database of SIGLE (System for Information on Grey Literature in Europe). The search strategies for each of the databases were as follows: (i) PubMed: ['Bruxism' (Mesh) or ‘tooth grinding’ or ‘tooth clenching’] AND ['Botulinum Toxins' (Mesh) or 'botulinum' or 'Botox']; (ii) Embase: ['bruxism' or 'tooth grinding' or 'tooth clenching'] AND ['botulinum' or 'botulinum toxin' or 'Botox']; (iii) Science Citation Index: ['bruxism' or 'tooth grinding' or 'tooth clenching'] AND ['botulinum' or 'botulinum toxin' or 'Botox']; (iv) CENTRAL: ['bruxism' or 'tooth grinding' or 'tooth clenching'] AND ['botulinum' or 'botulinum toxin' or 'Botox']; (v) ClinicalTrials.gov: 'bruxism' AND 'botulinum'; (vi) SIGLE: ['bruxism' or 'tooth grinding' or 'tooth clenching'] AND ['botulinum' or 'botulinum toxin' or 'Botox']. The electronic search was performed from January 1990 to April 2011 and there was no language restriction.

Data collection, analysis and quality assessment

Data collection and analysis

The general data, including study design, participant information, follow-up period, and primary and secondary outcomes, were extracted and collected. The primary outcome included the decrease in frequency of bruxism events. Secondary outcomes included the decrease in pain scores, subjective evaluation of efficacy and sleep quality improvement. Any adverse effects noted in the included studies, either locally or systemically, were also extracted and collected. Originally, the collected data were analyzed in Review Manager 5 (http://ims.cochrane.org/revman/download).

Quality assessment

The strengths and weaknesses of all the included studies were assessed with reference to the Cochrane Reviewers’ Handbook. The main items included were as follows: (i) was the sequence generation adequate?; (ii) was the allocation adequately concealed?; (iii) was blinding performed in the study?; (iv) were incomplete outcome data adequately addressed?; (v) was the study free of selective outcome reporting?; (vi) was the study free of other apparent risk of bias?

RESULTS

Literature

The procedures of the search strategy and selection are presented in Figure 1. We finally included four studies in this systematic review. Of these, two were randomised controlled trials and two were controlled before-and-after studies. The details and quality assessment of the four studies are presented in Table 1 and Table 2, respectively.

Primary outcome

Comparison of bruxism frequency reduction between botulinum toxins and saline placebo

Of the four identified studies, only one, by Lee et al.12, a randomised controlled trial of 12 adults, compared the effectiveness of botulinum toxins against placebo on the reduction in the frequency of bruxism events after injection (4, 8 and 12 weeks after injection). Post-injection bruxism events detected by electromyogram (EMG) were significantly less frequent in the botulinum group than in the placebo group (Table 3).

Secondary outcomes

Of the four identified studies, those by Guarda-Nardini et al.13, Bolayir et al.14 and Sener et al.15 reported the effectiveness of botulinum toxins on pain improvement. Guarda-Nardini et al.13 conducted a randomised controlled trial of 20 participants and compared the efficacy of botulinum toxins with saline placebo on pain reduction. Bolayir et al.14 conducted a controlled before-and-after study and compared visual analog...
scale (VAS) scores of pain before and after botulinum toxin injections. Sener et al.\textsuperscript{15} conducted a two-phase study and, during the two phases, the same 13 participants received botulinum toxin injections and oral splints sequentially. Pain levels were compared before and after each treatment, and pain level reductions were compared between botulinum toxin injections and oral splint.

### Comparison of pain improvement between botulinum toxins and saline placebo

The study by Guarda-Nardini et al.\textsuperscript{13} reported pain levels at rest and on chewing assessed by VAS scores in the range 0–10. Pain reductions on chewing from baseline to the 6-month follow-up were significantly greater in the botulinum toxin group than in the saline placebo group ($P < 0.05$). However, pain reductions on chewing from baseline to 1 week or 1 month after injection, or at rest from baseline to 1 week, 1 month or 6 months after injection, showed no difference between the two groups.

### Comparison of pain levels before and after botulinum toxin injections

Bolayir et al.\textsuperscript{14} reported the comparison of pain levels measured by VAS before and after botulinum toxin injections. This study revealed that pain levels decreased significantly in both masseter muscles, 1 month and 3 months after botulinum toxin injections ($P < 0.05$).
**Comparison of pain improvement between botulinum toxins and nocturnal oral splint**

The study by Sener et al.\(^{15}\) reported that both botulinum toxins and nocturnal oral splint decreased pain significantly from baseline, and that the two treatments were equally effective for bruxism.

**Comparison of subjective evaluations of the effectiveness of botulinum toxins on bruxism**

Of the four studies, those by Lee et al.\(^ {12}\) and Guarda-Nardini et al.\(^ {13}\) reported subjective evaluations of the efficacy of botulinum toxin injections. However, they used different standards to evaluate the effectiveness: Lee et al.\(^ {12}\) employed a bruxism questionnaire, whereas Guarda-Nardini et al.\(^ {13}\) used a subjective efficacy scale (0, poor; 1, slight, 2, moderate; 3, good; 4, excellent). Thus, their results cannot be pooled, and were analyzed separately.

Lee et al.\(^ {12}\) reported that the subjective assessment of efficacy did not differ between the botulinum toxin group and the saline placebo group, 4, 8 or 12 weeks after the injections \( [P = 0.27, P = 0.26 \text{ and } P = 0.11 \text{ (all > 0.05) for } 4, 8 \text{ and } 12 \text{ weeks after injection, respectively}] \). Guarda-Nardini et al.\(^ {13}\) reported that subjective assessment of efficacy did not differ between the botulinum toxin group and saline placebo group, 1 week and 1 month after injection, but was significantly higher in the botulinum toxin group than in the saline placebo group 6 months after injection.

**Safety assessment of botulinum toxin injections**

Of the four studies included, two (Guarda-Nardini et al.\(^ {13}\) and Sener et al.\(^ {15}\) ) did not report the adverse effects of botulinum toxin injections. Lee et al.\(^ {12}\) and Bolayir et al.\(^ {14}\) reported no post-injection adverse effects, either locally or systemically.

**Sleep quality improvement**

Unfortunately, none of the identified studies reported on this specific topic. Thus, more research is needed to investigate the effects of botulinum toxin injections on sleep quality improvement.

**DISCUSSION**

Botulinum toxins, purified exotoxins of *Clostridium botulinum*, have long been used for numerous neuromuscular disorders\(^ {16,17}\). These toxins can inhibit neuromuscular transmission, justifying their clinical application in the treatment of bruxism, as recent evidence has indicated that bruxism is caused by centrally mediated high levels of motor activity in jaw muscles\(^ {6,7}\). Through an intensive literature search, we found a total of four studies evaluating the efficacy of botulinum toxins on bruxism. Of these, two were randomised controlled clinical trials and two were controlled before-and-after studies.

In contrast with placebo (saline), botulinum toxins were found to reduce significantly the frequency of bruxism events\(^ {12}\). As bruxism events were detected through an objective method (EMG) in this study, the results are convincing.

Another randomised controlled trial (Guarda-Nardini et al.\(^ {13}\) ) reported that pain level reductions on chewing after 6 months, assessed through a VAS score, were significantly greater in the botulinum injection group than in the placebo group (saline), indicative of the long-term pain improvement effects of botulinum toxin injections.

Compared with the pain levels before botulinum toxin injections, the study by Bolayir et al.\(^ {14}\) revealed that the pain levels assessed through a VAS score decreased significantly after botulinum injections. However, the results may suffer from bias because of the absence of controls.

In addition to botulinum, several modalities have been used for bruxism, including oral splint. One study (Sener et al.\(^ {15}\)) revealed that botulinum toxins were equally effective as nocturnal oral splint, which further justifies the clinical use of botulinum toxins. However, as this study compared the pain level reductions of botulinum toxins and oral splint in the same subjects in two sequential phases, bias also exists in this study. Therefore, further research is warranted on this specific topic.

Two studies (Lee et al.\(^ {12}\) and Guarda-Nardini et al.\(^ {13}\) ) reported the subjective evaluation of the effectiveness of botulinum toxins on bruxism. Their results were divergent: subjective assessment did not differ between the botulinum group and the placebo group in Lee et al.\(^ {12}\), whereas it was significantly higher in the botulinum group than in the placebo group in Guarda-Nardini et al.\(^ {13}\). This disagreement may be a result of the different standards of subjective assessment and the longer follow-up period in Guarda-Nardini et al.\(^ {13}\). Thus, botulinum may only have long-term effects on subjective evaluation. Unfortunately, none of the studies reported on the improvement of sleep quality after botulinum injections.

The effects of botulinum toxins are transient and largely limited to the area of injection. A review by Ihde and Konstantinovic\(^ {18}\) has indicated that the most common adverse effects of botulinum toxins are localised effects, e.g. tenderness and mild skin reaction at the injection site, systemic effects, e.g. headache and reversible denervation atrophy, and specific effects, including dysphonia, dysphagia and dry mouth. However, the adverse effects reported in the
above-mentioned review were most common in patients receiving high doses (>100 U), and almost all the adverse effects were from indications for uses other than bruxism, e.g. cervical dystonia. In our review, the dosages in all the four included studies were no higher than 100 U. In addition, only two studies investigated the adverse effects of botulinum injections, but neither reported post-injection adverse effects, either locally or systemically. In the literature, two studies have reported the adverse effects of botulinum injections, but neither than 100 U. In addition, only two studies investigated dosages in all the four included studies were no higher adverse effects were from indications for uses other receiving high doses (>100 U), and almost all the above-mentioned review were most common in patients are safe.

Taken together, botulinum toxin injections can reduce the frequency of bruxism events, decrease bruxism-induced pain levels and satisfy patients' self-assessment of the effectiveness on bruxism. Botulinum toxin injections are equally as effective as nocturnal oral splint for bruxism. Furthermore, botulinum toxin injections at a dosage below 100 U of the masseter or temporalis muscles in otherwise healthy patients are safe.

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Declaration of interests

None declared.

REFERENCES


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