REVIEW ARTICLE

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# 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[1,2]. Although several therapeutic modalities have been employed, including oral splint, medications and behavioral approaches, none has been reported to be fully effective[3–5]. 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[6,7], 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[8–11]. 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.

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### *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

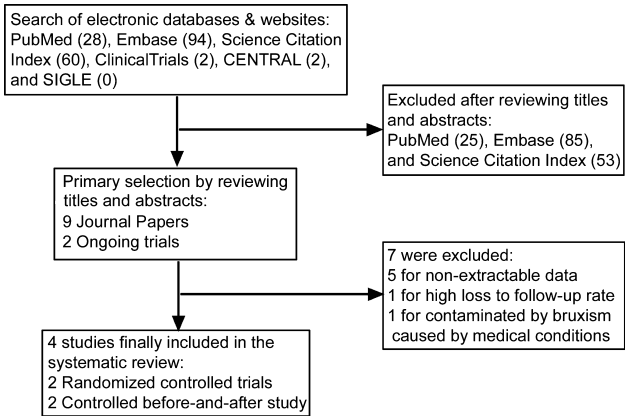



***Figure 1.*** Systematic search and selection strategy.


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**Table 1** General information on the four included studies

| Item | Lee *et al.*[12] | Guarda-Nardini *et al.*[13] | Sener *et al.*[15] | Bolayir *et al.*[14] |
|---|---|---|---|---|
| Study design | RCT | RCT | Controlled before-and-after study | Controlled before-and-after study |
| Population | 6 + 6 (20–30 years)<br>FU: 4, 8 and 12 weeks<br>FU rate: 100% | 10 + 10 (25–45 years)<br>FU: 1 week, 1 and 6 months<br>FU rate: NS | 13 (age range: NS)<br>FU: 2, 4 and 6 months<br>FU rate: NS | 12 (18–35 years)<br>FU: 1 and 3 months<br>FU: NS |
| Treatment | Group 1: each masseter [80 U Dysport (0.8 mL)]<br>Group 2: each masseter (0.8 mL saline) | Group 1: each masseter (30 U Botox); each anterior temporalis (20 U Botox)<br>Group 2: saline placebo | First stage (0–2 months): nocturnal oral splint for 2 months. Second stage (2–4 months): wash out period. Third stage (4–6 months): 60 U Botox into masseters | 50 U Dysport into masseters |
| Efficacy | A significant decrease in bruxism frequency compared with saline group | Significant decrease in pain on chewing and improvement in subjective efficacy compared with saline group | Significant decrease in pain, sensitivity and weakness for both Botox and splint after treatment<br>The two are equally effective | Subjectively reported less frequency of bruxism after injection<br>VAS pain scores decreased significantly after treatment |
| Safety | No adverse effects | NS | NS | No adverse effects |

FU, follow-up; NS, not stated; RCT, randomised controlled trial; VAS, visual analog scale.

**Table 2** Quality assessment of the included studies

| Study | Adequate sequence generation? | Allocation concealment? | Blinding? | Incomplete outcome data addressed? | Free of selective reporting? | Free of other bias? |
|---|---|---|---|---|---|---|
| Lee *et al.*[12] | Unclear | Unclear | Yes | Yes | Yes | Yes |
| Guarda-Nardini *et al.*[13] | Unclear | Unclear | Unclear | Unclear | No | No |
| Sener *et al.*[15] | No | No | No | Unclear | No | No |
| Bolayir *et al.*[14] | No | No | No | Yes | Yes | No |

**Table 3** Comparison of effectiveness between botulinum toxins and placebo on bruxism events assessed through electromyogram (EMG)

| Study or subgroup | Botulinum toxins (*n*) | Mean (SD) | Saline (*n*) | Mean (SD) | Mean difference inverse variance, random, 95% |
|---|---|---|---|---|---|
| 4 weeks after injection | 6 | 0.59 (0.57) | 6 | 4.13 (1.31) | −3.54 [−4.68, −2.40] |
| 8 weeks after injection | 6 | 1.33 (1.1) | 6 | 4.12 (0.89) | −2.79 [−3.92, −1.66] |
| 12 weeks after injection | 6 | 1.7 (0.91) | 6 | 4.4 (1.52) | −2.70 [−3.92, −1.66] |

scale (VAS) scores of pain before and after botulinum toxin injections. Sener *et al.*[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.*[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.*[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 ($P < 0.05$).

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### *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 [$P = 0.27$, $P = 0.26$ and $P = 0.11$ (all $> 0.05$) for 4, 8 and 12 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


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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 that botulinum toxins used in bruxism can cause dysphagia[10] or mild soreness at the injection site and temporal drooling[19]. However, the patients who suffered from these adverse effects in the two studies either received a large dosage (>100 U) or had a condition complicated by other medical problems. Thus, botulinum toxin injections at a dosage below 100 U in the masseter or temporalis muscles in otherwise healthy 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 for otherwise healthy patients are safe. However, only two of the studies – randomised controlled trials – were of high quality and no research has been performed on the effects of botulinum on sleep quality improvement. Therefore, further studies, especially randomised controlled trials of high quality, directed towards the comparison of botulinum toxin injections and oral nocturnal splint, and the effect of botulinum on sleep quality, are urgently needed to explore the advantages of botulinum toxin injections and to promote their wider clinical application.

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## Declaration of interests

None declared.

## REFERENCES

1. Bader G, Lavigne G. Sleep bruxism; an overview of an oromandibular sleep movement disorder. *Sleep Med Rev* 2000 4: 27–43.
2. Pavone BW. Bruxism and its effect on the natural teeth. *J Prosthet Dent* 1985 53: 692–696.
3. Okeson JP. The effects of hard and soft occlusal splints on nocturnal bruxism. *J Am Dent Assoc* 1987 114: 788–791.
4. Saletu A, Parapatics S, Saletu B *et al.* On the pharmacotherapy of sleep bruxism: placebo-controlled polysomnographic and psychometric studies with clonazepam. *Neuropsychobiology* 2005 51: 214–225.
5. Lobbezoo F, Van der Zaag J, Van Selms MK *et al.* Principles for the management of bruxism. *J Oral Rehabil* 2008 35: 509–523.
6. Kato T, Thie NM, Huynh N *et al.* Topical review: sleep bruxism and the role of peripheral sensory influences. *J Orofac Pain* 2003 17: 191–213.
7. Lavigne GJ, Huynh N, Kato T *et al.* Genesis of sleep bruxism: motor and autonomic–cardiac interactions. *Arch Oral Biol* 2007 52: 381–384.
8. Van Zandijcke M, Marchau MM. Treatment of bruxism with botulinum toxin injections. *J Neurol Neurosurg Psychiatry* 1990 53: 530.
9. Ivanhoe CB, Lai JM, Francisco GE. Bruxism after brain injury: successful treatment with botulinum toxin-A. *Arch Phys Med Rehabil* 1997 78: 1272–1273.
10. Tan EK, Jankovic J. Treating severe bruxism with botulinum toxin. *J Am Dent Assoc* 2000 131: 211–216.
11. Pidcock FS, Wise JM, Christensen JR. Treatment of severe post-traumatic bruxism with botulinum toxin-A: case report. *J Oral Maxillofac Surg* 2002 60: 115–117.
12. Lee SJ, McCall WD Jr, Kim YK *et al.* Effect of botulinum toxin injection on nocturnal bruxism: a randomised controlled trial. *Am J Phys Med Rehabil* 2009 89: 16–23.
13. Guarda-Nardini L, Manfredini D, Salamone M *et al.* Efficacy of botulinum toxin in treating myofascial pain in bruxers: a controlled placebo pilot study. *Cranio* 2008 26: 126–135.
14. Bolayir G, Bolayir E, Coskun A *et al.* Botulinum toxin type-A practice in bruxism cases. *Neurol Psychiat Br* 2005 12: 43–45.
15. Sener HO, Oral N, Keyf F. Intramasseteric botulinum toxin injection is as effective as oral overnight splint in nocturnal bruxism. *Cephalalgia* 2007 27: 1191.
16. Blitzer A, Sulica L. Botulinum toxin: basic science and clinical uses in otolaryngology. *Laryngoscope* 2001 111: 218–226.
17. Yin S, Stucker FJ, Nathan CO. Clinical application of botulinum toxin in otolaryngology, head and neck practice (brief review). *J LA State Med Soc* 2001 153: 92–97.
18. Ihde SK, Konstantinovic VS. The therapeutic use of botulinum toxin in cervical and maxillofacial conditions: an evidence-based review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007 104: e1–e11.
19. Monroy PG, Da Fonseca MA. The use of botulinum toxin-a in the treatment of severe bruxism in a patient with autism: a case report. *Spec Care Dentist* 2006 26: 37–39.

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