# Botulinum toxin for facial neuralgia

## Abstracted from

**Shackleton T, Ram S, Black M, Ryder J, Clark GT, Enciso R.**

The efficacy of botulinum toxin for the treatment of trigeminal and postherpetic neuralgia: a systematic review with meta-analyses. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2016; **122:** 61-71.

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## Question: Is botulinum toxin injection effective for the treatment of trigeminal or postherpetic neuralgia?

Data sources Medline via PubMed, the Web of Science and the Cochrane Library were searched until April 2014.

Study selection Randomised controlled trials (RCTs) comparing the efficacy of botulinum toxin type A (BoTN-A) with placebo in patients with painful trigeminal (TN) and postherpetic neuralgia (PHN) reporting changes in pain intensity in patients aged 19 years and older available in English were included.

Data extraction and synthesis Three authors independently assessed for inclusion, extracted standard data and assessed for risk of bias. The primary outcomes were baseline and post treatment intensity of pain and patients reporting pain relief of 50% or greater.

For continuous outcomes the treatment effect was measured as mean differences with 95% confidence intervals (CIs). For dichotomous outcome of reduction of pain of 50% or more, relative risk (risk ratio) with 95% CIs was reported. Statistical heterogeneity was tested with Cochran's test for heterogeneity and quantified by the I2 statistic. Results were combined using random-effects model in the presence of statistical heterogeneity otherwise fixed effect model was used.

Results Six studies were included. The effects of the interventions were presented in three meta-analyses. Mean difference in post treatment pain (six studies) pooled results showed a reduction of -3.009 in the VAS (95% CI -4.566 to -1.453 p<0.001) with the use of BoTN-A. Standardised difference in mean post treatment pain (six studies) was -0.918 (95% CI -1.197 to -0.639 p<0.001) in favor of BoTN-A. For the percentage of patients experiencing 50% pain reduction (three studies) absolute risk difference and relative risk were calculated (RR 2.892, 95% CI 1.726 to 4.848 p<0.001) in favour of the use of BoTN-A.

Conclusions The authors concluded that there is moderate evidence regarding the efficacy of BoTN-A in treating patients with trigeminal neuralgia and postherpetic neuralgia.

## Commentary

This meta-analysis reviews four studies for the effectiveness of BoTN-A on TN and two studies on PHN. While TN and PHN are both neuralgias they are very different conditions. TN is characterised by episodic paroxysmal lancinating pain triggered by a stimulus. TN can often be well managed with full pain relief with anticonvulsant medications. The medications do have side effects and may become less effective over time, warranting the need to increase doses or change medications. When medications are not effective or cannot be tolerated, invasive procedures like microvascular decompression may be considered which can have serious risks.

PHN is a debilitating complication of herpes zoster (HZ) characterised by intense continuous pain following an outbreak of HZ. The International Headache society diagnostic criteria for PHN include a unilateral facial pain recurring over three months after acute HZ, and the pain is located in the distribution of the same trigeminal nerve branch. It is mostly treated with topical lidocaine, anticonvulsants or anti-depressants. Symptoms of PHN are continuous stabbing pain, burning and allodynia along a dermatome where the mucocutaneous eruptions of HZ are found. In most cases PHN is self-limiting.

Botulinum toxin type A is a potent neurotoxin that inhibits the release of the neurotransmitter acetylcholine from presynaptic neurons as well as pain modulating neurotransmitters, which is why it has been studied for its effectiveness in treating neuropathic pain.1 BoTN-A does not have the systemic side effects of medications and does not carry the same risk as microvascular decompression, so if it proves to be effective and with minimal risk, it may be considered as an alternative treatment if medications may not be used.

This meta-analysis reviews four studies for the effectiveness of BoTN-A on TN and two studies on PHN. The pooled results suggest that BoTN-A significantly reduced pain on average of 3.009 on the VAS compared with placebo.

In this well designed meta-analysis all included studies used the same scale (VAS) for evaluating changes in pain. The TN studies all utilised MRI or CT to rule out secondary causes and followed accepted criteria for diagnosis. The two PHN studies used the criteria of pain three months after HZ rash has healed.

There were specific study design differences between the PHN and TN studies. The two PHN studies excluded the use of other medications, except paracetamol if needed in one study and opioids in another study. The four TN studies allowed

patients in the treatment and control groups to remain on their anticonvulsant or other medications throughout the study.

Aside from VAS, frequency of attacks were evaluated in three of the TN studies. In all three of the studies there was a significant reduction in frequency of attacks/ paroxysms at the time of the first measurement after treatment and sustained throughout the studies. Frequency of attacks is as important of a measurement as pain severity (VAS) when assessing pain relief in trigeminal neuralgia.

The authors do suggest that since there are potential differences in the patient populations related to age (TN patients typically are ten years younger than the PHN patients) that can have an impact in tolerance of medications and co-morbidities.

They also recognise that there is a blinding bias inherent in studying BoTN-A injections because of the potential of visible effects of botulinum on facial expression. They did rate five of the studies as having an unclear bias and one study with a high bias. The authors also state that the evidence was moderate because of the small number of studies that qualified. Other limitations are that the studies had small sample sizes, with variable treatment doses and injection sites and limited long term follow-up, the shortest being eight weeks.

No significant adverse side effects were reported. The few side effects reported included: facial asymmetry, transient oedema and hematomas, as well as pain on injection in the PHN patients.

Because of the inherent differences between the two neuralgias: TN being paroxysmal, while PHN is continuous and may be self-limiting, it would be prudent to analyse the results on each of the neuralgias separately.

Considering the small number of studies and the limitations of the evidence, BoTN-A might be an adjunct for the treatment of PHN and TN in patients refractory to anticonvulsant medication.

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