Editorial

# Is botulinum toxin the future of orofacial pain management? Evidence and perspectives

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**Botulinum toxin (BTX) demonstrates potential as a complementary therapy in managing chronic orofacial pain (OFP), but challenges in the standardization of protocols and indications remain.**

The orofacial region is anatomically intricate, housing a dense network of muscles, nerves and blood vessels. This complexity often makes diagnosing and treating orofacial pain (OFP) a challenging endeavor. While OFP is commonly conflated with intraoral pain caused by dental or periodontal pathology, problems with differential diagnosis emerge when it extends to non-odontogenic pain, such as temporomandibular disorder (TMD) or neuropathic pain. Most of these conditions are associated with a high risk for chronicization and impairment, and they often necessitate multidisciplinary approaches for effective management.[1] Amongst the emerging therapies, botulinum toxin (BTX), a neuromodulator known for its cosmetic applications, has gained attention for its potential to manage several pain conditions. The perception is that in several clinical communities, BTX is even emerging as the one-fits-all solution, so questions and concerns about its potential misuse and abuse arise. For this reason, a short recap of the available information supporting its applications, as well as a look at future perspectives, are needed.

Botulinum toxin exerts its effects primarily by inhibiting the release of acetylcholine at neuromuscular junctions, leading to temporary muscle relaxation. This effect is well-known and is the backbone for all applications in cosmetic medicine and dentistry, as well as for claims about its use within the framework of bruxism and/or musculoskeletal pain management. Beyond the modulation of muscle activity, BTX has demonstrated antinociceptive properties by reducing the release of pain mediators, like glutamate, substance P and calcitonin gene-related peptide (CGRP), in sensory neurons. This dual action makes it a promising candidate for managing chronic pain conditions, including those in the orofacial region.[2] The question is: Has BTX type A (BTX-A) ever done the step from promising to evidence-based treatment?

With regard to the orofacial area, most research has focused on the application of BTX in patients with TMDs and/or bruxism.

Temporomandibular disorders are the most common source of non-odontogenic OFP, and include disorders of the temporomandibular joint (TMJ), masticatory muscles and related structures. Traditional treatment ranges from physical therapy to oral splints and pharmacological interventions.[3] Various studies, including a systematic review by Delcanho et al.,[4] have highlighted the efficacy of BTX in alleviating pain, improving jaw mobility and enhancing the quality of life (QoL). Patients receiving BTX injections showed significantly reduced pain scores on the visual analog scale (VAS) and improved functional outcomes as compared to the placebo group.[5] These effects are particularly evident in patients with myelogenous TMDs, where muscle hyperactivity is the primary pain source.[6] Bruxism is a risk factor for muscle fatigue, TMJ pain[7,8] and dental complications.[9–11] Consequently, BTX has gained traction as effective treatment for bruxism by reducing masseter and temporalis muscle activity. The same review by Delcanho et al. reported significant decreases in muscle hypertrophy among patients treated with BTX, with minimal adverse effects.[4] De la Torre Canales et al. also supported that, despite the limited number of studies on this subject, BTX appears to be a feasible management option for bruxism-related symptoms.[12] However, additional research is essential, particularly regarding the specific treatment indications for the reduction of bruxism itself, a target that is often confused with the management of its potential consequences.

Other potential applications vary from neuropathic to neurovascular pain. Botulinum toxin has shown interesting effects in managing conditions like trigeminal neuralgia (TN) and post-herpetic neuralgia (PHN).[8]

Trigeminal neuralgia is severe, electric shock-like pain affecting the trigeminal nerve. Evidence from studies suggests that BTX injections provide substantial pain relief and reduce the frequency of attacks in refractory TN cases, with the benefits sustained for several months post-injection.[13,14]

Post-herpetic neuralgia is a chronic complication of shingles, and it can cause persistent facial pain. Botulinum toxin has demonstrated efficacy in reducing pain intensity and improving QoL, as highlighted in trials by Xiao et al.[15]

As for headaches and migraines, the approval of BTX by the Food and Drug Administration (FDA) for chronic migraine treatment can be seen as a milestone achievement to pave the track for its application in the orofacial region. Chronic migraine, often associated with referred pain in the jaw and neck, responds well to the neuromodulatory activity of BTX.[11] Research by Lanteri-Minet et al. showed a significant reduction in the number of headache days and headache intensity, with parallel improvement in associated facial pain.[16]

Moreover, preliminary studies suggest that BTX-A significantly reduces referred myofascial pain from the neck muscles, as well as orofacial myofascial pain, at 2–6 months post-treatment, with no major adverse events reported,[17] and that it might alleviate pain and improve oral function in patients with burning mouth syndrome (BMS).[18]

Despite its benefits and encouraging claims, some of the early problems that emerged with BTX therapy are still unchallenged, such as the poor standardization of injection techniques or dosages.[19] Protocols lack uniformity across studies and clinical practices, leading to very different outcomes at the individual level. Also, the high cost and subsequent low accessibility of BTX are impacting its diffusion in the clinical setting and the design of proper investigation in the research setting. The good news is that very few side effects have been reported, although the risk of temporary weakness or facial asymmetry should always be discussed with the candidate patients.

Thus, the role of BTX in OFP management continues to evolve, and future research should prioritize factors such as:

– standardized protocols: Developing evidence-based guidelines for BTX administration in different OFP conditions;
– long-term studies: Assessing the sustainability of therapeutic effects and their impact on patient QoL;
– combined therapies: Exploring BTX as part of multimodal treatment strategies, including physical therapy, pharmacology and cognitive-behavioral interventions[20]; and
– defined diagnosis: Individualizing the use of BTX in different conditions, with the focus on the psychosocial impairment as an outcome variable.

Additionally, advancement in imaging technologies and biomarker studies may refine patient selection, ensuring personalized and effective BTX treatment.

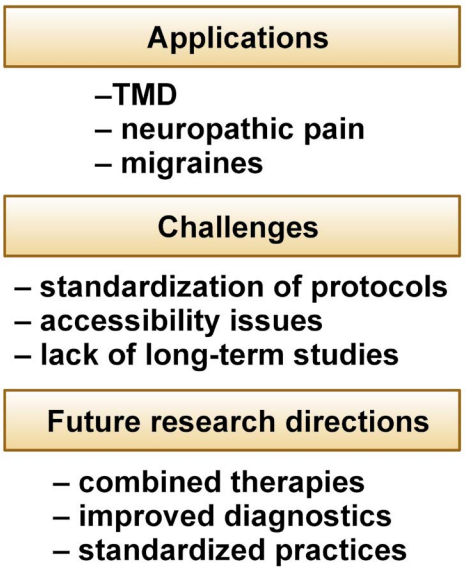


Fig. 1. Key aspects of botulinum toxin (BTX) in orofacial pain (OFP) management, highlighting applications, challenges and future research directions to improve clinical efficacy and standardization

TMD – temporomandibular disorders.

Botulinum toxin represents a transformative approach in OFP management, offering hope to patients with refractory or chronic conditions (Fig. 1). While not a universal solution, its role as an adjunct therapy is partially supported by scientific evidence. The current problem lies in the lack of development as far as the specific indications and protocols are concerned, which may lead to false claims and clinical misuse. Continued research and innovation are essential to overcome the current limitations and fully integrate BTX into mainstream OFP treatment protocols.

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