Chapter 2

Orofacial Dystonia and Other Oromandibular Movement Disorders

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Additional information is available at the end of the chapter

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Abstract

Orofacial movement disorders (OMD) are a group of conditions that affect the motor aspect of the trigeminal, facial, and hypoglossal cranial nerves. These alterations are produced by pathologic disorders affecting the central nervous system, manifesting as isolated or combined hyperkinetic dysfunctional activities on the masticatory, facial mimic, or tongue musculatures. A comprehensive understanding of orofacial dystonias is essential to identify different variants of OMD that could be easily mislabeled or misdiagnosed. In this chapter, the authors focus on different aspects of the pathophysiology, epidemiology, clinical features, and management of orofacial dystonias and other movement disorders that are poorly recognized but not uncommon presentations of OMD, such as orofacial dyskinesias, drug-induced orofacial reactions, tardive orofacial syndromes, and bruxism.

Keywords: oromandibular dystonia, orofacial dystonias, orofacial dyskinesias, tardive dyskinesias, drug-induced extrapyramidal reactions, sleep bruxism/awake bruxism

1. Introduction

The first written medical description of OMD was made in 1910 in Dr. Meige's paper entitled "Le convulsion de la Face, une forme clinique de convulsione faciale Bilateral et Mediane." However, the clinical features outlined by Dr. Meige were not the first description of the phenomena, some pictorial representations dating from the sixteenth century were the first recorded description of OMD. Meige's description summarized the clinical signs featured in orofacial dystonia, differentiating them from other movement disorders that affect the lower half of the face. He also emphasized relevant details such as the involvement of different

structures of the lower face, the description of specific precipitating factors, maneuvers that tended to milden and restrained the involuntary movement disorders, or their complete remission during sleep. Almost half a century later, OMD started to gain attention again [1].

Oromandibular dystonias (OMDy) are focal dystonias affecting the motor aspects of trigeminal, facial, and hypoglossal cranial nerves. Most OMDy are diagnostically challenging, mainly because they may have numerous presentations and severities, triggers may be hard to recognize, and orofacial movements may be quiescence during periods being often primary or idiopathic [2]. Consequently, OMDy may be commonly mistaken with temporomandibular disorders, spontaneous condylar dislocation, hemimasticatory or hemifacial spasm, and psychogenic disorders [3–7]. In this chapter, the authors focus on different aspects of the pathophysiology, epidemiology, clinical features, and management of OMDy that may be useful to identify them from other movement disorders that are poorly recognized but not uncommon, such as orofacial dyskinesias, tardive orofacial syndromes, and bruxism.

2. Oromandibular dystonia

2.1. Definition and clinical presentation

Oromandibular dystonia is an infrequent form of focal dystonia, which affects the lower half of the face and mandible [8]. It manifests like sustained or intermittent, involuntary muscle contractions, which can cause repetitive movements of the lower facial, masticatory or tongue muscles or sustained abnormal postures in the lower face [9]. Dystonic oromandibular movements may present as isolated or combined movements, affecting an isolated group of mandibular muscles (e.g., symmetric contraction of the elevators of the mandible, producing jaw closing dystonia) or various groups of muscles (asymmetric or alternated contraction of jaw depressors and elevators resulting in mandibular tremor or jaw deviating dystonia) [9].

Because clinical presentations are not uniform, focal OMDy can be characterized phenomenologically by the functional motor activity involved in the oromandibular movement. Consequently, OMDy can be subdivided into different subtypes: jaw-opening dystonia, jaw-closing dystonia, jaw-deviating oromandibular dystonia, perioral dystonias, and/or lingual oromandibular dystonia [10]. When OMDy occurs together with blepharospasm, it is usually called cranial dystonia or Meige syndrome [11]. Toloza and Marti suggested that most cases of OMDy occur in combination with blepharospasm, only manifesting independently in 2–23% of the cases [12]. Isolated jaw-closing dystonia seems to be the more prevalent form of OMD and is less likely to be associated with other craniocervical dystonias. Approximately 32% of jaw OMDy are associated with facial grimacing, lip pursing, or other facial contortions [13]. Spontaneous remission is uncommon but may occur within the first 5 years [11]. Morning benefit (milder symptoms during morning) and overflown phenomenon (aberrant muscle activation during certain tasks) are also relatively common in OMDy patients [14].

The dystonic muscle contractions may interfere with several orofacial motor activities like mastication, swallowing, and verbal and non-verbal communication, explained probably by the uncoordinated and deviated muscle masticatory activity with antagonist cocontractions

found in electromyographic studies [15]. Also, depending on the subtype of OMDy, patients may present trismus, dental wear, uncontrollable tooth clenching or grinding, frequent oral ulcers, forceful involuntary closures, jaw dislocation, dental restorations damage or fractures, temporomandibular joint overload, facial contortions, lip sucking or smacking, lip pursing, chewing-like movements, mouth retraction, and platysma contractions [13, 16–18]. Generally, the masticatory spams disappear during sleep [19].

OMDy can be triggered by mandibular activities, such as talking, yawning, chewing, or swallowing, often causing severe social impairment, reduced quality of life, and weight loss [20–22]. Also, patients frequently report exacerbating factors such as emotional stress and other daily activities like driving, reading, praying, looking upward/downward, or chewing [11]. Jaw and facial pain is also frequent and can often mislead the clinician, especially because OMDy are rare, may have remittance periods, and triggers are usually hard to identify [23]. Sensory trick ("geste antagonistique") may ameliorate OMDy symptoms temporarily, being more effective in jaw-opening dystonia more than jaw-closing dystonia [24, 25].

2.2. Epidemiology

The prevalence of the dystonic oromandibular movements varies within the different reports. In the United States, the estimated prevalence has been reported from 0.52 to 30 cases per 100,000 [26–28]. Other studies have reported a prevalence of 6.9 cases per 100,000 and an incidence of 3.3 cases per million [26, 29]. Women seem to be more affected than men, in a female: male ratio of 3:1, typically with adult age onset near the sixth decade of life (more prevalent between 45 and 75 years) [9, 29]. A recent multicentric study featuring centers from the United States, Canada, Germany, Australia, England, France, and Italy reported that from all forms focal dystonia, OMDy had a prevalence of 8.7%, being one of the less prevalent subtypes of focal dystonia [30] (**Table 1**).

2.3. Etiology

The etiology of OMDy may be primary (idiopathic) or secondary. The primary form is the most common form of OMDy, not involving any central nervous system pathology, brain lesion, or tumor. Studies by Tan and Jankovic reported that most of OMDy were primary, accounting for 63% of the cases reported [31]. The pathophysiology of OMDy is currently

	Number of cases	%
Primary	11	44
Neurodegenerative diseases (Parkinson's disease, Huntington's disease, other)	9	36
Secondary neuroleptic	3	12
Functional	2	8

Table 1. Prevalence and etiology OMD from Movement Disorders Tertiary Center, Centro de Trastornos de Movimientos (CETRAM), Chile, January 2014–October 2015.

unknown, but several pathophysiological explanations have been pondered as probable causes, such as basal ganglia dysfunction, hyperexcitability of motor neurons interneurons related to signaling pathways, loss of inhibition, aberrant dopamine signaling, monoaminergic dysfunction, abnormal plasticity, and abnormal sensory function [32–34].

The most common cause of secondary dystonia is tardive dystonia (drug-induced) reported in 22.8% of the cases. Other causes described are peripheral-induced OMDy in 9.3% of the cases, postanoxic states OMDy representing 2.5% of the cases, neurodegenerative disorders 1.8%, and head injury-associated OMDy accounting for 0.9% of the cases [13].

Tardive OMDy produced by haloperidol, thioridazine, and metoclopramide accounts for the majority of the reports of drug-induced cases. Also, calcium channel blockers antivertiginous drugs such as flunarizine and cinnarizine have also been associated with OMDy [35].

Secondary OMDy can be caused by brainstem lesions, cerebrovascular disease, traumatic brain injury, and neurodegenerative disorders including multiple system atrophy, progressive supranuclear palsy, Huntington's disease, and neuroacanthocytosis. OMDy secondary to neurodegenerative disorders often present coexisting symptoms, such as chorea, seizures, amyotrophy, or subcortical dementia [19].

Peripheral trauma is a known to be causative or predisposing factors in several neurological disorders. Despite that most reports relating orofacial or dental trauma/procedures to OMDy are mostly anecdotal, the precise relation of peripheral trigeminal trauma and the onset of OMDy is still unclear [36].

Traumatic injuries, fractures, surgeries, and peripheral trigeminal nerve deafferentation or amputation have been associated with the onset of OMDy [37]. Also, numerous ambulatory dental procedures have been described as possible causative or predisposing factors of OMDy [38]. Ill-fitting dentures, endodontic treatments, gingivectomy, tooth extraction, apicectomy, prosthodontics, TMJ arthroscopy, and dental implants had been reported in dental and neurological literature [8, 39–44].

Sankhla et al., in a review of 9083 patients, reported that of a total 197 patients diagnosed with OMDy, 27 cases had a history of facial trauma prior the onset of the dystonia [45]. Jankovic and Van der Linden noticed that 65% of the dystonia and tremors were associated with trauma-induced events [37]. Causation, however, is scarce as dental interventions are widespread while OMDy is very infrequent [29].

Eleven gene mutations have been identified as putative causes of dystonia. Of those, DYT6/THAP1 gene variations have been involved in early-onset, progressive craniocervical dystonia (OMDy, spasmodic dysphonia, and cervical dystonia) [46].

2.4. Treatment approaches

The treatment of OMDy is challenging and often requires multidisciplinary evaluation. Proper dental and oral evaluation is needed to assess orofacial and oropharyngeal function [29]. Triggers (especially relevant to sensory tricks) and the subtype of OMDy should be carefully identified.

Audiovisual recordings may be helpful in analyzing both. Adequate nutrition must be maintained when OMDy interferes with nutrition [29].

Physical therapy or speech therapy can be helpful sometimes. Peripheral afferent blocks targeted to the muscles with 5–10 ml 0.5% lidocaine solutions seem to improve unless temporarily OMDy, suggesting that somatosensory input may be relevant in the pathogenesis of dystonia [47].

Sensory tricks (geste antagoniste) do not seem to provide adequate long-term relief and many times requires actions that interfere with normal functional activities [29]. Reports indicate that sensory tricks like pressing the teeth or lips with the fingers, placing objects in the mouth (cigarettes, gum, or object between the molars or chin), singing, or humming may be helpful in one-third of the patients [24, 25, 45]. Oral appliances have shown to be useful in some cases [24, 42], especially when they successfully mimic the patient's sensory tricks. Singer and Papapetropoulus suggested that sensory tricks worked better for jaw-opening dystonia rather than in jaw closing dystonia [16].

A recent study by Yoshida et al. found that older patients with intraoral sensory tricks were more likely to respond to an oral appliance treatment compared to patients who do not have sensory tricks. Also, the authors reported that splint therapy was more effective in patients with jaw-closing dystonia who reported sensory tricks that involved mastication [14].

Deep brain stimulation targeting the externus globus pallidus has shown some continued efficacy, reporting interesting result in patients with Meige syndrome, but the evidence is still preliminary [48–50].

Pharmacological treatment of dystonia is mostly based on empirical experience rather than supported by rationale scientific evidence [51]. Oral medications are rarely beneficial in improving dystonic symptoms and may include anticholinergic drugs, baclofen, dopaminergic drugs, and benzodiazepines [52]. Tetrabenazine reported benefits in the treatment of the symptoms in 26 to 60% of OMDy patients but is frequently associated with important side effects like parkinsonism and suicidal ideation [7, 53]. Zolpidem in doses ranging from 5 to 20 mg has shown some promising results, but since these findings are only in a relatively small number of cases, prospective clinical trials are needed to determine its effectiveness [54, 55].

Chemodenervation with botulinum toxin (BT) is considered by most to be the first line of treatment. However, there are no high-level clinical trials to support this claim, and the evidence is mainly based on small series of cases [56]. Hallett et al. in an evidence-based review concluded that abobotulinumtoxin A and onabotulinumtoxin A have level C recommendation according to American Academy of Neurology Classification for the Quality of Evidence (AANC) and level U for incobotulinumtoxin A and rimabotulinumtoxin B (inadequate data or treatment still unproven) [57]. As expected, a recent systematic review that intended to evaluate the effectiveness of BT in OMDy concluded that due to the variability of the outcomes there is insufficient evidence to recommend or refute BT as a treatment option [58]. Nonetheless the scarce data, empirical experience over past 20 years has shown that BT is an effective and safe approach in the treatment of OMDy [59]. Because OMDy encompasses a broad range of musculature, it is among the most challenging forms of focal dystonias to treat

with BT [60]. The outcome of the injection depends critically on proper muscle identification, dose selection, and managing patient's expectations [29].

2.5. Subtypes of OMDy, muscle selection, and botulinum toxin application technique

2.5.1. Jaw-closing dystonia

The muscles responsible for jaw closing are the masseters, temporalis muscles, and medial pterygoid muscles. In jaw-closing dystonia, the masseter and temporalis are the primary targeted muscles, mainly because BT application is percutaneously and relatively easy to perform.

2.5.1.1. Masseter muscle

The masseter muscle is one of the major muscles of the mastication, with a thick quadrilateral muscle disposition. It is primarily involved in the elevation of the jaw and the deviation during its ipsilateral activity. The anterior two-thirds (superficial Masseter) originates from the lower border of the zygomatic arch and the lateral surface of the ascending mandibular ramus, projecting downward and posterior to the lateral aspect of the lower border of the ramus (near the second molar in its anterior border) and mandibular angle (posterior border). The last third has a more posterior origin in the zygomatic arch projecting in a vertical direction towards the central part of the ramus [61, 62] (**Figure 1**).

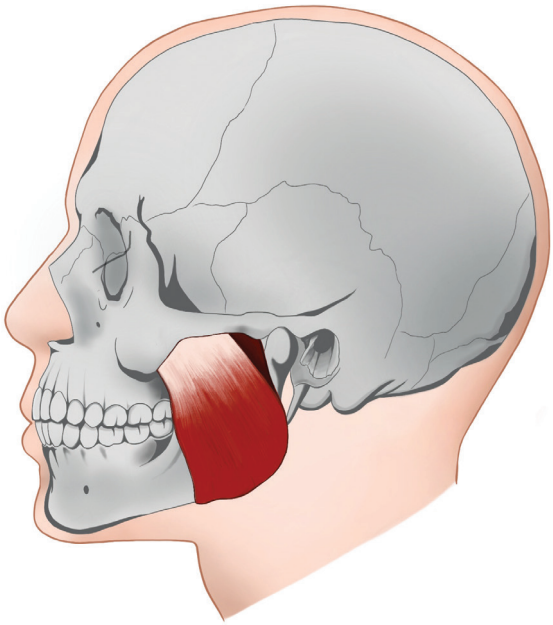

Figure 1. Masseter muscle anatomy.

The alignment of masseter muscle fibers is mostly oriented to give a biomechanical advantage towards performing jaw closing and elevation, also having some importance in lateral deviation and protrusion of the mandible. Hence it is of primary importance in the treatment of jaw-closing dystonia.

The application of botulinum toxin must be individualized for each patient. Usually, 2–3 points of injection are recommended since the masseter is a superficial muscle, clinically palpable the technique can be performed without EMG guidance. The muscle is usually approached by inserting the needle injection 1 cm anterior to the posterior border of the ramus and is easily palpable by making the patient clench. If EMG is used, the EMG discharges will ensure that the needle is in the masseter and not in the parotid gland [19] (**Figure 2**).

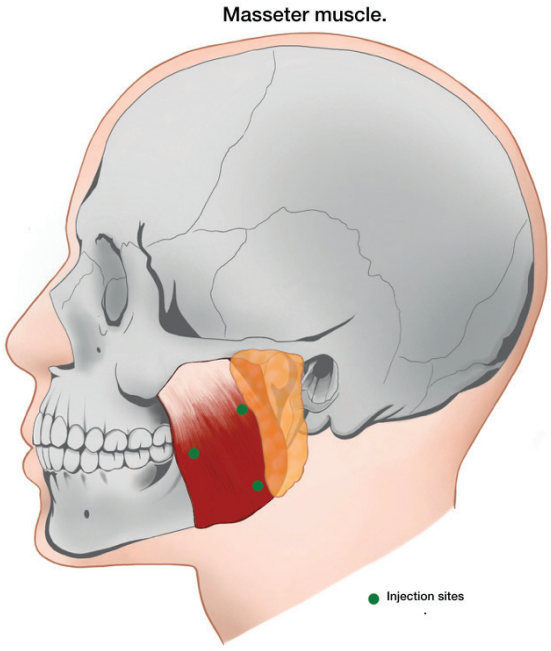

Figure 2. Masseter muscle recommended injection sites.

2.5.1.2. Temporalis muscle

The temporalis muscle is also one of the major mandibular elevators, consisting of three separate muscular fascicles with different vectorial orientations, displaying a distinctive fun shape and occupying almost the entire temporal fossa (conformed by the parietal, sphenoid, temporal, and zygomatic bones) on the lateral aspect of the skull.

It has three different fascicles (anterior, middle, and posterior) that merge into one sole muscle coursing inferiorly and medially to the zygomatic arch, where they converge in the temporalis tendon to insert in the coronoid process.

The three fascicles are aligned in a different disposition. The anterior fibers are oriented vertically, the middle fibers are disposed on a diagonal orientation, and the posterior fibers possess a more horizontal disposition. The three fascicles functioning altogether are involved in mandibular vertical closure. Anterior and the middle fibers are primarily involved in jaw-closing activities. The posterior fibers involved in jaw closure, but also are influential in promoting the settlement of the temporomandibular joint condylar disc complex into the glenoid fossa and helping retrusion of the mandible after it is protruded. Lastly, it is described that the ipsilateral three fascicles may be relevant in stabilizing the jaw during lateral excursive movements [61, 62] (**Figure 3**).

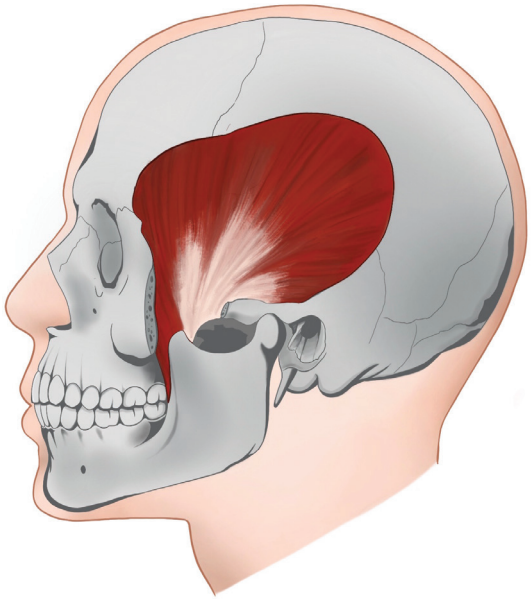

Figure 3. Temporalis muscle anatomy.

The injection technique should be performing at least one point per fascicle. Identification of the anterior portion of the temporalis muscle can be challenging in certain occasions. An easy way to rapidly identify this fascicle is to ask the patient to perform opening, closing, and clench movements repeatedly. This maneuver will contract the anterior temporalis fibers and will help identify the puncture points. The muscle is approached perpendicular to its plane and as highly possible in the temporal fossa. Because of this wide radiating pattern, it is best to give 3–4 injections into the muscle [19] (**Figure 4**).

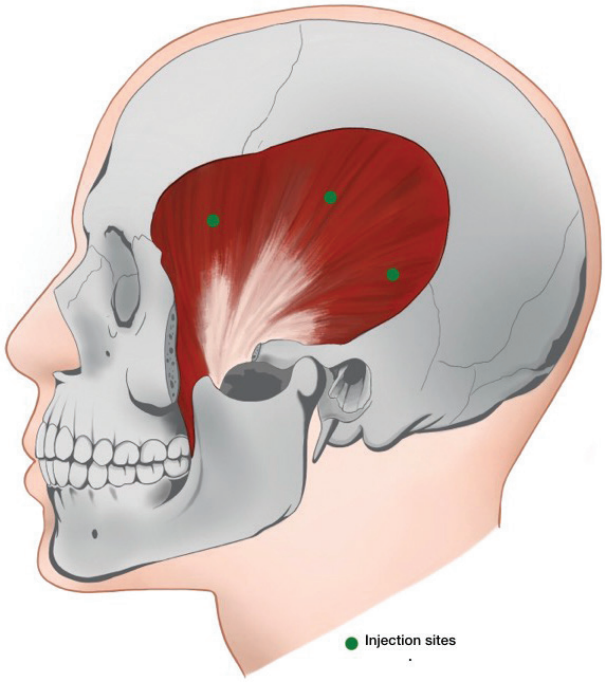

Figure 4. Temporalis muscle recommended injection sites.

2.5.1.3. Medial pterygoid muscle

The medial pterygoid muscle or internal pterygoid muscle is a deep quadrilateral muscle of mastication, primarily involved in the elevation of the mandible. It has two distinct points of origin: first, the "deep head" emerging from the medial surface of the lateral pterygoid plate of the sphenoid. The second point, the "superficial head" arises from the maxillary tuberosity and the pyramidal process of the palatine bone. Both heads orientate in a posterior and inferior direction, inserting at the medial surface of the ramus and mandibular angle via a shared tendinous insertion [62] (**Figure 5**).

The function of the medial pterygoid muscle is primary jaw closure and is considered a functional analog of the masseter muscle. During contralateral mandibular deviation, it acts in conjunction with the ipsilateral inferior head of the lateral pterygoid muscle producing contralateral translatory movement of the mandible and ipsilateral translation of the mandibular condyle. The bilateral activity of these muscles in conjunction with the bilateral activity of the inferior head of the lateral pterygoids results in jaw protrusion [63].

As the lateral pterygoid muscle, the medial pterygoid botulinum toxin application can be performed using an intraoral or extraoral approach.

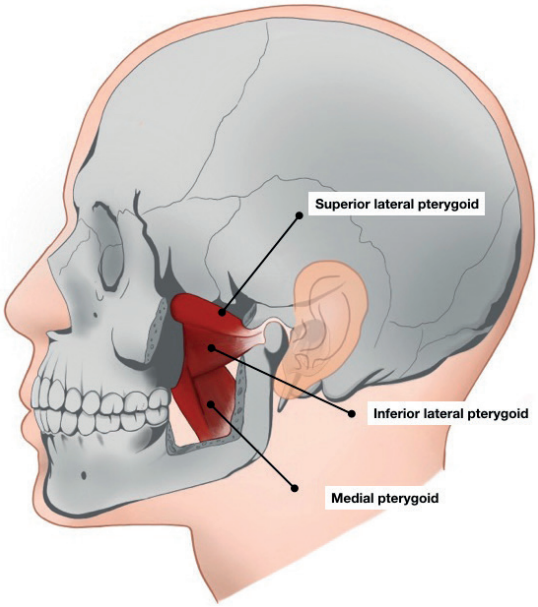

Figure 5. Medial and lateral pterygoid muscle anatomy.

There are two different forms of performing the extraoral injection into the medial pterygoid muscle. From below, inserting the EMG electrode about 0.5–1 cm anterior to the angle of the mandible along the interior aspect of the mandible and angled perpendicularly to the ascending mandibular ramus, the adequate positioning of the electrode should be verified by asking the patient to clench. While performing this approach, the clinician should be careful in avoiding the facial artery [19] (**Figure 6**).

The other approach is more technically complex because the electrode must traverse deep through an extensive amount of tissues and network of vessels (the pterygoid venous plexus). This extraoral approach requires to position the patient in a supine position with the mouth open wide. The punction site should be selected in the window bounded by the lower border of the zygomatic arch, the mandibular notch, the mandibular condyle, and the coronoid process. Then, the needle electrode is directed caudally towards the medial pterygoid muscle [64].

The intraoral technique is easier to perform, especially for those who are more familiar with intraoral injections. The technique must be executed by palping the muscle intraorally and inserting the needle electrode through the pharyngeal wall until the muscle is reached [64].

2.5.2. Jaw-opening dystonia

The muscles involved in jaw opening are the inferior lateral pterygoids and the submental complex (which includes the digastrics, mylohyoid, and geniohyoid muscles). The primary in promoting jaw opening is the inferior lateral pterygoid. The submental complex has a secondary role in promoting jaw opening, primarily assisting jaw opening at the beginning of the aperture.

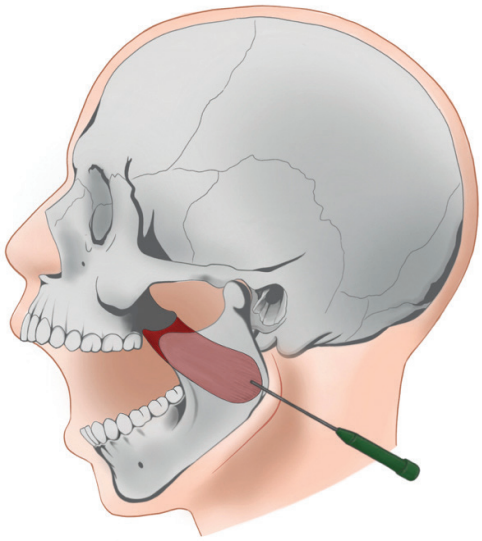

Figure 6. Medial pterygoid muscle extraoral botulinum toxin application technique.

2.5.2.1. Lateral pterygoid muscle

The lateral pterygoid muscle is a nonpalpable masticatory muscle located in the lateral portion of the infratemporal region, primarily involved in both jaw closure and opening. Lateral pterygoid muscle consists of two independent "heads" or "belies" (superior and inferior) that have two separate functional roles. The superior head has his origin in the greater wing of the sphenoid bone. The fibers of the superior head primarily insert in the articular fovea of the mandibular condylar head (accounting 60–70% of the times). A less frequent anatomic variant is the insertion at the temporomandibular joint disc and capsular complex (30–40% of the times). Functionally, the superior head of the lateral pterygoid muscle acts as an active stabilizer of the condyle during the closure [62].

The inferior head of the lateral pterygoid has less diverse anatomic variations, having its origin in the outer surface of the pterygoid plate and inserting in the lower part of the anterior fovea of the condyle and condylar neck. When acting bilaterally, the inferior head of the pterygoid muscle produces jaw protrusion and jaw opening when it acts in conjunction with the suprahyoid muscles. During these activities, the superior head of the pterygoid muscle is inhibited, giving this muscle a unique role in mandibular movement depending on which part of the muscle is activated. Conversely, when the inferior head of the muscle is activated unilaterally, a contralateral deviation of the jaw is produced [63]. Therefore, the inferior head of lateral pterygoid is one of the main targets in jaw-opening dystonia and jaw-deviating dystonia (**Figure 5**).

The access to the lateral pterygoid is complicated and can be performed intraorally or extraorally. Both approaches (intraoral or extraoral) require the use of electromyographic guidance to ensure intramuscular injection.

In the intraoral injection, the patient should be semi-reclined with his/her mouth slightly open and deviated to the contralaterally to the side of the procedure. The insertion of the needle electrode is above the second molar mucobuccal fold. The electrode is directed inward, upward, and backward sliding close to the tuberosity until hitting the pterygoid plate (to inject the inferior head) [65]. The direction of the injection should be oriented towards the middle point of a virtual line connecting the ipsilateral ear's tragus and lobe [66]. A counter-resistance contralateral mandibular deviation can be performed once the needle electrode is placed to ensure EMG discharge (**Figure 7**).

The extraoral technique needs a more profound anatomical knowledge of the infratemporal fossa. The patient should be in a supine position, with the jaw opened at least 20–30 mm wide or sufficiently to create a window bounded by the zygomatic arch (above) and the mandibular notch (below), coronoid process limiting the anterior border, and the mandibular condyle to posterior. To perform the extraoral technique, the clinician should palpate the bony margins with the index and middle fingers. Once located the tentative puncture the needle electrode should be placed anteriorly to the temporomandibular joint and directed upward, forward, and deep under the zygomatic arch towards the sphenoid bones (which forms the sealing within the muscles lies) [67]. Some descriptions suggest that the point of entry to the technique is 35 mm from the external auditory canal (anterior to the condylar neck of the mandible) and 10 mm from the inferior margin of the zygomatic arch. Then, the needle is angled upward about 15° and directed towards the roots of the lasts upper molars to reach the inferior head of the lateral pterygoid [19]. The needle must penetrate (at least

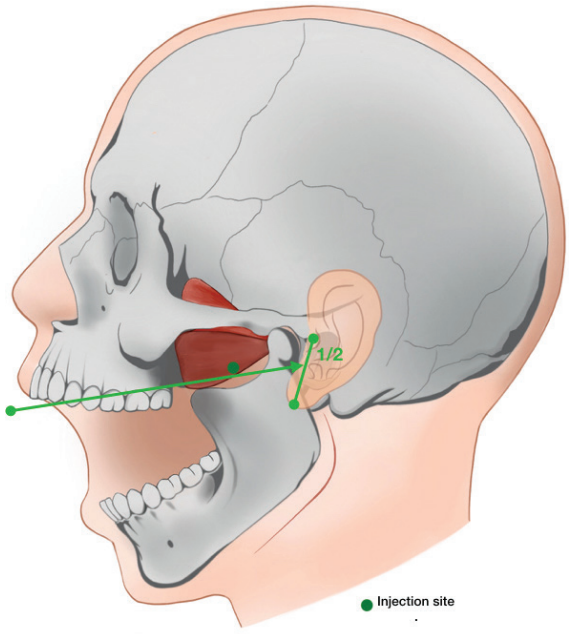

Figure 7. Intraoral injection technique to the inferior head of the lateral pterygoid muscle.

30–40 mm) through the masseter muscle and temporalis tendon before reaching the inferior lateral pterygoid head (**Figure 8a** and **b**).

2.5.2.2. Submental complex

The submental complex is primarily involved in jaw-opening oromandibular dystonia. This complex of muscles is constituted by three of muscles: the digastric muscle, the mylohyoid muscle, and geniohyoid muscle.

2.5.2.2.1. Digastric muscle

Similar to the lateral pterygoid muscle, the digastric muscle has two distinct components: the anterior belly and the posterior belly. The anterior belly has origin at the digastric fossa located in the submental area near the midline. Its fibers extend posteriorly and inferiorly. The posterior belly has its origin in the mastoid notch of the temporal bone and extends inferiorly and anteriorly to join with the anterior belly at the intermediate tendon attached to the hyoid bone. Both bellies participate in the mandible depression (opening). However, the anterior has more functional activity during jaw opening, while the posterior belly is also involved in elevating the hyoid bone during mastication and swallowing.

2.5.2.2.2. Mylohyoid muscle

The mylohyoid muscle is flat triangular muscle immediately situated superior to the anterior belly of the digastric muscle. It has his origin at the mandibular mylohyoid line, extending from the mandibular symphysis to the last inferior molar. The more medial fibers go inferior-medially and posterior towards the midline, where they meet with their contralateral

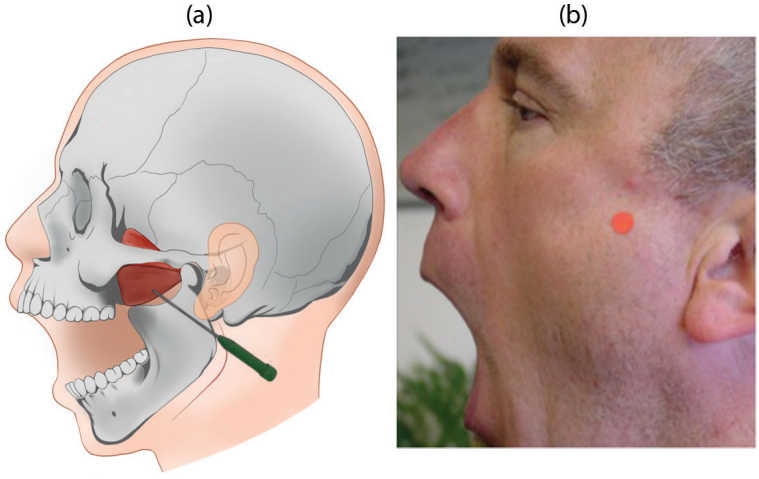

Figure 8. (a) Anatomical landmarks for extraoral injection technique to the inferior head of the lateral pterygoid muscle. (b) Extraoral puncture site for the inferior head of the lateral pterygoid muscle.

counterpart via mylohyoid raphe (where both muscles intermesh). The posterior fibers insert in the anterior surface of the hyoid bone. The mylohyoid assists mandibular opening and draws forward the hyoid bone during swallowing, thereby it also tends to push the tongue upwards (tongue protrusion). Likewise, the capacity to move the lingual floor from side to side helps mastication.

2.5.2.2.3. Geniohyoid muscle

The geniohyoid muscle is part of the oral cavity floor, primarily involved in drawing the hyoid bone forward during swallowing and assisting the opening of the mandible. It is a narrow muscle located superior to the medial border of the mylohyoid muscle. It originates from the mandibular inferior genial spine, extending backward and slightly downwards until it inserts on the anterior surface of the body of the hyoid bone.

In most occasions, the submental complex is almost fused together, making it difficult to separate one from another. These muscles can be palpated with the patient on an open mouth position. The recommended technique is performed by inserting the needle injection about 1 cm from the inferior border of the mandible, slightly lateral from the midline in both sides where the anterior digastric should be located. The anterior digastrics are easy to localize and are usually the initial muscles injected. If the clinical results are not satisfactory or the jaw-opening dystonia is severe, injections into the lateral pterygoids should be considered [19] (**Figure 9a** and **b**).

2.5.3. Jaw-deviating dystonia

The contralateral lateral pterygoid works in conjunction with the ipsilateral medial pterygoid to deviate the mouth to opposite side. The temporalis pulls the jaw to the same side. The injections follow the abovementioned techniques.

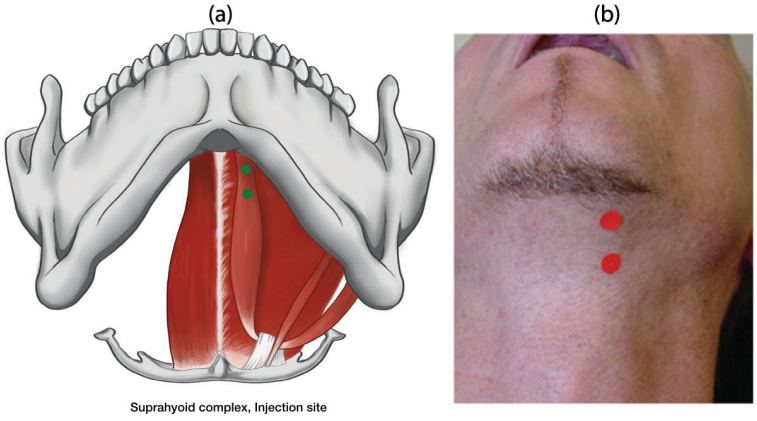

Figure 9. (a) Suprahyoid complex anatomy and injection sites. (b) Extraoral puncture site for the suprahyoid complex.

2.5.4. Perioral dystonia

The orbicularis oris is an intricated facial expression muscle that acts as an oral sphincter, consisting of numerous muscle fibers, partly from the orbicularis and partly from other facial muscles, that encircle the mouth. The angle and more lateral part of the muscle is formed by the buccinator, levator anguli oris, and the depressor anguli oris originating at the median plane of the lips (deep surface of the skin) in the maxilla and mandible. The fiber follows the trajectory of the upper and lower lips, inserting in the mucous membrane of the median lips. The orbicularis oris protrudes and purses the lips, producing grimacing of the mouth. Perioral BT application has been found beneficial in cases that produce severe social disability [68].

2.5.5. Lingual dystonia

Lingual dystonia is a rare but recognized form of OMDy, since the early descriptions made by Meige [11], only being present in about 7.6% of the OMDy cases [13]. Some authors have suggested that more severe forms may indicate the presence of heredodegenerative disease or secondary OMDy [69, 70]. However, there are also reports of severe forms of idiopathic tongue dystonia [70]. The most frequent form of lingual dystonia involves protrusive tongue movements that can be repetitive or sustained. Action-induced lingual dystonia can be triggered by regular physiologic activities such as chewing, swallowing, or speaking [11, 71–73]. Lingual dystonia can be substantially disabling and social embarrassing. Pronounced drooling is frequent in these patients. Also, patients may experience severe difficulties in feeding or wearing dental dentures if the dystonic movements tend to push food or objects out of the mouth [74]. Severe forms, only reported in secondary forms, may obstruct the upper airways and may even require intubation and respiratory support. If lingual dystonia coexists with jaw-closing dystonia, tongue biting may cause severe lingual mutilation [69]. BT injection seems to be an effective treatment approach in dystonic tongue protruding cases [74].

Since that most lingual dystonia cases are involved with tongue protrusive movements, the BT application often targets the genioglossus muscle.

Anatomically, the tongue is divided into two distinct sets of muscles: the extrinsic tongue muscles insert into the tongue from outside origins and the intrinsic tongue muscles insert into the tongue from origins within it. The extrinsic muscles move the whole tongue in different directions, whereas the intrinsic muscles allow the tongue to change its shape (such as curling the tongue in a loop or flattening it).

The genioglossus (genio = "chin") is an extrinsic tongue muscle that originates on the mandible and allows the tongue to move downward and forward. It is a fan-shaped muscle that occupies the majority of the volume tongue body. It originates from the superior genial spine to insert into the hyoid body (inferior fibers) and ventral surface of the tongue (superior fibers of the muscle were then mix with the intrinsic muscles of the tongue). When both genioglossus muscles act bilaterally, it promotes tongue protrusion and makes the lingual dorsum concave. Unilateral action produces deviation of the tongue to the contralateral side. BT application can be performed with a direct injection on the dorsal anterior surface of the tongue, starting at first 5–10 units per side to prevent dysphagia (**Figure 10**).

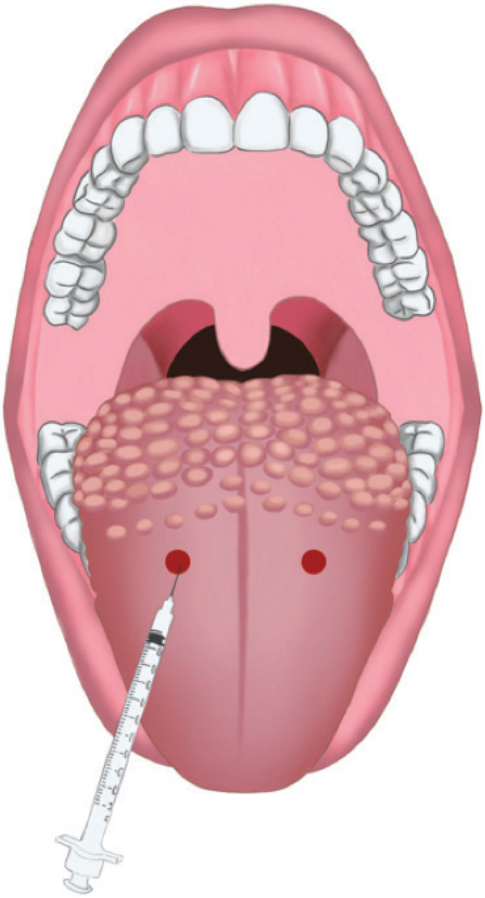

Figure 10. Genioglossus muscle injection sites.

2.6. Evaluation of treatment outcome

Response to BT application can be assessed by self-reported, observation, or a few available rating scales. The Movement Disorders Society Task Force on dystonia rating scales suggested that Oromandibular Dystonias Questionnaire (OMDQ-25) still needs further assessment to be validated and recommended [75]. However, the OMDQ-25 is clinimetrically valid, reliable, and sensitive to change in evaluating psychosocial and health-related change and improvement in OMDy [22]. Generalized dystonia rating scales, such as Burke-Fahn-Marsden Scale and the Unified Dystonia Ranking Scale, include orofacial subcomponents that can be useful in assessing the severity of the OMDy, guiding the treatment, and assessing the clinical response [29] (**Table 2**).

Type of Dystonia	Muscles Involved	Targeted Muscles	Botox®	Dysport®
			BT dose per side (Units)	
Jaw Closing Dystonia	Masseters	✔	25-50U	100-200U
	Temporalis	✔	20-40U	80-100U
	Medial Pterygoids	☑severe cases or not satisfactory results	15-50U	60-200U
Jaw Opening Dystonia				
	Submental Complex	✔	10-20U	40 - 80U
	Inf.Lateral Pterygoids	☑severe cases or not satisfactory results	15-25U	60 -100U
Jaw Deviating Dystonia	Contralateral Inf.Lateral Pterygoid	✔	15-25U	60-100U
	Ipsilateral Temporalis	✔	20-40U	80-100U
	Contralateral Medial Pterygoid	✔	15-50U	60-200U
Lingual Dystonia	Genioglossus	✔	10-50U	40-200U

Doses and muscle selection cited from [19], [29] and [76].
✔commonly injected in BT application opatative.

Table 2. Oromandibular dystonia subtypes, muscle identification and BT application.

3. Oromandibular dyskinesia and drug-induced extrapyramidal reactions

Orofacial dyskinesias are described as involuntary rhythmic, repetitive, and stereotypic movements of the face, lips, and tongue [77]. Clinical phenomenology varies in complexity and severity, ranging from almost being unnoticeable to complete social impairment (inability to eat, wear prosthetic dental devices, or perform social activities). As OMDy, oral dyskinesias can be spontaneous (primary) or secondary. Secondary dyskinesias are mostly part of drug-induced reactions or tardive syndromes but can also be secondary by subcortical infarcts, peripherally induced (related to edentulism and ill-fitting dentures), or be concomitant with neuropsychiatric conditions, dementia, or mental retardation [17, 78].

Milder forms of oral dyskinesias, featuring patterned and predictable stereotypies, are more common in spontaneous dyskinesia, dementia, neuropsychiatric conditions, and peripherally induced orofacial dyskinesias [2, 17]. Tardive orofacial dyskinesias are often more complex and severe, commonly labeled “Oro-Bucco-lingual” dyskinesias or “classic tardive dyskinesias” when the movements disorders manifest isolated [79].

3.1. Spontaneous orofacial dyskinesias

Spontaneous orofacial dyskinesia (SOD) is one of the less common forms of orofacial dyskinesias [17]. This subset is difficult to identify, mainly because of the inadvertent exposure to an offending drug is hard to discard. Hence, this term is usually coined when a detailed clinical description and characterization are lacking. SOD seems to be more prevalent in elderly, more commonly affecting females than men. Reports indicate that oral dyskinesias tend to fluctuate in time and their prevalence is highly variable [80].

Estimations on the prevalence rates vary from 1.5 to 38% among the population [81]. Reports on prevalence vary from 1.5 to 4% in healthy elderlies, 3.7% daycare centers elderlies, and 18–31.7% in elderly living at retirement homes [82–85]. The age-related factors involved in the onset of SOD are unknown and need further research.

Chronic schizophrenia patients have been reported to present more frequently SOD [86]. Descriptions of this coexistence between SOD and chronic schizophrenia patients have been made since before the introduction of antipsychotics drugs [87]. A study by Owens et al. showed that dyskinetic orofacial movements were present in chronic schizophrenia institutionalized patients with and without a history of chronic exposure to antipsychotic drugs, leading the author to suggest that the dyskinetic movements were probably related to the schizophrenia. However, some differences were observed between the two groups, showing more severe orofacial dyskinesias the group exposed to antipsychotic drugs [88]. The presence of SOD in chronic schizophrenia and other neurological disorders, such as autism, mental retardation, Alzheimer's disease, and Rett syndrome seems to be non-specific and needs further clarification [78].

3.2. Peripheral-induced dyskinesia

Peripherally oral factors have been suspected to play an important role in inducing orofacial dyskinesia. Edentulism, ill-fitting dentures, oral pain, and low perceived oral health seem to be strongly associated with oral dyskinesias [89].

Koller in a study, which compared 75 consecutive edentulous subjects to age-matched controls with teeth, found that 16% (12 individuals) of the edentulous subjects presented oral dyskinesia. Of them, nine presented mild oromandibular stereotypes and three subjects presented more marked dyskinesia, all of them displaying less complex dyskinesias compared to drug-induced dyskinesias [90].

A cross-sectional study in 1018 non-institutionalized patients found a 3.7% rate of prevalence of SOD. Interestingly, the subjects affected by oral dyskinesias reported more frequently edentulism with a high prevalence of ill-fitting dentures, oral pain, and poor buccal health perception. Furthermore, 52% of the edentulous subjects reported ill-fitting problems with their dentures in a higher proportion than the nondyskinetic controls and the tardive dyskinesia patients, leading the authors to suggest that in the absence of other putative factors, edentulism and orodental problems may trigger oral dyskinesia [89]. The nature of this association between orofacial dyskinesias and oral health factors requires further investigation and clarification and could be especially important to identify which dental factors may be amenable by good dental healthcare.

3.3. Drug-induced orofacial reactions and tardive orofacial dyskinesias

Shortly after the introduction of conventional neuroleptics, Frank Ayd in 1961, published a list of medications associated with various movement disorders, which he named drug-induced extrapyramidal reactions [91]. Since then, various reports associated with the use of medications and drugs were described and probably remain an important source of adult and pediatric movement disorders [92–95].

The terminology "Extrapyramidal Syndrome Reactions (ESR)" is commonly used in psychiatry to refer drug-induced dystonia, akathisia, and parkinsonism [96]. However, phenomenologically the term ERS lacks clarity, and clinically, the spectrum of persistent hyperkinetic and hypokinetic motor abnormalities is more precisely fitted into three distinct categories regarding their temporal profiles: acute and subacute drug-induced movement disorders and tardive syndromes. Acute drug-induced movement disorders often occurs within hours or days after the offending drug exposure; in subacute drug-induced movement disorders, the onset of the abnormal movements builds up slowly, after days or weeks of exposure [97]. Finally, tardive syndromes are due to the chronic exposure, almost never before than 3 months or 1 month in patients older than 60 years old, primarily after the exposure to dopamine receptor blocking agents (DRBA) [98].

3.3.1. Acute orofacial drug-induced movement disorders

Acute orofacial drug-induced movement disorders are primarily related to acute dystonic reactions, seen after the consumption of neuroleptics, emetics and gastrointestinal promotility agents, antidepressants, amphetamines, antiepileptics, and recreational drugs, among many others [99–101].

Typically, acute dystonic orofacial reactions start after a few days the offending drug is introduced, with 50% of the cases occurring during the first 24 hours and 90% of the cases within the first 5 days [99]. Motor symptoms are usually restricted to the head and neck, particularly as OMDy and complex cervical dystonias. Prevalence ranges from 2.3 to 60% and 2 to 3% in patients treated with typical DRBA and atypical DRBA, respectively [102].

Management consists in the suspension of the implicated drug, whenever is possible. Intramuscular or intravenous anticholinergic drugs are the most effective agents in treating acute dystonic reactions until the offending drug wears off. Benzodiazepines may be helpful but are not as effective as anticholinergics [99].

3.3.2. Tardive syndromes and tardive orofacial dyskinesias

The term "tardive syndromes" refer to a group of iatrogenic delayed onset of drug-induced persistent movement disorders [103]. Two essential aspects must be present to configure a tardive syndromes diagnosis. The first aspect is that continuous exposure to the offending drug must be present, more frequently seen in prolonged treatments with DRBA. If there is no medical history of prolonged exposure, another diagnostic should be considered. The second essential aspect is that regardless of the duration of the exposure, the abnormal movements will persist, continue, and often worsen after the offending drug is withdrawn [96].

In some patients, dyskinetic movements may appear immediately after the discontinuation, change, or reduction in dosage of neuroleptic medications, in which case the condition is called neuroleptic withdrawal-emergent dyskinesia. Because withdrawal emergent dyskinesia is usually time-limited, lasting less than 4–8 weeks, dyskinetic movements that persists beyond this window are considered as tardive dyskinesia [104].

Since the introduction of neuroleptics (DRBA), numerous reports emerged describing delayed orofacial involuntary stereotypies. Faurbye in 1964 initially coined the term "tardive dyskinesia" to describe late onset rhythmic, repetitive, persistent orofacial movements after long exposure to antipsychotic drugs [105, 106]. Other drugs distinct than DRBA have been related to tardive syndromes such as anti-emetics, tricyclic antidepressants, calcium channel blockers, norepinephrine selective reuptake inhibitors, and serotonin selective reuptake inhibitors can cause abnormal movements clinically indistinguishable from the DRBA-induced dyskinesias [107] (**Table 3**).

Typical antipsychotics
Chlorpromazine
Chlorprothixene
Droperidol
Flupentixol
Fluphenazine
Haloperidol
Levomepromazine
Loxapine
Mesoridazine
Molindone
Perazine
Perphenazine
Pimozide
Prochlorperazine
Thiothixene
Trifluprom azine
Zuclopenthixol
Atypical antipsychotics
Amisulpride
Aripiprazole
Asenapine
Clozapine
Iloperidone

Levosulpiride
Olanzapine
Paliperidone
Quetiapine
Remoxipride
Risperidone
Sulpiride
Ziprasidone
Antiemetics
Cisapride
Clebopride
Metoclopramide
Calcium channel blockers
Cinnarizine
Flunarizine
Serotonin/norepinephrine reuptake inhibitors
Duloxetine
Citalopram
Sertraline
Paroxetine
Fluoxetine
Tricyclic antidepressants
Amoxapine
Others
Lithium

Cited from: [78, 98, 107].

Table 3. Medications with the potential to cause orofacial tardive dyskinesia and drug-induced reactions (listed alphabetically).

In literature, this term is often used to define various types of hyperkinetic tardive manifestations. However, because many patients may present a combination of tardive abnormal movements, it is more appropriate to use the term "tardive syndromes" to classify all the different tardive phenomenologies including classic tardive dyskinesia, tardive stereotypy, tardive dystonia, tardive akathisia, tardive tremor, tardive parkinsonism, and tardive gait, among others [98].

Of the aforementioned tardive syndromes, the more prevalent presentations are classical tardive dyskinesia 30%, tardive akathisia 20%, and tardive dystonia 5–15% of the cases. Tics, myoclonus, tremors, pain, and other tardive syndromes are far less frequent [79].

A study by Orti-Pareja et al. described the frequencies of the different types of phenomenologies in a population of 100 patients diagnosed with tardive syndromes. The authors found that 72% of the patients presented oro-bucco-lingual dyskinesias, 30% tardive tremor, 22% tardive akathisia, and 16% tardive dystonia. In this study, 35% of the patients presented a combination of two or more tardive syndromes [108].

The presumed pathophysiology is thought to be related to chronic blockage of D2 and D3 dopamine receptors. Typical antipsychotics are more tightly bind and for more time to dopamine receptors than "atypical" antipsychotics, being more prone to produce tardive dyskinesia [109]. Other prominent mechanisms may be the facilitation of dopaminergic neurotransmission, postsynaptic supersensitivity, maladaptive neuroplasticity, increased neurodegeneration (neuronal loss, gliosis in the basal ganglia), and genetic susceptibility [110–112].

3.3.3. Tardive orofacial dyskinesias

Classical tardive dyskinesias or "tardive orofacial dyskinesias" are characterized by having an insidious onset of the symptoms, predominantly manifesting as relatively rhythmic, repetitive, and stereotypic movements of the face, mouth, tongue, and chewing movements (oro-bucco-lingual) [96].

Tardive dyskinesias tend to evolve into a full syndrome over days or weeks, persisting years or even decades after the offending drug is discontinued [107].

The clinical features often involve repetitive jaw movements, tongue protrusion, puffing of cheeks, lip smacking, lip puckering, or lip pursing affecting speech, swallowing, chewing, and occasionally producing tongue injuries. The onset of vertical, rhythmic perioral movements of the jaw with frequencies of 2.5–5.5 Hz (rabbit syndrome) or jaw tremor have also been described in chronic exposure to neuroleptics [77]. The abnormal oro-buccal-lingual movements can also extend to other body parts, including the trunk or the extremities [98].

With typical antipsychotics, the estimated prevalence is between 20 and 50% [113]. The estimated incidence is about 5% in younger individuals but tends to increase in middle age individuals and elderlies, particularly in women, probably due to the cumulative exposure to DRBA [107].

Tardive orofacial dyskinesia is potentially reversible in a subset of patients. However, remission rates after the discontinuation of the offending drug is relatively low, about 13% of the patients experienced complete resolution after 3 years and only 2% without having to include other pharmacological agents [114].

Treatment recommendations focus on patient selection (paramount for preventing tardive dyskinesias), use alternative medications whenever is possible, and making emphasis on avoiding long DRBA treatments. Slowly tapering of the offending drug is recommended mostly because sudden withdrawn can trigger withdrawn emergent dyskinesia [98, 107]. Evidence supports the idea that as sooner the causative drug is retrieved, the more likely is that tardive dyskinesia will

resolve [111]. Patients requiring antipsychotic drugs switching to atypical neuroleptics may still have risk of developing tardive dyskinesia [115]. About 60% of the patients will benefit with the reintroduction of the drug, but only for a low period of time [24].

Dopamine-depleting agents like tetrabenazine can be used in severe cases with moderate to good results. Other agents such as amantadine, clonazepam (only for short periods of time), vitamins, and antioxidants may help lessen tardive orofacial dyskinesia, but the evidence available is still inconclusive. Botulinum toxin injections have shown efficacy in reducing tardive dyskinesia in several clinical reports and small studies [98, 107].

4. Sleep and awake bruxism

4.1. Definition

Bruxism comes from the Greek term brukhein "to gnash the teeth" [116]. Research on sleep medicine, the pathophysiology of sleep and awake bruxism, and related comorbidities has changed old dental mechanistic beliefs based on dental occlusion to a more medical concept, hardly influenced by peripheral factors [117–119].

Bruxism is a trigeminal motor activity characterized by a repetitive and episodic muscle contractions producing grinding or clenching of the teeth, or bracing or thrusting of the mandible. By consensus, it can be categorized into two different circadian manifestations, occurring during sleep (Sleep Bruxism) or wakefulness (Awake Bruxism), being tooth grinding dominant during sleep and clenching activities more prevalent during wakefulness [120–122]. Evidence suggests that sleep bruxism and awake bruxism are probably not part of the same nosologic entity, each having some substantial similarities but probably having different etiologies and pathophysiology [123]. Sleep bruxism is considered a sleep-related movement disorder, and it is hardly controllable during sleep [124]; meanwhile, awake bruxism is an unaware stereotypic mandibular activity during wakefulness, when cognizant can be voluntarily controlled and terminated [116].

4.2. Diagnosis

During sleep, bruxism can be registered by quantifying the episodes of rhythmic activity of the masticatory muscles (also known as rhythmic masticatory muscle activity or RMMA) [125]. The RMMA corresponds to a rise in the electromyographic activity of the electrodes placed in the masticatory muscles and the chin, and it is produced by muscle contractions with a frequency of 1 Hz, helping distinguish it from other oromandibular movements or disorders during sleep (e.g., mandibular myoclonus, nocturnal vocalization, snoring, or swallowing) [126]. RMMA can take three forms of bursting patterns: (1) isolated muscle contraction lasting >2 s called "tonic"; (2) more than three bursts lasting 0.25–2.0 each, called "phasic"; and (3) the mixture between tonic and phasic bursts. It is important to note that RMMA may present with little or no tooth grinding at all [127].

A panel of international experts defined a diagnostic criterion, grading sleep bruxism into three diagnostic levels: The first criteria consists only in the anamnestic report, the second criteria adds to the anamnetic report a clinical assessment, and the third and definitive diagnostic level is based on a polysomnographic study [120, 124]. From the anamnestic standpoint, the presence of recent self-reported tooth grinding sounds during sleep is necessary, noted also or confirmed by a parent or a sleep partner. The second diagnostic level includes the anamnestic report plus clinical signs of abnormal tooth wear, the presence of jaw muscle fatigue or pain, temporal headache, or jaw locking upon wakefulness. Not better explained by other sleep disorders, medical or neurologic disease, medication use, or drug abuse [120].

Regardless that these two first diagnostic levels are widely accepted, evidence shows that report-based diagnosis in bruxism are subjective, possibly bias, lacks of acceptable specificity and sensitivity and needs further validation [125]. Then, some considerations should be taken into account before making an anamnesis-based or clinical diagnosis. First and foremost, studies have shown almost 50% discordance between PSG recording and self-reports, showing that self-report studies tend to overestimate bruxism [128, 129]. Also, it should be considered that tooth grinding tends to fluctuate with time and decline with age [130, 131]. Recent data shows that the assessment of sleep bruxism using subjective methods alone tends to overestimate the prevalence in 12.5% compared to PSG recordings [129, 132]. Moreover, a recent study aiming to assess the sensibility, specificity, and positive and negative predictive value among the different clinical diagnostics compared to PSG recordings found that the more sensitive clinical criteria corresponded to jaw fatigue upon awakening followed by a temporal headache. The most specific diagnostic criteria were jaw locking and muscle pain [133].

Awake bruxism is usually more difficult to diagnose, mostly because diagnosis relies on self-awareness of individual [134]. However, there is increasing evidence suggesting that once a person is made aware of their awake bruxism habits, he or she is more likely to give accurate feedback [135, 136].

4.3. Epidemiology

The prevalence of sleep bruxism is estimated mainly based on reports, being it highest during childhood approximately 14–20%, consolidating around 8–12% during adolescence and adulthood, and decreasing over 50 years to 3–5%. Several studies have found that when SB is present during childhood, it may persist into adulthood. However, as previously mentioned, most subjects show fluctuations and alternating periods of SB during the lifespan. Awake bruxism has been reported to have an estimated prevalence of 22.1–31% among the adult population [130, 131, 137].

4.4. Sleep and awake bruxism pathophysiology

Current understanding of the etiology and pathophysiology of SB is not based on a single factor explanatory model [138]. Instead, much of the pathological mechanisms are unknown or not well understand and are subject to interindividual variability [139].

Sleep bruxism starts with a cascade of physiological events that are temporally related to the onset of the RMMA episode [139]. Four to eight minutes before the onset, a cardiac sympathetic activity dominance can be observed [140, 141]. The cardiac autonomic activity is followed by an increase of electroencephalographic activity dominated by rapid frequency brain activity, i.e. arousal, in 50–80% of the episodes [142, 143]. Then, a rise in heart rate, fluctuations in respiratory breaths and oxygen saturation, a rise in the systolic and diastolic pressure, and an increase of suprahyoid muscles tone usually precede the onset of the RMMA [144–146]. This sequence of event is not always constant to all RMMA but highlights that sleep bruxism involves a complex interaction between the sympathetic system, cortical arousability, and respiratory functions. Posterior to the RMMA onset and the tooth grinding, most of the episodes are followed by swallowing (~60%) [147]. Sporadic RMMA is not infrequent in general population. However, individuals presenting sleep bruxism have more RMMA with more intense bursting patterns, manifesting primarily in pre-REM sleep during transitions between NREM1 and NREM2 stages [126, 138]. Sleep bruxism-induced muscle activity during REM sleep is less concurrent accounting for less than 10% of the RMMA episodes during sleep [125]. Individuals with sleep bruxism do not present alterations in their sleep architecture unless they present a comorbidities [129] (**Figure 11**).

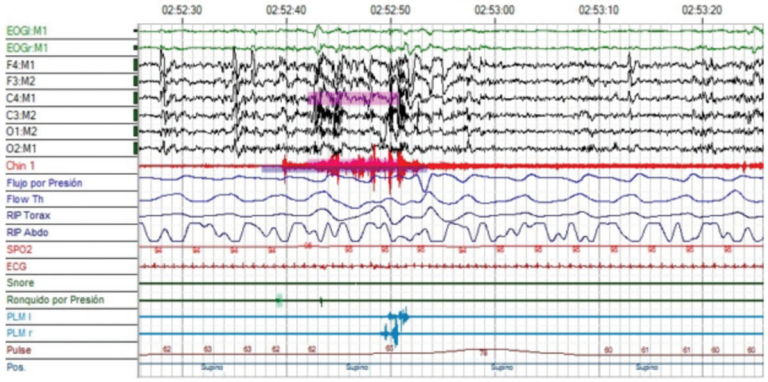

Figure 11. Sleep bruxism episode in a polysomnography study. Courtesy of Somno Clinic, Chile. www.somno.cl.

4.5. Sleep bruxism etiology

Multifactorial etiology of SB includes individual factors such as personality traits, environmental factors, genetics, circadian and ultradian rhythms, coping skills (anxiety/stress), neurotransmitters (more probably serotoninergic-related pathways), anatomic characteristics, sleep arousability, airway patency, and sleep disturbances among other factors.

Stress, anxiety, and maladaptive coping skills have been related to sleep and awake bruxism. Individuals with sleep bruxism usually are more stressed and exhibit more goal-oriented personalities and higher anxiety levels [148–151]. In children and adolescents, psychological factors have been found to be a putative risk for bruxism [152]. Personality traits and behaviors

like bullying, aggressiveness, neuroticism, increased sense of responsibility, tense personality traits, and antisocial conduct are associated with sleep bruxism [153–155].

Genetic predisposition is also postulated as an important etiologic factor, accounting for 48–52% of sleep bruxism phenotypic variance [156]. Heritability strongly correlates with sleep bruxism having a relative risk of 4.6 [157–159]. Single nucleotide polymorphisms of serotoninergic and dopaminergic neurotransmission have emerged as potential candidates showing strong association with an increased risk of sleep bruxism [160, 161]. These associations have not been found in awake bruxism which further support the idea that sleep and awake bruxism are two different nosologic manifestations [161].

Caffeine intake in high quantity is linked with an increased risk of sleep bruxisms in 1.5 times [162] through mechanisms currently unknown [163]. Heavy drinking and frequent alcohol intake during the day have also been associated with sleep bruxism. It is thought that fragmentation of sleep architecture and accumulation of neurotransmitters related to dopaminergic and serotoninergic pathways may be associated with the exacerbation of sleep bruxism [162, 163]. Similarly, tobacco consumption increases the risk of having sleep bruxism two times [162]. As well, several drugs and medications have shown activity in exacerbating sleep bruxism such as levodopa, selective serotonin reuptake inhibitors, tricyclic antidepressants, amphetamines, and MMDA, among others [127, 164, 165].

Airway patency studies have shown a positive association between sleep bruxism and sleep breathing disorders [166, 167]. In fact, about 50% of adults and children with obstructive sleep apnea present concomitant sleep bruxism [168–170]. Furthermore, self-reports studies in sleep apnea patients increase the risk of having bruxism, probably mediated by the occurrence of sleep arousals during respiratory events [171]. It has been hypothesized that the relation of sleep bruxism concomitant or posterior to hypopnea or apnea episodes may have a role in reinstating airway permeability during the events, suggesting a causative link [172]. However, there is not enough evidence to support this claim [173].

Nocturnal gastroesophageal reflux is another factor associated with sleep bruxism. Higher frequencies of SB episodes were associated with having more time of esophageal pH below 5.0 [174]. Miyawaki et al. showed a concomitance of RMMA events and gastroesophageal reflux episodes, more particularly when episodes had a pH lower than 3.0–4.0 [174]. Also finding the sleep position during sleep was influential in reducing RMMA and episodes of gastroesophageal reflux alike [175]. Moreover, clinical trials measuring the effect of proton pump inhibitors (PPI) in patients with comorbidity of sleep bruxism and gastroesophageal reflux have shown that the consumption of PPI reduces RMMA episodes of sand grinding noises significantly [176].

4.6. Management

In the absence of treatable comorbidities, treatment of sleep bruxism is not plausible. Instead, management should be focused on preventing tooth destruction and grinding and alleviating temporomandibular pain or concomitant headaches [125, 177]. Oral appliances tend to reduce

sleep bruxism episodes only in short-term, returning to the baseline activity within 7–10 days [178]. A recent systematic review showed the effectiveness of almost every type of oral appliances, providing a higher decrease of sleep bruxism episodes those that produce a certain extent of mandibular advancement (mandibular advancement devices) [178, 179].

In the presence of concomitant sleep breathing disorders, the first step should be taken towards managing sleep breathing disorders depending on the severity. In these cases, a mandibular advancement device or the use of CPAP should be preferred over upper maxillary appliances, mostly because evidence suggests that they may produce aggravation of hypopnea and apnea episodes [180, 181].

Pharmacotherapy for management sleep bruxism is mainly based on the use of off-label medication; only a few medications have shown some degree of effectiveness in reducing sleep bruxism. Clonazepam and clonidine have proven to reduce bruxism with respect to placebo [179]. A single-blinded, randomized controlled trial suggested that the use of gabapentin may be effective for the management of sleep bruxism especially in those patients with poor quality of sleep, but these preliminary results still need further corroboration with better designed clinical trials and more number of participants [182].

Botulinum toxin effects are in line with the expected pharmacologic effects; they are superior to placebo [183]. However, studies have shown that the use of botulinum toxin reduces the intensity of the RMMA bursts but not the frequency, which further confirms the central genesis of sleep bruxism episodes [184].

Regarding awake bruxism, EMG-based biofeedback programs seem to reduce tonic episodes of awake and sleep bruxism alike [185, 186].

A pilot study using mindfulness-based stress reduction programs has also shown efficacy in the management of awake bruxism (Unpublished data from Skarmeta et al.).

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