Four Oral Motor Disorders: Bruxism, Dystonia, Dyskinesia and Drug-Induced Dystonic Extrapyramidal Reactions

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Four oral movement disorders

The literature is replete with articles that discuss motor disorders, such as Parkinson's disease, Bell's palsy, essential tremor, poststroke paralysis, dystonia, and dyskinesia. The focus of this article is on those motor disorders that are known to affect the masticatory system and its adjacent muscles. The term ''orofacial motor disorder'' (OMD) encompasses a spectrum of movement aberrations, both hyperactive and hypoactive, which involves the muscles of the orofacial complex and are innervated by cranial nerves V, VII, and XII. OMDs generally present as localized problems that affect only the masticatory system, but they are driven by alterations in central nervous system (CNS) functioning. Dentists must be able to recognize and become involved with management of these problems, because such behaviors cause pain and dysfunction of the jaw and interfere with needed dental care on patients [1–3].

The most common OMDs are sleep bruxism and sustained habitual forceful clenching (day or night). In addition to bruxism, this article reviews three other vexing oral motor disorders: focal orofacial dystonia, oromandibular dyskinesia, and medication-induced extrapyramidal syndrome (EPS)–dystonic reactions. Table 1 provides a brief definition, the main clinical features, and management approaches that are used for these four OMDs. When severe, these motor disorders may cause strong headaches,

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Table 1
Oral motor disorders: dystonia, dyskinesia, bruxism and dystonic extrapyramidal reactions

Oral motor disorders	Definition	Clinical features	Management
Bruxism (ICD-9 #306.8)	Sleep bruxism can be defined as nonfunctional jaw movement that includes clenching, grinding, clicking, and gnashing of teeth during sleep.	Dental attrition Tooth pain TMJ dysfunction Headaches	Pharmacologic treatment data not convincing. Most cases treated with an occlusal appliance, severe cases treated with botulinum toxin injections.
Oromandibular dystonia (ICD-9 #333.6)	Involuntary, repetitive, sustained muscle contraction that results in an abnormal posturing of a structure. Depending on the muscle involved, it may produce a twisting motion of involved structure.	Involuntary jaw opening. Lateral movements of the jaw. Protrusion of the tongue. Present during the day. Disappears during deep sleep. Dystonic spasms increase in intensity during stress, emotional upset, or fatigue.	Pharmacologic treatment. Chemodenervation with botulinum toxin injections. Select use of neurosurgical treatment.
Orofacial dyskinesia (ICD9 #333.82)	The presence of excessive, repetitive, stereotypic oral movements.	Facial grimacing. Repetitive tongue protrusion. Puckering, smacking and licking of the lips. Side-to-side motion of the jaw.	Withdrawal of neuroleptic medications or other offending agent. Pharmacologic treatment.
Drug induced dystonic-type extrapyramidal reactions (ICD-9 #333.9)	Medications and illegal drugs produce a motor response that is classified better as an unspecified extrapyramidal syndrome reaction.	3 presentations: Dystonia Akathisia Parkinsonism	Withdraw offending drug. Pharmacologic trials.

damage the temporomandibular joint (TMJ), or create such motor control difficulty that patients are unable to eat and may start to lose weight. These motor disorders can affect the tongue musculature to such a degree that it compromises the patient's ability to speak clearly. The social embarrassment that patients must endure affects their daily living; many patients refuse or strongly avoid leaving their homes. Fortunately, there are various

medications, including botulinum toxin injections, and surgical interventions that reduce the severity of the OMDs.

Bruxism

The prevalence of chronic bruxism is unknown, because no large, probability-based, random sample study has been performed using polysomnography (which is needed to measure bruxism). Based on a combination of attrition assessment and reports by parents, spouses, or roommates, it is estimated that 5% to 21% of the population has substantial sleep bruxism [4,5]. Many bruxers do not have substantial attrition and many do not make tooth-grinding sounds during sleep, so sleep partner or parental reports are not always accurate. The pathophysiology of bruxism is unknown. The most cogent theory describes bruxism as a neuromotor dysregulation disorder. This theory proposes that bruxism occurs because of the failure to inhibit jaw motor activity during a sleep state arousal. There are numerous clear-cut neuromotor diseases that exhibit bruxism as a feature of the disease (eg, cerebral palsy). The disorder of periodic limb movements is similar to an OMD, except that it occurs in the leg muscles [6]. There are many articles that describe the clinical presentation and consequences of bruxism; most agree that the single most effective way to protect the teeth from progressive attrition, fracture, or clenching-induced pulpitis is to fabricate an occlusal appliance and have the patient use it at night [7]. The problem with an occlusal-covering appliance is that it does little or nothing to stop the bruxism in the long term. Most alter the behavior for a few weeks when first used, but this only offers a brief respite from some headaches and bruxism-induced TMJ derangement or arthritis problems. In cases in which the disorder is severe and the damaging consequences are well beyond the teeth, one option is to inject the masseter or temporalis about every 3 to 6 months to minimize the power of the bruxism activity. The literature supports this concept; one of the first reports was by Van Zandijcke and Marchau [8] in 1990 who provided a brief note on the treatment of a brain-injured patient who exhibited severe bruxism with botulinum toxin type-A injections (100 U total into the masseter and temporalis). Seven years later, Ivanhoe and colleagues [9] described the successful treatment of a brain-injured patient who had severe bruxism with botulinum toxin type-A. In this case, the patient was injected with a total of 50 U to each of four muscles (right and left masseter and temporalis) for a total of 200 U. Of course, the successful treatment of a single case of brain injury–induced bruxism does not make a compelling story for its routine use in managing bruxism. The story was extended by a more recent report [10]. The investigators reported on the long-term treatment of 18 cases of severe bruxism with botulinum toxin type-A. These patients all had severe bruxism, which had been causing symptoms for an average of 14.8 ± 10.0 years and all had no success with previous medical or dental

treatment. Similar to previous reports, the masseter muscle was injected with a mean dose of 61.7 ± 11.1 U per side. The efficacy of these injections was rated by the subjects as a 3.4 on a scale from 0 to 4 (with 4 being equal to total cessation of the behavior). The investigators described one subject who experienced dysphagia as a side effect of the injections. Finally, another investigator described a young child (age 7) who had severe brain injury–induced bruxism that was treated successfully with botulinum toxin [11]. The primary management method for strong bruxism and clenching is still a full-arch occlusal appliance, which does not stop the behavior but limits its dental damage [12]. Fortunately, the most severe cases of bruxism and clenching now have several motor suppressive medications; in extreme cases, botulinum toxin injections can be added to occlusal appliance treatment.

Oromandibular dystonia

Oromandibular dystonia is one form of a focal dystonia that affects the orofacial region and involves the jaw openers (lateral pterygoids and anterior digastrics), tongue muscles, facial muscles (especially orbicularis oris and buccinator), and platysma. When this occurs in association with blethrospasm (focal dystonia of the orbiculares oculi muscles), it is called Meige's syndrome [13]. Dystonia is considered present when repeated, often asynchronous spasms of muscles are present. Most dystonias are idiopathic and the focal form of dystonia occurs 10 times more often than does the generalized systemic form [14]. The prevalence of all forms of idiopathic dystonia ranges between 3 and 30 per 100,000 [15]. Focal dystonias can be primary or secondary; the secondary form of dystonias occurs as a result of a trauma (peripheral or central), brainstem lesion, systemic disease (eg, multiple sclerosis, Parkinson's disease), vascular disease (eg, basal ganglia infarct), or drug use [16]. Most dystonias are primary or "idiopathic" and demonstrate no specific CNS disease. Of course, various pathophysiologic mechanisms have been proposed to explain dystonia (eg, basal ganglia dysfunction, hyperexcitability of interneurons involved in motor signaling [15], reduced inhibition of spinal cord and brainstem signals coming from supraspinal input and dysfunction of neurochemical systems involving dopamine, serotonin, and noradrenaline [14]). All dystonias are involuntary but tend to be more intermittent than dyskinesias (see later discussion) and are compromised of short, but sustained, muscle contractions that produce twisting and repetitive movements or abnormal postures [17,18].

One interesting aspect of the involuntary motor disorders is that patients can control or suppress the movement partially with the use of tactile stimulation (eg, touching the chin in the case of orofacial dystonia or holding an object in their mouth). This suppressive effect has been called "geste antagonistique" [19]. These tactile maneuvers may lead physicians to the erroneous diagnosis of malingering or hysteria. Other examples of sensory tricks include placing a hand on the side of the face, the chin, or the back of the

head, or touching these areas with one or more fingers, which, at times, will reduce the neck contractions that are associated with cervical dystonia. With some dystonias, patients have discovered that placing an object in the mouth (eg, toothpick, piece of gum) may reduce dystonic behaviors of the jaw, mouth, and lower face (oromandibular dystonia). Finally, most of the focal and segmental dystonias only occur during waking periods and disappear entirely during sleep.

For treatment, there are several medications that can be used to suppress hyperkinetic muscles (see later discussion). After medications, the other primary method for treating dystonia is chemodenervation using botulinum toxin. In 1989, Blitzer and colleagues [20] first described the injection of botulinum toxin for oromandibular dystonia. They described injecting many of the orofacial muscles in oromandibular dystonia and claimed that masseter and temporalis injections helped with suppressing the overall oromandibular dystonia. These early reports did not specifically look at tongue movement changes nor were tongue botulinum toxin injection performed. In 1991, Blitzer and colleagues [21] described the first use of botulinum toxin in patients who had lingual dystonia, but cautioned clinicians that dysphagia was a problem in some of their cases; unfortunately, doses and injections sites were not described carefully. In 1997, Charles and colleagues [22] reported on nine patients who had repetitive tongue protrusion that resulted from oromandibular dystonia or Meige's syndrome. They were treated with botulinum toxin injections into the genioglossus muscle at four sites by way of a submandibular approach. Six of these patients were helped, and the average dose injected was 34 U, which produced a 3- to 4-month effect. Clearly, there is a need to explore when, where, and to what degree botulinum toxin may become useful in the management of the patient who has galloping tongue or tongue-based severe dyskinesia. There are many variations of oromandibular dystonia, but one common one is involuntary jaw-opening dystonia. One complication of jaw-opening dystonia is that the TMJ can become locked physically in the wide-open position, so that even after the dystonic contraction stops, the jaw will not close easily. In 1997, Moore and Wood [23] described the treatment of recurrent, involuntary TMJ dislocation using botulinum toxin A. The injected target was the lateral pterygoid muscle, and they injected each lateral pterygoid using electromyographic guidance. The investigators described that the effect lasted for 10 months. The lateral pterygoid is the muscle that is most responsible for opening; it is a difficult injection, which has a high potential for misplacement of the solution into other adjacent muscles.

Dyskinesia

Risk factors for the development of tardive dyskinesia are older age, female sex, and the presence of affective disorders [24]. For spontaneous dyskinesias, the prevalence rate is 1.5% to 38% in elderly individuals,

depending on age and definition. Elderly women are twice as likely to develop the disorder [25]. When this disorder is associated with a drug use, the medications that are implicated most commonly are the neuroleptic medications that are now in widespread use as a component of behavioral therapy. The prevalence of drug-induced dyskinesia (tardive form) is approximately 15% to 30% in patients who receive long-term treatment with neuroleptic medications [26]. These medications chronically block dopamine receptors in the basal ganglia. The result would be a chemically-induced denervation supersensitivity of the dopamine receptors which leads to excessive movement; however, other neurotransmitter abnormalities in γ-aminobutyric acid (GABA)ergic and cholinergic pathways have been suggested. There are isolated reports in the literature that implicate dental treatment as a factor in the onset of spontaneous orofacial dyskinesia. Orofacial dyskinesia occurs as involuntary, repetitive, stereotypical movement of the lips, tongue, and sometimes the jaw during the day [27,28]. Sometimes the dyskinesia is induced by medication (tardive) or it can occur spontaneously. The spontaneous form of dyskinesia often affects the elderly. Typically, the tardive form of dyskinesia occurs in mentally ill patients who have a long-term exposure to medications that are used to treat the mental illness [29]. By definition, tardive dyskinesia requires at least 3 months of total cumulative drug exposure, which can be continuous or discontinuous. Moreover, the dyskinesia must persist more than 3 months after cessation of the medications in question. Most dopamine receptor antagonists cause oral tardive dyskinesia to one degree or another. The typical antipsychotics—and in recent years, even the atypical antipsychotics—including clozapine, olanzapine, and risperidone were reported to cause tardive dystonia and tardive dyskinesia. No adequate epidemiologic data exist regarding whether any particular psychiatric diagnosis constitutes a risk factor for the development of tardive reactions to medications; however, the duration of exposure to antipsychotics that is required to cause tardive reaction is from months to years. Exposure to antipsychotics need not be long, and a minimum safe period is not apparent. This duration of neuroleptic exposure seems to be shorter for women. A longer duration of exposure to neuroleptics does not correlate with the severity of the reaction. Treatment of orofacial dyskinesia is largely with medications (see later discussion).

Drug-induced dystonic-type extrapyramidal reactions

There are patients who have developed a medication-induced oral motor hyperactivity that does not fit into the dyskinesia category [30]. These medications and illegal drugs produce a motor response that is classified better as an unspecified extrapyramidal syndrome (EPS) reaction. EPS responses typically have three presentations: dystonia, akathisia, and parkinsonism. Dystonic reactions consist of involuntary, tonic contractions of skeletal muscles [31–33]. Akathisia reactions occur as a subjective experience of

motor restlessness [34,35]. Patients may complain of an inability to sit or stand still, or a compulsion to pace or cross and uncross their legs. Parkinsonian reactions manifest themselves as tremor, rigidity, and akinesia, which shows as a slowness in initiating motor tasks and fatigue when performing activities that require repetitive movements (bradykinesia). When a medication or drug induces a dystonic EPS reaction, it typically involves the muscles of the head, face, and jaw that produce spasm, grimacing, tics, or trismus. Most of the literature has focused on the more severe acute dystonic EPS reactions that occur with use of antipsychotic medications. In addition to the antipsychotics, several antiemetics with dopamine receptor–blocking properties have been associated with tardive dystonia. These include prochlorperazine, promethazine, and metoclopramide. Of course, other less severe reactions do occur that vary in intensity and even wax and wane over time. The most commonly reported offending agents that are not neuroleptics are the selective serotonin reuptake inhibitors (SSRIs) and the stimulant medications and illegal drugs.

Serotonergic agents that cause extrapyramidal reactions

SSRIs (eg, fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, escitalopram) are used for depression and a variety of other mental illnesses. Unfortunately, these drugs are reported to produce the side effect of increased clenching and bruxism [36–39]. Actually the term ''SSRI-induced bruxism'' may not be accurate in that the actual motor behavior does not present as brief, strong, sleep state–related contractions as seen in bruxism, but more of an increased sustained nonspecific activation of the jaw and tongue musculature. Patients generally describe an elevated headache and tightness in their jaw, tongue, and facial structures. The best information available about the effect of SSRI class medications on oromandibular structures comes from a study in 1999, which examined the acute effects of paroxetine on genioglossus activity in obstructive sleep apnea [40]. It found that paroxetine, 40 mg, produced a clear augmentation of peak inspiratory genioglossus activity during non-rapid eye movement (NREM) sleep. Of course, the recent widespread use of SSRIs is based on a perception that these drugs have a lower side effect profile than do other categories of antidepressant medications (eg, tricyclics and monoamine oxidase inhibitors). Unfortunately, only case-based literature exists at this time; further polysomnographic studies on the motor effects of SSRIs are necessary to define prevalence and risk factors and to establish a causal relationship between SSRI use and oral motor disorders.

Stimulant drugs and other medications that cause extrapyramidal reactions

Illegal drugs, such as methamphetamine cocaine and 3,4-methylenedioxymethamphetamine (Ecstasy), and legal prescription stimulants, such as methylphenidate, phentermine, pemoline, dextroamphetamine, amphetamines,

and diethylproprion, have been reported to induce bruxism and dystonic extrapyramidal reactions [41–45]. All stimulant drugs have the potential to cause extrapyramidal reactions and they are being used in greater numbers to treat obesity or as stimulants for children who have attention deficit hyperactivity disorder or narcolepsy and even for severe depression [46].

Differential diagnosis of orofacial motor disorder

The most important aspect of any clinician's skill is the ability to provide a differential diagnosis. With the exception of bruxism, all of the other motor disorders require a neurologic consultation to achieve a definitive diagnosis. This includes Bell's palsy, essential tremor, the focal and multifocal dystonias, the dyskinesias, the motor and vocal tics, and hemifacial spasm. Although the dentist will not be doing this examination, it is necessary to identify whether a patient has had a correct assessment before participating in the management of the patient. A proper initial diagnostic work-up for a movement disorder involves a full clinical examination, including a thorough neurologic examination. This is necessary to rule out the possibility that the motor dysfunction may be due to a central degenerative, demyelinating, or sclerotic lesion of the nervous system. Depending on the exact nature of the motor disorder, the examining physician may add a thorough medication and illegal drug history to the work-up. Standard, enhanced, and angiographic-type MRI will be taken of the brain and spinal cord to rule in or out a neurologic infarct or tumor or compression of these tissue; an electromyographic assessment may be ordered to identify specifically which muscles are involved and to assess the patient for a motor nerve or sensory nerve conduction deficit or a peripheral-origin myopathic disease or motor neuron abnormality; and for the most severe forms of bruxism and some myoclonic-type bruxism problems, it will be necessary to conduct a nocturnal polysomnogram, which includes an electroencephalogram. For the dystonias that affect a specific motor system (eg, blepharospasm or torticollis), it is necessary to assess that system thoroughly to ensure that no local infection or neoplastic or arthritic disease is present, to name only a few of the considerations. For disorders that involve the masticatory muscles, the tongue, or the perioral muscles, it is necessary for the dentist to conduct a careful examination to rule out local pathologic entities.

Treatment of orofacial motor disorders

If the dentist chooses to become involved in medicating patients who have OMDs, it is essential to be familiar with the pharmacodynamic and pharmacokinetic effects of medications that are prescribed as well as risk/benefit considerations. For dystonia and dyskinesia that have undergone a confirming medical differential diagnosis, it is preferable for the dentist

to work in conjunction with a neurologist or psychiatrist who specializes in movement disorder, because pharmacologic management can be exceedingly complex and frustrating. This frustration is that although the medications described below can work effectively, more often only a small effect is seen and side effects can be substantial. Only a dentist who is well versed in pharmacologic approaches should attempt drug management, albeit this also should be done with continuing medical interaction. As far as surgical approaches for movement disorder, these are reserved for the most severe cases (see later discussion on interventional approaches).

There is no impressive data in the literature that suggest that a medication (other than botulinum toxin injections) can suppress bruxism reliably for more than a few days. Behavioral approaches should be addressed by the appropriate health care provider; they offer some help to patients who are having an acute stress problem that is influencing bruxism and clenching behavior, but again, data on true suppression of bruxism with a straight behavioral approach is lacking. Most of the time, the best treatment for bruxism is to fabricate an occlusal guard and try to protect the teeth from further attrition. Botulinum toxin injections are helpful for the more severe motor disorders, including bruxism.

General medical treatment strategy

For most OMDs, there is no well-defined treatment protocol except to rule out CNS disease and local pathology and to try one or more of the medications that may be helpful in these cases. If the disorder is severe enough and focal enough to consider, and the medications are not adequate, botulinum toxin injections can be considered. For patients who cannot be helped with the above, it is reasonable to consider neurosurgical therapy or implanted medication pumps that can deliver intrathecal medications. The use of motor blocking injections (botulinum toxin) can be considered. This method has proven to be most helpful for the focal dystonias and dyskinesias. In these disorders, injection of botulinum toxin is used successfully to block the transmission from the motor nerve to the motor end plate on the muscle for a period of 2 to 3 months (until the nerve sprouts and reconnects to the muscle). In the specific case of bruxism, some of the damage that is done by this behavior can be mitigated with the use of an intraoral appliance. For hemifacial spasm of spontaneous origin, intracranial surgical decompression surgery is used occasionally to remove the source of the irritation on the nerve.

Overview of interventional approaches

Surgical microvascular decompression

This approach can be used for hemifacial spasm if the clinician has determined that there is a compressive lesion of the facial nerve [47]. The involved

blood vessel is lifted off from the facial nerve and often a sponge is placed between the vessel and the nerve bundle.

Myectomy

If a specific muscle is involved (focal dystonia) or predominates on the OMD presentation, severing it may offer a solution when the patient has been refractory to other, more conservative approaches and cannot function. Blepharospasm may respond to cutting of the orbicularis oculi muscle [48].

Pallidotomy

The globus pallidus is a functional entity within the basal ganglia in the brain. This procedure involves creating a surgical lesion (localized damage) in this area of the brain that is involved with motion control; this can be of value for certain dystonias and torticollis [49]. This is one surgical approach that is used for managing Parkinson's disease.

Deep brain stimulation

Deep brain stimulation uses an implanted electrode to deliver continuous high-frequency electrical stimulation to the thalamus, globus pallidus, or any part of the brain that is involved with the control of movement [50]. In spite of these methods, the prognosis for curing a specific OMD is poor; however, some of them can be managed successfully with a combination of education, medications, and selective injections of botulinum toxin.

Treatment of drug-induced dyskinesia and dystonic extrapyramidal reactions

The general rule is that the offending medication is withdrawn and it is hoped that the dyskinesia or dystonic reaction goes away [51]. Fortunately, acute dystonic reactions secondary to neuroleptic drugs are infrequent and disappear upon discontinuation of the medication; however, this may take days to months, depending upon the drug, its dose, and the patient. The same is true for less severe dystonic EPS reactions that are associated with SSRIs and stimulant drugs.

If the suspected medication cannot be stopped or if the motor hyperactivity is severe, the following methods are used to treat the motor hyperactivity: diphenhydramine, 50 mg, or benztropine, 2 mg intravenously (IV) or intramuscularly (IM) [52–54]. The preferred route of administration is IV, but if this is not feasible, IM drug administration can be used. Finally, amantadine, 200 to 400 mg/d by mouth [55], and diazepam, 5 mg IV [56], have been shown to be effective for recurrent neuroleptic-induced dystonic reactions. Some patients who have SSRI-induced dystonic EPS have relief when the dosage of SSRI or the other stimulant drug is reduced (eg, fluoxetine changed from 20 mg/d to 10 mg/d). Other patients respond to the addition of buspirone in dosages of 5 to 15 mg/d [57,58]. Other patients developed bruxism

within the first few weeks of SSRI therapy; however, they were treated successfully with buspirone, 10 mg two to three times daily. Buspirone seems to be an effective treatment based on a few case reports. This drug may have an additional benefit of relieving anxiety if it is present. It is usually tolerated well and carries a low risk for significant side effects. Finally, switching to antidepressants that have not been associated with bruxism, such as mirtazapine or nefazodone, is an option.

Treatment of spontaneous dyskinesias and dystonias

With any new-onset movement disorders without obvious cause, a motor suppressive medication trial is logical. The commonly used medications are presented in Table 2. If the disorder is severe enough and focal enough to consider, and the medications are not adequate, botulinum toxin injections should be considered. Finally, for patients who cannot be helped with the above methods, and the scientific evidence to support alternative approaches is reasonable, consider neurosurgical therapy or implanted medication pumps that can deliver intrathecal medications. Regarding the prognosis of motor suppressive medications, a recent meta-analysis of the literature made several conclusions that should be shared with patients before starting treatment [59]. First, this review suggested that botulinum toxin has obvious benefit for the treatment of focal dystonias, such as cervical dystonia and blepharospasm. Second, trihexyphenidyl in high dosages is effective for the treatment of segmental and generalized dystonia in younger patients. Third, all other methods of pharmacologic intervention for generalized or focal dystonia, including botulinum toxin injections, have not been confirmed as being highly effective according to accepted evidence-based criteria.

Motor suppressive medications

There are multiple motor suppressive medications used in motor disorder management.

Anticholinergic therapy

The anticholinergic drugs, such as trihexyphenidyl hydrochloride, biperiden, or benztropine are the first line of motor suppressive medications used for dystonia, although they are only partially effective when compared with botulinum toxin injections [60,61]. It is critical to start at a low dose and increase the dose very slowly to try to minimize the adverse effects (dry mouth, blurred vision, urinary retention, confusion, memory loss).

Gamma-aminobutyric acid receptor agonist therapy

Baclofen is a GABA-ergic agent that is used in spasm [62]. The starting dosage is 10 mg at bedtime. The dosage should be increased by 10 mg

Table 2
Medications used for management of hyperkinetic motor disorders

Drug	Group	Starting dose	Usual dose	Indications	Receptor action
Trihexyphenidyl HCl (Artane)	Cholinergic antagonists	1 mg/d	6–15mg/d	Idiopathic parkinson's, extrapyramidal reactions, primary dystonias	Antagonizes acetylcholine receptors
Benztropine (Cogentin)	Cholinergic antagonists	1 mg bid	6 mg/d	Parkinsonism, extrapyramidal reactions, acute-onset secondary dystonias	Antagonizes acetylcholine and histamine receptors
Biperiden (Akineton)	Cholinergic antagonists	2 mg tid	16 mg/d	Parkinsonism, extrapyramidal disorders	Antagonizes acetylcholine receptors
Baclofen (Lioresal)	GABA agonist/ antispasmodic	10 mg/d	30–80 mg/d	Spasticity	Mechanism unclear, but most likely a GABA effect
Clonazepam (Klonipin)	GABA agonist/ tricyclic antidepressant	0.25 mg/d	1–4 mg/d	Seizures, absence anxiety, panic disorder, periodic leg movements, neuralgia	Binds to benzodiazepine receptors and enhances GABA effect
Tiagabine (Gabitril)	Anticonvulsant	4 mg/d	8–32 mg/d	Partial seizures	GABA reuptake inhibitor
Buspirone (Buspar)	Anxiolytic/hypnotic	7.5 mg bid	20–30 mg/d	Anxiety	Nonbenzodiazepine, but mechanism unclear

Amantadine (Symmetrel)	Antiviral/ antiparkinsonian	100 mg bid	100–300 mg/d	Influenza A, extrapyramidal reactions, parkinsonism	Mechanism unclear
Carbi/levodopa (Sinemet)	Antiparkinsonian	25–100 mg tid	200–2000 mg/d	Parkinson's associated tremor	Inhibits peripheral dopamine decarboxylation, dopamine precursor
Diphenhydramine (Benadryl)	Antihistamine	25 mg tid	400 mg/d	Dystonic reactions	Antagonizes central and peripheral H1 receptors (nonselective)
Clonidine (Catapres)	α-2 adrenergic agonist	0.1 mg bid	0.3 mg bid	Shown helpful for tardive dyskinesia	Stimulates α-2 adrenergic receptor
Botulinum toxin type A (Botox)	Neuromuscular blocker	20–50 U per large jaw closer muscle	Max: 200 units every 3 months	Focal dystonia	Blocks release of acetylcholine from motor end plate

Abbreviations: bid, twice a day; Max, maximum; tid, three times a day.

each week to a maximum of 30 mg three or four times daily. The best data
for baclofen is not for oral medications, but for intrathecal injections of
baclofen that are delivered with an implantable pump [63,64]. The main
side effects include drowsiness, confusion, dizziness, and weakness. Finally,
a recent report suggests that tiagabine, a GABA reuptake inhibitor that is
used as an adjunctive anticonvulsant treatment for partial seizures, can be
helpful in bruxism reduction [65]. The dosages of tiagabine that are used
to suppress nocturnal bruxism at bedtime (4–8 mg) are lower than those
that are used to treat seizures.

Benzodiazepine therapy

Benzodiazepines can be effective for suppression of focal, segmental, and
generalized dystonia [66]. They bind to a specific benzodiazepine receptor on
GABA receptor complex, which increases GABA affinity for its receptor. No
study has found a significant difference between the various benzodiazepines
and clonazepam, which has been widely used in movement disorders. The
starting dose for clonazepam is 0.25 mg at bedtime and gradually increasing
the dosage to a maximum of 1 mg four times daily. The main side effects
include drowsiness, confusion, trouble concentrating, and dizziness.

Dopamine therapy

A specific subset of dystonias that have an onset in childhood was shown
to respond remarkably well to low-dosage L-dopa, such as carbi/levodopa.
These dystonias are referred to as dopa-responsive dystonias (DRD), and
have been shown in recent years to encompass adult parkinsonism, adult-
onset parkinsonism, adult-onset oromandibular dystonia, spontaneously
remitting dystonia, developmental delay and spasticity mimicking cerebral
palsy, and limb dystonia that is not only diurnal but related clearly to exer-
cise [67,68].

Miscellaneous drugs for movement disorder therapy

There are several miscellaneous drugs that have been reported to sup-
press motor disorders. One medication that is used to suppress motor activ-
ity is buspirone, which is a nonbenzodiazepine anxiolytic drug [60,69].
Another drug whose mechanism is unclear is amantadine, which is used
to suppress extrapyramidal reactions [70]. Other drugs that suppress motor
activity are diphenhydramine [71] and clonidine [72].

Skeletal muscle relaxants

There are numerous drugs that are approved by the US Food and Drug
Administration and used for relief of local regional musculoskeletal pain
and spasm, including carisoprodol, chlorzoxazone, cyclobenzaprine
hydrochloride, metaxalone, methocarbamol, and orphenadrine citrate [73].

Generally, these medications are used only for acute clinical proven spasm and are not recommended for long-term use. This is because the evidence is weak that these muscle relaxants are beneficial for individuals who have chronic muscle pain that affects the neck and lower back [74,75]. As far as chronic involuntary oral motor disorders are concerned, these drugs are ineffective and do not play a role in their management.

Botulinum toxin

In 2003, a thorough review of botulinum toxin for oral motor disorders was published; it described the potential uses and current evidence basis for using this medication in the orofacial region [76]. The toxin that is used in botulinum toxin injections is produced by the anaerobic bacterium *Clostridium botulinum*. This injectable drug is able to block motor nerve conduction, and once injected, it suppresses muscle activity for a time period that ranges from 8 weeks to 16 weeks for botulinum toxin type-A. Any clinician who has used this medication will testify to its powerful and dramatic effect in some cases. Unfortunately, this treatment is only palliative. Botulinum acts by interfering with vesicular exocytosis, which blocks the release of neurotransmitters that are contained within these vesicles. The blockage occurs when the toxin enters the nerve and cleaves proteins that are needed for the docking and release of the vesicle contents into the synaptic cleft [77]. Acetylcholine is believed to be the main neurotransmitter that is blocked by the BoNT/A. BoNT/A is manufactured by Allergan, Inc. (Irvine, California), as Botox [78]. This agent is supplied in vials in a lyophilized form, at a dose of 100 U per vial. The typical expiration date is 24 months when stored at -5 to $-20°$C. Another serotype, BoNT/B, is marketed by Solstice Neurosciences, Inc. (San Diego, California) as Myobloc®. Another BoNT/A formulation, Dysport, is marketed outside of the United States by Ipsen Ltd. in Europe. All of these preparations—Botox, Myobloc, and Dysport—differ in formulation and potency; hence, their units are not interchangeable. Side effects can be divided into site-of-injection side effects and medication-related side effects. With regard to site-of-injection side effects, the needles that are used for most injections are small (27–30-gauge needles); if the skin is cleaned properly, then the chances of local hematoma, infection, or persistent pain in the injection site is extremely low. Medication-related side effects generally are few, transitory, and tolerated well by patients. The most common medication-related side effect is adjacent muscle weakness (eg, an inadvertent weakening of the muscles of facial expression or swallowing when this is not desired). For patients who have had injections into the lateral pterygoid or palatal muscles, slurred speech with palatal weakness also is a distinct possibility. In general, these "inadvertent weakness" complications that are due to local diffusion of the drug can and do occur. Moreover, this complication is technique and dose-dependent [79–81]. A second side effect with botulinum toxin injections of the masticatory

muscle is an alteration in the character of the saliva of patients who have not had direct salivary gland injections. Although this is an uncommon problem, some patients report that their saliva is diminished and thicker (ie, ropy saliva); it is more likely with higher doses and for injections around the parotid or submandibular gland. Obviously, this effect is desired at times if there is a substantial sialorrhea problem.

In most cases, the above complications are less problematic than are the untreated original motor disorder and generally do not stop the patient from seeking additional injections. If the injections are being used primarily to treat pain secondary to contraction, these complications might be more bothersome. Fortunately, persistent, more significant complications are distinctly rare. For example, systemic complications are uncommon and although several studies have reported a flulike syndrome, particularly after the first injection, such symptoms also have been reported following placebo injection. Finally, some patients develop antibodies to the toxin. It is unclear exactly what factors predispose to development of antibodies, but some studies suggest that the risk is increased by higher-dose and more frequent injections. For this reason, injections are not done more often than once every 12 weeks.

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