



Medical Management of Oral Motor Disorders: Dystonia, Dyskinesia and Drug-Induced Dystonic Extrapyramidal Reactions

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ABSTRACT

This article reviews three of the involuntary hyperkinetic motor disorders that affect the orofacial region, namely orofacial dystonia, oromandibular dyskinesia, as well as medication-induced extrapyramidal syndrome-dystonic reactions. Specifically, it discusses and contrasts the clinical features and management strategies for spontaneous primary and drug-induced motor disorders in the orofacial region. The article provides a list of medications reported to cause drug-related extrapyramidal motor activity above and beyond the more commonly known antipsychotics medications. It provides a needed update because the number and use of medications causing involuntary jaw muscle activity are increasing. For example, selective serotonin reuptake inhibitors (SSRI), stimulant medications and illegal drugs have all been reported to induce an orofacial motor activation as adverse reactions.

This article also discusses briefly the genetic and traumatic events associated with spontaneous dystonia. Finally, this article presents an approach for management of the orofacial motor disorders that involves the following three steps: (1) collect a full clinical history and examination, including magnetic resonance imaging of the brain; (2) after ruling out CNS disease, adverse medications reactions and local pathology, try one or more of the motor-suppressive medications that may be helpful in these cases (e.g., cholinergic receptor antagonizers or blockers, and GABA-ergic including benzodiazepines); and (3) if the disorder is severe enough and focal enough to consider, and motor-suppressive medications are not adequate, then consider botulinum toxin injections. The contraindications, side effects, and usual approach for these medications and injections are discussed.

Dentists must be able to recognize and become involved with management of oral motor disorders because such behaviors cause pain and dysfunction of the jaw. If the motor activation abnormality is severe, these disorders can also make it more difficult to perform needed dental care on patients and sometimes dental treatments aggravate these movement disorders. As used in this article, the term “orofacial motor disorders,” OMD, encompasses a spectrum of movement aberrations, both hyperactive and hypoactive that involve the muscles of the orofacial complex. Numerous involuntary motor disorders with varying consequences to the patient and can affect the orofacial musculature.¹⁻³ A partial list of these medications is provided in **Table 1**. The most common motor disorders of concern to dentists everywhere are excessive sleep bruxism and sustained habitual forceful clenching, day or night.

The primary management method for strong bruxism and clenching is still



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Table 1 Partial List of the Hyperkinetic Oral Motor Disorders	
Bruxism	Nonfunctional jaw movement that includes clenching, grinding, clicking, and gnashing of teeth during sleep. Based on EMG recording of the jaw closers during sleep, there are two basic patterns of bruxism reported: (1) rhythmic, side-to-side motions and, 2) prolonged, maximal isotonic contractions of the jaw muscles (up to 300 seconds in length). Bruxism has been reported during each stage of sleep; however, the majority of episodes appear during stage II sleep.
Orofacial dyskinesia	Excessive, repetitive, stereotypic oral movements such as facial grimacing, repetitive tongue protrusion, puckering, smacking, and licking of the lips and side-to-side motion of the jaw. The most common form is tardive dyskinesia and it appears in patients who have taken neuroleptic medications. However, dyskinesias may also be spontaneous and can be caused by systemic, metabolic, endocrine, structural, vascular, infectious, psychologic, or inherited degenerative conditions.
Meige's syndrome	Uncontrollable blinking of the bilateral eyelids which makes it appear as if the person is continually winking. When there is no obvious other cause (e.g., dry eyes), blepharospasm is called benign essential blepharospasm. It often affects both eyes at once, but it can also affect only one eye. Severe blepharospasm can cause the eyelids to be forcibly closed for a period which is longer than the typical blink reflex, thus causing a variable interruption in the ability to see. Meige's syndrome is a combination of blepharospasm and oromandibular dystonia (see below).
Oromandibular dystonia	Involuntary, repetitive, sustained muscle contraction, which results in an abnormal posturing of a structure. Depending on the muscle involved, it may produce a twisting movement of the involved structure. Dystonia is typically present throughout the day and disappears during deep sleep. Dystonic spasms typically increase in intensity during stress, emotional upset, or fatigue. If the affected muscles are in the oral region, it can produce involuntary jaw opening, lateral movements of the jaw and/or protrusion of the tongue.
Hemi-facial spasm	Hyperkinetic movement disorder affecting the unilateral facial muscles. It will start with an intermittent periorbital twitching, usually of the inferior orbicularis oculi muscle. Over months to years this abnormality can progress to involve half of the face and the platysma muscle. Since this is a disorder of CN VII, the muscles of mastication are not involved. Sometimes these twitching movements may progress to a sustained, chronic contraction of the involved facial muscles.
Facial and oral tics	Brief, intermittent, repetitive, nonrhythmic, unpredictable, purposeless, stereotyped movements. Rather than a voluntary movement, a tic is a movement which relieves a voluntary urge, and this is the key characteristic which differentiates a tic from another movement disorder. Motor tics of the orofacial area include tongue protrusion, facial grimacing, blinking, and facial twitching, and cheek sucking. Tourette's syndrome include motor and vocal tics and is the most common and severe form of a multiple tic disorder.

a full-arch occlusal appliance, which does not stop the behavior but limits its dental damage.⁴ Fortunately, the most severe cases of bruxism and clenching now have several motor-suppressive medications and in extreme cases, botulinum toxin injections that can be

added to occlusal appliance treatment. However, this article focuses not on bruxism but on three other vexing disorders of focal orofacial dystonia, oromandibular dyskinesia, and medication-induced extrapyramidal syndrome-dystonic reactions in the orofacial region.

When severe, these motor disorders may actually cause strong headaches, damage the temporomandibular joint, or create such motor control difficulty that patients will be unable to eat and may start to lose weight. Sometimes 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, which patients must endure, affects their daily living and many patients will refuse, or strongly avoid, leaving their homes. Fortunately there are various medications, including botulinum toxin injections that can offer partial help (Table 1).

Dystonia

Dystonias are involuntary but tend to be more intermittent than dyskinesias and they are a syndrome of short but sustained muscle contractions that produce twisting and repetitive movements or abnormal postures.^{5,6} Dystonias are called focal if they involve a single area, e.g., face, oromandibular area, arm, or neck. They are called segmental if two or more contiguous areas are affected, e.g., cranial and cervical areas or the face, jaw, and tongue. They are multifocal if two or more noncontiguous body regions are involved, e.g., an arm and a leg with cranial muscle involvement. Most dentists who have an elderly population have encountered orofacial dyskinesia, but few have seen a true dystonia problem affecting the jaw or tongue area. Focal primary dystonia occurs in 29.5 per 100,000 individuals.⁷ Oromandibular dystonia is one of these focal dystonias and it affects the orofacial region and involves the jaw openers (both lateral pterygoids and anterior digastrics), tongue muscles, facial muscles (especially orbicular oris and buccinator), and platysma are involved. When this occurs in association with blethrospasm, this is called Meige's syndrome.⁸

Oromandibular dystonias typically produce intermittent pulling, twisting of the jaw forward or sideways, and if they involve the tongue musculature, it

may effect a rolling of the tongue, lips, and cheek or even a spontaneous opening of the jaw. One interesting aspect of the involuntary motor disorders is that patients can partially control or suppress the movement with the use of tactile stimulation, such as touching the chin in the case of orofacial dystonia or holding an object in their mouth. This suppressive effect has been called geste antagonistique.⁹ These tactile maneuvers may mislead physicians to the erroneous diagnosis of malingering or hysteria.

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Other examples of sensory tricks include placing a hand on the side of the face, chin, or back of the head, or touching these areas with one or more fingers, which at times will reduce neck contractions associated with cervical dystonia. With some dystonias, patients will have discovered that placing an object in the mouth, such as a toothpick or a piece of gum may reduce dystonic behaviors of the jaw, mouth, and lower face (oromandibular dystonia). Finally, the majority of the focal and segmental dystonias only occurs during waking periods and disappears entirely during sleep.

Dyskinesia

Orofacial dyskinesia occurs as involuntary orofacial movement of the lips, tongue, and sometimes the jaw during the day.^{10,11} These problems are char-

acterized as repetitive, stereotypical, orofacial lip, and tongue movements. Sometimes the dyskinesia is medication-induced, called "tardive," or it can occur spontaneously. The spontaneous form of dyskinesia often affects the elderly. The tardive form of dyskinesia typically occurs in mentally ill patients who have taken long-term exposure to medications used to treat the mental illness.¹² Tardive dyskinesia by definition requires at least within three months of total cumulative drug exposure, which can be continuous or discontinuous.

Moreover, the dyskinesia must persist more than three 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 (Clozaril), olanzapine (Zyprexa), and risperidone (Risperadal), have been reported to cause both tardive dystonia (see next section) 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, but the duration of exposure to antipsychotics 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.

Dystonic-type Extrapyramidal Reactions

There are patients who have developed a medication-induced oral motor hyperactivity which do not fit into the dyskinesia category.¹³ These medi-



cations and illegal drugs produce a motor response which is better classified as an unspecified extrapyramidal syndrome, EPS, reaction. These EPS reactions have an international classification of disease (version 9) number of 333.90. EPS responses typically have three presentations: dystonic, akathisia and Parkinsonism. Dystonic reactions consist of involuntary, tonic contractions of skeletal muscles.¹⁴⁻¹⁶ Akathisia reactions occur as a subjective experience of motor restlessness.^{17,18} 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 requiring repetitive movements, bradykinesia. When a medication or drug induces a dystonic EPS reaction, it typically involves the muscles of the head, face, and jaw producing spasm, grimacing, tics, or trismus. Most of the literature has focused on the more severe acute dystonic EPS reactions which occur with use of antipsychotic medications. In addition to the antipsychotics, several antiemetics with dopamine receptor-blocking properties have also been associated with tardive dystonia. These include prochlorperazine (Compazine), promethazine (Phenergan), and metoclopramide (Reglan). Of course, other less severe reaction does occur, which 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, SSRI, and the stimulant medications and illegal drugs.

Serotonergic Agents

Selective serotonin reuptake inhibitors, e.g., fluoxetine, (Prozac), fluvoxamine (Luvox), paroxetine (Paxil),

sertraline (Zoloft), citalopram (Celexa), escitalopram (Lexapro) are used for depression and a variety of other mental illness. Unfortunately, these drugs are reported to produce the side effect of increased clenching and bruxism.¹⁹⁻²² 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 gen-

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erally describe an elevated headache and tightness in their jaw, tongue, and facial structures and 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.²³ They found that 40 mg of paroxetine produced a clear augmentation of peak inspiratory genioglossus activity during 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 other categories of antidepressant medications, e.g., tricyclics and monoamine oxidase inhibitors. Unfortunately, only case-based literature exists at this time and further studies, full polysomnographic studies on the motor effects of SSRIs

are necessary in order to define prevalence, risk factors, and establish a causal relationship between SSRI use and oral motor disorders.

Stimulant Drugs and Medications

Illegal drugs such as methamphetamine; cocaine; 3,4-methylenedioxy-methamphetamine (Ecstasy) and legal prescription stimulants such as methylphenidate (Ritalin), phentermine (Adipex-P), pemoline (Cylert), dextroamphetamine (Dexedrine), amphetamines (Adderall), and diethylpropion (Tenuate) have all been reported to induce bruxism and dystonic extrapyramidal reactions.²⁴⁻²⁸ All stimulant drugs have the potential to cause extrapyramidal reactions and they are being used in greater numbers to treat obesity and or as stimulants for children with attention deficit hyperactivity disorder or narcolepsy, and even for severe depression²⁹ (Table 2).

Etiology

Certainly in those with a family history of spontaneous dystonia or dyskinesia, genetic factors must be prominent. With the exception of familial idiopathic torsion dystonia, ITD, the specific genetic dysfunction is not known. With ITD, a mutation of the DYT1 gene on band 9q34 has been identified.³⁰ This gene encodes a protein called torsin A, which binds to adenosine triphosphate. In the absence of any family history, spontaneous dystonia or dyskinesia could be a new mutation. Unfortunately, the pathophysiology of motor disorders is not well understood, partly because it describes a symptom that may arise from a variety of cerebral structures, such as the basal ganglia, cerebellum, thalamus, or brainstem, or cortex. One question not yet answered is whether

Table 2**Partial List of SSRI and Other Stimulants Reported to Cause Jaw Motor Hyperactivity****Selective serotonin reuptake inhibitor medications**

Citalopram (Celexa)	Ellison and Stanziani, 1993; Romanelli et al., 1996; Gerber and Lynd, 1998; Lobbezoo et al., 2001
Fluvoxamine (Luvox)	
Paroxetine (Paxil)	
Fluoxetine (Prozac)	
Sertraline (Zoloft)	
Escitalopram (Lexapro)	

Illegal drugs

Ecstasy	Peroutka et al., 1988; Vollenweider et al., 1998; Fazzi et al., 1999; Winocur et al., 2001; See and Tan, 2003
Cocaine	
Amphetamine	

Stimulant medications

Pemoline (Cylert)	Malki et al., 2004
Methylphenidate (Ritalin)	
Dextroamphetamine (Dexadrine)	

those susceptible to tardive dyskinesia are individuals who are also vulnerable to drug-induced extrapyramidal dystonia, with the medication serving as a trigger to this mutation.

For a few cases, there is some evidence to support a role of trauma including injury to the head or other body parts. For example, a closed head injury can sometimes result in severe dystonia, but the injury has to be severe enough to result in damage to the basal ganglia, which can be visualized on brain imaging studies. Peripheral, non-CNS, injury to a limb may also result in severe dystonic postures, but the mechanism underlying this “peripheral injury-induced dystonia” is not clear. It is speculated that people who are carriers of the gene for dystonia may be more likely to have trauma as a triggering factor for the development of dystonia. One study reported on the role of peripherally induced oromandibular dystonia.³¹ Specifically, they reported on several cases with a history of a recent oromandibular

dystonia that: (1) developed within a few days or months, up to a year, after the injury; (2) the trauma was well documented by the patient’s history or a review of their medical and dental records; and (3) the onset of dystonia was anatomically related to the site of injury, facial and oral. They found 27 patients identified with an oral motor disorder temporally and anatomically related to prior injury or surgery and nothing else. The mean age at onset was 50 ± 14 year and there was a 2:1 female preponderance.

More important to the dentist was the reported association of new onset cranial dystonias which developed within hours to months following a dental procedure.³² In these cases, there was no family history of dystonia or prior use of neuroleptics. The authors suggested that the close association in time and location of the procedure and onset of symptoms suggested a causal link between the dystonia and the dental intervention and asked for better epidemiologic studies on the topic.

Management of Disease

Anytime a patient exhibits a new onset involuntary oral motor disorder, a three-step process is suggested. The first step is to collect a full clinical history and examination, including magnetic resonance imaging of the brain. The second step (after ruling out CNS disease, adverse medications reactions, and local pathology) is to try one or more of the motor-suppressive medications that may be helpful in these cases (e.g., cholinergic receptor antagonizers or blockers and GABAergic including benzodiazepines). The third step, if the disorder is severe enough and focal enough and motor-suppressive medications are not adequate, is to consider botulinum toxin injections.

History and Examination

The first step in all suspected oral motor disorders is to perform a proper diagnostic work-up for a movement disorder. This involves a full clinical history and examination and magnetic



resonance imaging examination. The history must include a thorough medication and illegal drug history, when tardive induced motor disorders are suspected. The imaging is necessary in order to rule out the possibility that the motor dysfunction may be due to a central degenerative, demyelinating, or sclerotic lesion of the nervous system. Moreover, in addition to a standard MRI, imaging might also include angiographic-type magnetic resonance imaging. These tests will rule in or out a neurologic infarct or tumor or compression of critical nerves or structures. For the most severe forms of bruxism and some sleep-related motor activity problems, it will be necessary to conduct a polysomnogram which includes an electroencephalogram and electromyographic monitoring of the involved structures.

In the absence of a clear-cut history of CNS damage, injury or new pathology, or a family history of similar movement disorders, it should be appreciated that the exact pathophysiologic mechanisms for the spontaneous onset hyperkinetic motor disorders is often not proven by examination or imaging. The two exceptions to this statement would be hemifacial and hemimasticatory spasm, where it is thought that there is a vascular compression of CN V and VII motor roots. Proceed with steps 2 and 3 only after a negative examination and imaging is achieved.

Treatment

Step 2 involves either removing medications, if a suspected drug-related motor disorder is present, or adding medications that effect the motor system.³³ If a patient has a proven tardive dyskinesia which does not stop with withdrawal from the offending medications, or these medications cannot be stopped, this is managed as a spontane-

ous movement disorders with motor-suppressive medications. These medications work well for acute onset spasms of the jaw, but often only a small effect is seen and side effects can be substantial in patients with hyperkinetic oral movement disorders.

Treatment of Tardive Dyskinesia and Drug-Induced Dystonic Extrapyrarnidal Reactions

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the dyskinesia or dystonic reaction will go away.³⁴ Fortunately, acute dystonic reactions secondary to neuroleptic drugs are infrequent and disappear upon discontinuation of the medication but this may take days to months, depending upon the drug, its dose, and the patient. The same goes for less severe dystonic EPS reactions associated with SSRIs and stimulant drugs. If the suspected medication cannot be stopped or it is severe, the following methods are used to treat them: diphenhydramine (Benadryl) 50 mg; benzotropine (Cogentin) 2 mg IV or IM.³⁵⁻³⁷ The preferred route of administration is intravenous. If this is not feasible, IM drug administration can be used.

Finally, both amantadine (Symmetrel) 200-400 mg/d po and diazepam (Valium) 5 mg IV have been shown to be effective for recurrent neuroleptic-induced dystonic reactions.^{38,39} Some

patients with SSRI-induced dystonic EPS have relief when the dose of SSRI or the other stimulant drug is reduced, e.g., fluoxetine (Prozac) changed from 20 mg/day to 10 mg/day. Other patients respond to the addition of buspirone (Buspar) in doses of 5-15 mg per day.^{40,41} Some patients developed bruxism within the first few weeks of SSRI therapy, however, they were successfully treated with buspirone in doses of 10 mg twice daily to three times daily. Buspirone appears 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 well tolerated and carries a low risk of significant side effects. Finally, switching to antidepressants that have not been associated with bruxism such as the mirtazapine (Remeron) or nefazodone (Serzone).

Treatment of Spontaneous Dyskinesias, 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 3. If the disorder is severe enough and focal enough to consider, and the medications are not adequate then consider botulinum toxin injections (see next page). Finally, for those who cannot be helped with steps 1 through 3, and the scientific evidence-supporting alternative approaches are 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.⁴² First, this review suggested that botulinum toxin has obvious benefit for the treatment of focal dystonias such as

Table 3**Oral Medications Used for Management of Hyperkinetic Motor Disorders**

Drug	Starting dose (mg/day)	Usual dose (mg/day)	FDA: Approved Use	Receptor Action
Trihexyphenidyl HCl (Artane)	1 mg/d	6-15 mg/d	Idiopathic Parkinson's extrapyramidal reactions	Antagonizes acetylcholine receptors
Biperiden (Akineton)	2 mg tid	16 mg/d	Parkinsonism extrapyramidal disorders	Antagonizes acetylcholine receptors
Baclofen (Lioresal)	10 mg/d	30-80 mg/d	Spasticity	Mechanism unclear but most likely a GABA effect
Tigabine (Gabitril)	4 mg/d	8-32 mg/d	Partial seizures	GABA-reuptake inhibitor
Clonazepam (Klonopin)	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
Buspirone (Buspar)	7.5 mg bid	20-30 mg/d	Anxiety	Non-benzodiazepine but mechanism unclear
Amantadine (Symmetrel)	100 mg bid	100-300 mg/d	Influenza A extrapyramidal reactions Parkinsonism	Mechanism unclear
Benzotropine (Cogentin)	1 mg bid	6 mg/d	Parkinsonism extrapyramidal reactions dystonic reaction, acute	Antagonizes acetylcholine and histamine receptors
Diphenhydramine (Benadryl)	25 mg tid	400 mg/d	Antihistamine dystonic reactions	Antagonizes central and peripheral H ₁ receptors (nonselective)
Botulinum toxin type-A	20-50 units per jaw closer muscle	Max: 200 units every 3 months	Focal dystonia	Blocks release of acetylcholine from motor end plate

cervical dystonia and blepharospasm. Second, trihexyphenidyl (Artane) in high dosages is effective for the treatment of segmental and generalized dystonia in younger patients. Third, all other methods of pharmacological intervention for generalized or focal dystonia, including botulinum toxin injections, have not been confirmed as being highly effective according to accepted evidence-based criteria (Table 3).

Anticholinergic Therapy

The anticholinergic drugs, such as trihexyphenidyl hydrochloride or biperiden (Akineton), are partially effective agents for dystonia, but even these drugs work in only a minority of patients. It is critical to start at a low dose and increase the dose very slowly to try to minimize the adverse effects such as dry mouth, blurred vision, urinary retention, confusion, and memory loss.

GABA-ergic Therapy

Baclofen (Lioresal) is a GABA-ergic agent which is used in spasm. The starting dose is 10 mg at bedtime. Increase the dose by 10 mg 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 delivered with an implantable pump.^{43,44} Main side effects include drowsiness, confusion, dizzi-



ness, and weakness. Finally, a recent report suggests tiagabine (Gabitril), a GABA-reuptake inhibitor which is used as an adjunctive anticonvulsant treatment of partial seizures, can be helpful in bruxism reduction.⁴⁵ The doses for tiagabine used to suppress nocturnal bruxism at bedtime (4 mg to 8 mg) are lower than those used to treat seizures.”

Benzodiazepines Therapy

Benzodiazepines can be effective for suppression of focal, segmental, and generalized dystonia.⁴⁶ They bind to a specific benzodiazepine receptor on GABA-receptor complex, thereby increasing GABA affinity for its receptor. No study has found a significant difference between the various benzodiazepines and clonazepam (Klonopin), 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.

Botulinum Toxin

Step 3 in the process of treatment for oral motor disorders involves the selected use of the toxin 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 ranging from eight weeks to 16 weeks with 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. The vast majority of the reports described in this paper relate to botulinum toxin type-A (Botox) unless specified other-

wise. When unit doses are provided, they refer to units of Botox, a product manufactured by Allergan since this is the primary product available and used in North America. The clear contraindications to the use of botulinum toxin are known allergy to the drug; infection or inflammation at the proposed injection site(s); pregnancy and/or women who are lactating; and an inability of a patient to cooperate, or high levels of fearfulness toward the method. The final caveat is that while

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botulinum toxin injections sound simple and safe, there are complications. In this regard, it should be reserved for patients with an unequivocal diagnosis. The specific applications and indications for botulinum toxins are presented below.

Oromandibular Dystonia (With Recurrent Jaw Opening Motion)

Oromandibular dystonia is a focal dystonia affecting the trigeminal and oral-perioral musculature. It is considered present when repeated, often asynchronous, spasms of muscles of these muscles are present. Treatment with botulinum toxin has been found helpful and 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 temporomandibular joint can become physically locked in the wide open

position so that even after the dystonic contraction stops, the jaw will not easily close. Several authors have described the use of botulinum toxin injections into the lateral pterygoid muscle when a patient exhibits focal dystonia which results in jaw opening.⁴⁷⁻⁴⁹ While the above authors have focused on injecting the lateral pterygoid muscles, sometimes the submandibular muscles e.g., anterior digastric and platysma, can play a role in jaw opening activity and here again there are several reports in the literature that report on botulinum injection of these muscles.^{50,51}

Hyperactivity of the Tongue

The tongue is often strongly active in tardive and spontaneous dyskinesia, some types of oromandibular dystonia, and can be involved as a manifestation of the motor effects seen in cerebral palsy. Botulinum toxin injections into the genioglossus and the intrinsic tongue muscles has been used to treat this motor problem with limited success.⁵²⁻⁵⁵

Injections Tips

Botulinum toxin is a safe therapy when administered in the appropriate doses by an experienced clinical specialist. A recent review discussed the dosage and injection sites for the commonly injected jaw muscles.⁵⁶ To become proficient with this method, it is recommended that the clinician spend some time in the anatomy laboratory injecting more than one cadaver with a colored dye and then dissecting the dye-injected cadavers to know if the injection was placed correctly. While for some, deep muscles, e.g., lateral pterygoid, it is advisable to use electromyographic localization method to ensure proper placement of the needle. Most times, this additional methodology is not required

in most patients since many of the primary target muscle (e.g., masseter, temporalis, anterior digastric, genio-glossus, orbicularis oris, muscles of facial expression, levator tensor palatae and the intrinsic tongue muscles) can be easily palpated or clear injection landmarks identified. For some of the injection targets, e.g., parotid, lacrimal and submandibular salivary glands, EMG will not help prove one is in the correct place, although it would help one to know one is in an incorrect location.

Side Effects From Botulinum Injection

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 being used for most injections are small (between 27- to 30-gauge needles), and if the skin is cleaned properly, then the chance of local hematoma, infection or persistent pain in the injection site is very, very low. Regarding medication-related side effects, they are generally few, transitory and well tolerated by patients if they occur. The most common medication-related side effect is adjacent muscle weakness, e.g., 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 is a distinct possibility as well. In general, these "inadvertent weakness" complications due to local diffusion of the drug can and does occur.

Moreover, this complication is technique and dose-dependent.⁵⁷⁻⁵⁹ 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. While this is an uncommon problem, some patients

report that their saliva is diminished and thicker, i.e. ropy saliva, and is more likely for higher doses and for injections around the parotid or submandibular gland. Obviously, sometimes this effect is desired if there is a substantial sialorrhea problem.

In most cases, the previously mentioned complications are usually less problematic than the untreated original motor disorder and will not generally stop the patient from seeking additional

The most common medication-related side effect is adjacent muscle weakness.

injections. However, if the injections are being used to primarily treat pain secondary to contraction, then 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 flu-like syndrome, particularly after the first injection, such symptoms have also been reported following a 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 risk is increased by higher and more frequent injections and for this reason, injections are not done more often than once every 12 weeks.

Summary Recommendations

The prognosis of patients with tardive dyskinesia or tardive dystonia is poor if the disorder persists after withdrawal of the medication. At best, the movements can be suppressed with motor-suppressive

medications but often the medications produce only a small change. The same can be said for the prognosis of spontaneous dyskinesia and dystonia, but if the disorders are reasonably localized, botulinum toxins can be quite helpful. A better prognosis is offered for the drug induced dystonic EPS reactions. In these cases, recognition and communication about the suspicion of a drug-induced EPS back to the prescribing clinician is the first step. Withdrawal from the medication or reduction of the medication is logical. There are several medications that can be used to help the patients manage this disorder, and when indicated, careful and cautious use of botulinum toxin in resistant cases is appropriate. ■■■■

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