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CERVICAL DYSTONIA : A CURRENT REVIEW

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Abstract

Cervical dystonia is a movement disorder and the most common form of focal dystonia, presents with sustained neck spasms, abnormal head posture, head tremor, and pain. One of the interesting and unique features of cervical dystonia is the geste antagoniste. There is not a well-clear pathophysiology for cervical dystonia, but several studies report involvement at the central and peripheral level. Although oral drug therapy has limited efficacy in the treatment of patients with cervical dystonia, botulinum toxin serotype A and B has satisfactory benefits. Surgery is an option when other treatments fail or become ineffective.

Keywords: Cervical dystonia, Botulinum toxin, Spasmodic torticollis.

Introduction

The term “dystonia” was coined by Oppenheim in 1911 to describe a disorder causing variable muscle tone and recurrent muscle spasm. This disorder was initially called dystonia musculorum deformans.[1,2] and was later called primary torsion dystonia. Generally Dystonia is a clinical syndrome characterized by sustained muscle contractions causing twisting and repetitive movements or abnormal postures.[3] Especially Cervical dystonia is the most common form of adult-onset focal dystonia.[4] Cervical dystonia is defined as involuntary twisting and turning of the neck caused by abnormal involuntary muscle contractions.[5] Cervical dystonia is also known as ‘spasmodic torticollis’. Even though cervical dystonia is the most common form of focal dystonia, only a few epidemiologic studies have been conducted to describe its incidence and prevalence. Separate studies of different geographic locations and times show the prevalence between 9 and 30 per 100 000 in the United States.[1,6,7] The current prevalence of cervical dystonia in the United States is estimated to exceed 90 000. Other studies show that its prevalence differs among ethnic groups.[8,9,10] Cervical dystonia affects women 1.3- to 2-fold more often than men. Cervical dystonia can occur at any time of life, but most individuals experience their first symptoms in middle age. A review stated about the clinical details of cervical dystonia in 266 patients. The median age of onset in their study was 41 years old, with a female/male ratio of 1.9:1. They found a familial history of dystonia in 12 of 100 cases. Remission was achieved in 9.8% of patients.[11]

Pathophysiology

The pathophysiology of Cervical dystonia is still not clear. But several studies show that cervical dystonia is considered neurochemical in nature, and does not result in structural neurodegenerative

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changes. Although no lesions are present in the basal ganglia in primary spasmodic torticollis, fMRI and PET studies have shown abnormalities of the basal ganglia and hyper activation of the cortical areas.[12] Studies have suggested that there is a functional imbalance in the striatal control of the globus pallidus, specifically the substantia nigra pars reticulate. The studies hypothesize the hyper activation of the cortical areas is due to reduced pallidal inhibition of the thalamus, leading to over activity of the medial and prefrontal cortical areas and under activity of the primary motor cortex during movement.[13] It has also been suggested that the functional imbalance is due to an imbalance of neurotransmitters such as dopamine, acetylcholine, and gamma-aminobutyric acid. These neurotransmitters are secreted from the basal ganglia and travel to muscle groups in the neck. Increases in neurotransmitters cause spasms to occur in the neck, resulting in spasmodic torticollis.[14] Studies of local field potentials have also shown an increase of 4–10 Hz oscillatory activity in the globus pallidus internus during myoclonic episodes and an increase of 5–7 Hz activity in dystonic muscles when compared to other primary dystonias. This indicates that oscillatory activity in these frequency bands may be involved in the pathophysiology of spasmodic torticollis.[15] Table 1 lists some common muscles involved in cervical dystonia, but any muscle in the neck may be involved.[16, 17]

Table No. 01: Commonly injected muscles in treating Cervical dystonia[16,17]

Muscle	Action
Sternocleidomastoid	Unilateral−ipsilateral flexion and contralateral rotation Bilateral−head and neck flexion
Splenius capitis	Bilateral−extends neck and head Unilateral−flex and rotates the head slightly to the same side
Semispinalis capitis	Extension, lateral flexion and rotation of neck
Scalenes	
Anterior	Bilateral−elevate ribs during inhalation
Medius	Unilateral−ipsilateral neck flexion, contralateral rotation
Posterior	Anterior−neck flexion
Levator scapulae	Elevates the superior angle of the scapula
Trapezius upper	Elevates, retracts, and rotates scapula

Causes of cervical dystonia

Several causes may contribute to Cervical dystonia. The first probable cause is loss of inhibition. Several studies show that dystonia is due to decreased central inhibition.[18] One hypothesis suggests that with a directed movement, a certain area of the motor cortex activates for the desired movement and unwanted movements are inhibited by surround inhibition, which is a concept similar to what has been shown in the visual system.[18,19] By applying transcranial magnetic stimulation to the motor cortex contralateral to the side of electromyographic (EMG) recording, showed that cortical motor excitability was increased in dystonia and that this was most likely secondary to a decrease of inhibition.[20] The brain γ-aminobutyric acid (GABA) level was impaired in cervical dystonia in 2002 by using magnetic resonance spectroscopy (MRS).[21] A potential cause of dystonia is sensory deficit and sensorimotor mismatch. Trauma and other abnormal inputs could lead to focal dystonia. The geste antagonistique, or sensory trick, is a sensory phenomenon used to improve abnormal postures in focal dystonia.[22] The final potential cause of dystonia is basal ganglia discharge. The comparison of the discharge rates and neuronal pattern in parkinsonian patients with dystonia is: In both dystonia and Parkinson disease the discharge rates in the putamen are very low, but discharge rates are much lower in the globus pallidus neurons in dystonia than in Parkinson disease. In dystonia there are no differences in discharge rates and patterns of neurons in globus pallidus, but in Parkinson disease patients, globus pallidus externa recording shows lower rates than globus pallidus internus.[23] Neuronal discharge in the globus pallidus internus, ventral thalamic nuclear group, ventral oral posterior/ventral intermediate (Vop/Vim) and subthalamic nucleus (STN) in patients with dystonia are also analyzed in a study.[24] Similar results were obtained, suggesting an association of dystonia and alteration in neuronal discharge in the basal ganglia and thalamus.

Clinical features

Head tremor, neck spasms, and pain are the main features of CD. Pain is not common in other focal dystonia except for writer's cramp.[25] Hand and arm, tremor can be seen in torticollis.[26,27] Rarely, head, arm, or trunk tremor is the initiative symptom or even the only manifestation of the disease.[28] Most patients with CD use geste antagoniste to diminish or even eliminate the muscle spasm. An example of geste antagoniste is touching the chin, the side of the face, or back of the neck without applying any pressure. Sometimes even thinking of geste antagoniste works, even though the mechanism is unknown.[26, 29] Besides the mentioned signs and symptoms, patients faces a high incidence of psychiatric comorbidities such as depression and anxiety, which as has been shown is not just secondary to a chronic, disfiguring disease.[30]

Treatment

Cervical dystonia is managed through several methods, including oral drug therapy, botulinum toxin injection, surgery and alternative treatments.

Oral drug therapies

Oral drug therapies have limited efficacy in control of the symptoms for cervical dystonia.[31] It includes:

- Trihexyphenidyl (anticholinergic agent) antagonizes cholinergic receptors in the CNS and smooth muscle. It possess antispasmodic action on smooth muscles. Shown to be effective in treating segmental and generalized dystonia.[32]
- Chlordiazepoxide, Clonazepam, Diazepam and Lorazepam (Benzodiazepines) enhance GABA receptors. It has the property of muscle relaxation.[33]
- Mexiletine (antiarrhythmic agent) shows the effectiveness in the treatment of cervical dystonia shown in an open label case study.[34]
- Riluzole is a glutamate believed to modulate glutamate release. Open label data showed success in the treatment of cervical dystonia.[35]
- Baclofen, GABA-B agonist works mainly at the spinal cord level by inhibiting firing of motor neurons. Some reports showed beneficial effects with the treatment of cervical dystonia by infusion of intrathecal baclofen.[36]
- Tetrabenazine, a benzoquinolizine derivative and a presynaptic catecholamine depleting agent acts as a effective and relatively safe agent for the treatment of hyperkinetic movement disorders.[37]
- Other agents like clozapine, olanzapine, valproate & ethanol injection are also providing a partial benefits against cervical dystonia.[38,39,40,41]

Botulinum Toxin Injection

Botulinum toxin serotypes A and B inhibit the release of acetylcholine into the neuromuscular junction. When injected into dystonic muscles, they reduce muscle spasm without systemic side effects. This is the treatment of choice for cervical dystonia, blepharospasm, spasmodic dysphonia, oromandibular dystonia, and limb dystonia,[42] because it provides long-term benefit in 70 to 90 percent of patients. Similar benefit has been seen with either serotype A or B in patients with cervical dystonia. [43] It may also be used in patients with generalized or multifocal dystonia to treat selected muscles. The frequency of neutralizing antibody-mediated resistance to botulinum toxin serotype A has declined since the introduction of a commercial preparation containing a smaller amount of complex protein.[44]

Cohrane Reviews about Botulinum toxins

BoNT treatment for cervical dystonia was analysed in four Cochrane reviews. The first review evaluated BoNTA therapy and included results from 13 randomized, placebo-controlled trials. They were short-term studies (6–16 weeks) of BoNT-A enrolling 680 patients overall. All trials reported a benefit of a single injection cycle of BoNT-A for cervical dystonia, but did not provide controlled evidence of the long-term effects of repeated BoNT-A injections. Enriched trials (using patients previously treated with BoNT-A), suggested that further injections maintained efficacy in most patients. The most frequently reported treatment-related adverse events were dysphagia, neck weakness, local pain at injection site, and sore throat/dry mouth. Most of the adverse events in patients receiving BoNT-A were mild or moderate; no serious adverse events or laboratory abnormalities were associated with the use of BoNT-A.[45] The second review evaluated BoNT-B and included three short-term (16 weeks) studies enrolling 308 participants. All were multicentre and conducted in the USA. All patients included had previously received BoNT-A. A single injection of BoNT-B improved cervical dystonia.[46] A similar

conclusion was reached in a different review, which included the same three trials.[47] The third review compared BoNT-A versus BoNT-B, but no preliminary results were yet available from two ongoing trials.[48] Evidence is currently lacking on direct comparison of the clinical efficacy and safety of BoNT-A versus BoNT-B. The fourth review analysed BoNT-A versus anticholinergics and found only one randomized trial comparing BoNT-A versus trihexyphenidyl in 66 patients with cervical dystonia. The results favoured BoNT-A.[49]

Surgical Management

Surgical therapy remains an option strictly when other treatments fail or become ineffective. Three surgical interventions are available for cervical dystonia: brain lesioning, brain stimulation, and peripheral surgical intervention.

Brain Lesioning

Several targets have been explored in the basal ganglia and thalamus to treat movement disorders since the early 1940.[50] Thalamotomy as a traditional stereotactic therapy for cervical dystonia shows controversial results.[51] Bilateral thalamotomy can be modestly effective to treat symptoms in cervical dystonia but can cause serious adverse effects, including weakness and dysphagia, in contrast with unilateral thalamotomy, which shows less beneficial response but a more favorable safety profile.[52] The posteroventral medial pallidotomy targets the pallidothalamic pathway and is hypothesized to interrupt abnormal neural circuitry involved in CD.[53] Of interest is that most reports show gradual improvements in dystonic patients after pallidotomy over several months.[52] A study has shown significantly better long-term results with pallidotomy compared with thalamotomy for all patients with dystonia, including CD.[54] Some studies reveal that thalamotomy is more effective in secondary dystonia than primary dystonia.[54,55,56]

Deep Brain Stimulation

Long-term electrical stimulation of the globus pallidus internus (GPi) or the thalamus has been applied in patients with various features of dystonia, mainly those who do not achieve adequate benefit with medical treatment. At this time, the consensus is that patients with primary (familial or sporadic) generalized or segmental dystonia and patients with complex CD are the best candidates for pallidal DBS.[57]

Deep brain stimulation was used initially in the 1960s to control chronic pain, and decades later it was used for various movement disorders such as Parkinson disease, tremor, and dystonia.[58] Posteroventral lateral globus pallidus internus is a target used for deep brain stimulation in dystonia and also Parkinson disease,[57,59,60] but for dystonia, the initial settings require higher voltages and pulse widths, followed by a gradual increase of intensity.[61]

Alternative treatments

In patients with loss of benefit from botulinum toxin treatment and mostly directional torticollis or laterocollis (eg, isolated head posture to one side), selective peripheral denervation procedures are considered the first-line alternative treatment.[62] These procedures include extradural ramisectomy and selective denervation of the dorsal rami of the cervical nerve roots (C1–C6), myectomies, and myotomies (in most cases, the sternocleidomastoid or muscles of the scaleni group), dependent on the pattern and location of dystonic muscle activity.[63] Peripheral denervation surgery, however, is not indicated in a subset of CD patients including those with head tremor and myoclonus, marked phasic dystonic movements, sagittal and lateral translation, anterocollis, and combined complex forms of CD.

Cervical spinal cord stimulation has been explored for treatment of patients with CD in the 1980s, but meanwhile it has been completely abandoned. Based on the gate, control theory that sensory input might modify sensory processing and on the hypothesis that sensorimotor integration is disturbed in dystonia patients underwent chronic high-frequency stimulation. Beneficial results were reported in some patients with CD.[64]

Conclusion

Cervical dystonia is the most common form of adult – onset focal dystonia. The patients with cervical dystonia have been suffering from involuntary twisting and turning of the neck caused by abnormal involuntary muscle contractions. Eventhough pathophysiology of cervical dystonia is still not clear, several studies revolve around the involvement of central and peripheral neural

mechanisms. Oral drug therapies have only limited efficacy to treat the cervical dystonia. But both Botulinum toxin serotypes A and B has showing compromising benefits in the treatment of patients with cervical dystonia without producing systemic side effects. When the treatments are ineffective or fails surgery is the final option.

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