



Treatment Approaches to Cervical Dystonia

Botulinum toxins are effective treatment.

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Dystonia is a movement disorder characterized by intermittent or sustained muscle contractions



causing abnormal, frequently repetitive movements and postures.¹ Cervical dystonia (CD) is also known as spasmodic torticollis and affects the neck and shoulder muscles. It is the most

common isolated focal dystonia and can vary in appearance, including a lateral head tilt (laterocollis), head flexion (anterocollis), head extension (retrocollis), or a combination of these.

Etiology and Diagnosis

Primary CD may be idiopathic or, in approximately 12% of cases, hereditary. Secondary CD is caused by another pathology that may be inherited or acquired; secondary causes include medication adverse effects, brain or cervical spinal cord structural lesions, vascular injury, or neurodegenerative diseases (eg, Huntington disease [HD] or Parkinson disease [PD]). CD is more common in women than men, with a prevalence of 5 to 20 per 100,000 individuals.²

People with CD may experience rigidity and pain from the contraction of the muscles, usually opposing agonist and antagonist muscles. Pain is often the main reason patients seek treatment for cervical dystonia and approximately two-thirds of CD patients require analgesics during the course of the disease.^{3,4} In a large survey of people with CD, 66% of patients reported feeling a significant amount of pain.⁴ In other studies pain was reported in up to 90% of cases.⁵

Patients report a diffuse pain over the neck and shoulders that radiates to the side of head deviation. There is also evidence for abnormal central processing of painful stimuli in patients with CD.^{6,7} A recent study found that the descending pain inhibitory control may be deficient in patients with CD compared to people without painful conditions and people with blepharospasm.⁶ Orthopedic complications, including spondylosis, disc herniation, fractures, radiculopathies, and myelopathies may also cause pain in people with CD.⁸

The diagnosis of CD is difficult to make, and people may be seen by multiple providers before being referred to a movement disorder specialist.⁶ Symptoms are often described nonspecifically such as a pulling in the neck or deviation of the head, such that incorrect diagnoses (eg, arthritis, cervical radiculopathy, psychiatric conditions, or even temporomandibular dysfunction) may be made at the initial presentation.^{4,9-11}

Pharmacologic Treatment

Botulinum Toxin Injections

Botulinum neurotoxins are the only treatment for CD approved by the Food and Drug Administration (FDA) and are the treatment of choice, although multiple oral medications are also used frequently (discussed later in this article).^{5,12} There are 4 botulinum neurotoxins approved for treatment of CD (Table). Efficacy depends on the dose used, the injection site in the affected muscle, experience of the injecting clinician, and managing expectations with discussion of symptoms before treatment. It is noteworthy that the toxin formulations are not interchangeable—the response to toxins may vary from patient to patient and even between various focal dystonias. Injections are frequently guided by EMG, which is useful to identify activated muscles to and locate the most active site of contrac-



TABLE. AVAILABLE BOTULINUM TOXINS FOR TREATMENT OF CERVICAL DYSTONIA

Agent	Trade name	Formulation	Notes
Onabotulinum-toxinA	Botox	Powder form reconstituted 1:1 to 1:2 in normal saline	
Abobotulinum-toxinA	Dysport	Powder form reconstituted in normal saline 1:1 to 1:2 depending on desired dose	Greater spread may lead to more diffuse distribution
Incobotulinum-toxinA	Xeomin	Powder reconstituted in saline 1:1	No complexing proteins, which may lead to more efficacy and reduced risk of antibody formation or sensitization ¹³
Rimabotulinum-toxinB	Myobloc	Liquid 500 U/0.1 mL	Acidic pH can cause more discomfort on injection

tion, as well as aiding in locating deeper muscles.

Approximately 50%-90% of patients experience improvements in dystonic symptoms and dystonia-related pain with botulinum toxin.¹⁴⁻¹⁶ Approximately 70% of patients report pain relief after 3 treatments with botulinum toxin injections with a mean time to pain relief close to 7 days, although level of pain relief achieved depends on the initial pain level.⁵ Improvements in pain can be seen after 1 to 14 days with a peak response between 2 to 6 weeks after the injections that usually wears off after 10 to 12 weeks.¹⁴

Pooling the results from 3 randomized controlled trials, a systematic review showed mean change from baseline to week 2 to 4 was 0.83 TWSTRS units higher (1.75 lower to 0.09 higher) with botulinum toxin B compared with botulinum toxin A group, and the authors concluded that there may be little or no difference on CD-associated pain (low level of evidence).¹⁷ A randomized double-blind multicenter noninferiority trial compared the efficacy, safety, and duration of onabotulinumtoxinA with rimabotulinumtoxinB in patients with CD and showed rimabotulinumtoxinB treatment resulted in significantly higher response rates on TWSTRS-Pain score at week 4 compared with onabotulinum toxin (59% vs 36%; $P < .05$). Mean TWSTRS-Pain scores decreased from 9.4 at baseline to 6.6 at week 4 with rimabotulinumtoxinB vs 10.4 at baseline to 8.5 at week 4 with onabotulinumtoxinA, although this difference did not reach statistical significance.¹⁸ Given similar efficacy and data from evidence-based reviews,^{7,8} the type of toxin used is frequently based on clinician or insurance preference.

Mechanism of Action. Botulinum toxin acts on CD by reducing excessive tone through acetylcholine inhibition to alleviate painful muscle spasms. Muscle atrophy is observed after 2 weeks with subsequent recovery of approximately 80% of muscle mass over the next 12 to 14 weeks is thought to contribute to decompression of nerves, increased tissue perfusion, and improved muscle metabolism.¹⁰ Pain relief, however, is not associated with dose, suggesting pain improvement is not related only to

muscle weakening.¹⁷ A central mechanism of pain relief is also hypothesized considering that botulinum toxin is associated with partial normalization of brain activity and connectivity within the basal ganglia and the sensorimotor network in patients with CD.¹⁹

Dose and Administration. The total dose of botulinum toxin used for CD varies with serotype and the specific botulinum toxin used and there is no consensus on dose because treatment requires individualization. Currently, there is little evidence to suggest significant differences between the available botulinum toxin A and B. The majority of trials evaluating botulinum toxin A used the Tsui scale as the primary outcome measure, which does not incorporate a pain item, whereas studies evaluating botulinum toxin B used the TWSTRS scale, including the pain subscale.¹⁷

Oral Medications

Anticholinergics. Benefits of anticholinergic treatment on CD and associated pain are well described.²⁰ In practice, anticholinergics are titrated up until benefit is seen or dose-limiting adverse effects (eg, dry mouth, urinary retention, blurred vision, confusion, hallucination) occur. Initial doses of trihexyphenidyl are low (1-2.5 mg/day) and the minimal dose providing adequate benefit should be used.

Baclofen. The GABA_B receptor agonist baclofen inhibits release of excitatory neurotransmitters glutamate and aspartate and is effective in alleviating skeletal muscle spasticity and pain. However, as little as 11% of patients with CD treated with baclofen have a good response,²¹ and adverse effects of fatigue, dizziness, gastrointestinal complaints, and urinary frequency limit use. Intrathecal baclofen has been reported to be more effective in patients with CD. Baclofen should always be tapered when discontinued because there is risk of withdrawal symptoms including seizures if stopped abruptly. Baclofen can also be administered intrathecally and significant improvement of CD and pain related to CD has been reported with baclofen pump in 2 patients with CD.²²



Benzodiazepines. Benzodiazepines also inhibit GABAergic transmission and have muscle relaxant properties that may be beneficial in up to 21% of people with dystonia.^{20,23} Benzodiazepines may be useful in CD with predominant head tremor.²³ Benzodiazepines are associated with a risk of misuse and dependence and adverse effects include sedation and confusion, therefore these drugs should also be tapered gradually.

Dopaminergic Agents. Paradoxically, patients with CD may report benefit from treatment that either increases or decreases dopaminergic neurotransmission. Results, however, have been less robust than those observed with the anticholinergic drugs. A review of the literature on the use of dopamine receptor antagonists and dopamine-depleting agents showed a response rates between 9% and 46%, and tetrabenazine has been successfully used in patients with tardive dystonia at doses of 75 to 250 mg/day.²⁴ Side effects include parkinsonism, sedation, hypotension, depression, and there is a risk of tardive dyskinesia associated with dopamine receptor blockers.

Adjunctive Analgesics. The therapeutic approach to adjunctive treatment of pain in CD should be tailored to individual needs. Opioids should be avoided in general, and potential risk factors for substance abuse in people with CD patients include male sex, age under 55, and comorbid psychiatric conditions.²⁵

Nonpharmacologic Treatment

Deep Brain Stimulation

Deep brain stimulation (DBS) of the globus pallidus internus (GPi) may be an effective treatment for CD.^{26,27} In a single-site, open-label study of 10 people who had DBS of the GPi, there were significant improvements in the TWSTRS total score and in the subscore for pain (50.5%) at 32 months with 6 of the 10 considered to have good response.²⁷ The mechanism of DBS in CD treatment is unknown. In a single case report, pain improvement with DBS of the globus pallidus internus (GPi) could be temporally dissociated from motor and postural improvement, suggesting that dysfunction of motor and somatosensory circuits in CD is not always in parallel.²⁸

Physical Therapy

There are no randomized clinical trials to assess overall efficacy of physical therapy for CD. Improvements in pain associated with CD have been reported with various adjunctive physical therapy techniques, including EMG biofeedback training, relaxation, stretching, postural exercises and electrotherapy, however.^{29,30} Although costs were decreased and patient-perceived effects of physical therapy and general health perception were more positive with adjunctive specialized physical therapy emphasizing motor

training to correct dystonic postures compared with adjunctive regular physical therapy, no objective difference between the 2 methods was observed.³⁰

Massage

Some patients with cervical dystonia find regular massages to be helpful, although data regarding efficacy is limited. A small randomized controlled trial reported improvements in pain and prolonged duration treatment effect after a 6-weeks of physical therapy and massage with botulinum toxin treatment compared with botulinum toxin alone.³¹

Psychotherapy

Behavioral interventions, including cognitive behavioral therapy (CBT) and mindfulness may improve quality of life for people with chronic pain.^{32,33} Further studies are needed to explore the benefit of behavioral interventions in CD.

Complementary and Alternative Treatments

Acupuncture

There is limited data for use of acupuncture as adjunctive treatment of CD. Studies have found that acupuncture is safe and feasible as adjunctive therapy although sample sizes are small.^{34,35} In a large study of acupuncture for chronic neck pain that included a cohort randomly assigned to no acupuncture, greater pain relief was seen in those who received acupuncture.³⁶

Cannabis

There has been a rise in use of medical marijuana for various neurologic conditions over the last decade, including CD, but as per American Association of Neurology (AAN) guidelines, there is insufficient evidence to demonstrate if Cannabis or the synthetic form of Δ^9 -tetrahydrocannabinol, dronabinol, is effective treatment for CD.³⁷

Dry Needling

Dry needling involves penetrating the skin, subcutaneous tissue, and muscle with a needle, without using an anesthetic to mechanically disrupt tissue.³⁸ Dry needling has been used several musculoskeletal conditions targeting myofascial trigger points, which are hypersensitive areas in palpable taut bands of muscle.³⁹ Although there is limited evidence that dry needling may be effective in the short term for musculoskeletal neck and back pain,^{38,40} data for treatment of CD specifically is lacking.

Conclusion

CD is a focal dystonia involving the muscles of the neck and shoulders, and pain resulting from sustained contrac-



tion of opposing muscles is often the reason people seek treatment. Botulinum neurotoxins are the only FDA-approved treatment for CD and are the treatment of choice. Botulinum toxins do not cause systemic symptoms (eg, sedation) that may be seen with oral pharmacologic therapies. Physical therapy, massage therapy, and cognitive behavioral therapy may have benefit as adjunctive, but not primary, treatment for CD. There is little evidence for alternatives therapies (eg dry needling or acupuncture). Further research is needed to compare efficacy of available botulinum neurotoxins on pain reduction and long-term benefits. ■

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