CERVICAL DYSTONIA: CLINICAL ASPECTS AND TREATMENT WITH BOTULINUM TOXIN

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Defining the disorder
The word dystonia stems from the ancient Greek, meaning altered muscle tone. Dystonia refers to a syndrome of involuntary sustained or spasmodic muscle contractions involving co-contractions of the agonist and the antagonist, that often occur in a repetitive and patterned manner. It may involve a single body part (focal dystonia); two or more contiguous regions of the body (segmental dystonia); noncontiguous body parts (multifocal dystonia); segmental crural dystonia and at least one other body part (generalized dystonia); half of the body (hemidystonia). This article addresses cervical dystonia (torticollis), the most common presentation of focal dystonia, often leading to painful twisting movements of the head and neck.

Terminology:
The term torticollis is derived from the Latin words tortus for twisted and collum for neck. It refers to dominating twisting spasmodic features of the disorder. Many (Jankovic et al, 1991 and Chan et al, 1991) prefer to avoid the popular term spasmodic torticollis and suggest the term cervical dystonia (CD) as a more appropriate, because many patients have neither simple torticollis (clinical term for rotation) nor spasmodic movements.

Pathophysiology:
Idiopathic CS is believed to arise from basal ganglia circuits dysfunction caused by an abnormal biochemical process. Low levels of metabolites of dopamine have been found in the cerebrospinal fluid (CSF) and modest improvements reported with levodopa as well as traditional neuroleptics, both of which possess equal D1 and D2 receptor-binding properties. Functional imaging studies (SPECT, PET) have shown reduced D2-receptor binding in the basal ganglia implying that underactivity occurs in the D2 dopamine receptors of the indirect pathway causing disinhibited thalamocortical output and dystonic postures. Relative imbalance between direct (D1-related) and indirect (D2-related) pathways may explain transient improvements and failure of both levodopa and traditional neuroleptic agents, which initially may reduce D1 activity and eventually both D1 and D2 activity in both pathways.

Symptomatology:
Patients with CD present with involuntary sustained or spasmodic muscle contractions, typically in a relatively patterned manner. The most common positions of head and neck can be described as:
- laterocollis: the head being tipped toward the shoulder
- rotational torticollis: the head being rotated along the longitudinal axis
- anterocollis: the head being forward flexed
- retrocollis: the head being hyperextended backward
However, very often these movements are combined in a pattern, unique to the patients. Torticollis with rotation of the head is the most common individual pattern followed by laterocollis and then retrocollis, with anterocollis being the
rarest form (Consky et al, 1994). However, very often these movements are combined in a mixed pattern, unique to the patient.
Muscle spasms and contraction may result in a limited range of motion of the head, in neck pain and headache, in stiffness and swelling of the neck muscles, in clonic and tremulous head movements, in changed posture of the shoulder. In dystonic CD, patient may alleviate the disorder with various sensory tricks (e.g. touching or holding the chin, leaning the head against the wall, bending forward, or lying down). About 30% to 40% of patients describe a brief beneficial effect of sleep with symptoms resuming within minutes of assuming the upright posture (Weiner et al, 1989).

Epidemiology:
Although CD can occur at any age, it most often begins between the ages of 40 and 70. Women are more likely to be affected by CD than men (Jankovic et al, 2007). Approximately 3 in every 10,000 people are believed to suffer from this dystonic disorder. If family history is present for CD or some other movement disorder, the patient is at higher risk of developing the disorder.

Causes:
In determining the cause of a ‘twisted neck’, one has to separate dystonic from nondystonic form. This separation will be of great importance also when planning a possible treatment with botulinum toxin (BTX) as nondystonic torticollis is not alleviated by BTX. Generally torticollis can be classified as:

- **inherited** - genetic,
- **congenital**: e.g. birth trauma, fibrosis in the muscle, intrauterine malposition, SCM cysts, vertebral anomalies, odontoid hyperplasia, spina bifida, hypertrophy or absence of cervical musculature, Arnold-Chiari syndrome. Congenital torticollis has a prevalence of less than 2% (Canale 1998)
- **acquired** (head, neck or shoulder injuries; infections, structural causes, such as odontoid fracture, cystic mass, cervical adenitis; antipsychotic and anti-nausea drugs).

Atlantoaxial rotary subluxation (AARS) of C1 on C2 may mimic torticollis. It occurs after minor trauma, pharyngeal surgery, an inflammatory process, or upper respiratory tract infection. In these conditions retropharyngeal edema may lead to abnormality of atlantoaxial structures, resulting in the rotational deformity. In can be distinguished from congenital muscular torticollis, because head tilts away from the affected SCM muscle.

**Compensatory torticollis**: Torticollis may often occur due to a compensatory mechanism for another disease: e.g. head tilt in an essential head tremor or congenital nystagmus; for diplopia secondary to an ocular muscle, nerve palsy or posterior fossa tumor.

**Acute torticollis**: this form of torticollis is particularly important for a clinician, as it does imply certain causes and specific treatment (with BTX in many cases not indicated). The most common type is wry neck, developing from simply sleeping in an awkward position. It can also be the result of trauma to head and neck. The condition is self-limited with symptoms usually resolving in a week or two, but a chronic or persistent form may reappear weeks after the quiescent interval. Acute torticollis may often be caused by ingestion of
certain medications (eg, traditional dopamine receptor blockers, metoclopramide, phenytoin, levodopa, carbamazepine), resulting in dramatic dystonic reactions causing not only CD, but also trismus, fixed upper gaze, clenched jaw, difficulty with speech, generalized spasms. Management of drug-induced CD can sometimes be managed merely by stopping the offending medication; if necessary, anticholinergics, diphenhydramine or benzodiazepines should be prescribed and the disorder usually quickly resolves.

If the condition occurs without a known cause, it is called idiopathic torticollis or idiopathic CD. It occurs in patients with a genetically determined susceptibility to environmental toxins, which, when encountered in threshold doses, activate cortico-striatal neuronal circuits deterioration.

**Diagnostic Tests**
The choice of diagnostic tests depends on the diagnostic (un)certainty:

- **Imaging of the cervical spine** - including plain cervical radiographs, computed tomography (CT) scans, or magnetic resonance imaging (MRI) – is needed to evaluate for bony trauma, suspected C1-C2 subluxation, congenital bony abnormalities, osteomyelitis.
- **MRI of the brain** may be needed to exclude tumors, retropharyngeal abscess, epiglottitis, spinal epidural abscesses and hematomas.
- **Eye examination** are needed particularly in children.
- **EMG** may support the diagnosis of dystonia or tremor and may be helpful in determining which muscles are most affected.

**Prognosis & Quality of Life:**
Although CD does not shorten the life span of affected individuals, there are several areas that may require additional treatment: (i) chronic pain due to dystonia or strain in attempts to compensate for abnormal postures, (ii) cervical spondylosis from chronic abnormal dystonic posture, which can lead to radiculopathies and/or spinal stenosis and (iii) stigma, leading to social embarrassment or social isolation with depression.

CD may dramatically worsen quality of life (QOL), as reported by Camfield et al. (2002). In this study patients with cervical dystonia were compared with patients with other neurological conditions: for energy/vitality, CD patients had scores comparable to those of stroke patients; CD pain scored similar to pain in Parkinsonism; and for physical role limitation, patients with CD scored significantly lower than both groups, despite having higher physical function scores.

**Treatment:**
The standard first line treatment for cranio-cervical dystonia (Ceballos Baumann et al, 2001; Albanese et al, 2006; Simpson et al, 2008;) is periodic administration of botulinum toxin to the affected muscles in a tertiary specialized centre; BTX treatment may be combined with physiotherapy. With BTX, large majority of patients may avoid pharmacological and surgical treatments.

*Before treating CD with BTX therapy for the focal dystonias make sure that*
  - you have thorough understanding of the toxin itself
- you are familiar with various preparation and advantages / disadvantages of various dilutions
- you have practical knowledge of typical dosages of selected preparation;
- you have practical knowledge of the neck functional anatomy - identify landmarks, such as the mastoid process, occiput, posterior and transverse spinous processes, and surface landmarks (basic electromyographic skills and understanding the kinesiology of different muscles may be of considerable help)

Select patients according to clearly set treatment goals. Do you intend to
- improve range of motion?
- decrease pain?
- decrease spasms?
- improve cosmesis?

What and how to inject?
Although selection of muscles and doses is very individual, there are certain general principles in choosing which muscle to inject and what dose to use (Walker 2003)
- muscles normally involved in the primary movement of the head and neck should be given priority
- muscles showing greater EMG activation during the primary movement should be given priority
- larger muscles should be given priority over smaller muscles
- muscles less likely to be associated with complications, including discomfort, should be given priority over muscles less likely to be involved.
- previously uninjected muscles should be given priority over injected muscles, if they are involved

The optimal dose of botulinum toxin (BTX) is the least amount of BTX needed to achieve a predetermined outcome. In principle:
- larger or hypertrophic muscles in general should be given more toxin
- muscles whose primary actions are aligned most closely with the dystonic movement should be given more toxin
- muscles that show more activation by EMG should be given more toxin
- muscles that are more superficial and more posterior (less likely to be painful or to have side effects, such as dysphagia)
- muscles that have never been previously injected but that are significantly involved should be given more toxin than muscles that have been injected.

For first-time injections, factors that favor the use of lower doses are smaller body size, female sex, need for injections of anterior cervical muscles (these injections are at greater risk for causing swallowing problems), milder forms of dystonia, experience of the injector, and risk aversiveness of the patient (Walker 2003)

Muscles are identified by clinical evaluation & needle movement & EMG.
The patient should be carefully examined in different positions: (a) by positioning the head in a comfortable upright posture, sitting and walking; (b) by passively adjusting the head and searching for additional neck extension, flexion, and rotation; (c) by actively flexing, extending, rotating and tilting the neck; (d) by palpating for spasms, hypertrophy and any point tenderness. The patient should then be asked to walk and the head position observed and recorded. The head position that is most abnormal is used to select the muscles for injection. EMG is recommended to localize involved muscles as it ensures to a larger degree that the needle is located in the affected muscle.

The most commonly injected muscles include relatively superficial muscles (sternocleidomastoid, trapezius, splenius capitis, levator scapulae, and scalene complex). In addition to superficial neck muscles, deep-cervical muscles (the prevertebral muscles for primary neck flexion, lateral vertebral muscles for shoulder elevation and head tilt and a posterior group of muscles for neck extension) may be involved additionally. However, injections of botulinum toxin given without the use of EMG needle guidance are effective in the majority of patients.

**What to expect?**
At the follow up or at the next visit patient should be asked about:
- response to therapy
- latency
- duration
- peak effect
- side effects
- any observed change pattern of abnormal movement

Up to ninety percent of patients will report some improvement in the postural deviation. In published studies 76-93% of patients reported pain relief following treatment with BTX. Latency between injections and onset of clinical benefit is around 7 - 10 days. Duration of effect is 3-5 months.

In the case of no response, the following possibilities should be considered:
- insufficient dose?
- wrong muscles?
- faulty preparation?
- improper handling?
- antibodies?
- primary unresponsiveness?

The most common adverse effects (Greene et al 1990) include neck weakness (20-30%), dysphagia (10-20%), and local pain (10%). They are transient and usually resolve spontaneously within 2-3 weeks. Serious adverse effects occur rarely and include severe dysphagia, respiratory compromise and pneumothorax, brachial plexopathy (Glanzman et al 1990) and polyradiculoneuritis (Burguera et al 2000) and systemic botulism-like reaction to botulinum toxin type A injections (Bakheit et al 1997).
Oral medications Two classes of therapeutic agents are worth trying: anticholinergics (benztropine and trihexyphenidyl) and benzodiazepines (particularly clonazepam, esp. in patients with myoclonic or jerky forms of dystonia). 1-week trial of Sinemet is also worth trying, but not very likely to be beneficial. Anticonvulsants and antispasticity agents have been reported to be successful in occasional case reports.

Surgical treatment: Although surgical treatment is not the topic of this article, a recent report on DBS is worth mentioning. Volkman and colleagues (2014) conducted a randomized, sham-controlled trial to ascertain whether bilateral DBS of the posteroventrolateral GPi would be effective for CT patients with a history of a poor response to oral treatment at the maximal effective dose and not received BTX for at least 6 months. The primary outcome showed a 26% improvement in the neurostimulation group at 3 months compared with 6% in the sham stimulation group (p = .0024) suggesting that DBS can be effective for refractory cases of cervical dystonia.

REFERENCES AND RECOMMENDED LITERATURE


Dressler D, Tacik P, Adib Saberi F. Botulinum toxin therapy of cervical dystonia: comparing onabotulinumtoxinA (Botox®) and incobotulinumtoxinA (Xeomin (®)). J Neural Transm. 2014 Jan;121(1):29-31


