Spasmodic Torticollis: Medical and Botulinum A Toxin Treatment

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The exact pathophysiologic mechanisms of spasmodic torticollis and other idiopathic torsion dystonias remain largely unknown. Thus, a variety of drugs have been used alone or in combination on an empirical basis to treat these disorders, but to date none have efficacy that is proven and consistent. The drugs in use include anticholinergics, benzodiazepines, dopaminergics and dopamine antagonists with variable degrees of clinical improvement. Botulinum toxin A injection treatment for spasmodic torticollis is safe and efficacious with minimal adverse effect. However, it is expensive and beneficial effects are short-lasting. Only when a spasmodic torticollis patient’s symptoms are refractory to combined treatment, using various drugs and Botulinum toxin injections, should the patient be considered a candidate for neurosurgical procedures.

Key Words: Spasmodic torticollis, dystonia, anticholinergics, dopaminergics, dopamine antagonists, botulinum toxin

Spasmodic torticollis (ST) and other idiopathic torsion dystonias are characterized by dystonic posturing and other abnormal hyperkinetic involuntary movements involving the head, neck, trunk and/or limbs. ST is the most common type among idiopathic torsion dystonias and produces stereotypical deviation of the head and neck to an abnormal position. Unlike Parkinson’s disease and Huntington’s chorea, where anatomical, neurochemical and neuropathologic information provides a rational basis for medical treatment, such an understanding of knowledge in ST is lacking (Lal 1979). Recent evidence, however, implicates altered neuro-transmitter functions involving noradrenergic pathways in the brain stem (Horny kiewicz et al. 1986; Jankovic et al. 1987).

The idiopathic torsion dystonias are of three types according to the involvement pattern-generalized, focal and segmental (Fahn 1988). Generalized dystonia usually occurs in childhood, is progressive, and eventually involves all extremities (e.g., dystonia musculorum deformans). The focal dystonias, of which ST is one (writer’s cramp is another), usually remain focal but may spread to involve other areas (segmental dystonia). Only rarely does it is progress to generalized from.

Clinical manifestations of ST vary considerably from patient to patient. The disorder usually begins after age 30, insidiously and progressively involving one or both sides of the head and neck over several years. Temporary or sustained improvement or remission occurs spontaneously in five to 20 percent of patients, but permanent remission is very rare (Jahanshahi et al. 1990; Lowenstein and Aminoff 1988).

In this report, we review medical management of patients with ST, particularly with regard to the use of botulinum A toxin.

Drug Treatment

As rational basis for therapy is lacking, many different drugs have been used on a non-specific empirical basis, alone or in combination in treatment of
ST. A number of drugs have been reported to be of some benefit in a variable number of patients with ST (Eldridge 1970; Fahn and Marsden 1987). However, to date, there has been no single drug with consistently-proven efficacy.

**Anticholinergics**

Trihexyphenidyl (Artane) is usually a first-line drug and may bring modest improvement in symptoms (Fahn 1983; Burke et al. 1986). Larger dosages in excess of 30 mgs per day were associated with more clinical improvement (Burke et al. 1986) and were better tolerated in children than in adults. In my experience, most patients developed intolerable common side effects following such high dosages, such as dryness of the mouth, blurred vision, memory impairment and confusion. To avoid these dose-limiting side effects, trihexyphenidyl should be started at a small dosage (2 to 4 mgs per day) and gradually increased to the maximum tolerable dosage. It is well known that benztropine (Cogentin) given intravenously relieves the acute dystonic reaction sometimes associated with phenothiazine use. In ST, no such dramatic response occurs. Combined use of small dosages of trihexyphenidyl and other drugs such as amantadine (Symmetrel) and haloperidol (Haldol) is often beneficial in ST patients (Lal et al. 1979; Gilbert 1972).

**Dopaminergics**

Apomorphine, a potent dopamine receptor agonist, has been reported to transiently relieve ST symptoms (Lal et al. 1979; Tolosa 1977). Anecdotal cases of remarkable improvement with the use of levodopa were reported (Coleman 1970; Chase 1970), but clinical results with levodopa have been largely disappointing in ST patients (Lang 1988). Green et al. reported favorable response to levodopa and dopamine agonists in dystonia patients who failed to obtain adequate response from anti-cholinergics (Green et al. 1988). Clinicians should be aware of the Segawa variant dystonia of childhood in which case dramatic improvement of symptoms is noted with the use of levodopa (Segawa et al. 1976). Dopamine agonists provide similar clinical results as levodopa in ST patients (Quinn et al. 1985; Lees et al. 1976).

**Dopamine antagonists**

Dopamine antagonists are regarded as the second most effective drugs after anti-cholinergics for ST patients. Significant improvement has been noted in more than 35 to 50 percent of ST patients with the use of haloperidol (Gilbert 1972; Green et al. 1988). Marsden, Marion and Quinn observed greater benefits with the combined use of haloperidol, tetrabenazine (a dopamine depletor) and anticholinergic (Marsden et al. 1984). However, chronic use of dopamine antagonists may induce Parkinsonism and/or tardive dyskinesia. Emergence of these side effects may mask ST symptoms and, therefore, throughout treatment with these drugs, patients should be carefully observed for these side effects.

**Benzodiazepines**

Diazepam (Valium) and other benzodiazepine derivatives have been widely used for non-specific treatment of ST symptoms. Beneficial effects may be related to anti-anxiety and anti-muscle spasm effects. Excellent results were observed by Bianchine and Bianchine (Bianchine and Bianchine 1971), and Ziegler (Ziegler 1981). In an attempt to increase brain levels of GABA, Korein et al. used a combination of isoniazid, pyridoxine, diazepam and L-Glutamine in ST patients (Korein et al. 1981). Of the 14 patients, seven improved to varying degrees. Baclofen, a GABAergic, was associated with significant improvement in only 11 percent of the 27 patients with ST (Green et al. 1988).

**Botulinum Toxin-A (Botox)**

The most important therapeutic development in the treatment of ST has been the use of Botox injections. The American Academy of Neurology declared its position regarding the clinical usefulness of Botox in the treatment ST in a statement in 1990 (Assessment, 1990). Its conclusion was that Botox injection treatment was a safe and efficacious modality for the treatment of ST.

Botox is produced by Clostridia botulinum. Type A is the most common cause of botulism and one of seven antigenically-distinct toxins (Simpson 1981). Botox acts presynaptically by preventing the calcium-dependent release of acetylcholine at neuromuscular junctions and causes muscle paralysis. Botox (Oculinum), provided as a crystallized, freeze-dried residue of the toxin in a concentration of 50 ng (140 U) per vial is stored at -20 degrees Celsius until used. One unit of Botox is equivalent to the amount of toxin found to kill 50 percent of female Swiss-Webster mice (LD-50) (Scott 1981). When in-
jected locally into the muscles, Botox causes focal muscle weakness related to local diffusion of the toxin. Although systemic effects are demonstrated using single fiber electromyography after Botox injections to the neck muscles, no serious consequences of these changes have been documented (Olney et al. 1988).

In ST patients, Botox is injected directly into the muscles with dystonic symptoms and signs. Doses in treating ST range from 50 to 200 units per treatment and are determined by both the site of involvement and severity of dystonic symptoms. There are a number of uncontrolled (Tsui et al. 1985; Brin et al. 1987; Stell et al. 1988; Jankovic and Schwartz 1990) and controlled (Tsui et al. Gelb et al. 1989; Greene et al. 1990; Jankovic and Orman 1987) studies assessing the clinical results of Botox injection treatment in ST patients. They reported significant improvement in 53 to 90 percent of treated patients. In Gelb's studies (Gelb et al. 1989), 80 percent of the treated patients reported subjective improvement, but no objective benefit was observed. Greene et al. (Jankovic and Schwartz 1990) reported statistically-significant improvement in both subjective and objective parameters in Botox-treated ST patients, and there were no serious side effects. Average duration of improvement was 11 weeks (Jankovic and Schwartz 1990). Clinical resistance to therapy has been noted in a small number of patients receiving repeated injection treatments. Circulating antibodies have been detected in these patients (Tsui et al. 1988). Pain, which is seen more often in ST than in other forms of dystonia, improves significantly, at times dramatically, in the majority of ST patients treated with Botox. Dysphagia and neck weakness are the most common side effects (Tsui et al. 1985; Brin et al. 1987; Stell et al. 1988; Jankovic and Schwartz 1990; Tsui et al. 1986; Gelb et al. 1989; Greene et al. 1990; Jankovic and Orman 1987) but they are usually transient and rarely a source of significant disability.

Practical Considerations/Recommendations

Prior to beginning drug treatment in a patient with ST, the exact etiology should be carefully and systematically sought. The need for the treatment of idiopathic ST should be carefully examined also, since clinical adverse effects of the drugs used are often worse than the ST symptoms. Indeed, minimal ST symptoms may not warrant drug therapy. It is necessary for the physician to appreciate the differences among individual patients and to realize that no drug treatment will be satisfactory to some ST patients. Chronic ST symptoms are often associated with considerable emotional problems (anxiety and depression) that require supportive psychotherapy and other counseling for resolution. Patients should be reassured about the basically benign nature of the disorder, and told of the fact that spontaneous remission occurs in significant percentage of ST patients. Relief or alleviation of emotional problems, along with judicious use of drugs, contributes to improvement.

In the majority of ST patients, physical therapy along with biofeedback and transcutaneous electrical nerve stimulation (TENS), may provide added benefit (Gildenberg 1981).

In my experience, trihexyphenidyl, benzodiazepine derivatives, amantadine and haloperidol generally provide better results than do other drugs. For mild ST patients in need of drug therapy, trihexyphenidyl in low dosages of 2 to 5 mg per day gradually increased up to 30 mg per day; dizepam (5 to 15 mg per dy); amantadine (100 to 300 mg per day); or varying combinations of these drugs can be used. If ST symptoms are moderately severe and include constant dystonic neck muscle contractions, haloperidol (1 to 8 mg) should be considered. Patients should be closely monitored for side effects of drug treatment; this is particularly important with the use of haloperidol, which has the potential for a variety of extrapyramidal side effects, including secondary Parkinsonism and tardive dyskinesia. Improvement with drug treatment is often of short duration, and dosage adjustment as well as changes in medication often becomes necessary.

Only when drug therapy fails to provide satisfactory improvement, should Botox injection treatment be considered. While Botox treatments is safe and efficacious in the majority of ST patients, it is very expensive and provides benefit for only two to three months. Botox should be used in combination with drug therapy. Dosage of Botox ranging from 100-200 IU should be given directly into the several sites of dystonic muscles in divided dosages.

Chronic dystonic contraction of the neck muscles may also cause or increase the severity of degenerative changes in the cervical spine, resulting in cervical radioculopathy which in return may require further evaluation and appropriate treatment.

With symptomatic improvement, many ST pa-
tients continue to function well. Only when symp-
toms are or become refractory to drug and Botox
treatment, should such neurosurgical pro-
cedures as cervical or peripheral nerve rhizotomy
or stereotactic thalamotomy be considered.

REFERENCES

Lal S: Pathophysiology and pharmacotherapy of spas-
1979
Hornykiewicz O, Kish SJ, Becker LE et al: Brain neuro-
transmitters in dystonia musculorum deformans. N
Jankovic J, Svendsen CN, Bird ED: Brain neurotransmit-
ters in dystonia (letter). N Engl J Med 316: 278-279,
1987
Fahn S: Concept and classification of dystonia. Adv
Press, 1988
Jahanshani M, Marion M, Marsden CD: Natural history
of adult onset idiopathic torticollis. Arch Neurol 47:
548-552, 1990
Lowenstein D, Aminoff MJ: The clinical course of spas-
modic torticollis. Neurology 38: 530-532, 1988
Eldridge R: The torsion dystonias: Literature review and
genetic and clinical studies. Neurology 20 (suppl. 2):
1, 1970
Fahn S, Marsden CD: The treatment of dystonia. Move-
ment Disorders 2. Butterworths, p359-382, 1987
Fahn S: High dosage anti-cholinergic therapy in dystonia.
Neurology 33: 1255-1261, 1983
Burke RF, Fahn S, Marsden CD: Torsion dystonia: A
Lal S, Hoyte K, Kiely ME et al: Neuropharmacological in-
vestigation and treatment of spasmodic torticollis.
Adv Neurol 24: 335-351, 1979
Gilbert GI: The medical treatment of spasmodic torticoli-
Tolosa E: Modification of tardive dyskinesia and spas-
modic torticollis by apomorphine: Possible role of
dopamine autoreceptors. Arch Neurol 35: 459-462,
1978
Coleman M: Preliminary remarks on the L dopa therapy
Chase TN: Biochemical and pharmacologic studies of
Lang AE: Dopamine agonists and antagonists in the
treatment of idiopathic dystonia. Adv Neurol 50:
561-570, 1988
Green PE, Shale E, Fahn S: Analysis of a large series of
patients with torsion dystonia treated with large

dosages of anticholinergics and other drugs. Adv
Neurol 50: 547-556, 1988
Segawa M, Hosaka A, Miyakawa F et al: Hereditary progres-
sive dystonia with marked diurnal variation. Adv
Neurol 14: 215-233, 1976
Quinn NP, Lang AE, Sheehy MP et al: Lisuride in
Lees A, Shaw KM, Stern GM: Bromocriptine and spas-
modic torticollis (letter). Brit Med J 1(6021): 1243,
1976
Marsden CD, Marion MH, Quinn N: The treatment of
severe dystonia in children and adults. J Neurol
Neurosurg Psy 47: 1166-1173, 1984
Blanchine JR, Blanchine JW: Treatment of spasmodic
torticollis with diazepam. South Med J 64: 893-894,
1971
Ziegler DK: Prolonged relief of dystonic movements with
Korein J, Lieberman A, Kupersmith M et al: Effects of L-
glutamine and isoniazid on torticollis and segmental
Assessment: The clinical usefulness of botulinum toxin-A
in treating neurologic disorders. Report of the ther-
apeutics and technology assessment subcommittee of
the American Academy of Neurology. Neurology
40: 1332-1336, 1990
Simpson LL: The origin, structure and pharmacological
activity of botulinum toxin. Pharmacol Rev 33: 155-
188, 1981
Scott AB: Botox injection of eye muscles to correct stra-
Olney RK, Aminoff MJ, Gelb DJ et al: Neuromuscular ef-
effects distant from the sites botulinum neurotoxin in-
jection. Neurology 38: 1780-1783, 1988
Tsui JK, Eisian A, Mak E et al: A pilot study on the use of
botulinum toxin in spasmodic torticollis. Canadian J
Neurosci 12: 314-316, 1985
Brin MF, Fahn S, Moskowitz C et al: Localized injections of
botulinum toxin for the treatment of focal
dystonia and hemifacial spasm. Movement Disorders
Stell R, Thompson PD, Marsden CD: Botulinum toxin in
spasmodic torticollis. J Neurol Neurosurg Psych 51:
920-923, 1988
Jankovic J, Schwartz K: Botulinum toxin injections for
Tsui JK, Eisen A, Stoessel AJ et al: double blind study of
Gelb DJ, Lowenstein DH, Aminoff MJ: Controlled trial of
botulinum toxin injections in the treatment of spas-
Greene P, Kang U, Fahn S et al: Double blind, Placebo-
controlled trial of botulinum toxin injections of the
treatment of spasmodic torticollis. Neurology 40:
1213-1218, 1990

292

Volume 33
Torticollis and Botox

