
Discussion

Botulinum Toxin A and Migraine Surgery

Discussion by David M. Knize, M.D.

This article is the authors' account of the evolution of botulinum toxin type A as a medical tool and how this experience led to their surgical techniques for the treatment of migraine headaches. They begin with a chronological account of how botulinum toxin A was used medically, and I will address that by reviewing the published record. Injections of dilute botulinum toxin A were used to weaken muscle action before 1973, when Scott, Rosenbaum, and Collins¹ reported the effectiveness of this toxin to correct extraocular muscle imbalance. Chemodenervation rapidly became an alternative to strabismus surgery.²⁻⁴ This application of botulinum toxin A injection soon was followed by its use for the treatment of tremors,⁵ blepharospasm,^{6,7} and other forms of head/neck spasm,^{8,9} including torticollis.¹⁰ Clark and Berris¹¹ reported treatment of facial asymmetry caused by facial nerve paralysis in 1989. In 1992, a husband/wife ophthalmologist/dermatologist team published the first description of botulinum toxin A use for cosmetic treatment (ablation of glabellar frown lines) in 18 patients.¹²⁻¹⁴ In 1994, Guyuron and Huddleston¹⁵ reported successful treatment of facial muscle asymmetry with injected botulinum toxin A, and they also treated hyperactivity of muscles in the glabellar area, noting the beneficial effect on the overlying skin lines.

Beginning in the early 1990s, there began to emerge a growing body of medical literature reporting headache relief with botulinum toxin A injections. Most of the earlier articles¹⁶⁻¹⁹ described pericranial muscle (temporalis, frontalis, glabellar muscle complex, procerus, occipitalis, and often even the trapezius muscle) function modification using botulinum toxin A injections into these muscles for relief of tension-type headaches. While the International Headache Society criteria for diag-

nosing tension-type headache are quite different from the symptom criteria for diagnosing migraine headache, it is believed by some authors^{20,21} that tension-type headache and migraine headache are conditions along a continuum of severity. In 1998, one article²² reported relief of migraine headache following the injection of botulinum toxin A into the pericranial muscles.

While there were no reports of successful migraine headache treatment from injecting the toxin into only the corrugator supercilii muscle, the senior author and his co-authors postulated that ablation of corrugator supercilii muscle function was the most likely basis for the benefit of these injections on migraine headaches.²³ In 2000, they did a retrospective study of 314 of their patients who had undergone surgical removal of the corrugator supercilii muscles. Of those patients in the group with a preoperative history of migraine headaches, they reported that a remarkable 79.5 percent had elimination or improvement of their migraine headaches immediately after the operation. In 2002, Guyuron, Tucker, and Davis²⁴ published a prospective, though uncontrolled, study of 22 patients treated with resection of the corrugator supercilii muscles in each case and transection of the zygomatico-temporal branches of the trigeminal nerve in some cases. They reported that another remarkable 95.5 percent of these patients experienced some degree of improvement in their headache frequency and/or intensity.

How corrugator supercilii muscle modification by resection or injection with botulinum toxin A produces migraine headache relief remains an unanswered question. The working premise is that the peripheral branches of the trigeminal nerve may act as trigger points that can start a stimulus cascade leading to a central

Received for publication February 19, 2003.

DOI: 10.1097/01.PRS.0000082207.54637.5B

or brain-level malfunction. If that is the mechanism, decompression of these nerve branches by modifying the surrounding muscle mass might alter a neurosensory pathway in which peripheral trigeminal nerve irritation from muscle action is the stimulus for a migraine headache. The authors postulate that these peripheral trigeminal nerve branches could be the supratrochlear, supraorbital, zygomaticotemporal, or intranasal branches of the trigeminal nerve. There are good data in the neurology literature to support that trigeminal sensory fibers participate in the pathogenesis of migraine headaches by causing vasodilation of the vessels of the brain and dura.²⁵

The authors further postulate that the greater occipital nerve, a branch of the second cervical nerve whose nucleus of origin is located in the spinal cord, could also play a role in stimulating migraine headaches. That potential mechanism is much less clear, and it is not based on any concepts of the mechanism of migraine headache production, to my knowledge.

Regardless of the mechanism, this observed 95.5 percent beneficial effect from the surgical treatment of migraine headaches is unprecedented. It appears that these surgical techniques successfully treat a chronically debilitating condition for which no prior form of treatment has enjoyed more than limited success. Of course, it will be important for other surgeons to confirm the authors' experience from their own practices. Ironically, this may be done best with a retrospective rather than a prospective study, because of the recognized placebo effect²⁶⁻²⁸ produced by patients' expectations of headache relief. Because the placebo effect is known to be very powerful, it is far more impressive if a patient experiences unexpected headache relief. A prospective controlled study would be difficult to accomplish, because sham surgery done in the control group would be problematic.

Within my surgical practice, I retrospectively examined a group of 29 patients who had a preoperative diagnosis of migraine headaches based on International Headache Society criteria and who had undergone corrugator muscle resection more than 1 year earlier. When questioned, 24 patients (82.8 percent) reported no change in their headache pattern or intensity, four patients (13.8 percent) thought that their headaches were less severe, and one patient (3.4 percent) said that she no longer

experienced migraine headaches. There was no reason to expect that the placebo effect was playing a role in these cases. These numbers pale in comparison to those reported by the authors, but the surgical treatment performed on these patients is a reasonable explanation for their change in symptoms. There was no attempt made to transect the zygomaticotemporal nerve branches, as the authors did in some of their cases.

The authors must be commended for actively pursuing this treatment avenue on behalf of the reported 28 million Americans who suffer from migraine headaches. They should be encouraged to continue exploration of the possibilities for surgical migraine headache management. The long-term, careful follow-up of the patients treated with this surgical approach by the authors and others to confirm a long-term benefit will be essential before the medical community will fully embrace this concept.

David M. Knize, M.D.
3701 South Clarkson Street
Suite 200
Englewood, Colo. 80110
dknize@aol.com

REFERENCES

1. Scott, A. B., Rosenbaum, A., and Collins, C. C. Pharmacologic weakening of extraocular muscles. *Invest. Ophthalmol.* 12: 924, 1973.
2. Scott, A. B. Botulinum toxin injection into extraocular muscles as an alternative to strabismus surgery. *Ophthalmology* 87: 1044, 1980.
3. Magoon, E., and Dakoske, C. Botulinum toxin injection for vertical strabismus. *Am. Orthop. J.* 35: 48, 1985.
4. Scott, A. B., Magoon, E. H., McNeer, K. W., and Stager, D. R. Botulinum treatment of strabismus in children. *Trans. Am. Ophthalmol. Soc.* 87: 174, 1990.
5. Ludlow, C. L., Sedory, S. E., Furita, M., and Naunton, R. F. Treatment of voice tremor with botulinum toxin injection. *Neurology* 39 (Suppl. 1): 353, 1989.
6. Frueh, B. R., Felt, D. P., Wojno, T. H., and Musch, D. C. Treatment of blepharospasm with botulinum toxin: A preliminary report. *Arch. Ophthalmol.* 102: 1464, 1984.
7. Elston, J. S. Botulinum toxin treatment of blepharospasm. *Adv. Neurol.* 50: 579, 1988.
8. Gonnering, R. S. Treatment of hemifacial spasm with botulinum A toxin: Results and rationale. *Ophthalmic Plast. Reconstr. Surg.* 2: 143, 1986.
9. Carruthers, J., and Stubbs, H. A. Botulinum toxin for benign essential blepharospasm, hemifacial spasm and age-related lower eyelid ectropion. *Can. J. Neurol. Sci.* 14: 42, 1987.
10. Tsui, J. K., Eisen, A., Mak, E., Carruthers, J., Scott, A., and Calne, D. B. A pilot study on the use of botulinum toxin in spasmodic torticollis. *Can. J. Neurol. Sci.* 12: 314, 1985.
11. Clark, R. P., and Berris, C. E. Botulinum toxin: A treatment for facial asymmetry caused by facial nerve paralysis. *Plast. Reconstr. Surg.* 84: 353, 1989.

12. Carruthers, J. D. A., and Carruthers, J. A. Treatment of glabellar frown lines with *C. botulinum*-A exotoxin. *J. Dermatol. Surg. Oncol.* 18: 17, 1992.
13. Carruthers, A., and Carruthers, J. History of the cosmetic use of botulinum A exotoxin. *Dermatol. Surg.* 24: 1168, 1998.
14. Kane, M. A. C. *The Botox Book*. New York: St. Martin's Press, 2002. P. 5.
15. Guyuron, B., and Huddleston, S. W. Aesthetic indications for botulinum toxin injection. *Plast. Reconstr. Surg.* 93: 913, 1993.
16. Zwart, J.-A., Bovim, G., Sand, T., and Sjaastad, O. Tension headache: Botulinum toxin paralysis of temporal muscles. *Headache* 34: 458, 1994.
17. Relja, M. Treatment of tension-type headache by local injection of botulinum toxin. *Eur. J. Neurol.* 4 (Suppl 2): 571, 1997.
18. Wheeler, A. H. Botulinum toxin A: Adjunctive therapy for refractory headaches associated with pericranial muscle tension. *Headache* 38: 468, 1998.
19. Schulte-Mattler, W. J., Wieser, T., and Zierz, S. Treatment of tension-type headache with botulinum toxin: A pilot study. *Eur. J. Med. Res.* 4: 183, 1999.
20. Featherstone, H. J. Migraine and muscle contraction headaches: A continuum. *Headache* 24: 194, 1985.
21. Silberstein, S. D., and Lipton, R. B. Epidemiology of migraine. *Neuroepidemiology* 12: 179, 1993.
22. Binder, W., Brin, M. F., Blitzer, A., Schoenrock, L. D., and Diamond, B. Botulinum toxin type A (BTX-A) for migraine: An open label assessment. *Mov. Disord.* 13 (Suppl. 2): 241, 1998.
23. Guyuron, B., Varghai, A., Michelow, B. J., Thomas, T., and Davis, J. Corrugator supercilii muscle resection and migraine headaches. *Plast. Reconstr. Surg.* 106: 429, 2000.
24. Guyuron, B., Tucker, T., and Davis, J. Surgical treatment of migraine headaches. *Plast. Reconstr. Surg.* 109: 2183, 2002.
25. Moskowitz, M. A. The neurobiology of vascular head pain. *Ann. Neurol.* 16: 157, 1984.
26. Jhee, S. S., Salazar, D. E., Ford, N. F., et al. Monitoring of acute migraine attacks: Placebo response and safety data. *Headache* 38: 35, 1998.
27. Pradalier, A., Bakouche, P., Baudesson, G., et al. Failure of omega-3 polyunsaturated fatty acids in prevention of migraine: A double-blind study versus placebo. *Cephalalgia* 21: 818, 2001.
28. Melmed, R. N. The placebo effect: New insights on a continuing debate. *Med. Crossfire* 3: 49, 2001.