Botulinum Toxin for Headache Treatment (2001)

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The literature contains many references about using botulinum toxin to treat various pain states. In the early 19th century Justinus Kerner ("Wurst-Kerner", the "Sausage Doctor"), who studied the toxin from crude extractions of bad sausage, had initially proposed that this most potent of neurotoxins might have therapeutic uses.

Dr. Edward Schantz, who isolated the toxin in crystalline form in 1946 at Fort Dix, also published an opinion that this agent, developed as a biologic weapon, might alleviate medical conditions. Schantz, working with Dr. Alan Scott in the 1970's, began work leading to the use of botulinum toxin type A first in non-human primates, then in human volunteers. By the 1980's, it was shown that this agent could be used for strabismus, and for dystonic movement disorders, such as cervical dystonia (spasticity).

Clinical experience has shown that even in those cases where the abnormal dystonic posture is little affected, pain is often still relieved.

Physicians therefore have wondered whether botulinum toxin might have an anti-nociceptive effect, besides lessening the intensity of muscle contraction. In fact, Dr. Aoki, a researcher at Allergan, has shown that botulinum toxin type A reduces inflammatory pain in "the rat formalin model" (formalin injected subcutaneously into the paw). The mechanism is uncertain, but might involve diminished release of substance P and/or other inflammatory mediators (Welch). Given the interest of headache doctors in neurogenic inflammation, the possible connection to headache treatment is fascinating.

Most of the literature on treating headaches involves the use of botulinum toxin type A (as Botox (from Allergan, or overseas as Dysport(which is a different preparation with a different potency). There are 7 antigenic types, but type B as Myobloc(in the US (same drug is called Neurobloc(elsewhere) is the only other antigenic form commercially available at present for therapeutic use. Botulinum toxin has been utilized for treating many different types of headache, including episodic migraine, tension-type headache, and chronic daily headache. The literature is replete with reports of efficacy, but also replete with reports or lack of proof of benefit. At present, it is a controversial and unproven therapy, yet there are patients who do respond to treatment, and some very vocal advocates.

My concern regarding this treatment is that there is no definite proof that it is effective, and I see no clear way to choose patients who might be good candidates to receive this treatment. In other words, there are at present no clear identifying co-morbid or co-existent medical conditions to help select potential responders. One study we participated in suggested a benefit in treating migraine (Silberstein), but a later, more complicated study failed to show efficacy.

The well-known mechanism of botulinum toxin is to prevent release of acetylcholine from cholinergic neurons, and to induce temporary paralysis of muscles. Interestingly, vascular endothelium receives cholinergic innervation as well, and perhaps another mechanism of headache prevention might be at the level of inhibiting nitric oxide release.

Both Allergan and Elan, the companies which produce Botox and Myobloc, respectively, have an interest in investigating potential effects of botulinum toxin on pain, including headache. Numerous studies, including one on chronic daily headache, are ongoing. Several members of the Headache Cooperative of New England are involved in these studies. If you have patients interested in enrolling in such studies, I would be happy to provide further information.

References

Silberstein SD et al. Botulinum toxin type A as a migraine preventative treatment. Headache 2000;40:445-450.

Welch MJ et al. Sensitivity of embryonic rat dorsal ganglia neurons to clostridium botulinum neurotoxins. Toxicon 2000; 38: 245-258.