

# Botulinum Toxin- Role in Headache Prophylaxis

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Botulinum toxin type A has been used for many different indications over the past three decades. In the early 1970s Botulinum toxin was used to weaken the medial rectus muscle for strabismus. In the 1980s injections were given into the skeletal muscles for dystonia and spasticity. Subsequently patients with tremors, tics and other hyperkinetic disorders were treated. In the late 1990s, plastic surgeons using botulinum toxin noted their patients' unexpected improvement in their migraines. Reduction in pain was also noted by patients in the initial dystonia and spasticity studies. Following this chance but important observation, further studies established that botulinum toxin could reduce migraine. In recent years the focus of research worldwide has been on the role of botulinum toxin in cosmetic applications and pain and headache management.

While pain reduction was initially thought to be due to a release of muscle contractility in spasm-related conditions, recent research suggests that botulinum toxin may inhibit release of substance P, calcitonin gene related peptide (CGRP) and glutamate. Physicians are therefore now beginning to explore the potential benefits of botulinum toxin for a variety of conditions characterized by pain including different headache disorders, cervical myofascial pain, low back pain, and post-herpetic neuralgia. For a systematic evaluation of the efficacy of botulinum toxin A in headache disorders, well-defined treatment procedures and an exact diagnosis of headache according to the criteria of the International Headache Society (IHS),<sup>1</sup> is mandatory.

Migraine is a primary neurovascular disorder of the brain that is characterized by headache, aura and autonomic dysfunction. Migraine is now not thought to be a principally vascular process but may be due to the dysfunction of ion channels in the aminergic brainstem nuclei that modulates sensory input. The pain of headache may be due to altered perception of craniovascular input that is not usually painful and then activation of biological processes that involve the first division of the trigeminal nerve (ophthalmic division). Thus, based on the clinical phenomenology, and the study of headache physiology and genetics, several alternative hypotheses have emerged. Initiation of migraine pain may be due to activation of peripheral sensory fibers that innervate intracranial vessels, activation of descending pathways that facilitate pain signals, or suppression of descending pathways.

The mechanism of action of botulinum toxin for its effect in migraine is thought to be through its ability to block nociception at the nerve fiber level and its effects on muscle spindle gamma efferent fibers, resulting in altered sensory feedback. Botulinum toxin may inhibit release of neuropeptides in the peripheral trigeminal vascular system and effect feedback onto the migraine generator to suppress the initial activation of the migraine.

Migraine affects 10 - 20% of the world's population and has significant consequences on patients' functional quality of life. Despite this, fewer than 20% of sufferers receive prophylactic treatment. For some migraineurs, migraine occurs so frequently or is of such intensity that prevention becomes critical. Lack of effective, well-tolerated drugs is thought to be one of the primary reasons for sub-optimal treatment. Unless one gets to see patients with severe chronic migraine one may not understand the difficulties in treating end-stage primary headaches and the need for better prophylactics.

Over the past few years, botulinum toxin has been systematically evaluated as a prophylactic for the treatment of migraine. Botulinum toxin is a new type of migraine preventative treatment that should be offered to patients for whom oral prophylactic medications are either not effective, not tolerated, contraindicated, or to those poorly compliant to oral medications. Patients may find treatment with botulinum toxin an appealing option because it has an excellent side effect profile and treatment may need to be repeated only once every 3-4 months.

In this issue, Mishra *et al* have reviewed the various trials conducted so far to study the role of botulinum toxin in headache and have discussed the probable mechanism of action and injection techniques.<sup>3</sup> More trials are being performed to learn more about botulinum toxin. These trials will provide additional information on very long-term safety and will guide physicians on the proper use and safety of the drug in these patient-popular approach.

Based on the experience to date, botulinum toxin should be considered principally as a treatment for chronic migraine and tension-type headaches. In future studies optimal patient selection criteria, the injection technique for headache subtypes and dose dilution should be clarified. A study design according to the IHS recommendations would be helpful for a reliable classification of the studies. Botulinum toxin A might be a sufficient therapy for defined subgroups of patients with idiopathic headache, but well-designed and controlled studies with a large number of patients are needed for a valid evaluation. Furthermore, the known standard

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therapies in headache treatment need to be compared with botulinum toxin A. This can be performed in blinded studies, which are, however, very difficult to design. It is nevertheless important for the development of treatment recommendations to discuss the advantages and disadvantages of this particular prophylactic procedure in comparison with oral medication.

In all the studies reviewed by the authors there were no reported serious adverse events due to botulinum toxin therapy and overall very few adverse events. There were significant reductions in the frequency, severity, duration, and disability associated with migraine and chronic tension-type headaches. These results of decreased headache frequency compare favorably with other prophylactic headache medications currently in use. Botulinum toxin is a

promising addition to the long list of prophylactics. Hopefully in the long term, with more physician experience and conviction we will see more of our chronic intractable headache patients benefiting from the use of botulinum toxin.

## REFERENCES

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