Type A Botulinum Toxin in the Treatment of Chronic Facial Pain Associated With Masticatory Hyperactivity

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Purpose: Chronic hyperactivity of the masticatory muscles is a common functional disorder associated with chronic facial pain and headache. The positive therapeutic effect of botulinum toxin type A on functional disorders and pain symptoms has been known in connection with the treatment of cervical dystonia. The purpose of this report is to assess whether the targeted reduction of masticatory muscular hyperactivity by local injection treatment with botulinum toxin type A can improve facial pain headache symptoms in the event that other treatment methods prove ineffective.

Materials and Methods: In an randomized blinded placebo-controlled study, 90 patients (60 verum and 30 placebo) with chronic facial pain were treated with botulinum toxin type A (Botox; Allergan, Ettlingen, Germany) injections into masticatory muscles.

Results: Ninety-one percent of patients who received botulinum toxin improved by a significant mean reduction of approximately 3.2 on a visual analog pain scale. By comparison with $t$ test and $\chi^2$ test, there was a significant difference compared with the placebo group ($P<.01$).

Conclusions: The local injection of botulinum toxin type A constitutes an innovative and adequately efficient treatment method for chronic facial pain associated with hyperactivity of the masticatory muscles. An improvement in the painful symptoms can be expected in up to 90% of patients who do not respond to conservative treatment methods.

Chronic myofascial facial pain and headache is a common, multicausal, functional disorder often associated with hyperactivity of the masticatory muscles and temporomandibular disorders. Etiologic factors include occlusal interferences, inadequate stress management, the general level of psychomotor activity, skills, and individual disposition. Changes in the proprioceptors and disturbances in the motor pathways are also discussed as potential causes of masticatory muscle hyperactivity and pain. Diagnosis and therapy of chronic facial pain are primarily based on relieving and eliminating the pathologic symptoms as determined by functional analysis.

General hyperactivity of the masticatory muscles manifests itself by various symptoms without necessarily involving functional disorders or pain. Indication of hyperactivity of the masticatory muscle groups are hypertrophy of the masseter and temporal muscles, condyle hypermobility, parafunctional movements with occlusal tooth surface attrition, and cases of dystonia.

Myofascial facial pain often results from general masticator muscle hyperactivity and condyle hypermobility, which tends to radiate in the region of the affected muscles when at rest or after excessive exercise. As a rule, the muscles that close the jaws (M. masseter, M. temporalis, M. pterygoideus medialis) and protract the jaws (M. pterygoideus lateralis) are affected.

Up until now, the conservative treatment of painful muscular hyperactivity in cases of chronic facial pain...
has primarily been based on occlusal, physical, and drug therapy. These include occlusal splint therapy, physiotherapy, and the systemic administration of muscle relaxants. Approximately 80% of all patients can have successful primary treatment with the help of these methods. Unfortunately the pain symptoms persist in approximately 20% of the patients, despite conservative treatment.

The temporary, positive therapeutic effect of type A botulinum toxin on functional disorders and pain symptoms has been known in connection with the treatment of cervical dystonia.5

Botulinum toxins are exotoxins of Clostridium botulinum, a gram-positive, anaerobic, spore-forming organism. In immunologic terms, a distinction can be made among 8 different subtypes. Botulinum toxin type A (Botox; Allergan, Ettlingen, Germany) is used in the treatment of motor disorders, one of the main indications.5

The specific action of botulinum toxin on peripheral cholinergic synapses has been known for a long time on the basis of the symptoms of botulism.6 The primary effect is receptor-mediated endocytosis of the botulinum toxin in the area of the synapses with subsequent selective proteolysis of the vesicular protein SNAP (synaptosomal-associated protein). This prevents the release of acetylcholine into the neuromuscular synaptic gap.7

The result is an inhibition of muscular hyperactivity up to 3 month. Additional effects (eg, changes in proprioceptors and muscle afferent nerves, inhibition of neuropeptides and local inflammation) are discussed.8,9

Thus, the question arises as to whether the targeted reduction of muscular hyperactivity by topical treatment with type A botulinum toxin can improve the pain symptoms in the event that other treatment methods prove ineffective.

Therefore, a prospective, randomized, blinded placebo controlled study was to be used as a basis for assessing the therapeutic potential of type A botulinum toxin in the treatment of painful hyperactivity of the masticatory muscles.

Materials and Methods

Since June 2000, 90 patients (60 verum group, 30 saline group) with chronic facial pain caused by hyperactivity of the masticatory muscles, parafunctional movement and hypermobility disorders were treated with botulinum toxin type A (Botox) in a prospective, single blinded, randomized placebo controlled study. All patients had previously received appropriate conservative treatment (3 months to a maximum of 34 months).

The conservative treatment methods involved flat planed occlusal splint therapy and special physiotherapy (eg, relaxing technique, massage). None of these methods had led to a decisive improvement in the symptoms up to that point.

The indication for treatment with type A botulinum toxin was determined on the basis of the examination and the functional analysis according to jaw movement, joint function, muscles hyperactivity and pain. Other causes, particularly arthropathy, were reliably ruled out clinically and by imaging diagnostics. Undefined pain syndromes with unclear patterns of radiation and no reference muscle were excluded from the study.

The development of the symptoms was recorded before and after therapy based on a modified visual analogue pain scale over a period of 4 weeks. Clinical function analysis was performed during the follow-up observation period between 1 to 3 months. Each patient gave informed consent by a standardized questionnaire. In all cases the rest of the injections were administered in accordance with the topography of the corresponding muscles (M. masseter, M. temporalis, M. pterygoideus medialis). The majority of the injections were administered intraorally. Only 23% required extraoral injection due to location (M. temporalis, M. masseter).

An average of 35 MU Botox liquidated in 0.7 mL NaCl saline, respectively 0.7 mL NaCl pure saline (placebo) was injected on each side of muscle. The injections into the muscles was given into the areas of maximal tenderness and pain. The patients were not informed whether they were treated with Botox or the placebo.

Subjective pain scores were assessed on a visual analogue scale (VAS) where 0 was no pain and 10 the worst facial pain the patient ever had in this context. Patients placed a mark on the visual analogue scale before the first injection and than over the next 4 weeks even at the same time of the day. Patients were also asked to stop any other treatment for their pain 7 days before the first injection (eg, analgesics).

Results

The results show that there was an improvement in the local facial pain symptoms in 55 cases (91%) in the verum group of the patients. The overall results show an average improvement of 3.2 points on the visual analogue pain scale (verum group). In the saline group there was only an improvement of local pain symptoms about 0.4 points on the VAS (Figs 1 A, B). By comparison with t-test and $\chi^2$-test there was a significant difference ($P < .01$). There was a correlation between the pretreatment pain intensity on the VAS and the improvement of local pain symptoms.
Patients with greater pain (>6.5 VAS) showed a major improvement (>3.5, n = 26) than those with less pain (<6.5 VAS) with only minor improvement (<3.5, n = 27).

In 19 cases similar symptoms recurred after the effect of the toxin had subsided (approximately 2 months), thus necessitating a repeat injection. In the other patients, the therapeutic effect lasted throughout the observation period (1 to 3 months).

Side effects in the form of swallowing difficulty or temporary paralysis of a muscle of facial expression occurred in only 1 patient. These disorders were
completely reversible after 4 weeks. Other side effects respectively temporary speech impairment or systemic botulism can not be observed.

Discussion

Type A botulinum toxin has been successfully used for diseases with increased muscle tone for about 20 years. Distinctive analgesic effects of botulinum toxin are already known in the treatment of painfully craniovascular dystonia. The pain that appears in that occasion results primary from neural structures and the muscles or from secondary irritation caused by the permanent contraction. Simultaneously, degenerative changes in the joints can result in chronic additional pain symptoms.

The results we obtained in the therapeutic application of botulinum toxin in our study confirm the general findings in the literature.

A literature review with regard to the improvement of pain in connection with botulinum toxin therapy for various indications (e.g., cervical dystonia) shows occasionally major improvements in the painful symptoms of the patients in 15 of 18 predominantly open label studies.

Freud and Schwartz conducted a study with 11 and 46 patients with muscular and arthrogenous pain symptoms and found that 90% of them showed an overall improvement in pain and function following topical injection of botulinum toxin type A in comparable doses. Girdler also reported an improvement in pain symptoms in 2 patients with chronic facial pain and muscle spasms.

In principle, the improvements in the pain symptoms in the region of the masticatory muscles correspond to experience gained in the treatment of focal dystonia, such as rotary tic. In this case, the local muscle-relaxing effect is known to also be accompanied by a significant reduction in pain in the region of the affected muscles. The example of facial dystonia induced by neuroleptic drugs demonstrates that muscular hyperactivity can result from a disturbance of the neurotransmitter balance between dopamine and acetylcholine. In this context, an excess of acetylcholine leads to undesirable and involuntary muscle contractions.

As a result of chemical denervation, botulinum toxin injection leads to the direct attenuation of these muscle contractions. An improvement in the aerobic muscular metabolism with regard to oxygen supply is also being postulated. In this context, chemical denervation at the neuromuscular end plate induces inactivity atrophy in the region of the affected muscles, thus counteracting the etiological factors.

In clinical terms, reduction of the masseter muscles by half can be induced by injecting botulinum toxin.

At the same time, changes also occur in the region of the myofibrils, muscle cells and the neuromuscular end plate. These processes are similar to the phenomena occurring after denervation by axotomy, but are completely reversible in a period of up to 3 months. A discussion is currently in progress as to the extent to which botulinum toxin affects the tonicity of the muscles by changing the muscle fiber afferents. However, this gives no consideration to the changes in the extrapyramidal locomotor centers, which may possibly be responsible for the hyperactivity of the masticatory muscles.

The harmonization of the disturbed muscle function may not be the only cause of the pain reduction in these patients. Clinical and experimental examinations speak for a much more complex analgesic mechanism of botulinum toxin. So the pain reduction with botulinum toxin frequently appears a few days after the injection, still before the excessive muscle contraction get reduced. Simultaneously, pain reduction occurs also in neighboring muscle groups. A possible reason for prolonged muscle relaxation in myofascial pain syndrome is that nociceptive neurons contract excessive muscle spindle activity.

Botulinum toxin hinders trigeminal nerves not only by the release by acetylcholine but also the release of substance P. Substance P is a potent neurotransmitter in the activation of neurological inflammations. Newest studies also show, that type A botulinum toxin reach the brain and spinal cord 48 hours after intramuscularly injection. It may have a direct analgetic effect on the sensory nozizeptive systems, that go far beyond the peripheral denervation of botulinum toxin in the neuromuscular junction.

References

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