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Type A Botulinum toxin in the treatment of chronic facial pain associated with temporo-mandibular dysfunction

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Abstract

In an open-label study 41 patients suffering from the muscular form of temporo-mandibular dysfunction were treated with botulinum toxin type A injections into masticatory muscles (average of 200 U on each side) and followed for an average of 6.7 months. Eighty percent of patients improved by a mean reduction of 45% on a visual analogue pain scale. During the observation period, 17% of patients had to receive a second injection because of recurrent pain. Reversible speech and swallowing difficulties occurred in only 1 patient. These encouraging results need to be confirmed by a randomized controlled trial.

Key words : Masticatory pain ; temporo-mandibular dysfunction ; botulinum toxin.

Introduction

Definition of muscular hyperactivity

Painful hyperactivity of the masticatory muscles is a common, multicausal, functional disorder associated with chronic facial pain.

The essential causes include occlusal and arthrogenous factors, the general level of psychomotor activity, inadequate stress-management skills and individual disposition (Hupfauf, 1995). Changes in the proprioceptors and disturbances in the motor pathways are also discussed as potential causes (Nishoika *et al*., 1988 ; Reich *et al*., 1988).

As a rule, it is not possible to precisely differentiate between the individual aetiological factors. Therefore, diagnosis and therapy are primarily based on relieving and eliminating the pathological symptoms determined by functional analysis.

General *hyperactivity of the masticatory muscles* in the stomatognathic system manifests itself by various symptoms without necessarily involving functional disorders or pain. Hypertrophy of the masseter and temporal muscles, condyle hypermobility, hypertrophy of the masseteric tuberosity at the mandibular angle and an elongation of the muscular process of the mandible indicate hyperactivity of the corresponding muscle groups (Krough-Poulsen, 1980). Additional symptoms of parafunctions include occlusal attritions and cases of dystonia.

In addition to general clinical indications, *painful hyperactivity* of the masticatory muscles and condyle hypermobility are particularly manifested by chronic facial pain, which tends to radiate in the region of the affected muscles when at rest or after exercise.

As a rule, the muscles which close the jaws (M. masseter, M. temporalis, M. pterygoideus medialis) and protract the jaws (M. pterygoideus lateralis) are affected.

Conservative treatment of painful muscular hyperactivity

Up to 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.

Approx. 80% of all patients can be given successful primary treatment with the help of these methods.

Unfortunately, the pain symptoms persist in approx. 20% of the patients, despite conservative treatment.

The temporary positive therapeutic effect of botulinum toxin on functional disorders and pain symptoms has been known for a long time in connection with the treatment of cervical dystonia.

Botulinum toxins are exotoxins of Clostridium botulinum, a gram-positive, anaerobic, spore-forming organism. In immunological terms, a distinction can be made between 8 different subtypes. Botulinum toxin type A (Dysport®, Speywood Pharmaceuticals Ltd. ; Botox®, Allergan) is used in the treatment of motor disorders, one of the main indications (Brin, 1991).

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 (Brin, 1991). 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 (synaptomal-associated protein). This prevents the release of acetylcholine into the neuromuscular synaptic gap (Binz *et al*., 1994).

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

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

Material and methods

Since June 1997, 41 patients with painful hyperactivity of the masticatory muscles, parafunctions and hypermobility disorders were treated with botulinum toxin type A (Dysport®). All patients had previously received appropriate conservative treatment (3 to max. 18 months).

The conservative treatment methods involved occlusal overlay therapy and special physiotherapy. None of the conservative methods had led to a decisive improvement in the symptoms up to that point.

The indication for treatment with botulinum toxin was diagnosed on the basis of the examination and the clinical function analysis (Krough-Poulsen, 1980). Other causes, particularly arthrogenous symptoms, 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 and with the help of clinical function analysis (Krough-Poulsen, 1980) (3, 6 weeks, 3 months). The follow-up observation period was 3 to 12 months (average : 6.7 ± 2.7 months).

In 8 cases, the intramuscular injection of botulinum toxin type A (Dysport) was administered under electromyographic control (M. pterygoideus lateralis, M. digastricus, M. pterygoideus medialis). The rest of the injections were administered in accordance with the topography of the corresponding muscles (M. masseter, M. temporalis, Platysma). The majority of the injections were administered intraorally. Only 19.5% required extraoral injection due to location (M. temporalis, M. digastricus, M. pterygoideus lateralis).

In most cases (n = 29), only one treatment was administered. Twelve patients required one or two repeat injections.

An average of 200 U Dysport (0.5 ml) was injected on each side.

Results

The results show that there was an improvement in the local pain symptoms in 80% of the patients with *painful hyperactivity*, *parafunctions and hypermobility* (n = 41). Thirteen patients reported a major improvement, all the way to the disappearance of the symptoms. As many as 20 patients reported an improvement in the symptoms for an effective period of 3 months . The overall results show an average improvement from 6.4 down to 3.5 points on the visual analogue pain scale. The same symptoms recurred in 7 patients (17%) after the effect of the toxin had subsided, thus necessitating a repeat injection. In the other patients, the therapeutic effect lasted throughout the observation period (3 to 12 months ; average : 6.7 ± 2.7).

Side effects in the form of temporary speech impairment and swallowing difficulty occurred in 1 patient. In this case, injections were also necessary in the M. pterygoideus medialis. These disorders were completely reversible after 3 to 5 weeks.

Discussion

The results we obtained in the therapeutic application of botulinum toxin confirm the few results in the literature, although it is not possible to make a direct comparison with our group of indications. *Freud and Schwartz* (Reich *et al*., 1988) conducted a study with 11 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* (Girdler, 1994 ; Brin *et al*., 1989) also reported an improvement in pain symptoms in 2 patients with chronic facial pain and muscle spasms.

Based on defined indications and a representative patient population (n = 41), our study showed improvements in the symptoms of *painful hyperactivity of the masticatory muscles* in up to 80% of the cases.

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 (Brin, 1991 ; Brin *et al*., 1989). 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. A literature review (Childers *et al*., 1998) 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 studies.

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 acetyl-

choline. In this context, an excess of acetylcholine leads to undesirable and involuntary muscle contractions (Nishioka *et al*., 1988).

As a result of chemical denervation, the 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 discussed (Brin, 1991). In this context, chemical denervation at the neuromuscular end plate induces inactivity atrophy in the region of the affected muscles, thus counteracting the aetiological factors (Moore *et al*., 1994).

In clinical terms, reduction of the masseter muscles by half can be induced by injecting botulinum toxin. This is confirmed by findings from animal experiments (Capra, 1991). 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 (Filippi *et al*., 1993). A discussion is currently in progress as to the extent to which botulinum toxin affects the tonicity of the muscles by changing the muscle fibre afferences (Filippi *et al*., 1993). However, this gives no consideration to the changes in the extrapyramidal locomotor centres, which may possibly be responsible for the hyperactivity of the masticatory muscles.

Conclusion

The local injection of botulinum toxin type A constitutes an innovative and adequately efficient treatment method for painful hyperactivity of the masticatory muscles. An improvement in the painful symptoms and function can be expected in up to 80% of patients who do not respond to conservative treatment methods.

In this context, attention must be drawn to local side effects, such as speech impairment and swallowing difficulty, as well as potential systemic side effects (botulism). However, these risks can be greatly minimised by taking the topography of the muscles into account and using standardised injection techniques.

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