Botulinum Toxin and Its Contribution to the Treatment of Masseteric Hypertrophy

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Summary

With discovery and use of botulinum toxin masseteric hypertrophy has become treatable in a minimal invasive way. The authors discuss the masseteric hypertrophy as such as well as they describe a technique of clinical application of botulinum toxin in its therapy. They introduce a significant contribution of botulinum toxin to patients with masseteric hypertrophy.

Key words: botulinum toxin – masseteric hypertrophy

Jurkovič R., Macák P.: Botulotoxin a jeho příspěvek k léčbě hypermassesterismu

Súhrn: Hypermasseterizmus sa objavením a používaním botulotoxínu stal liečiteľný aj minimálnou invazívnou cestou. Autori článku sa zaoberajú problematikou hypermasseterizmu, ako aj popisom techniky použitia botuloxotínu pri jeho terapii. Uvádzajú jeho podstatný prínos pre pacientov s hypermasseterizmom.

Kľúčové slová: botulotoxín – hypermasseterizmus

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INTRODUCTION

The protein botulinum toxin type A is one of seven immunologically distinct neurotoxins produced by the anaerobic organism Clostridium botulinum. It is the most potent bacterial toxin known to man and is responsible for the botulism infection. The toxin is available for pharmacological use as the botulinum toxin type A-haemagglutinin complex and is currently licensed for use in blepharospasm and hemifacial spasm. Local injection of a very small dose of the toxin into a muscle produces local paralysis and therefore individual muscles can be selectively weakened. The toxin exerts its action by permanent binding to the motor end plate at the neuromuscular junction which prevents the release of acetylcholine from the presynaptic vesicles – an action probably mediated by blocking the re-uptake of acetylcholine from the neuromuscular cleft. This accounts for the delayed onset of action of the toxin which is usually between 2 to 4 days after administration, as the storage vesicles of acetylcholine within the presynaptic motor and plate are used up. This produces an effective functional denervation of the muscle which subsequently atrophies. Although the toxin binds to the neuromuscular junction permanently, a recovery of muscle function does occur. The process, by

which a function returns, was demonstrated by Duchen [1] who showed that new neuromuscular junctions are formed by a process of presynaptic axonal sprouting. The duration of muscle paralysis is usually between 2 to 4 months with a gradual recovery of full function thereafter.

The first clinical application of botulinum toxin was for the treatment of strabismus [2]. Since then indications for its use have widened, in particular, for the use in dystonic conditions, such as blepharospasm [3, 4], spasmodic torticollis [5], spasmodic dysphonia [6], and also in hemifacial spasm [7]. Larger doses of toxin produces a more intense and prolonged paralysis and repeated injections are effective. Drug resistance due to antitoxin antibody formation was initially consideredas a potential problem, however this has not been the case in clinical practice with only sporadic reports of clinical resistance to the effects of repeated large doses of botulinum toxin [8]. No serious side effects of botulinum toxin therapy have been reported to date, and the side effects which have occurred are minor, such as local bruising or unwanted spread of action to adjacent muscles.

Bilateral masseteric hypertrophy is a benign condition characterised by bilateral enlargement of masseter muscles. It was for the first time described by Legg [9] in 1880. The highest inci-

dence is in the second and third decades of life and there is no sex predilection. The aetiology is obscure, however most, if not all cases, have a clenching/grinding habit of jaws which is frequently present also during a sleep. This habit induces the hypertrophy of the masseter muscles which are often asymmetric in size and this is the basis of the 'work hypertrophy' theory of Gurney [10]. Occasionally also other muscles of mastication may be hypertrophied, such as the temporalis muscles. Patients also frequently complain of a dull aching pain deep within the masseter muscles and occasionally symptoms of temporomandibular joint disfunction are present too. Examination often reveals a square-shaped lower face with bilateral, often asymmetric swellings over the ramus and angle of the mandible which become far more pronounced when the patient is asked to clench the teeth together.

The masseter muscles are often tender on deep palpation and become almost 'bony hard' on clenching. Longstanding cases may exhibit bony changes with hyperostosis formation and 'winging' of the mandible.

Conventional treatment consists of masseteric resection and reduction of bony hyperostosis. Surgical reduction can be performed from intraor extra-oral routes. Adams [11] described the extra-oral submandibular approach to excise the medial part of the muscle whilst Gurney [10] removed only the lateral portion of the muscle, which is more hazardous due to close proximity of the mandibular and buccal branches of the facial nerve.

Converse later described the intra-oral route to resect the medial part of the muscle and to reduce the bony prominence. Many conservative treatments (including occlusal adjustment, splint therapy, relaxation therapy, spasmolytics, tranquillisers and antidepressants) were advocated in the past, however these are almost always unsuccessful.

The known actions of botulinum toxin offer potential benefit to patients requiring treatment for bilateral masseteric hypertrophy and therefore it was decided to test the efficacy of this toxin in a series of patients.

THERAPEUTIC PROCEDURE

Botulinum toxin type A-haemagglutinin complex is available as a white freeze-dried powder ready for reconstitution with normal saline. Each vial contains 500 units (1 unit is the LD50 dose in mice) of the toxin which is dissolved in 2.5 ml of normal saline giving a concentration of 200 units/ml. Once prepared, the solution must be used within 1 hour. The toxin is administered

intramuscularly using a 2.0 ml syringe and a 25 gauge needle. The percutaneous route is preferred and small volumes of the toxin are deposited in two sites within each muscle. The first injection is given into the site of maximal swelling on clenching which is usually over the angle of the mandible. A second injection is given a centimetre or two more superiorly towards the zygomatic origin of the muscle. It is essential to deposit the toxin within the muscle and to avoid a superficial injection – the needle is inserted down to bone and then withdrawn by about 5–10 mm to ensure that the tip is within the bulk of muscle. Following aspiration of the syringe, the solution is deposited [12]. Electromyographic localisation is not necessary. In a bilateral case, the total dose of 500 units is administered, usually with 300 units into the worst side and 200 units into the other side. In the cases with also temporalis hypertrophy, about 100 units of toxin are deposited into the anterior vertical fibres only on each side. The patients are asked to massage the muscles regularly for the following 48 hours to assist the spread of the toxin throughout the muscle. The above dosages only apply to the botulinum toxin which is available in the United Kingdom (Dysport) and do not correlate with other preparations such as Botox (Allergan Inc) which is available in America. If a partial or asymmetrical result is seen after a month, then a second injection is placed into the area of inadequate response. Also the patients who are still able to clench the jaws together receive further injection either into the masseters, if palpable contraction is present, or into the temporalis muscles if these are particularly active.

Patients need to be warned of potential sideeffects such as facial bruising, painful injection site or facial muscle weakness.

The newest international research, which follows the efficacy of the botulinum toxin used for treatment of masseteric hypertrophy, confirms its excellent effects based also on objective assessment of ultrasound and CT examinations of the treated muscles [13, 14].

DISCUSSION

The pharmacological action of botulinum toxin and the clinical efficacy of this drug in the treatment of masseteric hypertrophy supports the 'work hypertrophy' theory of aetiology. A jaw clenching or tooth grinding habit is prevalent in this condition and it is believed that this produces the hypertrophic change in masseters and occasionally also in temporalis muscles. After the injection of botulinum toxin patients are impossible to clench their teeth firmly together due to

the functional denervation of the jaw closing muscles and it is assumed that this period of enforced inactivity is sufficient for the clenching/grinding habit to stop completely.

To date, the longest follow-up interval is 8 months; however, the first results are very encouraging and represent a major advancement in the treatment of this condition. Many surgeons are hesitant to recommend a conventional surgery for this benign but distressing condition. Particular problems associated with this surgery are:

- 1. difficulty in judging the correct amount of muscle to resect;
 - 2. occasional need for an extra-oral incision;
- 3. risk to the lower branches of the facial nerve;
- 4. significant post-operative morbidity, which includes pain, swelling, haemorrage and trismus, may persist for months.

Botulinum toxin injection can be used also for the treatment of temporalis muscles if these are hypertrophied too. Unlike the surgery, the treatment is performed in the out-patient setting without a need for a local anaesthesia and the dosage of the toxin can be divided between the muscles in a bilateral case to suit the individual clinical situation. The long-term results of this treatment are unknown yet. So far, no patient has shown a tendency towards a recurrence of the muscle hypertrophy. However, if this occurs, repeated injections can be expected to be effective.

It remains to be seen whether bony changes of the mandible reverse after this treatment and the patients with significant hyperostosis and flaring of the mandible will be assessed carefully for evidence of this. If, as is believed, the bony changes are secondary to the primary muscle hypertrophy, then it can be presumed that these bony abnormalities will also remodel back towards a normal shape after the correction of the bilateral masseteric hypertrophy with botulinum toxin.

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