

SHORT REPORT

Botulinum toxin treatment of synkinesia and hyperlacrimation after facial palsy

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Abstract

Objectives—To investigate the effects of injection of botulinum toxin type A (BTX A) into the orbicularis oculi muscle and lacrimal gland in patients with aberrant regeneration after facial palsy (facial synkinesias and hyperlacrimation).

Methods—The effect of the toxin injection (on average 75 mouse units of BTX A) into the orbicularis oculi muscle on facial synkinesias was assessed on a five point (0 to 4) scale in 10 patients with aberrant regeneration of facial nerve fibres after a peripheral facial nerve palsy. Six patients underwent a videographic control, which was assessed by a blinded independent investigator. In two patients with hyperlacrimation an extra dose of botulinum toxin (on average 20 mouse units BTX A) was injected into the lacrimal gland and the effect was assessed using the Schirmer test and on a three point scale.

Results—Botulinum toxin type A had a good to excellent (grades 3 and 4) effect over an average of six months after 91% of injections. In 9% the injections had a moderate (grade 2) effect. Patients with hyperlacrimation showed a nearly complete recovery. There were no systemic side effects but focal side effects due to a temporary weakness of the orbicularis oculi muscle were not uncommon.

Conclusions—Botulinum toxin type A is the treatment of choice in motor and autonomic effects of aberrant regeneration of facial nerve after a peripheral palsy. The required dose is similar to or slightly lower than the dose usually recommended for hemifacial spasm.

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Aberrant regeneration of fibres after facial palsy may lead to several unwanted effects, such as involuntary synkinesia between the orbicularis oculi and orbicularis oris muscle, or increased lacrimation of the affected eye.¹⁻³ Before the introduction of botulinum toxin therapy, there was no effective medical or surgical therapy for these troublesome symptoms.^{4,5} Botulinum toxin blocks the presynaptic release of acetyl-

choline and causes a functional denervation of neuromuscular endplates. Collateral sprouting re-establishes the pathological state after a period of three to five months.^{6,7} The toxin affects the neuromuscular junction as well as the autonomic cholinergic transmission.^{8,9} Recurrent local injections of botulinum toxin type A (BTX A) into the orbicularis oculi muscle with 100-200 mouse units Dysport in cases of blepharospasm and 50-100 units Dysport in cases of hemifacial spasm every three to five months are usually required.¹⁰ Theoretically botulinum toxin could not only have an effect on ephaptic motor symptoms (facial synkinesias) but also on vegetative phenomena (hyperlacrimation) occurring after facial nerve palsy. The latter effects have not been investigated systematically.

Secretomotor fibres of the facial nerve innervate the lacrimal gland through the greater superficial petrosal nerve. After a facial palsy, an aberrant connection of the visceromotor fibres, originally innervating the salivatory gland to the fibres of the lacrimal gland may develop, causing a hyperlacrimation whenever the patient salivates (crocodile tears). As the fibres to the lacrimal gland use acetylcholine as a transmitter, local injections of botulinum toxin into the gland may remedy this symptom. In Frey's syndrome (gustatory sweating after traumatic lesions of the auriculotemporal nerve and aberrant regeneration of cholinergic fibres to sweat glands) a beneficial effect of the local intracutaneous injections of BTX A has been reported as well.¹¹

We have investigated the effects of BTX A in ephaptic motor (facial synkinesias) and vegetative phenomena (hyperlacrimation) occurring after a facial nerve palsy.

Patients and methods

We treated eight women and two men with facial palsy with a total of 32 injections. The average age of the patients was 59 (range 26 to 85) years. Six patients were treated in the Department of Neurology in Kassel and four in Aachen. An informed written consent was obtained from all patients. The table contains a list of the patients including their clinical and treatment features.

BTX A (Dysport) was used; 500 mouse units were dissolved in 2.5 ml normal saline and an average dose of 75 (range 40-120)

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List of the patients, clinical, and treatment data

Patient	Age (y)	Sex	Clinical symptoms	Aetiology of facial palsy	Duration before treatment (y)	Injection sessions (n)	Dose of injected toxin in different injection sessions (range (mu))	Range of clinical effect on synkinesia (S) and hyperlacrimation (H)	Mean difference (%)
1	67	F	A: Yes B: No C: No	Idiopathic	?	2	60–120	S: 4	—
2	85	F	A: Yes B: No C: No	Idiopathic	2	8	40–120	S: 2–4	+57
3	58	F	A: Yes B: Yes C: No	Idiopathic	30	5	60–120	S: 4 H: 1–2	—
4	74	F	A: Yes B: Yes C: No	Idiopathic	1	1	70	S: 3 H: 2	—
5	80	F	A: Yes B: No C: No	Idiopathic	1	5	60–100	S: 2–4	+47
6	70	M	A: Yes B: Yes C: No	Zoster oticus		5	70–80	S: 2–4 H: 2	+45
7	68	M	A: Yes B: Yes C: No	Resection of acoustic neurinoma	7	1	80	S: 3 H: 1	+67
8	31	F	A: Yes B: Yes C: No	Idiopathic	5	2	80–100	S: 4 H: 2	+26
9	34	F	A: Yes B: Yes C: No	Idiopathic	4	1	60	S: 4 H: 2	—
10	26	F	A: Yes Hypolacrimation C: No	Idiopathic	4	2	60	S: 4 H: No clinical effect on hypolacrimation	+40

Videographic assessment of the width of the affected lid was performed before and 2–4 weeks after the BTX A injection in patients 2, 5, 6, 7, 8, and 10.

A=synkinesias; B=hyperlacrimation; C=gustatory sweating.

Mean difference=mean difference between relative width of affected lid before and 2–4 weeks after treatment *v* unaffected side.

mouse units was injected into four points in the orbital part of the orbicularis oculi muscle. In two patients an extra dose of 20 units was injected into the lacrimal gland (two injections in patient 6 and one injection in patient 8). These patients were asked to look to the contralateral side and the toxin was injected 2–3 mm subcutaneously into the lateral part of the frontopalpebral sulcus into the palpebral part of the lacrimal gland. In four patients with hyperlacrimation (patients 3,4,7, and 9) we did not perform any injections into the lacrimal gland because there was a moderate to good effect on the hyperlacrimation after injections of the toxin into the lateral part of the orbicularis oculi muscle. The clinical effect of the toxin on the synkinesia was assessed on a five point scale (0 points: no effect; 4 points: nearly complete resolution of synkinesia). In six patients (13 injections) the patient was videoed and the width of the affected lid during movement of the mouth (saying: “oooh...”) was compared with the unaffected side both before and two to four weeks after the injection by a blinded independent investigator (MS). Statistical evaluation was performed using a paired *t* test between data acquired before and after injections of botulinum toxin. A possible correlation between the injected toxin dose and the clinical effect was assessed using the Spearman rank correlation test. The treatment effect on the hyperlacrimation was assessed using a Schirmer test (Dr Winzer, GmbH, FRG) both before and two to four weeks after the injection, and on a three point scale (0 points: no effect; 1 point: moderate effect; 2 points: nearly complete effect). The side effects were assessed by a questionnaire.

Results

Injection of botulinum toxin into the orbicularis oculi muscle had a good (grade 3 and 4) clinical effect on the facial synkinesias after 29 injections (91%) and a moderate (grade 2) effect after three injections (9%). The average duration of the effect was 23.9 (range 13–40) weeks. The relative width of the affected lid compared with the unaffected side was measured both before and a few weeks after the treatment. A highly significant increase (47 (SD 18)%; $p < 0.01$) of the lid diameter during innervation of the orbicularis oris muscle was found (figure A, B).

The potential correlation between the dose and the subjective rating of the effect of the botulinum toxin was assessed in two ways: Firstly, all individual recordings of the dose and effect rating ($k=32$) were considered irrespective of whether several of them were obtained from the same patient. Secondly, the median dose level and the median effect rating were computed for each patient and the correlation was determined for these averaged values ($n=10$). The Spearman rank correlation coefficient “*r*” was computed to assess monotone relations between dose level and effect rating. For the individual values the correlation coefficient was $r = -0.052$ ($p = 0.788$, $k = 32$), indicating no systematic correlation between these two indices. For the median values the correlation coefficient was $r = -0.431$ ($p = 0.213$, $n = 10$), which was still not significantly different from zero.

Patients with hyperlacrimation who were treated with botulinum toxin injection into the lacrimal gland (patients 6 and 8) had a nearly complete recovery of this symptom. In patients 3,4,7, and 9 botulinum toxin was only injected



A 31 year old woman with right sided idiopathic facial palsy for five years before the botulinum toxin injection (patient 8). (A) Involuntary synkinetic closure of the right eyelid with facial movement before injection. (B) Four weeks after injection of 80 units of BTX A into the orbicularis muscle there is a substantial reduction of the amplitude of the synkinetic lid closure. (C) Hyperlacrimation on the affected right side, confirmed by a Schirmer test before treatment. (D) A Schirmer test four weeks after the injection of 20 units of BTX A into the lacrimal gland showed a nearly equal lacrimation on both sides. As an identical duration of the Schirmer test before and after the treatment was not chosen, only the differences between both sides are reliable. (Written consent for publication was obtained from the patient.)

into the orbicularis oculi muscle. All these patients showed a moderate to complete recovery of hyperlacrimation. The clinical effect of the injection was assessed using a Schirmer test before and after the toxin injection into the lacrimal gland, which showed a nearly equal lacrimation on both sides after the treatment (figure C, D).

Six patients (after 14 injections) had side effects, which lasted from a few days to two weeks. There were 12 episodes of incomplete lid closure, two episodes of ptosis, one episode of double vision, and two episodes of conjunctivitis. No patient showed dry eyes. There were neither serious nor systemic side effects. In three patients (patients 1, 3, and 6) only the highest doses of BTX A (100–120 mouse units) led to side effects, whereas with doses of 60–80 units no side effects could be found. In two patients (patients 2 and 3) no apparent relation between the dose and the incidence of side effects could be obtained, although these patients reported a subjective decline in the severity of their unwanted symptoms with decreasing doses of injected BTX A.

Discussion

With botulinum toxin type A we now have a powerful method to treat the synkinesia due to the aberrant regeneration of the facial nerve after a peripheral lesion. Moreover, our results suggest that it may be very effective in treating hyperlacrimation.

All patients investigated had a moderate to good recovery of their motor symptoms (facial

synkinesias) and hyperlacrimation. We treated facial synkinesias with an average dose of 75 mouse units BTX A and hyperlacrimation with 20 mouse units in two patients. The administered dose was comparable with that used in other studies.^{12 13} There are no reports in the literature on the treatment of hyperlacrimation after facial nerve palsy. Although injections of BTX A into the lacrimal gland had an excellent clinical effect on hyperlacrimation, a considerable recovery could be found after subcutaneous toxin injections into the lateral part of the orbicularis oculi muscle, possibly due to diffusion of BTX A into the lacrimal gland.

Duration of the effect of the toxin in our patients was somewhat longer than that reported and lasted about 24 weeks; in the literature there is a reported duration of 11 to 20 weeks in patients with facial synkinesias after facial nerve palsy.^{12 13}

Statistical analysis disclosed no significant correlation between the injected dose and the clinical effect of the toxin. One of the most important criteria for choosing the appropriate dose of the toxin was the rate and the subjective severity of the side effects. Accordingly the injected dose was not always chosen on the basis of the effect, but also on that of the expected side effects. This could possibly explain the lack of correlation between the dose and the clinical effect of the toxin. In addition, the size of the treatment group may have been too small to allow statistical significance and the dose range used by us was

probably not large enough to establish such a correlation.

As in some patients only highest doses of BTX A (100–120 units) led to side effects, a starting dose of 60–80 units may be recommended to reduce the incidence of undesirable effects.

On average the patients in the present study needed a lower toxin dose, which showed a longer duration of the clinical effects than was the case for patients with blepharospasm. The required dose was comparable with or slightly lower than the dose given to patients with hemifacial spasm.¹⁰ The pre-existing denervation in the facial muscles after a peripheral palsy seems to make the neuromuscular transmission more sensitive to the toxin. Hemifacial spasm is also known to be associated with facial weakness and electromyographic evidence of denervation.¹⁴ Therefore these different clinical entities may require similar doses of botulinum toxin.

Due to the few patients investigated, this study presents insufficient data to comment on the long term effects of the therapy of facial synkinesias and hyperlacrimation with the toxin. The effect of the injection on hyperlacrimation seems to be more stable than the effect on synkinesias.

Local injection of BTX A into the orbicularis oculi muscle is a very effective treatment of the facial synkinesias occurring after a peripheral facial nerve palsy. With doses of slightly less than half of the required dosage for blepharospasm and similar to that required in hemifacial spasm a good clinical effect may be obtained over about six months. Subcutaneous toxin injections into the lateral part of the orbicularis oculi muscle may have a beneficial

effect on hyperlacrimation in most cases. With a suboptimal response to this treatment, injection of BTX A into the lacrimal gland may be more effective.

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