SHORT REPORT

Treatment of sialorrhoea with ultrasound guided botulinum toxin type A injection in patients with neurological disorders

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Abstract

***Objectives*—To investigate the safety and efficacy of ultrasound guided botulinum toxin type A (BTX-A) injections into salivary glands for the treatment of sialorrhoea in patients with neurological disorders.**

***Methods*—The parotid and submandibular glands of 10 patients were injected with BTX-A using ultrasound guidance. Before injection, the baseline rate of salivation was assessed using a visual analogue scale. Postinjection, assessments were repeated at regular intervals for up to 1 year.**

***Results*—Of the 10 patients treated, nine (90%) reported a subjective reduction in salivation post-treatment and one patient (10%) found no improvement. Visual analogue scale scores showed a reduction of 55% in the mean rate of salivation for all patients and a reduction of 60.8% for the group of responders. No serious adverse events occurred and no procedure related complications were reported.**

***Conclusions*—This is the first study to report (1) the injection of BTX-A (BOTOX®) into both parotid and submandibular glands, and (2) the use of ultrasound guidance during the administration of BTX-A into salivary glands. The results suggest that the technique is safe and that BTX-A injections are effective for the treatment of sialorrhoea in patients with neurological disorders.**

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Keywords: botulinum toxin type A; sialorrhoea; ultrasound; neurological diseases

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Sialorrhoea, or excessive salivation and drooling, is commonly associated with many neurological and systemic conditions and often results from a disturbance in the coordination of swallowing. The condition affects about 10% of patients with chronic neurological diseases such as cerebral palsy, Parkinson's disease, amyotrophic lateral sclerosis, and post-traumatic encephalopathy[1]; primary sialorrhoea is comparatively rare. Persistent sialorrhoea creates major hygienic and psychosocial difficulties for patients and their caregivers; these include maceration of skin around the mouth, chin, and neck, which may result in secondary bacterial infections. In addition, sialorrhoea can interfere with speech and feeding and thus contribute to embarrassing and disabling social problems, which result in a decrease in quality of life.

Salivary glands are controlled by the autonomic nervous system, mediated by adrenergic and cholinergic nerve endings, and are primarily under parasympathetic cholinergic control. In adults, about 1.5 litres of saliva are secreted daily by three pairs of major salivary glands. The submandibular glands, the parotid glands, and the sublingual glands account for about 95% of the total secretion and the remaining 5% is produced by the lingual and other minor glands.

The treatments currently available for sialorrhoea are unsatisfactory. Systemic anticholinergic drugs are often ineffective and produce unacceptable side effects such as blurred vision, urinary retention, and cardiac arrhythmia.[2] Surgical intervention[3] and local irradiation of salivary glands[4] may also be considered, but these are invasive procedures that are often unacceptable to patients and their caregivers.

Botulinum toxin type A (BTX-A) is widely used in the treatment of focal dystonia, spasticity, and other conditions characterised by focal muscle hyperactivity.[5 6] Recent reports have indicated that BTX-A is both safe and effective in the treatment of focal hyperhidrosis.[7] In the late 1990s, Bushara[8] proposed "blind" intraparotid injections of BTX-A for treatment of sialorrhoea and this technique has subsequently been used by others in two preliminary studies.[9 10] Both of these studies reported reductions in salivary secretions and drooling in patients with neurological diseases; furthermore, side effects were absent or minimal in both studies.

We report the results of a preliminary study investigating the efficacy and safety of ultrasound guided BTX-A injections into the parotid and submandibular glands of patients with sialorrhoea that is either primary or secondary to other neurological disorders.

Patients and methods

Ten patients (seven men, three women) with sialorrhoea or drooling were treated with injections of BTX-A (BOTOX®, Allergan Inc,

Table 1 Reduction in sialorrhoea estimated by patients after BTX-A injection

Relative reduction in sialorrhoea after BTX-A injection	*Patients (%)*
Complete reduction	20
Moderate* to marked† reduction	70
No reduction	10

*Moderate=<50% reduction in sialorrhoea; †marked=≥50% reduction in sialorrhoea.

Irvine, USA) into the salivary glands. None of the patients had previously responded to systemic drug therapies commonly used to treat sialorrhoea. All patients gave written informed consent for participation in the study.

Before injection, the vascular anatomy of the parotid and submandibular glands and the intraparotideal tract of the facial nerve was carefully assessed by ultrasound using a linear electronic probe of 7.5 MHz (Aloka 1700-SD). BTX-A was injected bilaterally into the parotid and submandibular glands using a 1 ml syringe and a 22 gauge needle. The total dose of BTX-A for each patient was calculated based on the rate of salivation before treatment and the patient's body weight. Using the probe to avoid areas of relative hypervascularisation, two separate injection sites were selected for each parotid gland and a single site was selected for each submandibular gland.

All patients underwent a general and neurological examination, routine laboratory tests, ECG and, if necessary, imaging and functional tests. Before treatment, each patient or carer provided a subjective estimate of the baseline rate of salivation using a visual analogue scale (VAS), where 0 indicates normal salivation and 100 indicates an extremely high rate of salivation.

All patients were monitored postinjection. Visual analogue scale assessments were recorded daily during the week after injection and then monthly for 1 year. Side effects and procedure related complications were carefully monitored and documented throughout the study.

Results

DEMOGRAPHIC CHARACTERISTICS

The mean age of the 10 patients in the study was 55.4 years (range 19–85 years). One patient had primary sialorrhoea and nine reported symptomatic sialorrhoea (four patients with amyotrophic lateral sclerosis, two with Parkinson's disease, one with cerebral palsy, one with post-traumatic encephalopathy, and one with subacute sclerosing panencephalitis). All patients presented with severe dysphagia and speech problems.

All patients successfully completed the study.

DOSAGE

The dose of BTX-A injected into each parotid gland ranged from 15 to 40 U (mean dose 27.7 U/gland) into two injection sites. The dose administered in the submandibular glands ranged from 10 to 15 U/gland (mean 11.9 U/gland). The total dose of BTX-A administered/patient ranged from 50 to 100 U (mean 76.6 U).

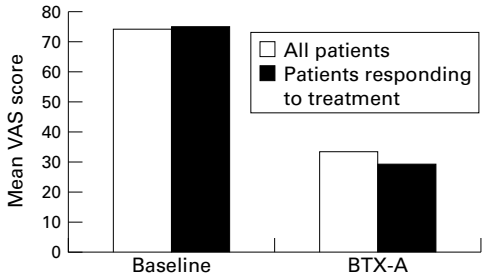

Figure 1 Patients' assessments of the level of sialorrhoea, as determined using a visual analogue scale, at baseline and the point of maximum benefit after injection of botulinum toxin type A.

EFFICACY

Patient assessment

Nine patients (90%) reported a lessening in hypersalivation after treatment (table 1). One patient (10%), a 67 year old woman with amyotrophic lateral sclerosis of bulbar onset, experienced no improvement after treatment. This patient had received the maximum study dose of BTX-A—that is, 100 U (40 U/parotid gland and 10 U/submandibular gland).

Visual analogue scale score

After injection of BTX-A, VAS scores showed an improvement in the mean rate of saliva secretion in the study group (fig 1). The mean rate of salivation as assessed by the VAS (range 0–100) for all patients in the study was reduced from 74.4 (range 60–90) at baseline to 33.8 (range 0–70) at maximum beneficial effect (peak). The mean difference in VAS score between peak effect and baseline was 40.6 (range 0–90), which indicated a mean overall reduction of 55% in salivation rate. In the group responding to BTX-A treatment (nine patients), the mean VAS score was 75.0 at baseline and 29.4 at peak. Thus, the mean difference in VAS score (baseline *v* peak) was 45.6, indicating a 61% reduction in salivation rate.

The reduction in the rate of salivation was first noted 3–8 days (mean 5 days) after injection and the response was maintained for 4–7 months (mean 4.7 months).

SAFETY

No serious side effects or procedure related complications occurred during the study. One patient who had received a total dose of 100 U BTX-A reported a dry mouth that was considered to be of mild severity.

Nine patients reported a moderate (<50%) to marked (≥50%) improvement in both dysphagia and speech problems.

Discussion

This is the first study to demonstrate the efficacy of ultrasound guided BTX-A injections into both parotid and submandibular glands for the treatment of sialorrhoea and drooling. All but one of the patients responded to treatment, reporting either complete relief or a marked reduction in saliva secretion. Overall, the maximum beneficial effect for BTX-A treatment resulted in a mean reduction of 55% in the rate of salivation. Exclusion of the patient

who did not respond to BTX-A treatment increased the mean reduction in salivation to 61%. The reason for the lack of response to BTX-A in this patient was unclear; further investigations were not performed owing to a lack of consent from the patient. A correlation between BTX-A dose and rate of response was not found in this study, but this was not expected considering that it was not the primary end point for the study and the few patients treated.

A beneficial response was found 3–8 days after injection. This latent period is similar to that reported for the use of BTX-A in the treatment of other conditions, such as focal spasticity[11 12] and hyperhidrosis.[13] However, the mean duration of action in this study was 4.7 months, slightly longer than that reported for focal dystonias (about 3 months) and similar to that for hyperhidrosis. The reason for this difference in duration of effect is unclear at present, but one possibility is that unlike voluntary motor fibres, there is no evidence of axonal sprouting and consecutive innervation in autonomic nerve fibres. A partial explanation may be the trophic effect of autonomic innervation on salivary glands.

The BTX-A was well tolerated and only one patient reported a side effect, which was transient dry mouth, and this was mild in severity. Larger studies are warranted to investigate the optimum dose of BTX-A, and to determine whether this varies depending on the baseline rate of salivation. From our clinical experience, we suggest that the initial dose should be about 20 U in each parotid gland and 10 U in each submandibular gland.

Two previous studies have reported beneficial effects resulting from "blind" (non-guided) intraparotid injections of BTX-A for the treatment of sialorrhoea in adults. Pal *et al*[9] treated nine patients with Parkinsons's disease and found a subjective improvement in over 65% of patients. Three of the four patients treated by Bhatia *et al*[10] showed a response to BTX-A therapy that lasted between 6 weeks and 4 months. The results of the present study show a higher response rate to treatment with a greater duration of effect than the earlier two studies.[9 10] Possible explanations for this discrepancy are the higher doses of BTX-A used in this study, the additional injection of the submandibular gland, which is known to account for up to 70% of salivary secretions, and the use of ultrasound guided injection resulting in more accurate placement of the injection. Indeed, Pal *et al*[9] suggested that the different degrees of response in their patients might have been related to the accuracy of their technique. The use of ultrasound guidance may also account for the absence of procedure related complications in the present study, although neither of the earlier studies reported procedure related complications. We think that this technique is essential for targeting the correct region of the gland to obtain maximum efficacy and safety. Using ultrasound guidance it is possible to set the needle in the correct position inside the gland, thus avoiding problems posed by the different anatomical location of the glands in different patients. The technique also facilitates circumvention of iatrogenic lesions of intraparotideal branches of the facial nerve.

In conclusion, injection of BTX-A (BOTOX®) into the parotid and submandibular glands is an effective treatment for sialorrhoea and drooling, regardless of the underlying cause of the condition. The use of ultrasound guidance during the injection procedure would seem to enhance efficacy and safety. Larger scale studies are warranted to verify these results and to determine the optimum dose of BTX-A.

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