

Preliminary Experience with Botulinum Toxin Type A Intracutaneous Injection for Frey's Syndrome

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Background: Gustatory sweating, the main symptom of Frey's syndrome, usually occurs after parotid gland surgery. Numerous medical and surgical treatments have been proposed to treat this condition, but there are various drawbacks. Botulinum toxin type A intracutaneous injection is a relatively new treatment modality; its use has never been reported in Taiwan. Here, we present our preliminary experience with this technique and review the literature.

Methods: Between March 2002 and June 2005, 10 consecutive patients with severe gustatory sweating were managed with intracutaneous injection of botulinum toxin type A for a total of 16 times. The affected skin was visualized by Minor's starch-iodine test and then recorded. The interinjection distance was 1 cm and a mean dose of 46.4 U (at a concentration of 2.5 U/0.1 mL) was used.

Results: In all 10 cases, gustatory sweating improved within 2 days after injection, with no side effects. Patients in whom the first 13 injections were performed experienced recurrence of gustatory sweating. Mean duration of effectiveness was 9.3 months; the shortest duration of effectiveness was 2 months and the longest was 28 months. One patient also had gustatory flushing, but this symptom did not improve even after 3 treatments.

Conclusion: Intracutaneous injection of botulinum toxin type A is a highly reliable, effective, safe, and minimally invasive treatment for gustatory sweating. Some patients had long-lasting therapeutic results. We recommend it as a valuable treatment option for severe cases of gustatory sweating. However, in our experience, it had no effect on facial skin flushing. Therefore, in addition to acetylcholine, there might be other neurotransmitters that are responsible for skin vasodilatation. [*J Chin Med Assoc* 2005;68(10):463–467]

Key Words: botulinum toxin type A, flushing, gustatory, hyperhidrosis, sweating

Introduction

In 1923, Lucie Frey, a neurologist at the University of Warsaw, published her landmark study on the "syndrome du nerf auriculotemporal". She described a 25-year-old patient who developed facial sweating and local facial skin flushing during meals 5 months after a gunshot trauma to the parotid region. The syndrome that bears Frey's name is characterized by sweating and flushing resulting from gustatory stimulation, independent of mastication.¹ Frey's syndrome has become a synonym that is usually used for gustatory sweating.

Currently, most cases of Frey's syndrome occur after surgery of the parotid gland. Various theories have been advocated to account for gustatory sweating occurring after parotidectomy. At the present time, the most widely accepted explanation is the aberrant regeneration theory, which was initially suggested by Ford and Woodhall.² According to the theory, Frey's syndrome is caused by aberrant regeneration of postganglionic parasympathetic fibers feeding the parotid gland that are severed during parotidectomy. These cholinergic parasympathetic fibers reach the distal end of the sympathetic fibers innervating the sweat gland and subcutaneous vessels.

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Because postganglionic parasympathetic nerve fibers and sympathetic nerve fibers share the same mediator, acetylcholine, once the aberrant regeneration takes place, the skin will flush and sweat during eating.

Botulinum toxin type A has been reported to block neurotransmission at the neuromuscular junction and at cholinergic autonomic nerve terminals.³ In patients with Frey's syndrome, the transmission of the neural input to the sweat gland and subcutaneous vessels is cholinergic, as previously mentioned. In 1995, Drobik and Laskawi⁴ reported the first successful management of Frey's syndrome with intracutaneous injection of botulinum toxin type A. In the ensuing years, several reports from Western countries have confirmed the effectiveness of this treatment for gustatory sweating.⁵⁻¹³ However, there are no reports about this treatment in Taiwanese patients. We, therefore, present our clinical experiences with botulinum toxin type A intracutaneous injection for the treatment of Frey's syndrome in Taiwanese patients, and review the background and details about Frey's syndrome and this particular treatment.

Methods

Between March 2002 and June 2005, we treated 10 consecutive patients, who developed severe gustatory sweating following parotidectomy, with botulinum toxin type A. All patients had gustatory sweating that occurred during every meal, causing annoyance and/or embarrassment. Criteria for treatment were intense gustatory sweating and the desire to be treated.

The exact location of the affected area was assessed and photographed by means of a starch-iodine test in an air-conditioned room. The affected cheek was painted

with 10% better iodine alcohol solution. After this had dried, powdered potato starch was applied onto the iodine-stained skin. The patient was then given a tablet of vitamin C to chew for 5 minutes. The extent of the hyperhidrotic area could then be visualized as small black spots when sweat from the sweat glands reacted with the iodine (Figure 1A). This black discoloration allowed us to delineate the involved skin surface.

None of the patients had contraindications to the use of botulinum toxin type A (BOTOX®; Allergan Inc, Westport, County Mayo, Ireland). One ampoule of BOTOX® contains 100 units of botulinum toxin type A as a freeze-dried powder. Immediately before injection, the toxin was reconstituted with 4 mL of sterile saline solution to a final concentration of 2.5 U/0.1 mL. The borders of the involved skin were marked with a waterproof pen according to the starch-iodine test, and then the whole area was divided into squares of about 1 cm² each. Intracutaneous injection was performed without local anesthesia during an office visit. Typically, 0.1 mL BOTOX® was infused into 1 cm² of involved skin with a 1 mL syringe usually used for insulin injection. However, the shape of involved skin was sometimes irregular, so some local concentrations of BOTOX® might have been higher than estimated in order to cover the entire area of involved skin. All patients were followed-up with self-assessment and starch-iodine tests in our department.

Results

The patients' characteristics are summarized in Table 1. There were 4 male and 6 female patients; mean

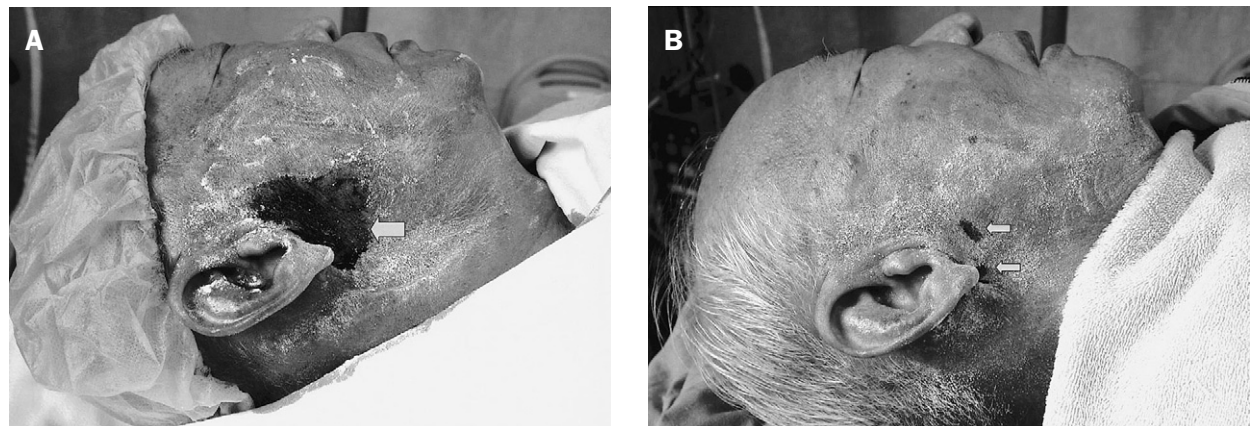


Figure 1. Minor's starch-iodine test in patient 1 demonstrated: (A) profuse gustatory sweating (arrow) before treatment with botulinum toxin type A intracutaneous injection; (B) small areas of slight gustatory sweating on the cheek (arrows) 6 months after treatment. This minimal reaction did not reach the symptomatic threshold and the patient had no complaints.

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