

# The Role Of Botulinum Toxin-A In The Treatment Of Post-Laryngectomy Pharyngocutaneous Fistula

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## Abstract

This paper describes our experience in the management of the pharyngocutaneous post-laryngectomy fistula with Botulinum neurotoxin-A injections into both parotid glands. It includes the rationale of the treatment, the physiological and pharmacological basis for this clinical application, the injection technique and the good results achieved. Our findings suggest that Botulinum neurotoxin offers a highly effective, safe and long-lasting conservative treatment in pharyngocutaneous fistula following major oncological pharyngolaryngeal surgery.

## INTRODUCTION

Pharyngocutaneous Fistula (PF) is the most frequent complication after major ablative pharyngolaryngeal surgery, despite improved reconstructive techniques, and occurs in 9 to 23% of cases (1). Post-surgical PFs remarkably increase the length of hospitalization and the morbidity of the patients with elevated costs.

Botulinum toxin (BTX) is a neurotoxin which selectively inhibits cholinergic neurotransmission. Because acetylcholine is the major neurotransmitter of the peripheral parasympathetic nervous system, it is possible to modulate parasympathetic stimulation by BTX.

The aim of this study is to report the personal experience in the use of BTX injections into both parotid glands, performed in order to transiently reduce salivation and to lead the closure of a post-surgical PF in a patient undergoing ablative oncological surgery of the larynx.

## MATERIAL AND METHODS

After obtaining institutional review board approval, we have performed an ultra-sound-guided injection of BTX type A into the parotid glands of a male patient aged 82 years undergoing total laryngectomy that developed post-operative a PF 12 days after surgery. A barium swallow showed a large extrapharyngeal spreading of the contrast medium, both to the left and right of the pharynx (fig.1). Despite strict nasogastric tube feeding and intensive local care, no spontaneous closure was achieved after 7 weeks. Because of the general conditions of the patient and the elevated

anaesthesiologic risk we have excluded the surgical closure of PF with myocutaneous flap.

The injection was performed according to the technique of Glickman & Deaney (2) using a 21G needle that should not breach the parotid fascia (fig.2). Lyophilized BTX type A (Dysport®, Ipsen Limited, Slough, Berkshire, England) was dissolved in normal sterile saline to a final concentration of 25 mouse units (MU)/0.1 ml (fig.3). The procedure was carried out with topical anesthesia with lidocaine. The BTX was injected at two different points into each parotid gland. At each point, 50 MU of BTX were injected. The procedure was well tolerated by the patient.

**Figure 1**

Figure 1: After 7 weeks of total laryngectomy, a barium swallow showed a large, extrapharyngeal spreading of contrast medium, both to the left and right of the pharynx, due to a pharyngocutaneous fistula.



**Figure 2**

Figure 2: Botulinum injection technique. The skin inferior to the tragus is lifted off the deep structures. The 21G needle is inserted at the mid-point between the tragus and the mandibular angle. It is advanced until the anterior border of masseter muscle, without damage of the parotid fascia.



**Figure 3**

Figure 3: Lyophilized Botulinum Neurotoxin type A (Dysport®, Ipsen Limited, Slough, Berkshire, England).



## RESULTS

After injection the salivation decreased dramatically within 2 days. The FP was dry 4 days later and a barium swallow revealed his definitive closure 1 week later. Massage of the injected parotid glands did not reveal any saliva at the relative orifices in the mouths. The patient started the physiological feeding after 10 days. The regular salivation started 6 weeks after BTX treatment. The patient reported no complication. On physical examination he exhibited no facial nerve or individual muscle deficits. Tongue movements, eye, lip and mouth closure and swallowing were monitored weekly for a follow-up period of 20 weeks. No other side-effects related to treatment were observed.

## DISCUSSION

The earlier hypothesis that local injection of BTX type A could be evaluative as a therapeutic option for the reduction of salivary gland secretion has been studied since 1997, especially in the treatment of drooling and/or dysphagia due to neurological diseases as cerebral and congenital suprabulbar palsy, strokes, amyotrophic lateral sclerosis, Parkinson's disease, operculum syndrome (3).

BTX is produced by the bacterium *Clostridium botulinum*. Seven serologically distinct neurotoxins designated A through G are known, each with its own antigenic specificity and therapeutic profile. BTX causes a chemical denervation by blocking neurotransmitter release at cholinergic nerve terminals; both motor nerves to skeletal muscles and cholinergic autonomic nerves are similarly blocked by the toxin. In the literature several reports have described the role of BTX in neurologic disorders and in some autonomic diseases such as achalasia (4), hyperhidrosis (5), migraine and tension-type headaches (6,7)

In otolaryngological field the Frey syndrome is the best documented indication for this clinical application. In this syndrome the misdirected secretory nerve fibers of parotid gland origin reinnervate the local sweat glands. The BTX injection in the area of sweating inhibits the release of acetylcholine and, then, blocks the misdirected secretory fibers. The local injections of BTX into the major salivary glands are commonly employed in various states of hypersalivation, drooling and sialorrhoea both neurological and otolaryngological disorders (2,3,8,9) (Tab.I).

On this basis, we have selected BTX as an alternative treatment of specific post-operative complication related to hypersalivation occurring in a patient with a post-laryngectomy PF. A persistent PF is a severe problem in this patient, protracting the healing time and the hospital stay.

Spontaneous closure of PF with local wound care is achieved in approximately 70% of cases. The other cases usually require surgical closure by direct suture or the use of myocutaneous flaps (deltopectoral or pectoralis major). In the literature, the successful management of PF obtained by BTX in the patients undergone major oncological pharyngolaryngeal surgery has been described (8,9).

The easy, safe and effective treatment with BTX injection suggests its significant and remarkable role as an useful option in the post-oncological surgery PFs and in any post-operative saliva-related complications. In the present case, the injection of 100 MU of BTX into each gland led to an intended temporary reduction of salivation for 6 weeks. We know that the effect of BTX is dose related and that there is no way to determine in advance the dose of BTX for therapeutic effect in a patient who has never been treated before. Larger, randomized studies with longer follow-up periods are necessary to determine accurately the outcome of this intriguing modality for the treatment of PF. Finally, studies evaluating BTX type A in the treatment of other salivary pathologic conditions is warranted based on the successful outcome of our experience.

**Figure 4**

Table 1

THERAPEUTIC APPLICATIONS OF BOTULINUM TOXIN-A INJECTION INTO SALIVARY GLANDS
- Postparotidectomy fistula
- Frey syndrome
- "Idiopathic hypersalivation"
- Sialocele
- Chronic sialoadentitis
- Pharyngocutaneous fistula following major oncological ablative oropharyngolaryngeal surgery
- Drooling as indirect effect of nasal obstruction, tongue size, malocclusion, head posture, sitting position, emotional state
- Dysphagia following stenosis of the upper esophageal segment
- Drooling and/or dysphagia after major ablative oropharyngolaryngeal surgery and/or reconstructive surgery of the head and neck
- Drooling following treatment with tranquilizers, anticonvulsants, anticholinesterases
- Drooling and/or dysphagia in neurologic disorders (Amyotrophic lateral sclerosis, operculum syndrome, cerebral palsy, strokes, Parkinson's disease, congenital suprabulbar palsy)

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