

# Ultrasound-Guided Botulinum Toxin Injections into the Salivary Glands for the Treatment of Drooling

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**ABSTRACT:** **Background:** Drooling is the unintentional loss of saliva from the mouth, usually caused by poor coordination of the swallowing mechanism. It is commonly seen in patients with chronic neurologic disorders, such as Parkinson's disease, amyotrophic lateral sclerosis (ALS), cerebral palsy, and stroke, as well as in patients with cognitive impairment and dementia.

**Objectives:** To evaluate the efficacy and safety of ultrasound-guided botulinum toxin injections into the parotid and submandibular salivary glands for the treatment of drooling.

**Methods:** We conducted a retrospective analysis of the medical records of 12 consecutive patients treated with botulinum toxin injections into the parotid and submandibular glands for the first time. The primary outcome variable was the subjective improvement of drooling on a 5-point scale. Secondary outcome variables were duration of the therapeutic effect, request to undergo additional treatment, and adverse events.

**Results:** Of 12 patients, 8 (67%) reported considerable improvement after treatment, 3 reported slight improvement, and 1 reported development of dry mouth. All patients stated that they felt the effects 1 week after the injections; the mean duration of the therapeutic effect was 4.5 months (range 3–9 months). One patient suffered from local hematoma and ecchymosis that did not require medical care. Another patient complained of difficulty swallowing, which did not require medical treatment and resolved spontaneously within 1 month.

**Conclusions:** Ultrasound-guided botulinum toxin injections into the parotid and submandibular glands seem to be a safe and effective therapy for the treatment of drooling. Further long-term prospective studies with varying doses are warranted.

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**KEY WORDS:** botulinum toxin, drooling, sialorrhea, salivary gland, ultrasound-guided injections

Swallowing is a complex neuromuscular activity that involves the rapid coordination of structures in the oral cavity, pharynx, and esophagus. The initial phase of swallowing, also called the oral phase, requires the complex neuromuscular coordination of the peri-oral, masticatory, lingual, and palatal muscles. Drooling is the unintentional loss of saliva from the mouth and is usually caused by poor coordination of the swallowing mechanism and not by over-production of saliva. Patients with chronic neurologic disorders, such as Parkinson's disease, amyotrophic lateral sclerosis (ALS), cerebral palsy, and stroke, as well as patients with cognitive impairment, dementia, facial palsy, post-laryngectomy, and post-mandibulectomy often suffer from drooling, which greatly adds to their disability, lowered self-esteem, and isolation [1].

Drooling has numerous negative sequelae affecting the psychosocial functions and physical condition of the patients. Soiling of clothes, dysfunctional eating, disturbed speech, wetting and damage to technical aids, peri-oral skin irritations and infections, halitosis, and aspiration-related pulmonary complications are among the complaints frequently reported by patients and caregivers [2-6].

Various therapeutic approaches exist for the treatment of drooling, the diversity of which emphasizes that no single treatment is effective in providing a satisfactory result with minimal side effects and risks. Pharmacological treatments attempt to decrease salivation by reducing cholinergic activity, and anticholinergic medications such as scopolamine, glycopyrrolate and benztropine are prescribed for this indication. These drugs, however, have many serious side effects [2-4] that may pose greater risks to the health of the patient than drooling itself. Many surgical techniques have been proposed to control drooling, with resection of the submandibular glands being one of the early surgical techniques described. It carries with it the risk of an irreversible xerostomia and paresis of the facial nerve developing [2]. Resection of the chorda tympani nerve and tympanic plexus neurectomy decrease salivary flow by interrupting the parasympathetic neural pathway. They carry the risk of taste loss and hearing loss and are associated with neural regrowth and waning of the effects

with time. Ligation of the submandibular ducts or the parotid ducts to obtain gland atrophy are other surgical options but are associated with varied periods of pain and swelling [3,5]. Submandibular duct rerouting with simultaneous sublingual gland excision has become a popular surgical procedure [6], although it may increase the risk of aspirations and respiratory complications due to posterior drooling, cause ranula formation, injure the lingual nerve, and predispose the patient to obstruction of the duct [7]. Parotid duct rerouting has also been reported with similar and additional surgical risks. Radiation therapy has been proposed to decrease salivary secretion; however, the results are unpredictable, and include the risk of xerostomia, loss of taste, mucositis, radiation caries, and potential of future malignancy [2,3,5,8].

Botulinum toxin (BTX) was introduced into medicine more than 40 years ago and became the first bacterial toxin used as a medication [9]. It causes temporary denervation of target organs by blocking the release of acetylcholine from nerve endings [10-12]. In 1997, Bushara [16] was the first to propose that if BTX is injected into salivary glands, it can disrupt the parasympathetic secretomotor pathway and reduce the amount of saliva. Today, even after numerous publications in the medical literature, the details of the technique are far from consistent and uniform. Which glands to inject – the submandibular, the parotid, or both? What is the optimal dose to be administered, and at what dilution? How important is ultrasound guidance? What is the recommended interval between injections? What is the accumulative effect of repeated injections on glandular tissue? And how safe is this procedure? In addition, the vast majority of published studies included a small number of patients, limiting the reader's ability to interpret the results thoroughly [14-16].

The purpose of the present study was to assess the results of BTX injection for the treatment of drooling. We aimed to evaluate subjective outcomes, duration of the therapeutic effect, and occurrence of adverse events.

**PATIENTS AND METHODS**

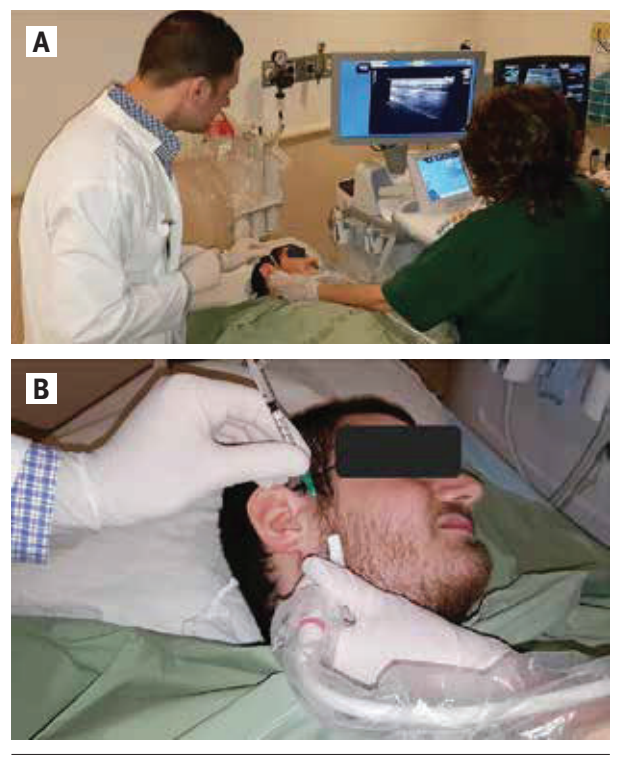
We conducted a retrospective analysis of the medical records of consecutive patients treated for drooling with BTX injections for the first time during a 3-year period (from November 2014 to July 2017). Patients were referred for BTX injections either as a primary treatment for drooling, or after the side effects of pharmacologic treatments had become intolerable.

The procedure was performed as outpatient ambulatory day care and no anesthesia was given. None of the patients had received a prior injection of BTX for any other indication within 4 months before the present injection. An ampoule of 100 MU of BTX type A (Botox, Allergan pharmaceuticals, Mayo, Ireland) was diluted in 4 ml of normal saline. After disinfecting the skin, the parotid and submandibular glands

were injected percutaneously, each gland receiving equally 25 MU of BTX diluted in 1 ml of saline. A 23 G 30-mm-long needle attached to a tuberculin syringe was used. Injections were performed transcutaneously with the guidance of a commercially available ultrasound system (Model ACUSON S200, Siemens, CA, USA) operated by an imaging technician. While the patient's head was turned away from the side to be injected, the transducer was positioned in such a way that injection with the needle was possible along the longitudinal axis of the transducer [Figure 1]. The needle could be visualized within the parenchyma of the gland to optimize needle placement and ensure that the BTX was injected within the confines of the capsule [Figure 2]. After injecting half the volume in the syringe, the needle was slowly withdrawn, during which, and as long as within the confines of the gland, small infiltrations were given. All injections were performed by the main author (W.A.).

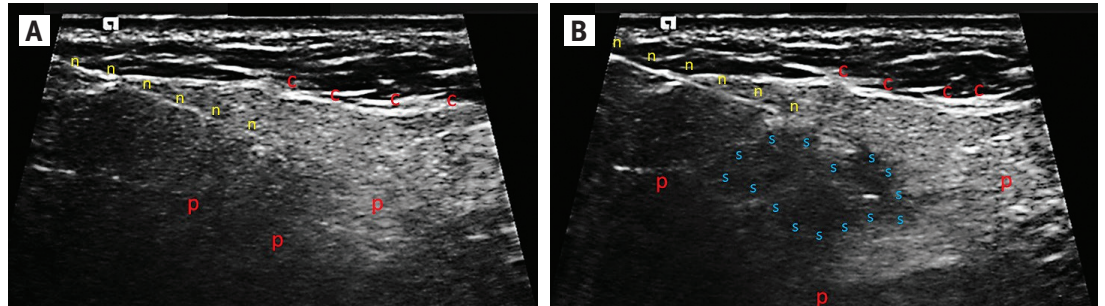
The severity of drooling was determined at each visit by interviewing the patients and/or caregivers, and conducting a physical examination. The findings of both were documented in

**Figure 1. [A]** Clinical setting of the injection procedure. The patient is lying in the supine position, the surgeon is standing on the side that will be injected, and the ultrasound technician is on the opposite side. Both the surgeon and technician can see, simultaneously, the needle in the surgeon's hand, the transducer in the technician's hand, and the monitor. **[B]** The needle and transducer are oriented parallel to each other



**Figure 2. [A]** Ultrasound image demonstrating the needle (n) appearing as a hyperechoic (bright) line within the parenchyma (p) of the parotid gland.

**[B]** Ultrasound image demonstrating the solution (s) injected appearing as a hypoechoic (dark) change in the gland. C = capsule of the gland



the medical records as a routine practice and not for conducting a clinical trial. Patients and/or caregivers were asked several questions regarding the number of shirts changed per day, the need to wear a bib or a towel around the neck, an estimation of the frequency of suctioning per hour (in patients with a portable suction machine), and the severity and frequency of daytime and night-time aspirations. The physical exam included observation of salivary spillage on the lips and chin, intra-oral evaluation of pooling of saliva in the floor of the mouth, and presence of peri-oral and commissural irritations and infections. The first author (W.A.) was responsible for evaluating all patients prior to the injections and throughout the follow-up period and for documentation in the medical files, and another author (S.N.) retrospectively drew the information from the files for the purpose of this study. The response to treatment was determined by comparing the data before and after the injection and was categorized into one of five categories as described by Sidebottom et al. [7]: "Worse drooling," "No change in drooling," "Slight improvement," "Considerable improvement," and "Too dry." This was considered the primary outcome parameter. Secondary outcome variables were duration of therapeutic effect, request to undergo additional treatment, and adverse events. Data from the follow-up appointments after the first injection and before performing additional intraglandular injections were used to assess the efficacy of treatment, duration of effect, and adverse events.

The study was approved by the Sheba Medical Center Institutional Review Board (number 4682-17-SMC). All data from the medical files were analyzed with the aid of an Excel spreadsheet.

**RESULTS**

Twelve consecutive patients were included in the study, 7 males and 5 females. Seven patients had Parkinson's disease, three suffered from amyotrophic lateral sclerosis (ALS), and two patients had Wilson's disease. Their demographic and medical details are presented in Table 1.

The first follow-up evaluation was performed after a mean of 4.7 weeks from the injections (range 2–8 weeks). Eight

patients and/or caregivers reported "Considerable improvement," three patients reported "Slight improvement," and one patient complained of "Dry mouth" [Table 2]. All patients stated that they felt the effects 1 week after the injections. Ten patients and/or caregivers requested a second BTX treatment after the effects had waned, while two patients did not. The mean duration of the therapeutic effect was 4.5 months, with a wide range of 3–9 months.

One patient suffered from local hematoma. This was observed at the 2-week follow-up visit as a residual ecchymosis in the left submandibular area. It did not require any medical care. Another patient complained of difficulty swallowing that developed soon after the injections. The dysphagia was not severe and he was able to eat solid foods and drink liquids; medical treatment was not required other than the usual follow-up visits. The dysphagia resolved after approximately 1 month, before the therapeutic effect of BTX on drooling subsided.

**Table 1.** Characteristics of the study population

<b>Age (yrs)</b>	
Mean	63.8
Range	22–91
<b>Gender</b>	
Male	7
Female	5
<b>Medical condition</b>	
Parkinson's disease	7
Amyotrophic lateral sclerosis	3
Wilson's disease	2

**Table 2.** Degree of efficacy, duration of effects, and patient's request for additional injections

<b>Outcome parameter</b>	<b>Result</b>
Efficacy of BTX on drooling	Considerable improvement, 67% (8 of 12) Slight improvement, 25% (3 of 12) Dry mouth, 8% (1 of 12)
Duration of therapeutic effect	Mean 4.5 months Range 3–9 months
Request to undergo additional BTX treatment	Yes, 10 of 12 No, 2 of 12

## DISCUSSION

The present study demonstrated that ultrasound-guided BTX injections into the salivary glands seems to be a safe and effective treatment for patients with drooling. The majority of patients benefited considerably from the treatment and asked for the procedure to be repeated after the effects of BTX had faded. The few adverse events were mild, localized, and temporary.

There is a lack of homogeneity in the injection protocols proposed in the literature [1,21,22]. The dosage given per gland in several trials was half the dosage given in other trials. In addition, while some authors injected the parotid glands only, others injected only the submandibular glands, and others injected both sets of glands. The conclusions were mixed, with some authors concluding that reducing the salivary secretion of either gland alone is insufficient to produce a clinically significant response [9,18,19], while others concluded the opposite [11,22,23]. In the present study, we injected each of the four major glands with 25 MU of Botox, which yielded better subjective results than those of our previously published trial [16] where we injected 15 MU of Botox into the parotid glands only. We believe that in addition to the dose increase, the present favorable results were probably due to the fact that because we injected the two sets of glands, a reduction in both the resting salivary flow (primarily from the submandibular glands) and the stimulated salivary flow (primarily from the parotid glands) was achieved.

In general, the complication rate reported in the literature is low, and the adverse events are usually localized and temporary. One patient in the present study experienced a mild dysphagia, which probably occurred due to diffusion of BTX into the surrounding musculature and resultant paresis of the muscles in the floor of the mouth. His complaint resolved within 1 month, which was less than the duration of the effect of BTX, which could probably be explained by the gradual muscular compensations that aided in improving the function of deglutition. All injections in the present study were performed by the same surgeon and ultrasound technician, and the dilution of BTX in saline was the same for all procedures. We could not identify the reason for the development of dysphagia in this one patient.

In conclusion, ultrasound-guided percutaneous intraglandular BTX injections seems to be safe and effective in reducing drooling in patients with various chronic neurologic disorders. A standard injection protocol whereby both the parotid and submandibular glands are injected with 25 MU of Botox proved beneficial in the majority of patients. Future controlled studies with larger cohorts and long-term follow-up are still needed to establish the lowest effective therapeutic dose and ideal number of glands to be injected.

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