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Research Article

# Onabotulinum Toxin-A Injection into Salivary Glands for Parkinson's Disease-related Drooling

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## Abstract

**Background:** Excessive drooling is common and problematic issue faced by Parkinson's disease (PD) patients and their caregivers. Drooling can cause both physical and psychosocial disability. Recent studies of Botulinum toxin type-A (BoNT-A) in PD-related drooling have shown favorable results with minimal side effects.

**Aim:** To evaluate the safety and efficacy of botulinum toxin injections into salivary glands in decreasing PD-related drooling.

**Study Design:** Prospective case series.

**Methodology:** A total of ten male patients of PD with excessive drooling, attending Movement disorder clinic with mean age of 71.6 ± 4.5 years (range 64 - 80 years), mean duration of PD of 7.5 years and duration of drooling of 6 months to 2 years were included in the study. Patients were given botulinum toxin injections in both parotids and/or submandibular glands. The frequency and severity of saliva secretion was assessed at baseline and then weekly for one month and subsequently every month.

**Results:** All patients treated with BoNT-A reported significant subjective improvement following treatment in both frequency and severity of drooling. All patients received injections in both parotids and in addition four received in submandibular glands. The mean BoNT-A dose in each parotid was 18.5 ± 6.3U and 10U in each submandibular gland. Onset of effect occurred after mean duration of 12.5 ± 1.9 days. The average duration of benefit was 5.7 ± 1.0 months. None of the patients had clinical adverse reactions.

**Conclusion:** This case series reaffirms that repeated BoNT-A injection into parotid and submandibular glands is safe and effective treatment in controlling PD-related drooling.

**Keywords:** Drooling; Sialorrhea; Parkinson's Disease; Botulinum Toxin Type A; Onabotulinum Toxin-A

## Introduction

Drooling saliva also known as ptyalism or sialorrhea is frequently reported symptom in patients with Parkinson's disease. It is an important non-motor symptom because it may cause secondary respiratory infections and aspiration pneumonia. It also leads to significant embarrassment and social isolation, thus impairing the quality of life. Pharmacotherapy is partially effective and has multiple side effects including cognitive impairment in elderly patients of PD. Botulinum toxin (BoNT- A) injections into the salivary glands can decrease production of saliva and thereby decrease drooling [1]. This study investigated the safety and efficacy of repeated BoNT-A injections in bilateral parotids and/or submandibular glands for PD related drooling.

## Methods

This study was conducted on the patients attending movement disorder clinic of Neurology outpatient of Dr Ram Manohar Lohia Hospital. Inclusion criteria were (1) patient with a diagnosis of Idiopathic Parkinson's disease in accordance with the UK Parkinson's Brain Bank criteria, (2) an excessive and troublesome drooling of saliva leading to impairment of personal and social functioning. Exclusion criteria were (1) currently receiving pharmaceutical treatment for drooling, (2) exclusion of secondary causes of drooling e.g. Stroke, head injury, drug induced and (3) history of hypersensitivity to botulinum toxin injections.

All were administered BoNT- A injection. First, the area was cleaned with alcohol swab. The botulinum toxin vial containing 50 mouse units (MU) of onabotulinum toxin A (Botox (®), Allergan, Inc., Irvine, CA) was dissolved in 2 ml saline solution (0.9%), giving a concentration of 25U/ ml. This was then drawn up with a 23 gauge needle on a 1-ml tuberculin syringe. We then injected transcutaneously directly into the salivary glands, a total of 20-30 units, placing 5-6 units at 4 points on each parotid and a total of 10 units, placing 5 units at 2 points on submandibular salivary glands guided by anatomical landmarks (Figure 1). The study was done as per the ethical standards of institutional ethical committee and prior written informed consent was obtained from all the participants of this study.

**Figure 1:** Landmark for injecting parotid and submandibular gland: (A) Parotid gland: Drawing the imaginary line starting from the tragus to angle of the mandible; then the mid-point of this line is the landmark for injecting botulinum neurotoxin into the gland. (B) Submandibular gland: Drawing the imaginary line, along the length of body of the mandible, starting from angle of the mandible to tip of the chin; then one finger breadth medial to the mid-point of this line is the landmark for injecting botulinum neurotoxin into the glands.

Patients were evaluated based on duration of complaint, and onset and duration of therapeutic effects. Subjective assessment in drooling using Drooling Severity and Frequency Scale (DSFS) as judged by caregivers were recorded before and after BoNT-A injections. In this scale, parents or caregivers were asked to rate the severity and frequency of drooling, classifying severity of drooling using a 5-level domain ranging from 1 (dry) to 5 (profuse drooling). The frequency of drooling was classified using a 4-level domain ranging from 1 (no drooling) to 4 (constant drooling). The frequency and severity of saliva secretion were assessed at baseline and then weekly for one month and subsequently every month (Table 1).

| **Drooling severity** | **Points** |
|---|---|
| Dry (never drools) | 1 |
| Mild (wet lips only) | 2 |
| Moderate (wet lips and chin) | 3 |
| Severe (clothing becomes damp) | 4 |
| Profuse (clothing, hands, tray, objects become wet) | 5 |
| **Drooling frequency** | |
| Never drools | 1 |
| Occasionally drools | 2 |
| Frequently drools | 3 |
| Constantly drools | 4 |

**Table 1:** Drooling frequency and severity scale.

## Results

The present series comprised of a total of ten cases of PD related drooling. All were males. Their age ranged from 64 - 80 years (mean age 71.6 ± 4.5). The mean duration of PD was 7.5 years and mean duration of symptoms 3.8 ± 3.7 years (range: 8 months-2 years). All patients received injections in bilateral parotid glands and four patients were given additional injections in bilateral submandibular glands. The total BoNT-A dose injected in each parotid gland ranged from 10 to 30U (mean dose 18.5 ± 6.3) and 10 U in each submandibular gland. Further repeat BoNT-A injection cycles were given on 16 occasions; 3 received once, 3 received additional two, and one patient received 7 injections respectively. Onset of effect occurred after mean duration of 12.5 ± 1.9 days (range 10 - 15 days). All patients experienced a consistent statistically significant reduction in both drooling frequency (DFS) and severity (DSS) from BoNT-A injections compared to baseline ($p < 0.001$). The average duration of benefit was 5.7 ± 1.0 months (range: 4-7 months). Follow-up ranged from 6 months to four years. The therapeutic effect was sustained as long as four years (Table 2-4).

| | |
|---|---|
| Total number of cases | 10 |
| Age (Mean ± SD) (years) | 71.6 ± 4.5 |
| M:F | 10:0 |
| Mean duration of Parkinson's Disease (years) | 7.5 |
| Mean Duration of drooling symptoms (years) | 3.8 ± 3.7 |

**Table 2**: Demographic and disease related parameters.

| Site of injection | |
|---|---|
| Bilateral parotid gland | 10 |
| Bilateral submandibular gland | 4 |
| Mean dose of BoNT-A | |
| Parotid gland (MU) | 18.5 ± 6.3 |
| Submandibular gland (MU) | 10 |
| Onset of effect | 12.5 ± 1.9 days |

**Table 3:** Treatment related parameters.

| | | | |
|---|---|---|---|
| DSS | 4.15 | 2.76 | P < 0.001 |
| DFS | 3.89 | 2.17 | |

**Table 4:** Before and after drooling severity and frequency scores.

## Discussion

Parkinson's disease is a progressive movement disorder having both motor and non-motor symptoms. Predominant motor symptoms are resting tremors, bradykinesia, cogwheel rigidity, freezing and postural instability. Drooling or excessive pooling of saliva in the oral cavity is one of the non-motor symptoms.

Medical treatment for drooling consists of anticholinergic/antagonistic drugs; trihexyphenidyl, atropine, scopolamine and glycopyrrolate. But these drugs have adverse side-effects especially in elderly patients. Botulinum toxin is most potent biological toxin put to its best use for treatment of various neurological and non-neurological indications. BoNT-A is an established and effective treatment for drooling; blocking the release of acetylcholine at the cholinergic parasympathetic terminals and postganglionic sympathetic activity of the salivary glands causing reduction of salivary secretion.

This study shows that injecting 18 U BoNT-A using external landmarks is a relatively safe and effective approach in reducing drooling in patients of Parkinson's Disease. Injection into submandibular glands may be required in selected number of patients. To minimize the side effects of the injection, the landmarks should be appropriately identified, if using the blind technique. Also starting with a lower dose may be a wise strategy.

Previously, studies have been done to assess the effect of BoNT-A for drooling in Parkinson's Disease. Seven studies including a single case series, four open label studies and two randomized controlled trials have assessed the use of onabotulinum toxin A for treating drooling patients with PD [2-6]. Onabotulinum toxin A was injected into the parotid glands in all studies. Su., *et al.* also included MSA and DLB patients, in whom injections were additionally given into submandibular gland [5]. There are no studies to compare injection of the parotid glands with the injection in submandibular glands for PD related drooling. Two of these studies used ultrasound guidance for injection, where as others relied on surface land marking only [3,6]. Santamato., *et al.* conducted an open label study using ultrasound-guided toxin injection in 18 drooling PD patients while Dogu., *et al.* conducted a randomized control study comparing toxin injection in 15 drooling PD patients divided into arms using (n = 8) and not-using (n = 7) ultrasound guidance to assess the effects of treatment, Jost., *et al.* and Santamato., *et al.* used only subjective assessment, Friedman., *et al.* used only objective assessment, and rest other studies used subjective as well as objective assessment [1-7]. The subjective assessment tools included reporting from patients and their spouses, and DSFS. The objective assessment included the change of dental roll weight after placement in the mouth for 2, 5 or 10 minutes. Duration of evaluation after initiation of treatment ranged from 1 to 16 weeks. All studies agreed that onabotulinum toxin A injection, dosage ranging from 5 to 50 units and 5 units per parotid and submandibular gland, respectively, significantly reduced drooling in PD, MSA and DLB patients and improved subjective or objective assessments for approximately 4 months. In addition, injecting the toxin under ultrasound guidance might have provided more accuracy and more reduction in salivary production compared to the blind injection technique.

We compared the results of different studies with our study, which are tabulated below (Table 5).

| Study | Type of study | Number of cases | Dose | Results | Adverse effects |
|---|---|---|---|---|---|
| Jost., *et al*. 1999 [2] | Case series | 5 | 5 units per each parotid gland | 2 with good (normal salivation), 2 with moderate (decreased salivation), 1 with no change | No |
| Pal., *et al* 2000 [8] | Open label | 9 | 7.5 units then, 8 weeks later 15 units per each parotid gland | 8 patients had significant improvement | Dry mouth |
| Su., *et al*. 2006 [5] | Open label | 15 | 15 units for each parotid gland and 5 unit per each submandibular gland | Significant improvement objectively and in DSFS score. | Dry mouth |
| Santamato., *et al*. 2008 [6] | Open label | 18 | 15 units for each parotid gland | Significant improvement in DSFS at 4 weeks | No |
| Friedman., *et al*. 2001 [7] | Open label | 5 | 5 units per each parotid gland | significant reduction in saliva production (by weighing dental rolls) | No |
| Dogu., *et al*. 2004 [3] | Randomized placebo controlled | 15 | 30 units for each parotid gland; 7 with and 8 without ultras | Significant reduction in saliva production. (VAS Score) | Dry mouth |
| Lagalla., *et al*. 2006 [4] | Randomized double-blind, placebo-control | 16 with treatment and 32 with placebo | 50 units per each parotid gland | Significant reduction in saliva production. (VAS Score) | Mild swallowing difficulty |
| Our Study | Case series | 10 | 18.5 units for each parotid and 10 units for each submandibular gland | Significant reduction in DSFS ($P < 0.001$) | No |

**Table 5:** Comparison of different studies related to Onabotulinum toxin A treatment for PD related drooling.

## Conclusion

Drooling is major cause of personal discomfort as well as social embarrassment for patients with Parkinson's Disease. Apart from medical treatment, Onabotulinum Toxin A injection is an effective alternative to medical management. Carefully selected technique with optimum doses of BoNT- A injection is the most effective therapeutic approach with some minor adverse effects. The major concerns for this technique being the cost of injection and repeated injections.

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