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Short communication

# Does botulinum toxin decrease frequency and severity of sialorrhea in Parkinson's disease? ☆

Ana Caline Nóbrega [a], Bernardo Rodrigues [a], Ana Catarina Torres [a], Alfredo Enzo [b], Ailton Melo [a,*]

[a] *Division of Neurology and Epidemiology, Federal University of Bahia, Brazil*
[b] *Service of Radiology, Federal University of Bahia, Brazil*

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**Abstract**

This study analysed if botulinum toxin type A (BTX-A) decreases drooling in 21 Parkinson's disease patients. BTX-A injections were given in the parotid glands. The severity of drooling decreased in 18 (86%) patients, while frequency was reduced in 8 (38%). In 11(52%) patients, the frequency of drooling remained constant, which may reflect more difficulties in swallowing, compared to the group that presented such improvement. Future trials assessing the level of swallowing dysfunction may be important to establish a prognosis for patients who keep the frequency of drooling in spite of decreased severity after BTX injection.


*Keywords:* Drooling; Sialorrhea; Parkinson's disease; Botulinum toxin

## 1. Introduction

Drooling is common in several neurological diseases [1,2]. In the late course of Parkinson's disease, it is associated with increased morbidity [3]. Although swallowing dysfunction is sometimes associated with drooling, there is no clear correlation among these phenomena. Some trials have shown that botulinum toxin (BTX-A) decreases the volume and frequency of drooling, however the authors analyzed the two phenomena together giving the idea that the frequency of sialorrhea is always decreased by BTX-A [3,5]. This study was carried out to establish if botulinum toxin decreases frequency and severity of diurnal drooling in advanced Parkinson's disease patients.

## 2. Method

This study was approved by the ethical committee of the Federal University of Bahia, and was performed according to the 1964 Declaration of Helsinki. All patients provided their informed consent prior to taking part in any procedure of this study.

The diagnosis of Parkinson's disease was based on the presence of bradykinesia associated with at least one of the following symptoms: muscular rigidity, 4–6 Hz rest tremor or postural instability. All patients were previously evaluated by a neurologist and sent to a speech therapist specialized in swallowing disorders, who calculated the drooling score, considering the sum of the scores for severity (1, dry: never drools; 2, mild: only lips wet; 3, moderate: lips and chin wet; 4, severe: clothing soiled; 5, profuse: clothing, hands and tray moist wet) and frequency (1: never drools; 2: occasional drooling — not every day; 3: frequent drooling — every day; 4: constant drooling) of drooling, according to the established rating scales [4]. Patients with Parkinson's disease and diurnal sialorrhea with grade 5 or over were subsequently admitted to the Unit of Movement Disorders of the University's tertiary care medical center. Exclusion criteria included those patients who presented with dementia or severe depression. Other exclusion criteria were previous stroke, repeated head injuries, encephalitis, previous treatment with neuroleptics within 1 year prior to the onset of

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* Corresponding author.
*E-mail address:* asm@ufba.br (A. Melo).

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Table 1
Drooling scale score changes 1 month after botulinum toxin

| Parameters | Pretreatment | Postreatment | *p* (95%) |
|---|---|---|---|
| Drooling severity | 3.42±0.92 | 2.14±0.79 | <0.001 |
| Drooling frequency | 3.42±0.59 | 3.00±1.00 | 0.021 |
| Total score | 6.85±1.15 | 5.14±1.62 | <0.001 |

symptoms, pyramidal or cerebellar signs, early autonomic involvement, and supranuclear gaze palsy, as well as previous treatment of drooling or use of anticholinergic drugs. Injections containing 125 U of BTX-A (Dysport) were given in two points of the parotid gland, guided by ultra-sound after dilution (500 U/2.5 mL of saline). Drooling evaluation was repeated 15 and 30 days after BTX-A injection by the speech therapist, following the described criteria used in the baseline.

### *2.1. Statistical analysis*

Statistical analysis was performed using the SPSS (version 10.0). The Wilcoxon signed rank test and the paired Student's *t*-test were used for dependent variables. Any *p* values $< 0.05$ were considered statistically significant.

## 3. Results

A total of 21 Parkinsonian outpatients, 18 males and 03 females, mean age 70 years, ranging from 55–84 years, were examined. All were on levodopa therapy associated to entacapone and/or pramipexole. All but two patients reported decrease of drooling after two weeks from the date of injection. One had his condition worsened, and the other presented no substantial change. In those who presented improvement, the severity of drooling decreased in 18 patients, while frequency was reduced in 8. In 11 patients, the frequency of drooling remained constant after BTX-A. As we can see in Table 1, the total score of drooling decreased an average of 1.71 points, whereas severity decreased 1.28 points, and frequency had a 0.42 point reduction. Patient 21 developed bilateral local edema after BTX-A injections. This edema was mild, self-limited, and disappeared after four days. Patient 15 and 10 experienced mild dry mouth, lasting 1 month.

## 4. Discussion

This paper shows that 250 U of BTX-A in the parotid glands under ultrasound guidance is effective and safe to treat PD disabled patients with diurnal drooling. However, in the published articles, there is a wide variety of dosages, brands, sites and methods of botulinum toxin injection (use of ultrasound, number of injected glands, dilution and number of injection points), which creates difficulty for the comparison of results.

The reduction of the total drooling rate presented by our patients is in accordance with results presented by authors who used the same scale to measure drooling before and after use of BTX-A [5] or BTX-B [3] in parotid and submandibular glands. However, 52% of our patients did not present improvement in the frequency of drooling. Previous authors observed that there is no association between decrease of saliva production and drooling due to swallowing dysfunction observed in this group of patients [1,5,6]. Our results suggest that unreduced frequency of drooling may reflect difficulties in swallowing, whereas reduction in severity may be related to a decrease of saliva production after use of BTX. Thus, future trials assessing the grade of swallowing dysfunction may be important to establish a prognosis for patients who keep the frequency of drooling in spite of decreased volume from the use of BTX.

In a recent study with botulin toxin type B in parotid and submandibular glands to treat drooling in 21 Parkinson's disease or ALS patients, Contarino et al observed decrease in severity and frequency of drooling in 100% of the cases. It must be mentioned, however, that these authors used a toxin with higher anticholinergic power, and injected the toxin in parotid and submandibular glands, which may account for the difference in the results.

Notwithstanding some papers stating that injection of BTX in the parotids and submandibular glands are more effective than injection in the parotid glands alone [7,8], there is no agreement among the authors [9]. In addition, it is unknown whether decreased sialorrhea would interfere with swallowing, oral hygiene, formation of ulcers or cavities. This uncertainty leads us to stress the risk of a marked decrease of salivation in neurologic patients, particularly the old ones.

In our patients, botulin toxin was injected, under direct monitoring, in two sites of each parotid gland. If these cautions are followed, we can assure the toxin will not reach masticatory muscles, and the mentioned side effects will be avoided [10]. It is to be stressed, however, that most authors who did not use ultrasound to guide BTX injection to treat Parkinson's disease or parkinsonism associated drooling did not find masticatory muscles compromised [1,3,6,11].

We can thus see that many aspects related to a decrease of drooling in Parkinson's patients are still open. Trials with longer follow-up periods are necessary for prognostic factors and side effects of the proposed treatment be more accurately assessed.

## References

[1] Friedman A, Potulska A. Quantitative assessment of parkinsonian sialorrhea and results of treatment with botulinum toxin. Parkinsonism Relat Disord 2001;7(4):329–32.
[2] Porta M, Gamba M, Bertacchi G, Vaj P. Treatment of sialorrhea with ultrasound guided botulinum toxin type A injection in patients with neurological disoders. J Neurol Neurosurg Psychiatry 2001;70(4):538–40.
[3] Ondo WG, Hunter C, Moore W. A double-blind placebo-controlled trial of botulinum toxin B for sialorrhea in Parkinson's disease. Neurology 2004;62(1):37–40.
[4] Crysdale WS, White A. Submandibular duct relocation for drooling: a 10-year experience with 194 patients. Otolaryngol Head Neck Surg 1989;101:87–92.

[5] Mancini F, Zangaglia R, Cristina S, Sommaruga MG, Martignoni E, Nappi G, et al. Double-blind, placebo-controlled study to evaluate the efficacy and safety of botulinum toxin type A in the treatment of drooling in Parkinsonism. Mov Disord 2003;18(6):685–8.
[6] Pal PK, Calne DB, Calne S, Tsui JKC. Botulinum toxin A as treatment for drooling saliva in Parkinson's disease. Neurology 2000;54:244–7.
[7] Contarino MF, Pompili M, Tittoto P, Vanacore N, Sabatelli M, Cedrone A, et al. Botulinum toxin B ultrasound-guided injections for sialorrhea in amyotrophic lateral sclerosis and Parkinson's disease. Parkinsonism Relat Disord, published online 27 June 2006, doi:10.1016/j.parkreldis.2006.05.005.
[8] Suskind DL, Tilton A. Clinical study of botulinum-A toxin in the treatment of sialorrhea in children with cerebral palsy. Laryngoscope 2002;112(1):73–81.
[9] Dogu O, Apaydin D, Sevin S, Talas DU, Aral M. Ultrasound-guided versus blind intraparotid injections of botulinum toxin-A for the treatment of sialorrhoea in patients with Parkinson's disease. Clin Neurol Neurosurg 2004;106(2):93–6.
[10] Jost WH. Treatment of drooling in Parkinson's disease with botulinum toxin. Mov Disord 1999;14(6):1057.
[11] Racette BA, Good L, Sagitto S, Perlmuter JS. Botulinum toxin B reduces sialorrhea in parkinsonism. Mov Disord 2003;18(9):1059–61.