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Brief Report

Severe Constipation in Parkinson's Disease Relieved by Botulinum Toxin

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Summary: A parkinsonian patient with severe outlet-type constipation was treated with injection of botulinum toxin into the puborectalis muscle. A total of 30 units (Botox) was injected in two sites. Resting anal pressure, maximum voluntary contraction, and pressure on straining were evaluated before treatment and 4, 8, 12, and 16 weeks afterward. Pressure values declined following treatment, the decline of pressure on straining ending by week 12. Proctography performed 8 weeks after treatment showed improvement in the anorectal angle and evacuation of barium paste. The clinical benefit lasted for ~12 weeks. The present data show that botulinum toxin is a promising tool for treating outlet-type constipation in Parkinson's disease. **Key Words:** Botulinum toxin—Gastrointestinal dysfunction—Outlet-type constipation—Parkinson's disease—Puborectalis muscle.

Constipation and defecatory dysfunction occur 2–3 times more frequently in patients with Parkinson's disease (PD) than in nonparkinsonian subjects (1,2). Constipation exacerbates with disease severity and duration (2), supporting the hypothesis that PD directly affects gastroenteric motility (3). Ineffective defecation in PD has been correlated with paradoxical activation of the puborectalis muscle during straining (4), which accentuates the flap-valve action of the anorectal angle resulting in an obstruction to the onward passage of stool. Slow intestinal transit may coexist with outlet obstructions to exacerbate constipation.

Botulinum toxin (BTX) has been already used to relieve hyperactivity of the smooth muscles controlling propulsion along the alimentary tract (5–7). The toxin has also been injected into the puborectalis muscle of some patients affected by anismus (8).

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PATIENT AND METHODS

A 55-year-old man had been affected by PD since age 42; for several years, he was successfully treated with levodopa and dopamine agonists. At the age of 50, he underwent a left stereotactic thalamotomy that abolished tremor on the right-hand side. In the last 5 years, he had motor fluctuations that were partially controlled by drugs. Severe chronic constipation, as commonly defined (9), was present since the onset of parkinsonian signs and progressively worsened. Domperidone and laxatives were used unsuccessfully. His constipation became severe and progressively worsened in the last 2 years; no spontaneous evacuations occurred for the last 6 months. The patient was studied by a standard protocol for constipation (10).

There were no signs of autonomic dysfunction. Intestinal transit time, as studied by plain abdominal radiography, showed a mild slowing of transit through the colon. A double-contrast barium enema revealed sigmoid and transverse dolichocolon, and findings on colonoscopy were unremarkable. No other bowel abnormalities were reported. Proctography during defecation enabled us to classify this case as outlet-type constipation due to

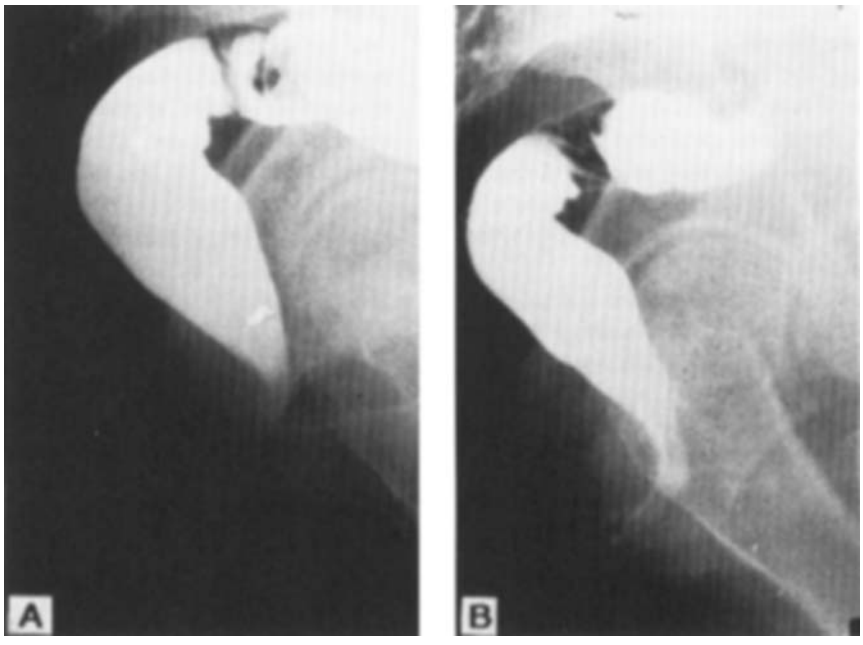

FIG 1. Defecatory proctography on straining. **A:** Before treatment, the anorectal angle is 115°; barium paste is not evacuated. **B:** At 8 weeks after botulinum toxin injection, the anorectal angle is 130°; evacuation of barium paste is shown.

puborectal syndrome (9). Anorectal manometry did not reveal a hypercontractile retrosphincteric reflex, as reported in some PD cases (11).

Antiparkinsonian medications consisted of levodopa preparations (a total of 1,400 mg of levodopa daily), pergolide (1 mg b.i.d.), and domperidone (10 mg t.i.d.). These were not varied throughout the study. Apomorphine, known to improve defecatory function in parkinsonian patients (12), was not used. The patient was studied with defecating proctography before treatment and 8 weeks afterward. Clinical evaluations and anal manometry were performed before treatment and every 4th week thereafter. All clinical and instrumental evaluations were performed 1 h after levodopa intake, with the patient in the *on* condition.

BTX A (Botox, Allergan, Irvine, CA) was injected into the puborectalis muscle with the patient lying on his side. No sedation or local anesthesia was used. The muscle was palpated and verified by recording with a unipolar electromyographic injection needle attached to the syringe containing the toxin solution (50 units/ml). A total of 30 units were injected in two sites: one injection was performed on each side of the puborectalis muscle close to the deep part of the external anal sphincter (8). After the injections, the patient's case was followed for 12 weeks.

TABLE 1. *Summary of quantitative evaluations (normal values are reported in the text)*

Weeks	0	4	8	12
Manometry (mm Hg)				
Resting pressure	95	50	40	40
Voluntary contraction	100	60	60	60
Pressure on straining	100	40	55	80
Proctography				
Anorectal angle (resting)	110°		115°	
Anorectal angle (on straining)	110°		130°	
Evacuation of barium paste	No		Yes	

RESULTS

Before treatment, on digital examination the anal orifice was closed, basal anal tone and voluntary contraction were detectable, and the anorectal angle could be appreciated normally, but no relaxation of the puborectalis muscle was detected when the patient strained. Pretreatment proctography demonstrated a resting anorectal angle of 110° (mean normal value, 90°; range, 70°–140°) that was not modified on straining (mean normal value, 135°; range, 110°–180°). Owing to impaired relaxation of the puborectalis muscle, the patient was unable to evacuate the barium paste (Fig. 1A). Anorectal manometry showed a resting pressure of 95 mm Hg. Pressure during maximum voluntary contraction did not vary and was not released by straining (Table 1). Normal values for manometry have been previously published (13).

The first spontaneous evacuation occurred 4 days after the injection. At 4 weeks after BTX treatment, the patient reported daily spontaneous evacuations that required

prolonged and effortful strain. Anal manometry revealed a decline in pressure values at rest, during maximum voluntary contraction, and on straining (Table 1).

At 8 weeks after BTX treatment, the patient had further clinical improvement: strain was brief though effortful, and anal pressure was lower than baseline (Table 1). The anorectal angle was 115° at rest (Fig. 1A) and widened, on straining, to 130°. The patient could evacuate the barium paste (Fig. 1B).

At 12 weeks after BTX treatment, the patient complained of a relapse. He reported that, starting 8 weeks after the treatment, defecation had gradually worsened, which forced him to take laxatives again. Defecatory difficulties, however, were not as severe as before treatment. Anorectal manometry showed a resting pressure of 40 mm Hg; pressure during maximum voluntary contraction was 60 mm Hg and, on straining, was 80 mm Hg (Table 1). No side effects were reported during the entire study period.

DISCUSSION

This observation provides new evidence of the usefulness of BTX in the management of alimentary tract dysfunction (6,14). This patient's constipation, predominantly of the outlet type as shown by pressure measurements and by proctography, improved following local chemodenervation of the puborectalis muscle. The effect was transient, confirming that the underlying cause of outlet constipation had not been cured.

Constipation in PD is usually of a mixed type, being partly due to slowing of intestinal transit and partly due to outlet obstruction. Based on such premises, prokinetic drugs were maintained in this patient during the treatment phase to improve delayed transit. Since distant effects of BTX cannot be detected clinically (15), it is concluded that local infiltration of BTX improved outlet obstruction, but had no appreciable effect on reduced transit. Considering that paradoxical activity of the puborectalis muscle in PD has been proposed to be a form of focal dystonia (4), the improvement observed in this case may be similar to that following local infiltration of BTX in other primary and secondary cases of focal dystonia.

As shown by anal manometry, the maximum voluntary pressure, as well as the resting pressure, decreased following BTX injections into the puborectalis muscle. The latter pressure variation indicates a diffusion of the toxin to the internal (smooth) sphincter. Such diffusion was not symptomatic, because no incontinence or other unwanted reactions were reported by the patient. Still, it is worth noting that, although minimal or no diffusion to the puborectalis occur following BTX injections into the internal sphincter (5), the toxin diffuses quite appreciably in the opposite direction. Fecal incontinence is, therefore, a potential complication of this procedure, and further investigation of its efficacy and safety are indicated before its general usage can be advocated.

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