

# Multidose Botulinum Toxin A for Intralaryngeal Injection: A Cost Analysis

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**Summary: Objectives.** Botulinum toxin A (BtxA) injection is the mainstay treatment for laryngeal dystonias. BtxA product labeling states that reconstituted toxin should be used within 4 hours on a single patient despite several studies that have demonstrated multidose BtxA to be safe and effective. Many insurance carriers mandate the use of an outside pharmacy which necessitates a single-use approach. This study compares the cost savings of multidose BtxA for laryngeal dystonia compared to single-use.

**Study Design.** This is a retrospective review and projected cost savings analysis.

**Methods.** Records and billing information were reviewed for patients receiving BtxA for intralaryngeal injection at a single laryngology division in 2015. Inclusion criteria included CPT 64617 or J0585; exclusion criteria included CPT 64616. The price of BtxA 100 unit vial for calculation was \$670.

**Results.** A total of 142 patients were seen for intralaryngeal BtxA injection resulting in 337 visits over 1 year. The average BtxA dose per visit was 2.86 units with an average of 3.06 procedure visits per year. The calculated cost of BtxA treatment using a single vial approach was found to be \$2,050 per patient per year. If billed instead for \$7/unit with 5 units wastage charge per visit, the yearly per patient charge is \$168. Single vial-use of BtxA injection thus represents a 1,118% price increase versus multidose use. When estimated for yearly prevalence of spasmodic dysphonia, multidose BtxA use would save almost \$100 million annually.

**Conclusions.** Multidose botulinum toxin A application utilizing per unit billing is significantly less expensive than per single-use vial billing and would save the health-care system significant amount of money without any sacrifice in safety or effectiveness.

**Key Words:** Health policy—Spasmodic dysphonia—Botulinum toxin A—Intralaryngeal injection—Cost analysis.

## INTRODUCTION

Spasmodic dysphonia (SD) is a focal dystonia involving the intrinsic muscles of the larynx. There are two well-accepted types of spasmodic dysphonia based on the predominant muscle involvement: adductor and abductor spasmodic dysphonia.<sup>1</sup> Spasmodic dysphonia is estimated by the National Spasmodic Dysphonia Association to afflict approximately 50,000 North Americans, although this number may be inaccurate due to misdiagnosis or undiagnosed cases.<sup>2</sup>

The gold standard treatment of spasmodic dysphonia has for over 20 years been intralaryngeal injection of botulinum toxin A, which requires repeat injections that are usually done as short in-office procedure done under local anesthesia every ~2–3 months.<sup>1,3,4</sup> There are several formulations of botulinum toxin A, including onabotulinumtoxinA (Botox, Allergan, Irvine, CA), incobotulinumtoxinA (Xeomin, Merz, Raleigh, NC), and abobotulinumtoxinA (Dysport, Ipsen, Basking Ridge, NJ). As all of the safety and efficacy literature for intralaryngeal injection has focused on the use of onabotulinumtoxinA, this paper will focus on that product, henceforth abbreviated as BtxA. BtxA comes in single-use 50 unit (labeled for cosmetic use only), 100

unit, or 200 unit vials consisting of a powder that, per manufacturer instructions, must be reconstituted and used within four hours on a single patient.<sup>5</sup> However, dosages for intralaryngeal injection typically range between 1 and 5 units per muscle complex targeted, which are significantly fewer units than the total vial contents.<sup>6,7</sup>

A previous study has shown that multidose usage of BtxA 100 unit vials for intralaryngeal injection is both safe and effective.<sup>5</sup> This multi-institution study involved a 10-year chart review of injection responses, questionnaires of patient's past injection experiences, and a prospective study of injection adverse events of multidose BtxA injections at three different laryngology centers of excellence. There was no evidence of infection-related complications associated with multidose use for any of the groups, and the self-reported efficacy rate of multidose injection was 96.6%. However, this study did not address cost differences between single vial and multidose usage. The present study aims to explore the cost-savings of using BtxA in a multidose approach compared to a single vial use.

## MATERIALS AND METHODS

The study was submitted and approved by the University of Pittsburgh's Institutional Review Board (Number PRO13030372). Medical records and billing information were reviewed for all patients who were billed for botulinum toxin A injection during a clinical visit at our institution in 2015. Inclusion criteria included CPT code 64617 ([chemodenervation of] larynx, unilateral, percutaneous (eg, for spasmodic dysphonia), includes guidance by needle electromyography, when performed) or J0585 (botulinum toxin, per unit (report the number of units injected)).<sup>8</sup> CPT code 64616, chemodenervation of muscles of the neck, and

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the older CPT 64613, which included chemodenervation of muscle(s); neck muscle(s) (eg, for spasmodic torticollis, spasmodic dysphonia), or any patients who did not have laryngeal injection specifically were excluded.

BtxA injections were performed using a percutaneous injection with electromyographic guidance via a transcricothyroid membrane approach in an in-office setting either using newly reconstituted single-use 100 unit vials or, as described previously, using 100 unit vials in a multidose fashion.<sup>5</sup> Demographic information collected included age (at first injection of the year), gender, insurance, visit dates, number of visits, indicated diagnosis for injection, and total units injected over the year. Based on the frequency of injection visits, an average number of injection visits per year was calculated for each patient. The average units injected per visit was similarly calculated. The overall average injection visits per year for the cohort was calculated and multiplied by the 2015 average wholesale price for a 100-unit vial of BtxA (\$670 USD) to calculate a per patient yearly BtxA cost. Based on the average units injected per visit, an alternate billing calculation was made for per unit billing based on average units injected per visit plus 5-unit wastage per visit based on \$7/unit billing.

## RESULTS

A total of 429 total separate procedure codes for CPT code 64617 (chemodenervation of the larynx) were billed. These procedures were cross-referenced with billing for botulinum toxin (J0585) to confirm BtxA injection. These injections involved 145 separate patient accounts—two patients were total laryngectomy patients who received injections into the neopharynx and one patient was listed under two different billing accounts and was combined. Thus, 142 patients received intralaryngeal BtxA injection. Demographics and diagnosis distribution are listed in Table 1. The vast majority of patients were women (83.8%), the most common diagnosis was adductor spasmodic dysphonia (75.4%), and the average age at first injection of the year was 63.1 years, with a range from 22.6 to 92.5 years old. Although some patients switched insurance during the year, 52 of the 142 patients used Medicare insurance during the year (36.6%), five

patients used Medicaid (3.5%), and four patients paid out-of-pocket (2.8%). The remainder of patients used private insurance.

The total number of visits was calculated by counting procedure codes for each patient and eliminating codes for multiple injections on the same date (eg, bilateral injections), leading to 337 total procedure visits. The frequency of visits (based on the time between the first and last visit of the year) was calculated for each patient, with an average frequency of 3.06 visits per year. An average of 2.86 units (total) were injected per visit. At \$7 per unit with 5 unit (\$35) wastage per visit, per unit billing leads to \$55.02 billed per patient visit, or \$168.36 per patient per annum. In contrast, if our patient cohort was billed for the whole 100 unit vial per visit at the 2015 average wholesale price of \$670, the total cost is \$2,050.20 per patient per annum. The difference equals an effective 1,118% increase in cost when the patient is billed using a single vial approach compared to a multidose approach. Assuming similar visit frequency for the estimated 50,000 patients with spasmodic dysphonia, the total difference in annual health-care expenditure in the United States of America is \$8,418,000 versus \$102,510,000, or a nationwide cost-savings of \$94,092,000 for multidose intralaryngeal injection approach of BtxA for spasmodic dysphonia.

## DISCUSSION

The gold standard treatment for a variety of laryngeal disorders, including laryngeal dystonias, such as spasmodic dysphonia, and essential tremor, is intralaryngeal BtxA injection.<sup>9</sup> OnabotulinumtoxinA (BtxA) is available in 50-, 100-, or 200-unit vials; however, only the 100-unit vial is typically used for intralaryngeal injection. Despite the fact that vials are labeled as single-use only, both anecdotal reports and formal surveys of physicians have indicated that many physicians re-use BtxA to minimize cost, without noticing a decrease in efficacy, and to increase the ease of customized dosing and patient scheduling.<sup>10,11</sup> BtxA has been demonstrated to maintain efficacy when stored for up to 2 weeks in several studies, and up to 6 weeks in one study.<sup>10,12–14</sup> Multidose BtxA for in-office intralaryngeal injection was previously shown to be safe and effective in a multi-institution study.<sup>5</sup> The present study is a follow-up cost analysis study that demonstrates the substantive cost-savings of this approach.

Multidose usage of BtxA has been not only approved but specifically suggested by the Center for Medicare & Medicaid Services (CMS): “The CMS encourages physicians, hospitals and other providers to schedule patients in such a way that they can use drugs or biologicals most efficiently, in a clinically appropriate manner” (Pub 100-04, Transmittal 1248, 5-25-07, section 40). Indeed, the example cited in the document was the usage of BtxA vials in a multidose fashion. Included in CMS instructions were the ability to bill CMS on a per-unit plus wastage basis or for the entire vial. This approach provides implicit approval for a multidose approach to the use of BtxA. Unfortunately, many private insurances, used by nearly 60% of the patients in our study, do not approve multidose injection, and many patients are required to obtain new single-use vials for each procedure visit. One of the reasons for this difference is ostensibly for cost-savings by bulk purchasing vials from a

**TABLE 1.**  
**Demographics of Study Cohort**

No. of patients	142	
Average age at first injection	63.1 ± 1.2 y (22.6–92.5)	
Gender	Female	119 (83.8%)
	Male	23 (16.2%)
Diagnosis	Adductor SD	107 (75.4%)
	Abductor SD	6 (4.2%)
	Essential tremor	23 (16.2%)
	PVFM	2 (1.4%)
	Mixed SD	2 (1.4%)
	Tremor/SD	1 (0.7%)
	Laryngeal myokymia	1 (0.7%)

Abbreviations: PVFM, Paradoxical Vocal Fold Motion Disorder; SD, spasmodic dysphonia.

third-party pharmacy service to send the provider an entire vial (100 units) for each patient.

Given the small number of BtxA units typically used for intralaryngeal BtxA injection, this situation creates a significant wastage and financial problem. Indeed, intralaryngeal injections, which use only between ~1% to 5% of a 100-unit vial, require the practitioner to discard nearly 97% of the purchased pharmaceutical.<sup>6,7</sup> Currently the recommended practice is single-use vials, but based on the spasmodic dysphonia population estimates, a switch to multidose vials would mean a reduction in health-care costs of almost \$100 million annually. Additionally, this estimate only grows if expanded to include other intralaryngeal injection indications, such as essential tremor, or nonlaryngology BtxA uses (orofacial dystonia, blepharospasm, etc).

Another advantage of multidose BtxA use is the ability for the clinician to have multiple different concentrations of BtxA on hand to allow easy personalization of BtxA use from patient to patient. Given the importance of delivering the smallest possible volume of BtxA to the vocal fold (for airway safety and to minimize diffusion of BtxA to adjacent muscles), it is clinically required to have a range of different BtxA concentrations available.<sup>15</sup> For example, our clinical group maintains BtxA concentrations of 10, 5, 2.5, 1.25, and 0.625 units per 0.1 mL for dedicated “Botox” clinics. In contrast, attempting injections with single-use BtxA dosing (eg, for a patient who requires significantly different dosages in different muscle complexes or contralaterally) causes a decreased clinical efficiency, significant waste of a precious medication, and is not cost-effective medical care. Another possible dispensing pattern is to have hospital pharmacies prepare standard dose aliquots using standard operating procedures. Such a dosing regimen may make multiple concentrations more difficult, but it does allow for dispensing pharmaceuticals in ways which maintain sterility under local regulations.

As health-care expenditures grow and insurance premiums continue to rise, efforts to reduce cost and waste have become more important. Chronic conditions that require maintenance therapy, like dystonias, are especially susceptible to creeping price increases. We believe the savings demonstrated in our study are so significant, without any decrease in safety or efficacy, that they warrant a re-evaluation of single-dose BtxA use and recommend multidose usage for BtxA intralaryngeal injection.

### CONCLUSION

Multidose usage of botulinum toxin A for intralaryngeal injection has been shown to be safe and effective but there are no data on the cost-benefit of such usage. Our study shows

that current recommendations to follow single-vial usage equals an effective 1,118% price increase compared to a multidose administration of BtxA. Estimates of nationwide usage suggest a potential health-care savings of \$100 million annually. We recommend implementation of multidose injection as the standard of care for intralaryngeal botulinum toxin A injections.

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