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MAIN ARTICLE

Spasmodic dysphonia: a seven-year audit of dose titration and demographics in the Indian population

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Abstract

Objectives: This study aimed to evaluate the demographics of spasmodic dysphonia in the Indian population and to analyse the optimum dose titration of botulinum toxin type A in this group. A comparative analysis with international studies was also performed.

Method: The study involved a retrospective analysis and audit of botulinum toxin type A dose titration in spasmodic dysphonia patients who visited our voice clinic between January 2005 and January 2012.

Results: The average total therapeutic dose required for patients with adductor spasmodic dysphonia was 4.2 U per patient per vocal fold (total 8.4 U per patient), and for patients with abductor spasmodic dysphonia, it was 4.6 U per patient.

Conclusion: Our audit revealed that 80 per cent of the spasmodic dysphonia patients were male, which contrasts dramatically with international studies, wherein around 80 per cent of spasmodic dysphonia patients were female. Our study also revealed a higher dose titration of botulinum toxin for the Indian spasmodic dysphonia population in both adductor and abductor spasmodic dysphonia cases.

Key words: Dysphonia; Larynx; Voice Disorders; Botulinum Toxin

Introduction

Spasmodic dysphonia is a focal laryngeal dystonia; it is an action-induced laryngeal movement disorder that affects laryngeal motor control. This voice disorder is characterised by abnormal, intermittent, intralaryngeal muscle spasms, which result in voice breaks. The action that triggers the spasms is speaking itself. Patients with spasmodic dysphonia classically have a spasmodic speech pattern with predominantly adductor or abductor spasms.

In the adductor variant of spasmodic dysphonia, spasms of the adductor muscles cause strangled voice breaks, and a strained or strangled voice quality. In the abductor variant, spasms of the posterior cricoarytenoid muscle cause breathy voice breaks often associated with flaring of the ala nasi, and a breathy voice quality. A study by Cannito and Johnson suggests that all spasmodic dysphonia patients have a mixed spasmodic dysphonia with either adductor or abductor spasms predominating the other.[1] These voice breaks lead to significant difficulty in daily communication, and limit the individual functionally, physically and emotionally.

Though spasmodic dysphonia may be present in both males and females, it is more prevalent among the female population, with some estimates as high as 80 per cent.[2] In spasmodic dysphonia, there seems to be a progression of symptoms for two years, following which there is usually a plateau of symptoms, though the patient may complain of a progressive increase in the effort required to phonate. Spasmodic dysphonia is a relatively rare disorder; however, accurate worldwide audited numbers are not available. With increasing awareness of spasmodic dysphonia, more cases are being accurately diagnosed and managed.

A provisional diagnosis of spasmodic dysphonia can often be made within a couple of minutes of talking to the patient, as the diagnosis is based primarily on auditory and perceptual features. Adductor spasmodic dysphonia patients have a typical choking voice and the spasms are heard on vowels. Thus, sentences with more vowels can highlight this voice disorder.[3] The adductor variety is more common than the abductor type, with the former affecting around 80 per cent of persons with spasmodic dysphonia.[4] In the case of abductor spasmodic dysphonia, a typical breathy spasm is observed and is almost always accompanied by a flaring of the ala nasi. In a prospective, double-blinded, controlled study of 24 cases of proven

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abductor spasmodic dysphonia, visible and detectable flaring of the ala nasi, as a constant recurring pattern, was observed (in contrast to a control group). In the control group, two patients demonstrated persistent flaring of the ala nasi during phonation; both of these patients were affected by vocal nodules.[5] The breathy bursts observed in cases of abductor spasmodic dysphonia take place when attempting to talk after voiceless consonants.[6,7]

Laryngoscopy and electromyography (EMG) can help to establish a diagnosis of spasmodic dysphonia. The findings of laryngoscopic evaluation (of vocal fold movement) in adductor spasmodic dysphonia range from normal, in very early spasmodic dysphonia, to obvious bursts of hyperadduction during speech.[8] This may reflect true vocal fold spasms only, or true and false vocal fold spasms with a complete anteroposterior and lateral compression of the supraglottis. Stroboscopy may be performed, ideally using the 'chip on the tip' flexible stroboscope. In patients with abductor spasmodic dysphonia, a sudden abduction is observed corresponding with the breathy spasm on phonation. Electromyography findings in patients with spasmodic dysphonia reveal an inappropriate dystonic muscular activity with significant electrical activity before the onset of voice, and persistent electrical activity despite voice breaks.[9]

One main hurdle to finding a cure for spasmodic dysphonia is the fact that the cause and pathophysiology remain unclear. A study by Simonyan and Ludlow suggests that the aetiology of spasmodic dysphonia is abnormality in the primary somatosensory cortex.[10] Lesions in the basal ganglia have been implicated by Marsden *et al.* as leading to spasmodic dysphonia.[11] The findings of a study by Blitzer and Brin, of a series of laryngeal dystonia patients, indicate that spasmodic dysphonia has a genetic aetiology.[12]

A team approach is vital in the diagnosis of spasmodic dysphonia. Together with the laryngologist, a speech therapist and a neurologist form the core team in the diagnosis of spasmodic dysphonia. Occasionally, the opinion of a gastroenterologist or a psychiatrist may be sought.

The 'gold standard' of treatment for adductor spasmodic dysphonia is botulinum toxin injection in the affected muscle, which causes chemodenervation, with resultant weakening of the muscle spasms. Botulinum toxin works at the level of the neuromuscular junction by binding presynaptically and blocking the release of acetylcholine, thus arresting the muscle contraction. Botulinum toxin does not affect the synthesis or storage of acetylcholine.[12,13]

Our aim was to study the demographics of spasmodic dysphonia patients, with an analysis of dose titration and response to botulinum toxin type A, in the Indian population. Laryngeal EMG with botulinum toxin injection is not currently covered by insurance in India; we hope that this study will help to improve the outcome for spasmodic dysphonia patients being injected with botulinum toxin for the first time. A comparative analysis with international studies was also performed.

Materials and methods

We performed a retrospective audit of all spasmodic dysphonia patients who visited our voice clinic between January 2005 and January 2012. Of the 76 patients identified, 56 had adductor spasmodic dysphonia, 13 had abductor spasmodic dysphonia and 7 had mixed spasmodic dysphonia (Figure 1). Sixty-one patients were males and 15 were females. All patients were diagnosed by the first author, perceptually and by flexible video laryngoscopy.

All patients were counselled regarding the expected outcome and side effects of botulinum toxin. Patients in the adductor spasmodic dysphonia group were informed about the possibility of a breathy voice, which may develop over a variable period of approximately 1–6 weeks, and that there may be aspiration of water (when drinking) for 2 days to 1 week following the injection.

All patients were followed up at one week to enable assessment of the voice. In patients who did not show any response to the injection at this time, a re-injection was performed free of cost using the previously reconstituted botulinum toxin, which had been preserved in a temperature-controlled environment.

Injection procedure

Our patients were injected under laryngeal EMG control using the AccuGuide injection monitor (Medtronic, Minneapolis, Minnesota, USA), with a 27-gauge,Teflon-coated unipolar needle. No local anaesthesia was used during this procedure.

At the time of the injection, patients were placed in a sitting position with their necks extended. The skin over the mandible and neck was cleaned with 95 per

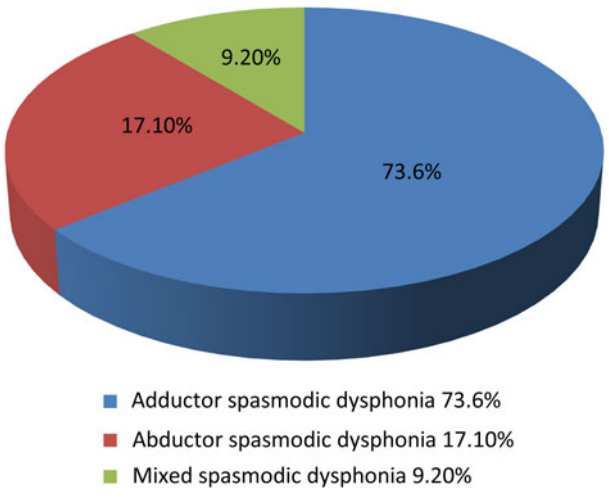

FIG. 1
Incidence of adductor, abductor and mixed spasmodic dysphonia at our voice clinic.

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cent methylated spirit, and surface electrodes were placed on the skin over the mandible on the side being injected. The patient was instructed not to swallow or move during the actual injection procedure.

In the adductor spasmodic dysphonia patients, after palpating the neck and identifying the cricothyroid membrane, the injection needle was angled at 30 degrees in males and 0–15 degrees in females, and introduced 1 cm from the midline with a 30-degree tilt of the needle laterally. Each patient was asked to say 'eee', and the corresponding signal was observed on the EMG machine. If the EMG reading showed a burst of activity, the needle was presumed to be in the thyroarytenoid muscle and botulinum toxin was injected. A similar procedure was carried out on the opposite side.

In the abductor spasmodic dysphonia patients, the lateral edge of the thyroid ala and the superior border of the cricoid cartilage were identified, and an imaginary cross-section of these two lines was formed. The injection needle was inserted at the upper and outer quadrant of this cross-section. The patient was asked to sniff; a burst in EMG activity confirmed entry into the posterior cricoarytenoid muscle.

For the patients with adductor spasmodic dysphonia, the dose of botulinum toxin type A was 2.5 U in both the vocal folds at the first visit. Voice and vocal fold movement were evaluated after a week. If there was no breathiness of voice or loss of spasms, a second injection of 2.5 U was given in each vocal fold. If the patient had a decrease in spasms but no breathiness of voice, 1.25 U was injected bilaterally. The botulinum toxin used for re-injection was the previously prepared and preserved botulinum toxin, which had been kept in a temperature-controlled environment.

Patients with abductor spasmodic dysphonia were injected with 3.75 U botulinum toxin type A unilaterally and re-evaluated after a week. They were subsequently injected with 1.25 U into the same vocal fold if no improvement was observed.

Results

Of the 76 patients with spasmodic dysphonia who visited our voice clinic between January 2005 and January 2012, 61 patients were male (80 per cent) and 15 were female (20 per cent). Only 31 spasmodic dysphonia patients opted for the botulinum toxin injection, of which 25 were adductor spasmodic dysphonia patients and 6 were abductor spasmodic dysphonia patients. None of the mixed spasmodic dysphonia patients opted for this treatment.

Of the 25 adductor spasmodic dysphonia patients, 4 patients had a breathy voice and an absence of spasms 1 week after the first injection of 2.5 U botulinum toxin in both vocal folds, and did not need a repeat injection. However, 21 patients (84 per cent) needed re-injecting after 1 week: 13 patients received 2.5 U bilaterally and 8 patients received 1.25 U bilaterally. Hence, the total dose of botulinum toxin in adductor spasmodic dysphonia patients was 5 U in 4 patients, 7.5 U in 8 patients and 10 U in 13 patients (Figure 2). The average total therapeutic dose required was 4.2 U per patient per vocal fold (total of 8.4 U per patient).

Following botulinum toxin injection, 24 per cent of the adductor spasmodic dysphonia patients experienced slight aspiration, which lasted for an average of 5 days. These patients were counselled regarding the aspiration and taught a special technique for swallowing. They were asked to drink water slowly, using a straw or a spoon. The voice of patients in this group remained breathy for an average of 13 days.

The six patients with abductor spasmodic dysphonia who opted for this treatment were injected with 3.75 U botulinum toxin unilaterally and re-evaluated after a week. They were re-injected with 1.25 U botulinum toxin if no improvement was observed. This was necessary in four of the six patients (66.6 per cent). The average total therapeutic dose required was 4.6 U per patient.

Discussion

Our study revealed a male predominance in spasmodic dysphonia patients; this is in contrast to international studies which show a female predominance. Adler *et al.*, in their study of 270 spasmodic dysphonia patients at the Mayo Clinic (Scottsdale, Arizona, USA), showed a female predominance of 79.2 per cent.[2] One possible explanation for the high number of males in our study of spasmodic dysphonia patients relates to the fact that the majority of the workforce in India are male. Non-working females may not have the confidence or receive adequate social support to tackle their voice problem.

In India, treatment with botulinum toxin is not covered by insurance. As many of our patients belong to the lower socioeconomic strata, most patients want

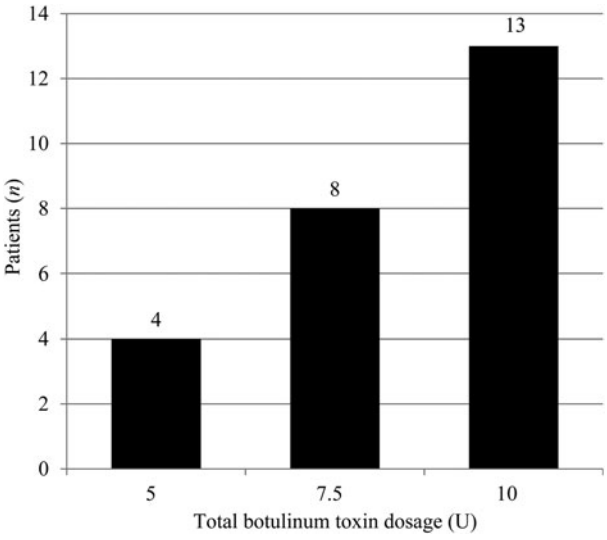

FIG. 2
Dose of botulinum toxin in our adductor spasmodic dysphonia patients.

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a guarantee of improvement in their vocal symptoms following the first botulinum toxin injection. To keep the costs of the procedure low, whilst still aiming to provide maximum benefit to our patients, the standard dose of 2.5 U botulinum toxin was injected bilaterally in adductor spasmodic dysphonia cases, and a dose of 3.75 U was injected unilaterally in abductor spasmodic dysphonia cases. However, all patients were counselled regarding a possible repeat injection, provided free of cost at one week, if there was no apparent response to the initial botulinum toxin injection. We used the same botulinum toxin that had been reconstituted for the patient one week previously and subsequently preserved in a temperature-controlled environment.

The average total dose was calculated by adding the first injection dose to any injection dose given one week later. In our study, 16 per cent of patients did not need a repeat injection. The average total dose injected was 4.2 U per vocal fold per patient for adductor spasmodic dysphonia and 4.6 U per patient for abductor spasmodic dysphonia (injections were unilateral for this latter group). As the re-injected botulinum toxin was 7 days old, it was probably less potent than the freshly prepared botulinum toxin. Therefore, we feel that the recommended total dose of botulinum toxin type A, in the Indian adductor spasmodic dysphonia population, should be more than 2.5 U and less than 4.2 U per vocal fold. For adductor spasmodic dysphonia patients, a dose of 3 U in each vocal fold may be injected at the first visit, and subsequent improvement in voice observed as an on-going study. For abductor spasmodic dysphonia patients, we recommend 4 U unilaterally.

Most clinicians begin with a bilateral injection of 1.25–2.5 U botulinum toxin into each vocal fold in adductor spasmodic dysphonia cases and 3.75 U unilaterally in abductor spasmodic dysphonia cases. The total dose can be increased incrementally over subsequent injections.[14] Blitzer and Brin developed an injection protocol wherein the starting dose for adductor spasmodic dysphonia was 3.75 U bilaterally. However, this was gradually brought down to 2.5 U and subsequently to 1 U bilaterally, in an attempt to minimise the duration of breathy voice symptoms (Table I).[12] Some patients are sensitive to the toxin; in these patients, small bilateral doses do not give the best results but larger doses lead to too much breathiness. Blitzer *et al.* recommended giving such patients a large unilateral dose, followed by a smaller dose in the contralateral vocal fold two weeks later.[4] In a 2013 study by Rosow *et al.*, it was observed that patients injected with 1.25 U bilaterally had a significantly shorter duration of breathiness of voice compared with patients in other studies that used standard doses of botulinum toxin (2.5 U), with no significant difference in clinical effectiveness or voice outcome. The authors therefore recommended a relatively low initial botulinum toxin A dose with subsequent titration, to improve voice outcomes (Table I).[15] An interesting study by Birkent *et al.* of long-term botulinum toxin users revealed that the dose needed for a constant response in the treatment of laryngeal dystonia decreases over time, without any accompanying change in the duration of good voice.[16]

- **In this study, 80 per cent of Indian spasmodic dysphonia patients were male; this is in contrast to international study findings which show an 80 per cent female predominance**
- **A higher total dose of botulinum toxin was required for the Indian spasmodic dysphonia population compared with international studies**
- **For Indian spasmodic dysphonia patients, we recommend 3 U botulinum toxin A bilaterally for adductor types and 4 U unilaterally for abductor types**

Although 24 per cent of our patients experienced occasional aspiration when drinking water, which lasted for 5 days after the botulinum toxin injection, the patients tolerated this well and were happy with the outcome of a 5–6-month spasm-free voice. Blitzer *et al.*, who studied over 900 patients injected with botulinum toxin, showed that aspiration affected 15–60 per cent of patients, and this resolved in 1–2 weeks.[4]

Conclusion

Our study revealed a high male to female ratio of spasmodic dysphonia in the Indian population. We feel that this could be attributed to social and financial compulsions, rather than being a true representation of the spasmodic dysphonia population. In our study, a higher dose of botulinum toxin was required for both adductor (8.4 U) and abductor (4.6 U) spasmodic dysphonia patients, as compared with international studies.

TABLE I
COMPARISON OF BOTULINUM TOXIN TYPE A DOSES FOR ADDUCTOR AND ABDUCTOR SPASMODIC DYSPHONIA

Study	Recommended dose for adductor spasmodic dysphonia	Recommended dose for abductor spasmodic dysphonia
Pou *et al.*[14]	1.25–2.5 U bilaterally in thyroarytenoid muscle	3.75 U unilaterally in posterior cricoarytenoid muscle
Blitzer & Brin[12]	1 U bilaterally in thyroarytenoid muscle	3.75 U unilaterally in posterior cricoarytenoid muscle
Rosow *et al.*[15]	1.25 U bilaterally in thyroarytenoid muscle	–
Current study	3 U bilaterally in thyroarytenoid muscle	4 U unilaterally in posterior cricoarytenoid muscle

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Following the botulinum toxin injection, the incidence of aspiration was 24 per cent; this lasted for an average of 5 days and was well tolerated by patients. We propose that the initial dose of botulinum toxin type A for Indian adductor spasmodic dysphonia patients should be higher than 2.5 U bilaterally, and instead recommend a dose of 3 U bilaterally. For abductor spasmodic dysphonia patients, we recommend 4 U unilaterally.

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