BOTULINUM TOXIN TREATMENT OF UPPER ESOPHAGEAL SPHINCTER HYPERFUNCTION

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Hyperfunction of the upper esophageal sphincter can cause severe dysphagia and appears to be the cause of Zenker's diverticulum. This condition may occur in the context of a number of neurologic conditions, such as stroke, postpolio syndrome, Parkinson's disease, and amyotrophic lateral sclerosis, or it may be idiopathic. Upper esophageal sphincter hyperfunction may also develop after laryngectomy, interfering with swallowing and, more commonly, preventing the successful use of a tracheoesophageal speech prosthesis, which depends on passage of air through the sphincter as a sound source.

Botulinum toxin (BTX)* treatment offers a nonsurgical treatment alternative for upper esophageal sphincter (UES) hyperfunction, which is useful because affected patients are often debilitated or may have had radiation treatment to the neck. BTX treatment may also be used as a diagnostic maneuver to identify patients who would benefit from a myotomy.[1]

THE UES

The UES is a 2- to 4-cm section of high intraluminal pressure separating the hypopharynx from the esophagus. Its most prominent component is the cricopharygeus (CP) muscle, making up approximately its lower-most third.[2,3] For that reason, the UES is sometimes called the CP sphincter. The balance of the UES comprises the lower portion of the inferior pharyngeal constrictor and the cricoid cartilage anteriorly.

The fibers of the CP originate and insert into the dorsolateral aspect of the cricoid cartilage, forming a semicircle that encompasses the esophageal lumen. Innervation of the CP muscle remains a matter of debate. It is principally supplied by the vagus, via the superior laryngeal nerve and the pharyngeal plexus, with contributions from the recurrent laryngeal nerve. It also appears to receive input from the glossopharygeal nerve and sympathetic nerve fibers.[4-6] Innervation is ipsilateral, without any contralateral component, and the two halves function as separate units.[3,7] Acetylcholine is the principal neurotransmitter, which acts on motor endplates believed to be distributed more or less evenly throughout the muscle tissue.[8]

The CP muscle is tonically active during respiration and phonation and, therefore, the UES maintains high intraluminal pressure. Alone of the muscles of the neck, CP activity is present at rest, which makes it uniquely suited for electromyography (EMG)-guided localization. The drop in UES pressure during swallowing is caused by relaxation of the CP combined with anterosuperior traction from elevation of the larynx.[9] By itself, the cessation of tonic neural input may not be enough to open the CP, and UES hypertonicity after laryngectomy has been hypothesized to be caused by the absence of laryngeal traction. Both UES opening time and the magnitude of the opening varies in direct proportion to bolus size.[2]

There is ample evidence that UES function deteriorates with age.[10-12] Both laryngeal excursion and sphincter opening are reduced in the elderly, and there appear to be delays in opening which impair bolus passage. In patients with radiographically demonstrable CP bars—a hallmark of CP achalasia—the principal abnormality appears to be reduced muscle compliance, resulting in reduced distension of the sphincter during swallowing.[13] In the nonlaryngectomized patient, UES hyperfunction may occur in both upper and lower motor neuron lesions, including both superior and recurrent laryngeal nerve injury, in various myopathies, of which oculopharyngeal dystrophy is the most notable, after stroke,[14] and in Parkinson's disease.[15] Usually, however, it is idiopathic.

Dysphagia to solids is a suggestive feature of the history, and flexible fiberoptic laryngoscopy may reveal pooling of secretions. Evaluation may include manometry but most commonly hinges on contrast radiography; a modified barium swallow demonstrating the typical CP bar—a crisp and well-defined soft-tissue projection into the lumen from the posterior aspect representing the inadequately relaxed CP muscle—is diagnostic. The absence of this finding does not, however, rule out UES hyperfunction if the history and symptoms are highly suggestive.

TREATMENT ALTERNATIVES TO BTX

The mainstay of treatment of UES hypertonicity has been CP myotomy via an open approach. Meta-analyses of the literature have shown the operation to be effective in 73% to 79% of cases.[16,17] Injury to the recurrent laryngeal nerve and esophageal perforation, with the potential for deep neck infection and mediastinitis or fistula, are the principal complications. Endoscopic approaches are possible in the presence of a Zenker's diverticulum, and these eliminate the possibility of recurrent nerve injury.[18,19] The diverticular pouch must be large enough to permit transection of the entire vertical height of the muscle, and perforation with leakage of esophageal contents into deep tissues of

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*Unless otherwise indicated, botulinum toxin (BTX) refers to botulinum toxin type A (Botox; Allergan, Irvine, CA). Dosages discussed in this article also refer to Botox, and the reader should note that they are not equivalent to those for botulinum toxin type B (Myobloc; Elan Pharmaceuticals, Dublin, Ireland) or Dysport (Ipsen Ltd, Slough, UK), which is another preparation of botulinum toxin type A.

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the neck remains a risk. Dilation may also be beneficial, particularly in cases where fibrosis of the sphincter is suspected.[20] Dilation is accomplished most safely under direct visualization or by using retrograde techniques. In patients with a diverticulum, blind bougienage is to be assiduously avoided, because perforation through the fundus of the sac is not only possible, but likely.

BTX TREATMENT OF UES HYPERFUNCTION

In noncontrolled prospective clinical studies, 70% to 100% of patients with dysphagia caused by UES hyperfunction benefited from BTX treatment.[1,15,21-24] Decreased spasm was confirmed by cineradiography and sometimes by manometry, but most importantly by improvement of symptoms. Treatment permitted the consumption of solid food, removal of feeding tubes, and weight gain. Benefit was greatest in those patients with CP spasm as an isolated abnormality, as opposed to those with associated dysmotilities, postsurgical defects, or dysphagia resulting from stroke.[1] The effects of BTX injection lasted from 4 months to over 1 year and, in some cases, injection did not need to be repeated. Occasionally, injection was combined with bougienage.[21] Injection was performed both percutaneously and endoscopically under a general anesthetic.

After laryngectomy, UES hyperfunction is not infrequent and prevents the effective use of tracheoesophageal speech. Under ideal circumstances, the UES functions as a vibratory sound source for exhaled air shunted from the trachea to the esophagus via a prosthesis.[25] Hypertonicity creates an excess of resistance to the passage of air and no useable sound results. This is thought to be responsible for as many as 80% of postlaryngectomy tracheoesophageal prosthesis voice failures.[26] Treatment includes myotomy and dilation, similar to the treatment of dysphagia from UES hyperfunction. Today, most surgeons include myotomy or pharyngeal plexus neurectomy as part of the initial operation in an effort to prevent the problem. If this effort is not successful, then BTX offers an alternative to surgery in the irradiated neck or the debilitated patient.

In several series, BTX treatment resulted in useable tracheoesophageal voice in 70% to 100% of patients.[27-31] The dose used varied from 15 to 90 U, and it was injected percutaneously, sometimes under fluoroscopic guidance. The duration of benefit was to some extent dose-dependent and ranged from 1 month[27] to indefinite.[27,28] As in the case of dysphagia, it appears that in some cases a single treatment is sufficient to resolve UES hyperfunction definitively.

Dysphagia is the most common adverse effect in CP injection, and it likely results from unintended diffusion to muscles other than the target muscle. Less likely but more dangerous is respiratory distress from diffusion to the posterior cricoarytenoid muscles. If this occurs bilaterally, then a life-threatening situation may result. As in all BTX injections, accuracy is important. BTX may be delivered under direct visualization under general anesthesia, or percutaneously in the awake patient, under radiographic or EMG guidance. Because it avoids morbidity of anesthesia, which is often not insignificant in this patient population, we prefer percutaneous injection and routinely use EMG guidance.

Because the CP muscle originates and inserts into the cricoid cartilage, the position of the cricoid can be used as a guide to the level of this muscle in the nonlaryngectomized patient (Figure 1A). The larynx is rotated away from the side of the injection and a 27-guage, Teflon-coated, hollow EMG recording needle is inserted just lateral to the cricoid cartilage but medial to the carotid sheath, which is located by palpation of the carotid pulse (Figure 1B). It is advanced medially until the characteristic electrical signal of the CP muscle appears. The CP is contracted at rest, so it yields a loud and unambiguous full interference pattern on EMG. For confirmation, the patient can be asked to swallow. Although this elevates the larynx and may displace the needle, swallowing relaxes the muscle and reduces or eliminated the electrical signal, even in

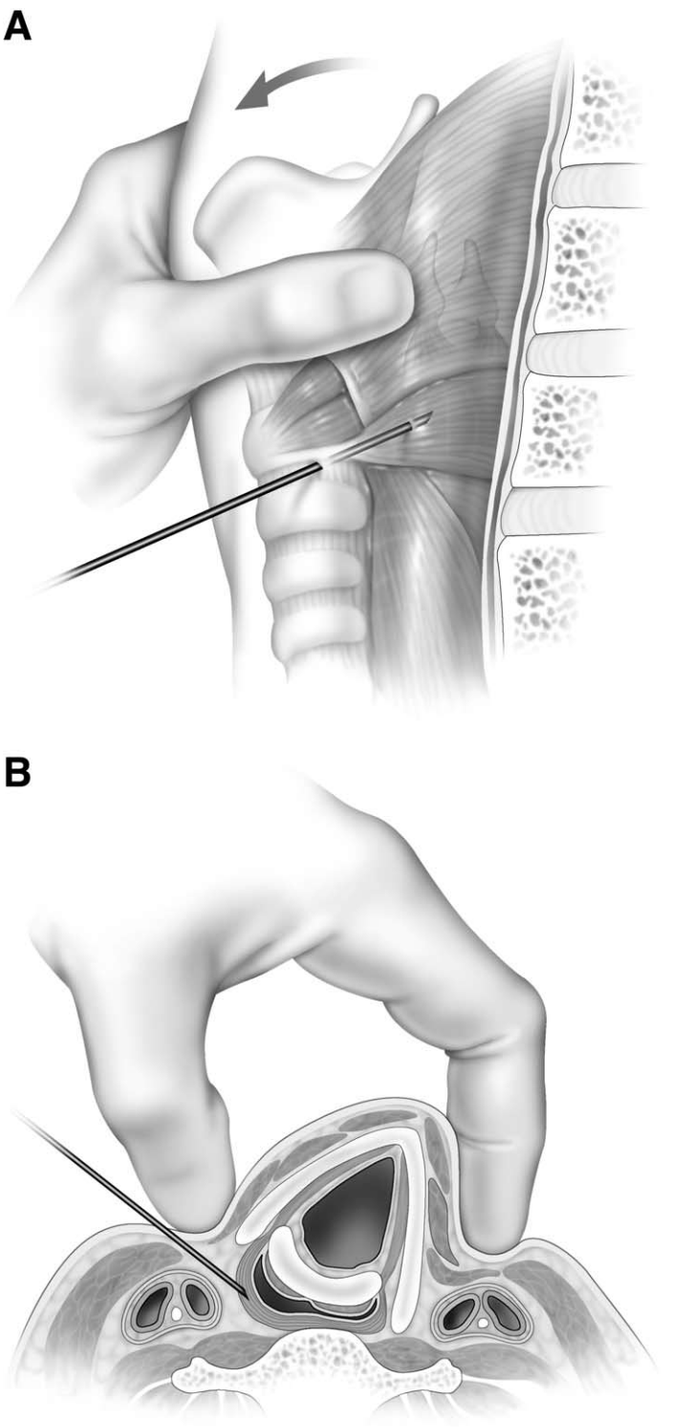

FIGURE 1. (A) EMG-guided percutaneous injection of the cricopharyngeus muscle. Note the proximity of posterior cricoarytenoid muscles. (B) This axial section shows the path of the injecting needle medial to the carotid sheath.

patients with UES hypertonicity. All other muscles in the area will demonstrate the reverse pattern, ie, silence at rest and activation during swallow. The CP muscle should be injected at multiple sites, and the routine should be repeated on the other side to treat both halves of the CP.

The muscle can be somewhat more difficult to find in laryngectomized patients because the cricoid cartilage is absent. Generally, it is located about 1 cm above the superior border of the stoma and gives the same signal as in the nonlaryngectomized patient.

Recommended doses vary widely. In our experience, 4 to 6 injections of 2.5 to 5.0 U of BTX suffice to improve UES hyperfunction. Heartburn has been noted as a complication of UES weakening,[24] and it is possible that reflux of gastric acid underlies some cases of UES hyperfunction, so it is advisable to treat this appropriately, especially in those patients with associated neurogenic compromise of the larynx.

CONCLUSION

BTX injection is an effective means of the nonoperative treatment of UES hyperfunction as well as a useful method of identifying patients likely to benefit from myotomy. In some cases, a single set of injections appears to provide long-lived relief, although the rule is repeat treatments. Adverse effects are limited and minimized by careful technique and knowledge of relevant anatomy.

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