Does Intraglandular Injection of Botulinum Toxin Improve Pediatric Sialorrhea?

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QUESTION

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BACKGROUND

Drooling, or sialorrhea, is a common problem among patients with cerebral palsy. The prevalence ranges from 37% to 58%.1 Drooling occurs when an individual’s ability to control and swallow oral secretions is limited. Common contributing factors include poor oropharyngeal coordination; dysphagia; poor posture or head position; dental abnormalities including malocclusion, nasal, or oropharyngeal obstruction; and gastroesophageal reflux. Patients may present with anterior drooling, posterior drooling, or both. Anterior drooling is defined as saliva spilled from the mouth that is clearly visible. This can have a significant medical and psychosocial impact on our patients and their families, including social rejection, damage to personal belongings, social isolation, frequent damp clothing, local skin irritation, and halitosis. Patients with posterior drooling, which occurs when saliva spills through the oropharynx and into the hypopharynx, can have serious medical consequences, including chronic aspiration leading to progressive lung disease.

Multiple interventions aimed at reducing or eliminating drooling have been described. These include physical and behavioral therapies, oral appliances, medications, botulinum toxin injections, and surgery. To date, there has been no clear consensus on which treatments of drooling are the safest and most effective. The goal of this review is to determine the role of botulinum toxin injections in the management of pediatric sialorrhea.

LITERATURE REVIEW

Localized injections of botulinum toxin result in denervation of the target organ without the systemic anticholinergic effect, making submandibular, parotid, or combination salivary gland injections a favorable alternative to anticholinergic medications. The maximum effect is typically seen between 2 and 8 weeks, with the average length of improvement from 3 to 6 months. Dosing paradigms vary among providers, but an individualized approach has been recommended.2 The performance of injections under ultrasound (US) guidance (see Fig. 1) is recommended to help decrease the risk of dysphagia from toxin diffusion to the surrounding musculature and tissue; injections under electromyography guidance have also been described.2 The majority of US guided injections occur under general anesthesia; however, Daniel has described his method using the local anesthetics tetracaine hydrochloride gel 4% or EMLA (eutectic mixture of local analgesics, Shaumburg, Illinois, U.S.A.) cream.2 Given the comorbidities within this patient population, an approach under local anesthesia may be favorable in the appropriately selected patient.

A controlled clinical trial (CCT) published in 2004 compared a single-dose botulinum toxin injection with scopolamine treatment in 45 children.3 The severity of sialorrhea was measured using objective tools, including the Drooling Quotient (DQ), the Teacher Drooling Scale, and visual analog scales. For patients treated with botulinum toxin, the mean DQ showed a significant decrease, with greatest reductions achieved 2 to 8 weeks postinjection. This improvement persisted the duration of the study (24 weeks) in 50% of patients. Scopolamine also showed favorable results, but 71.7% of the patients experienced moderate to severe side effects. The most common adverse effects were xerostomia (66.7%), restlessness (35.6%), somnolence (35.6%), blurred vision, and confusion (20%). Four patients left the study secondary to scopolamine side effects. After botulinum toxin injections, two patients (5.1%) had transient flu-like symptoms, and three patients complained of mild dysphagia (6.7%). This study suggests that scopolamine and
botulinum toxin have similar efficacies; however, botulinum toxin is a better tolerated treatment.\textsuperscript{3}

In 2012, a Cochrane review examined the management of drooling.\textsuperscript{1} The authors reviewed randomized controlled trials (RCTs) and CCTs, which limited their investigation to four studies examining the efficacy of botulinum toxin A (BoNT-A) and two studies on pharmacologic interventions, specifically glycopyrrolate and benztropine. Although all included trials showed a positive reduction in drooling that remained statistically significant 1-month postintervention, the authors had insufficient evidence to conclude on either the effectiveness or safety of benztropine and glycopyrrolate or BoNT-A. The authors commented that the lack of trials on interventions did not suggest such interventions were ineffective, but that well-powered and well-designed trials are required to make such conclusions.

A meta-analysis of intraglandular botulinum toxin injections published in 2014\textsuperscript{4} reviewed eight studies, including three RCTs. Among the studies, there was lack of treatment homogeneity that limited the authors’ ability to formulate a specific protocol; however, the authors did recommend using US guidance and injecting BoNT-A at 2 U/kg (1 mL/100 units) divided equally between all four glands, under local or general anesthesia. The most commonly noted side effect was xerostomia, with transient dysphagia, thickened saliva, altered salivary flow, and an initial increase in saliva also reported. The authors concluded that although higher levels of evidence are needed, the efficacy results were encouraging, and they supported the use of botulinum toxin as part of the therapeutic regimen for sialorrhea management.

In 2016, Lungren et al. published their experience with US-guided Botox injections and proposed a unified protocol.\textsuperscript{5} Lungren et al. recommended injecting 15 U/gland in patients < 15 kg, 20 U/gland for patients weighing 15 to 25 kg and 25 U/gland for a weight of > 25 kg. All injections were performed using US guidance under general anesthesia. A total of 144 procedures in 111 patients were performed. Improvement was graded as 0 = none, 1 = partial effectiveness, 2 = good effectiveness, 3 = very effective, or 4 = lost to follow-up or death. The procedure was very effective 41% (59 of 144) of the time, and only 25% (36 of 144) of procedures had no benefit.

Six patients with no benefit went on to schedule surgical intervention. There were three complications, including one patient with cellulitis and two patients with temporary unilateral muscle of mastication weakness. There was no statistically significant weight-adjusted dose response associated with effectiveness or complications. The authors recommended that their procedure and protocol be considered as part of the therapeutic strategy for sialorrhea management.

**BEST PRACTICE**

The published data on sialorrhea management is limited for all interventions, yet current literature supports the use of botulinum toxin injections as part of a therapeutic regimen. We are unable to conclude that botulinum toxin injections should be offered in lieu of anticholinergic medications; however, the CCT published by Jongerius et al. demonstrated a significant decrease in sialorrhea with both interventions but a more favorable side-effect profile for injections.\textsuperscript{3} This suggests that botulinum toxin injection may be ideal, especially for patients who are candidates for injections under local anesthesia. In patients who fail to improve following botulinum toxin, surgical intervention may be warranted.

**LEVEL OF EVIDENCE**

The levels of evidence included in this review are level 1 for the Cochrane review and level 2 for the CCT by Jongerius.\textsuperscript{3} The other references were level 3 because they were retrospective reviews and a meta-analysis based on retrospective studies.

**BIBLIOGRAPHY**