The Repetitive Usage of Onabotulinum Toxin type A into Salivary Glands for the Management of Sialorrhea in the Pediatric Population: an Ultrasound Measurement.

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ABSTRACT

Introduction: Drooling, also known as sialorrhea, carries severe clinical, functional and social burdens in its care and management. There are several modalities for the management of sialorrhea, one being the repetitive use of Onabotulinum Toxin A (OBTXA) injections, which is an excellent option for salivary control.

Objectives: We aimed to assess quantitative salivary gland changes via ultrasound imaging after intragladular injection of OBTXA for sialorrhea treatment in children, as a method that suggests possible permanent changes in gladular size can suggest decrease in functionality or atrophy.

Methods: The parotid and submandibular glands of 22 patients with sialorrhea with previous repetitive OBTXA treatments were measured via ultrasound before new injection with OBTXA using bimanual palpation or by EMG guidance. Children with various causes for drooling were included. Patients were compared with a group control of 38 healthy children.

Results: A total of 60 patients were included in the study (38 boys, 22 females). BMI, sex, age were defined as confounders. The mean age was 7 (SD ±2.3) and 9 (SD±3.8) for treatment and control groups respectively. There were no post-injection complications. We found a significant decrease in the size dimensions (area and Anterior-Posterior dimension) of both submandibular glands and one parotid gland in the treatment group (P<0.05). Significant smaller medio-lateral dimension of the submandibular glands (P<0.01) was also found. BMI was also correlated to salivary gland size.

Conclusion: The chronic use of intraglandular OBTXA reduced the size of the salivary glands measured ultrasonographically. Results were correlated with clinical outcomes. Pathological studies should be done to correlate whether ultrasound changes result in atrophy or apoptosis of the glands.

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INTRODUCTION

Drooling, or sialorrhea, is excessive production of saliva. There are several modalities for the management of sialorrhea such as the repetitive use of Onabotulinum Toxin A (OBTXA) injections, which has proven to be successful for salivary control. Many children require repetitive injections (every 3 to 6 months). The long-term effect of the repetitive OBTXA injection in pediatric salivary glands is still not well known.

The present study aimed to assess quantitative salivary gland changes via ultrasound imaging after intraglandular injection of OBTXA for sialorrhea treatment in children, as a method that suggests possible permanent changes in glandular size can suggest decrease in functionality or atrophy.

METHODS AND MATERIALS

The parotid and submandibular glands of 22 patients with sialorrhea with previous repetitive OBTXA treatments were measured via ultrasound using bimanual palpation or by EMG guidance.

Inclusion criteria:

- Children between 4 to 18 years old, with a minimum of 3 OBTXA injections.
- Children with various causes for drooling were included, having had previous scores of at least 6 on the drooling frequency and severity scales [1] and scores of 5 and 1 or 2 on the teacher Drooling Scale and Thomas-Stonell and Greenberg scales [2,3] pre and post OBTXA treatments.
- Children without any surgical procedure nor medical treatment that could interrupt salivary flow or production.

Patients were compared with a control group of 38 healthy children. Both submandibular and parotid glands of each patient were scanned in two planes, transverse and longitudinal to the mandibular plane and evaluated by the same physician.

RESULTS

Table 1: Patients Baseline Characteristics

	Control Group	Treatment Group Patients	P value
Gender			
Male	28(73%)	10 (45%)	
Female	10(26%)	12 (54%)	
Age (mean SD)	7.09 (±2.3)	9.3 (±3.8)	-2.72
BMI (mean SD)	18.5 (±4.3)	17.6 (±5.1)	0.71

Table 1: Age (years) and BMI (kg/m^2), compared using the T-Test. Gender Fischer's Exact test

RESULTS

Table 2: Mean glandular size and comparison in univariate analysis combining right and left glands.

	Treatment	Control	P-value (ANOVA)	Percentage difference of salivary glands
AREA				
-PAROTID	2.58 (±0.94)	2.90 (±0.68)	0.34	11%
-SMG	2.57 (±0.54)	3.10 (±0.63)	<0.001**	17%
AP				
-PAROT	1.59(±0.26)	1.62(±0.21)	0.47	2%
-SMG	1.33(±0.16)	1.48(±0.24)	0.01*	10%
ML				
(Depth)	2.68(±0.72)	3.23(±0.40)	<0.001**	17%
-PAROT	2.87(±0.51)	3.06(±0.36)	0.018*	6%
-SMG				

Table 2: P-values using ANOVA test. Parotid (parotid gland); SMG (submandibular gland); AP (anterior-posterior), ML (mediolateral), Area (surface area). Significant P<0.05, ** significant P<0.001

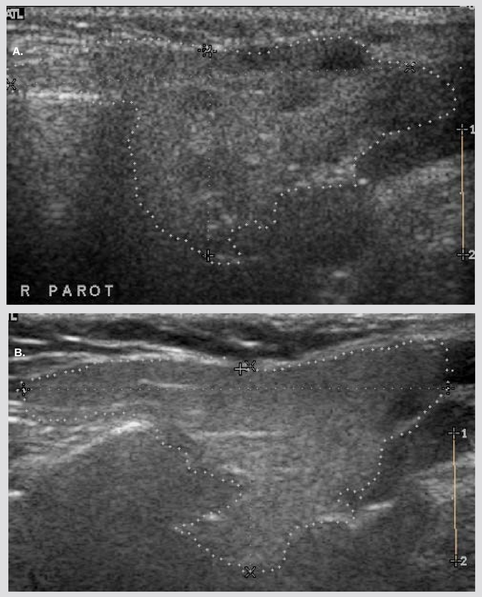

Figure 1. Right parotid gland measurement via ultrasound guidance.

A: treatment group
B: control group.
Note the increase in heterogenicity, irregular, lobulated contours with a loss of convexity in the treatment group.

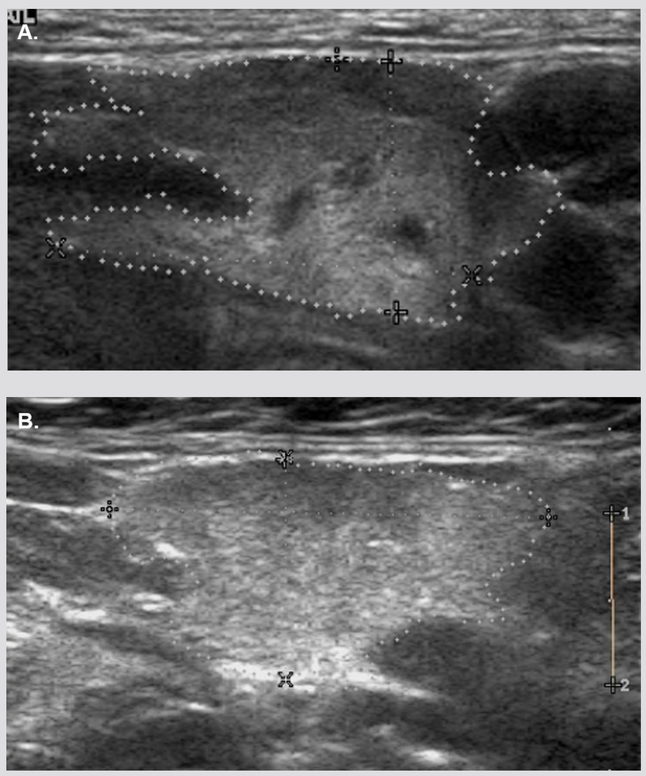

Figure 2. Right submandibular gland via ultrasound guidance. A: treatment group. B: control group. Note the different echogenicity, irregular contours in the treatment group.

DISCUSSION

OBTXA is currently available as a novel effective treatment to treat sialorrhea with an efficacy range of 89% to 95% [4]. Botulinum toxin blocks Acetylcholine (Ach) release at the neuroglandular junction of the salivary glands, thus diminishing the release of saliva [5]. The therapeutic use of OBTXA for excessive drooling is rapidly growing, although the complication rates and long-term safety are still not well delineated [6]. The common side effects of OBTXA injections are usually minor and temporary. These include local hematoma, pain and erythema (0% to 18.7%), mild dysphagia, viscous saliva and dry mouth [16]. Most severe complications require hospitalization and are associated with high doses of OBTXA injections.

We report a significant reduction in the size of submandibular glands which was greater than the reduction observed in parotid glands. This correlates well with drooling scores, hence resting saliva, responsible for drooling, is primarily controlled by the submandibular glands.

We suggest a more extensive treatment towards all four major salivary glands for sialorrhea treatment, to control drooling at rest and during meals. We also report changes in appearance of the salivary gland parenchyma. These anatomical changes could be multifactorial in origin. Either related to trauma or post inflammatory caused by the injection or to OBTXA neurotoxin-induced histological changes.

CONCLUSIONS

The chronic use of intraglandular OBTXA reduced the size of the salivary glands measured ultrasonographically. Results were correlated with clinical outcomes. Pathological studies should be done in order to correlate whether ultrasound changes result in atrophy or apoptosis of the glands. OBTXA injection into the major salivary glands of children with sialorrhea should be considered as the first line of treatment before more definite surgical procedures are considered.

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