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Salivary botulinum toxin injection may reduce aspiration pneumonia in neurologically impaired children

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ABSTRACT

Objectives: Neurologically impaired children often drool and aspirate saliva leading to recurrent aspiration pneumonia and frequent hospitalizations. Salivary botulinum toxin injection is known to reduce sialorrhea. This study evaluates whether this intervention affects the frequency and duration of respiratory infections including aspiration pneumonia and hospitalizations in neurologically impaired children.

Methods: Retrospective review of patients treated with salivary botulinum toxin at a tertiary care pediatric hospital from January 2009 to December 2013. Each patient was their own control and 180 day pre-injection and post-injection time periods were compared. Outcomes evaluated included: number of hospital days, intensive care unit days, days of antibiotic treatment, chest X-rays, and infiltrates on chest X-ray.

Results: 13 patients accumulated 539 hospital days. All children were gastrostomy tube dependent. 54% were tracheostomy tube dependent. Amongst all patients, the total hospital days decreased from 385 to 154 ($P = 0.02$), the mean days treated with antibiotics decreased from 214 to 47 ($P = 0.02$), and the number of chest X-ray confirmed infiltrates decreased from 20 to 6 ($P = 0.02$) after injection.

Conclusion: In this review, there was a decrease in hospitalized days, antibiotic usage, and chest X-ray infiltrates after the salivary botulinum toxin injection. A prospective study is needed to evaluate whether this treatment can prevent aspiration pneumonia in neurologically impaired children.

1. Introduction

Sialorrhea, or drooling, is an extremely common problem in children with neurologic disorders such as cerebral palsy. Between 40 and 58% of cerebral palsy patients have drooling and in 15–33% it is severe [1,2]. In children with severe neurological disabilities, low oral sensitivity, infrequent swallowing, poor posture, and dysfunctional oral motor control can lead to pooling of saliva in the anterior oral cavity [3,4]. The pooled saliva can be swallowed, lost through the lips, or travel posteriorly and be aspirated into the lungs. Drooling causes significant caregiver burden, maceration of the lips and chin, dehydration, foul odors, and social isolation [5]. While less common, aspiration of saliva can cause recurrent bouts of aspiration pneumonia, extended hospital admissions, intensive care unit (ICU) care, and possibly invasive mechanical ventilation [6].

Despite the availability of multiple treatment approaches, these problems are notoriously difficult to treat [5,7–12]. Anticholinergics such as glycopyrrolate, scopolamine, and benztropine are often the first line treatment for sialorrhea, but side effects such as dry mouth, thickened secretions, urinary retention, flushing, constipation, agitation, and many others limit their clinical utility in many patients [12,13]. Surgical treatments are an effective option to reduce the incidence of drooling and aspiration pneumonia in neurologically impaired children. Salivary duct ligation, salivary gland excision, and laryngotracheal separation have been studied and shown to effectively reduce episodes of aspiration pneumonia in selected patients [7,8,10,14–16]. However, they are invasive options that suffer from disadvantages specific to each technique.

Botulinum toxin has a wide range of clinical uses, including the treatment of focal dystonias, vocal tics, headaches, temporomandibular joint dysfunction, and many others [17]. Its action is temporary, nondestructive, and localized to the region of the injection. It inhibits acetylcholine release from nerve terminals, resulting in flaccid paralysis [17]. The efficacy of botulinum toxin

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as a minimally invasive treatment for sialorrhea is well studied and it can be used as part of a combined treatment effort [11,18–23]. However, to our knowledge, there are no studies that evaluate the effect of botulinum toxin injections on aspiration pneumonia and hospitalizations in neurologically impaired children. The goal of this study is to determine whether salivary botulinum toxin (SBT) decreases the rate of respiratory infections requiring inpatient hospital care in a high risk population of neurologically impaired children.

2. Materials and methods

The University at Buffalo Children and Youth Institutional Review Board approved this review. Billing records were used to identify all patients treated with SBT between January 2009 and December 2013 at the Women and Children's Hospital of Buffalo, New York. Inclusion criteria included: age less than 21 years, a 180-day period before and after the injection free of additional injections, diagnosis of sialorrhea, diagnosis of neurologic disease that resulted in severe disability, and at least one inpatient hospitalization for respiratory distress. The presence of respiratory distress was diagnosed by the admitting pediatrician and was defined as any of the following: increased work of breathing, need for increased or supplemental oxygen, or the need for increasing external respiratory support such as mechanical ventilation. Exclusion criteria included prior salivary gland surgery, prior laryngotracheal separation, primary immunodeficiency, and an evolving neurological disability.

One hundred and seven SBT injections were administered to 42 unique patients during the study period. Eighteen patients met the inclusion criteria. Among those excluded, 8 patients had injections more frequently than every 180 days, 1 patient was older than 21 years, 1 patient did not have a neurologic diagnosis, and 16 patients did not have an inpatient hospitalization with an associated respiratory diagnosis. One patient was excluded due to an evolving neurologic disorder secondary to recovery after severe head trauma. Two patients were excluded because of salivary gland surgery during the study period. Ultimately, 15 patients were eligible for the study.

Information was collected regarding gender, age, medical conditions, gastrostomy and tracheostomy tube status, home ventilator status, prior attempts at secretion management with anticholinergic medications, surgical procedures including prior salivary gland surgeries, and evidence of penetration or aspiration via salivagram or swallow study. During the 180 days before and after the SBT injection, we gathered hospital and ICU length of stay, days of antibiotic usage, number of chest X-rays (CXR) performed, and the number of CXRs that showed a radiologist diagnosed infiltrate. Serial CXRs would show the same lung infiltrate, therefore a radiologist-reported infiltrate would not be considered a new infiltrate until 14 days elapsed, which seemed a reasonable estimate based on the average age of patients [24].

Patients were evaluated by the otolaryngology service at the request of the treating pediatricians. The decision to recommend SBT injection was made by the attending pediatric otolaryngologist on the basis of the patient's overall clinical condition. An injection would only be recommended if there was failure of systemic anticholinergic medications to manage secretions.

The injection was done by a pediatric interventional radiologist using aseptic technique. The parotid and submandibular glands were identified with ultrasound guidance. Ultrasound was used to ensure correct intraglandular position of the needle prior to the injection. A 25-gauge needle was used for injection, the family was present, and the head was gently controlled by the nursing staff. There was one strong teenage patient who could not cooperate with the procedure and required general anesthesia for safe and precise placement of the drug. The injections were done preferentially with the child awake. If there was an indication for a general anesthetic for a different procedure, the SBT injection could be performed under general anesthesia as a combined treatment. OnabotulinumtoxinA (Allergan, Inc.) was used for all injections. A total of 100 unit of botulinum toxin was the preferred dose with 35 unit injected into each submandibular gland and 15 unit into each parotid gland for a total of 4 injections per treatment (Table 1). An alternate dose of 50–60 unit could be used if the child was less than 2 years of age, if it was the first time they were being treated with SBT, if their clinical condition was less severe, of if there was significant parental anxiety about potential side effects. Ultimately the exact dosage and distribution of botulinum toxin into the salivary glands was determined by the clinical judgment of the attending interventional radiologist.

General statistical analysis was performed with version 11.00.01 of SYSTAT and Kaplan–Meier testing was done with Minitab 17.1.0. A P value less than 0.05 was considered significant for all testing and was obtained via a paired-samples *t*-test. Survival analysis was conducted via Kaplan–Meier methodology.

3. Results

Upon first review of the data, 2/15 (13%) of the patients were outliers and were removed from subsequent analysis as their inclusion would have strongly favored the SBT treatment group. The first patient was hospitalized for 180/180 (100%) days before and 9/180 (5%) days after while the second patient was hospitalized for 154 (86%) days before and 9 (5%) days after the injection. In both cases, detailed review of the medical record

Table 1
Patient information.

Patient	Age (yr)	Gender	Neurological disorder	Gastrostomy tube	Trach tube	Home ventilator	Total units injected	Submandibular units injected	General anesthesia	First ever injection
1	14	Female	Aicardi, GDD	Yes	No	No	100	35	No	Yes
2	18	Male	CP, GDD, TBI	Yes	Yes	Yes	100	35	No	Yes
3	2	Female	17q21 deletion	Yes	Yes	No	100	35	No	Yes
4	1	Female	Apert, GDD	Yes	Yes	No	100	30	No	No
5	4	Male	CP, GDD, microcephaly	Yes	Yes	No	100	35	No	Yes
6	1	Female	Aicardi, GDD	Yes	No	No	60	20	No	Yes
7	4	Female	GDD	Yes	No	No	60	15	No	Yes
8	3	Female	Pontocerebellar hypoplasia	Yes	No	No	100	30	No	Yes
9	21	Male	CP, HIE	Yes	No	No	100	25	No	Yes
10	13	Male	Batten disease	Yes	Yes	No	100	35	Yes	Yes
11	13	Male	GDD, HIE	Yes	Yes	No	100	35	No	Yes
12	3	Female	GDD	Yes	No	No	100	25	No	Yes
13	2	Male	SMA Type 1	Yes	Yes	Yes	60	15	Yes	Yes

Abbreviations: GDD, global developmental delay; CP, cerebral palsy; TBI, traumatic brain injury; HIE, hypoxic ischemic encephalopathy; SMA, spinal muscular atrophy.