Management of Sialorrhea in Children with Cerebral Palsy

Ali Alrefai and Samah K Aburahma

Affiliation: Department of Neuroscience, Jordan University of Science and Technology (JUST), Irbid, Jordan

ABSTRACT

Drooling, the overflowing of saliva from the mouth, is mainly due to neurological disorder and, less frequently, to hypersalivation. Drooling is prevalent among children with cerebral palsy (CP) and has a negative impact on their social and physical wellbeing. Treatment options include oral medications, chemodenervation, and submandibular duct relocation. Although no treatment option has proven to be ideal, an optimum approach needs to be tailored to the needs of the child. This article provides an overview of the different treatment approaches and significant research findings.

Keywords: drooling, cerebral palsy, botulinum toxin

Correspondence: Ali Alrefai, Department of Neuroscience, Jordan University of Science and Technology (JUST), PO Box 3030, Irbid, Jordan 22110. Tel: (962)-2720-0600, Ext 40708; Fax: (962)-2720-0621; e-mail: aalrefai@just.edu.jo

INTRODUCTION

Sialorrhea (drooling) is the unintentional loss of saliva and other oral contents from the mouth. It is a normal phenomenon of infancy that subsides in early childhood, usually by 15–18 months, as a consequence of physiological maturity of oral motor function [1].

Drooling children frequently have irritated facial skin, foul odor, and in cold weather the dampness from saliva is chilling. Their dehydration experience can be a recurrent problem from chronic fluid loss. They may also damage books, toys, computers, and other communication aids [2].

Drooling affects the social and physical wellbeing of children with cerebral palsy (CP), and may represent problems for caregivers. The unsightly nature of drooling, speech spray, and a cough or sneeze can lead to social avoidance [2].

Reported treatment options have included behavioral modification therapy, oral or topical anticholinergic medications, surgical excision of salivary glands or duct relocation, and chemodenervation with botulinum toxin. Despite the abundance of reports on the efficacy and safety profiles of each treatment option, definitive conclusions are difficult to draw, given the heterogeneous nature of the patient populations studied and the different outcome measures used in the various studies. In this review, an analysis of outcome measures commonly used for assessing response to treatment and a study of recent reports on the various therapeutic options available will be presented.

BASIC PHYSIOLOGY

Healthy subjects secrete variable amounts of saliva, averaging 0.5–1.5 L/day. The parotid and submandibular glands produce about 90% of saliva [3]. The submandibular and sublingual salivary glands produce about 70% of saliva in the resting state, although when stimulated, the parotid glands provide most of the saliva. The submandibular glands produce a high-viscosity fluid, whereas the parotids produce watery saliva. Saliva serves a number of important functions, including: (1) providing a protective effect from tooth decay and the gingival tissues from inflammation; (2) acting as a lubricant for swallowing and a solvent for facilitating taste; (3) providing an antibacterial action in the mouth; and (4) promoting protein and carbohydrate breakdown.

Salivary secretion is regulated by a reflex arc. The afferent part is mainly activated by stimulation of chemoreceptors located in the taste buds and mechanoreceptors located in the periodontal ligament. The afferent arc is mediated through cranial nerves V, VII, IX, and X, which carry impulses to the salivary nuclei in the medulla oblongata [4]. The efferent part of the reflex is mainly parasympathetic. Cranial nerve VII provides control of the submandibular, sublingual, and minor glands, whereas cranial nerve IX controls the parotid glands [4]. The flow of saliva is enhanced by sympathetic innervation, which promotes contraction of muscle fibers around the salivary ducts [5].

ETIOLOGY AND EPIDEMIOLOGY OF DROOLING

Hypersalivation, which is excessive saliva production, is not synonymous with drooling. Drooling in children with CP is usually not due to hypersalivation; in fact, in most cases, the volume of saliva produced is normal [6]. It was found that there was no statistical difference in the rate of salivary flow, the buffering capacity, and the concentration of sodium and potassium between children with CP who drool and unaffected age-matched children [6]. Drooling occurs as a result of central or peripheral etiologies. Of the central

AMERICAN JOURNAL OF CLINICAL NEUROLOGY REVIEW ARTICLE

AJCN 2010; 000:(000). Month 2010 1 www.slm-americanneurology.com
etiolologies, CP is the most common cause in children. The factors that contribute to drooling in children with CP include an inefficient coordination of the oral phase of swallowing and poor lip closure [7]. This has been confirmed by comparing drinking tasks in normal children with children with CP [8]. Drooling children with CP had more trouble initiating swallowing than normal children or children with CP who did not drool. Other factors that might contribute to drooling include muscle hypotonia, macroglossia, dental malocclusion, abnormal posture, and impaired nasal airway patency [7].

Drooling is reported to be a significant problem in 10–37% of patients with CP [9, 10], especially children with quadriplegic CP attending special schools, where drooling of patients with CP [9, 10], especially children with CP who did not drool. Other factors that might contribute to drooling include muscle hypotonia, macroglossia, dental malocclusion, abnormal posture, and impaired nasal airway patency [7].

**ASSESSMENT OF DROOLING**

A detailed history helps to assess the severity of drooling, its effects on quality of life for the patient and family, and to decide the therapeutic intervention. Both objective and subjective measures need to be utilized in assessing therapeutic intervention. Objective measures are usually aimed at measuring the amount of saliva. The commonly reported and utilized objective measures include calculating the weight of drool using dental bibs [12], weighing dental rolls placed in different areas of the mouth, positioning absorbent cotton rolls at the salivary gland duct orifice [13], and the drool quantification method [14]. The drool quantification method is an effective non-invasive evaluation tool that includes a cup-like collection device, a vacuum pump, plastic tubing, an airtight collection chamber, and a calibrated test tube. The commonly reported subjective tools include the drooling severity and frequency rating scale, Teacher Drooling Scale (TDS), Drooling Quotient (DQ), caregivers’ questionnaires, and a visual analog scale for frequency and severity of drooling [15–18]. Table 1 shows the drooling severity and frequency rating scale. The TDS is a useful tool for outpatient visits, in which the classroom teachers indicate the degree of drooling by means of a five-point scale. The DQ is a validated, semiquantitative, direct observational method; it is defined as the number of times when drool was present or absent measured at 15-s intervals during two 10-min periods separated by a 60-min break. Despite the absence of studies comparing subjective and objective measures of saliva production, subjective measures frequently show an earlier and more significant response to the therapeutic intervention being studied than objective measures, and appear to parallel changes in quality of life assessments [19]. This may be because objective measures assess drooling at a given fixed period of time, whereas most subjective measures assess drooling from observations over a more extended period of time. However, as drooling is variable throughout the day, subjective tools may actually be more reflective of the true nature and burden of the problem for children with drooling, and necessarily complement information obtained from objective tools.

A questionnaire was developed to document the social impact and self-esteem of treating drooling [20]. It consists of sets of multiple choice questions and a visual analog scale in which parents evaluate their experiences as well as the personal reactions of the child.

**BEHAVIORAL TREATMENT**

Various behavioral techniques have been described for the treatment of drooling. Despite their appeal because of their non-invasive nature, there is a paucity of clinical research documenting their efficacy, and most reports are based on anecdotal case descriptions. Proposed techniques include various oral appliances to modify and improve oral motor function and aid lip closure [21], oral motor stimulation techniques that emphasize the enhancement of sensorimotor feedback mechanisms [22, 23], and biofeedback and automatic cueing techniques [24, 25]. However, with the complex and demanding nature of these techniques, and their dependency on the cognitive abilities of the patient, they seem to have fallen out of favor. In the authors’ opinion, behavioral techniques may have a role as adjunctive therapy with other treatment modalities; however, this requires further investigation before definitive recommendations can be made.

**SURGICAL TREATMENT**

Surgery is indicated when conservative treatment has been tried for at least 6 months without reduction in drooling [19]. It is best deferred until the patient is 6 years old as, by this age, there should be full maturation of oral motor function and coordination.

Various surgical approaches have been reported, such as parotid duct ligation with submandibular gland excision, submandibular gland duct relocation with or without sublingual gland excision, and parasympathetic neurectomy [26–29]. Salivary gland resection is associated with significant morbidity including external scar, xerostomia, and, in the worst cases, facial weakness [26]. Nowadays, the gold standard surgical procedure is submandibular duct relocation. Crysdale and White [27] reported significant reduction

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = Never drools</td>
<td>1 = Dry (never drools)</td>
</tr>
<tr>
<td>2 = Occasionally drools (not every day)</td>
<td>2 = Mild (only lips wet)</td>
</tr>
<tr>
<td>3 = Frequently drools (part of every day)</td>
<td>3 = Moderate (wet on lips and chin)</td>
</tr>
<tr>
<td>4 = Constantly drools</td>
<td>4 = Severe (drool extends to clothes)</td>
</tr>
<tr>
<td></td>
<td>5 = Profuse (hands, tray, and objects wet)</td>
</tr>
</tbody>
</table>
in drooling in the majority of children who underwent this procedure as the salivary flow is redirected to the back of the mouth, a site more conducive to swallowing than drooling. The absence of an external scar is appealing to both the patient and the surgeon. The disadvantages of this procedure include the need for hospitalization and ranula formation in 8% of patients. The addition of sublingual gland resection to avoid this complication was found to be ineffective and increases the chance of bleeding and pain [28]. Patients with a history of recurrent tonsillitis should have a tonsillectomy 2 or 3 months before the duct relocation.

### PHARMACOLOGICAL THERAPY

Salivation is mediated through the autonomic nervous system, primarily by way of the cholinergic system muscarinic receptor sites. Blockage of these receptors inhibits nervous stimulation to the salivary glands. Anticholinergic drugs used to decrease drooling have widespread effects on all end-organs that are governed by muscarinic stimulation.

Several clinical trials have used anticholinergic drugs to decrease drooling, but the response was usually partial and at the price of side-effects [30–32]. A double-blind, placebo-controlled, crossover trial reported that transdermal scopo-lamine demonstrated “a significant reduction in drooling” with low toxicity [30]. However, the patient population was heterogeneous, and the method of measurement of improvement was not sufficiently described. Benztrapine in one double-blind trial produced a 65% decrease in drooling, but the trial term was short and had a 30% dropout rate [31]. Glycopyrrolate, a synthetic antimuscarinic agent that does not cross the blood–brain barrier, making it an interesting compound to use, has been investigated in a double-blind, dose-ranging clinical trial, and showed reduction in drooling. However, 20% had adverse effects leading to drug withdrawal [32].

Botulinum toxin (BoNT-A), a potent exotoxin produced by Clostridium botulinum, the same organism responsible for tetanus, is another medication that may be effective in the treatment of drooling. It blocks the release of acetylcholine at the cholinergic neurosecretory junction of the target organs including the salivary glands. The first published results of BoNT-A injection to treat drooling appeared in 2000 in patients with Parkinson’s disease (PD) [33]. Since then, several case series and unblinded, open-label cohort studies have reported its effect on drooling in children with CP and other neurological disorders [34–37]. The injected salivary glands were the parotid gland alone in one study [34], the submandibular gland alone in two studies [35, 36], and both sets of glands in the third study [37]. Three controlled trials have recently been published [38–40]. A double-blind, placebo-controlled trial studying the effect of unilateral injection of the parotid and bilateral submandibular glands with BoNT-A reported that this approach reduced the drooling frequency and severity scale and drooling quotients at most follow-up periods [38]. The investigators adopted this approach with the intention of keeping at least 50% of resting and post-prandial saliva production in an attempt to decrease side-effects. However, this study is limited by small sample size. In another double-blind, placebo-controlled, dose-escalating trial, we reported that bilateral parotid gland injection with BoNT-A significantly reduced the frequency and severity of drooling compared with placebo in the smaller dose, but the reduction was not statistically significant with a higher dose due to a high dropout rate from the placebo group [39]. Another dose-finding trial comparing injections into the submandibular glands alone with injections into the submandibular and parotid glands found more responders with the second approach, but no conclusions were made regarding the ideal dose [17]. In an open-label, randomized controlled trial, Reid and his group [40] reported that injection with BoNT-A into the parotid and submandibular glands in children with CP significantly reduced drooling compared with a control group. This reduction was maximal at 1 month after injection and remained significant for 6 months; nine families were still happy with the results at 1 year. No child was reinjected during this time. This is the first study with long-term follow-up.

Botulinum toxin type B (BTxB) has been proposed as a treatment for drooling in patients with neurological disorders such as PD and amyotrophic lateral sclerosis (ALS) [41, 42]. In a double-blind, placebo-controlled trial in 20 patients with ALS, 2500 U of BTxB or placebo was injected into the bilateral parotid and submandibular glands under electromyography (EMG) guidance [42]. Patients treated with BTxB reported a global impression of improvement of 82% at 2 weeks compared with 38% of those treated with placebo. At 12 weeks, 50% of patients who received BTxB continued to report improvement compared with 14% of those who received placebo. Based on this study, in a recent practice parameter update, the Quality Standards Subcommittee of the American Academy of Neurology has recommended the use of BTxB for patients with ALS who have medically refractory drooling (level B evidence) [43].

In children with CP, Wilken et al [44] randomly assigned children to receive BoNT-A or BTxB into the parotid and submandibular glands on both sides, and found that reduction of drooling was achieved 2 weeks after injection, with a positive effect lasting about 3–4 months, but this reduction was not significant between both types of botulinum toxin.

Although most trials have used ultrasound guidance for injection, our group reported that injection using anatomical landmarks was also effective [39]. Trials comparing blind injection based on anatomical landmarks and injection with ultrasound guidance are limited.

Side-effects reported with botulinum toxin injection included thicker, more viscous saliva. The parotid glands produce thin, serous secretions unlike the submandibular glands, which produce more viscous saliva. Therefore, this side-effect is believed to be secondary to decreased parotid saliva production. Another reported side-effect is difficulty swallowing, and this is believed to be secondary to local diffusion of botulinum toxin producing weakness of surrounding muscles. Some children might require general
anesthesia to administer botulinum toxin, which could increase the cost and risk of complications and side-effects. Other potential effects are hematoma, salivary duct calculi, and local injuries to the carotid arteries or branches of the facial nerve.

Despite the fact that many studies have reported that botulinum toxin is effective in treating drooling in children, there are still unanswered questions. Most studies have used small heterogeneous patient samples and subjective measures to evaluate response. Optimally, future studies should use large homogeneous patient samples and both subjective and objective outcome measures. The optimum dose, the dilution, and the number of injection sites need to be standardized. Table 2 lists some of the recent randomized clinical trials using BoNT in treating drooling in children with CP, showing the differences in the dosages used, outcome measures, and injection sites.

**Table 2. Effect of Botulinum Toxin on Drooling in Children with Cerebral Palsy**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Study group</th>
<th>Study type</th>
<th>Outcome</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suskind et al</td>
<td>22 children</td>
<td>Prospective, open-label, dose-escalating study; 12 children with only submandibular gland injection 10, 20, 30 units and 10 children with 30 units in submandibular and 20, 30, 40 units in parotid</td>
<td>Drooling rating scale, dental roll weight, DQ</td>
<td>DQ: 33% responders in group 1 and 80% responders in group 2; DQ: eight patients in group 2 have decreased DQ</td>
<td>Different outcome measures between groups, no ideal dose</td>
</tr>
<tr>
<td>Jongerius et al</td>
<td>45 children</td>
<td>Controlled, open-label, clinical trial. Treatment with scopolamine patches, then with BoNT-A into submandibular glands. Total dose: 30 U if &lt;15 kg; 40 U if 15–25 kg; 50 U if &gt;25 kg</td>
<td>Saliva secretion (measured by DQ, TDS, and VAS)</td>
<td>DQ: 53% responded to scopolamine and 64% responded to BTX-A at 2 weeks and 49% at 24 weeks. TDS: 61.5% good responders 8 weeks post BTX-A and 36% at 24 weeks</td>
<td>71% patients experienced moderate–severe side-effects with scopolamine. With BTX-A, only non-severe side-effects</td>
</tr>
<tr>
<td>Lin et al</td>
<td>13 children</td>
<td>Double-blind, placebo-controlled, randomized clinical trial. Treatment with BoNT-A 2 u/kg into one parotid and the contralateral submandibular gland; control group, 1.5 mL of saline</td>
<td>Drooling severity and frequency scale, saliva weight, DQ</td>
<td>Significant improvement in all three measures within 14 weeks, except drooling severity and frequency scale and DQ at week 4 of BoNT-A</td>
<td>Small sample size with statistical power only 59.5%</td>
</tr>
<tr>
<td>Alrefai et al</td>
<td>24 children</td>
<td>Double-blind, placebo-controlled, randomized clinical trial. Treatment with BoNT-A 50 u into each parotid; control group, 0.5 mL of saline</td>
<td>Drooling severity and frequency scale</td>
<td>Significant reduction in median severity and median frequency scale in treatment group</td>
<td>High dropout rate in the placebo group with the higher dose (70 U into each parotid)</td>
</tr>
<tr>
<td>Reid et al</td>
<td>48 children</td>
<td>Placebo-controlled, randomized clinical trial. Treatment with BoNT-A 25 U into each parotid and submandibular glands; control group, no treatment</td>
<td>DrI</td>
<td>Significant difference between treatment and control groups in DrI scale at 1 month up to 6 months</td>
<td>Measurement bias as the placebo group received no treatment</td>
</tr>
<tr>
<td>Wilken et al</td>
<td>30 children</td>
<td>Randomized, repeated, open-label clinical trial. Treatment with BoNT-A total dose 80 u up to 100 u or serotype B 100 u/kg up to 120 u/kg (parotid and submandibular)</td>
<td>TDS</td>
<td>83% of all children responded. No significant difference between serotypes A and B</td>
<td>Five children developed viscous saliva; only 50% of children continued treatment</td>
</tr>
</tbody>
</table>

DQ, drooling quotient; DrI, Drooling Impact Scale questionnaire; TDS, Teacher Drooling Scale; VAS, visual analog scale.
malignancy in the irradiated field [46]. However, this risk is minimal, particularly in patients with ALS, as these patients have limited life expectancy.

RT has been criticized and abandoned from use for the pediatric population because of its long-term hazards of growth retardation and risk of malignancy [48–50].

ETHICAL CONSIDERATIONS

From the above discussion on the treatment options for drooling in children with CP, it is clear that, with the exception of non-invasive behavior modification techniques, adequate explanation of the advantages and disadvantages of each treatment option is required, and treatment can only be offered after appropriate consent is obtained. Obtaining consent before providing care is both a fundamental part of good practice and a legal requirement. The process of obtaining consent will vary from simple situations such as providing behavior modifications or administering oral medications to more complex situations where a considerable amount of information would be needed to support the decision-making process, as is the case with surgical options or botulinum toxin injections. There are unique issues relating to obtaining consent from children under 16 years of age. It is automatically assumed in these cases that obtaining parental consent is sufficient. The authors stress the importance of confirming that the consenting parent is indeed the parent with legal parental responsibility as defined by regional laws and regulations. Once children reach the age of 16 years, they are considered to have reached the age of legal capacity in most countries, and are considered to be able to provide consent to medical interventions. However, physicians are urged to encourage children between the ages of 16 and 18 years to involve their families in decision-making, especially when the young person is making the decision to refuse a certain treatment. In addition, in many countries, for treatment decisions that are unlikely to have grave consequences, even a young person under 16 years can legally consent to treatment provided he or she is competent to understand the nature, purpose, and possible consequences of the treatment proposed, as stated in the landmark Gillick case [51]. Consent considerations are more complex for children with CP, as many are not deemed competent to make such decisions. However, a disabled child should never automatically be presumed to be incapable of making decisions regarding care, and many will be able to contribute to the decision-making process if information is presented to them appropriately and they are adequately supported during the decision-making process. Even where children are not able to give consent for themselves, it is very important to involve them as much as possible in decisions about their own health and care. Even very young children will have opinions about their health and care, and methods appropriate to their age and understanding should be used to enable these views to be taken into account.

Complex situations arise at times, such as when parental responsibility cannot be verified, or when the competent child and his/her caregivers cannot agree on a certain treatment option. In these situations, regional regulations regarding the age of legal capacity and consent procedures must be consulted, and physicians are urged to seek legal advice.

CONCLUSIONS

Drooling can be a significant source of functional and social disability for a child with CP. Treatment of drooling is part of the multidisciplinary care that these patients require, which should consist of a pediatric neurologist, an otolaryngologist, a pediatric dentist, and a speech pathologist. Treatment recommendations are developed through a group decision-making process and are based on clinical evaluation of the type and severity of drooling and associated structural or neurodevelopmental problems. The parents and patients are included in developing a stepwise plan of no immediate treatment, intervention with oral motor techniques or equipment, biofeedback, pharmacotherapy, or surgery. There are no clinical trials comparing different treatment options (e.g., pharmacotherapy vs surgery or pharmacotherapy vs behavioral treatment), making treatment guidelines more difficult.

Future long-term studies with a large, homogeneous patient population should provide guidelines for the best treatment approach for this problem.

Disclosure: The authors have nothing to disclose.

REFERENCES