Chapter 3

Sialorrhea: A Guide to Etiology, Assessment, and Management

Işıl Adadan Güvenç

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Abstract

Sialorrhea, also known as hypersalivation or ptyalism, is excessive salivation associated with neurological disorders or localized anatomical abnormalities in the oral cavity. Pathologic sialorrhea may develop due to hypersalivation, together with various neurologic disorders including cerebral palsy, Parkinson's disease, and amyotrophic lateral sclerosis, or as an adverse effect of medications. Sialorrhea results in numerous problematic physical and psychosocial complications and has a significant negative impact on quality of life for both the patient and caregiver. The management of sialorrhea is best accomplished with a multidisciplinary team approach. Treatment options range from conservative measures such as observation, positioning, behavioral therapies, and pharmacological therapy to more aggressive methods such as botulinum toxin injections or surgery. The physiology, etiology, assessment, and treatment of sialorrhea are outlined in this review.

Keywords: sialorrhea, hypersalivation, drooling, ptyalism, etiology, assessment, management

1. Introduction

Sialorrhea, also known as hypersalivation or ptyalism, is excessive salivation associated with neurological disorders or localized anatomical abnormalities in the oral cavity. Sialorrhea can be classified as anterior and posterior; both can occur separately or simultaneously. Posterior sialorrhea is the flowing of saliva from the tongue to the pharynx. Anterior sialorrhea results in salivary incontinence or involuntary spillage of saliva over the lower lip, known as drooling. The underlying etiology is the excessive production of saliva or inability to retain saliva within the mouth due to reduced neuromuscular control of the tongue, oral tissues, and

impairment in the swallowing mechanism, all of which are necessary to move saliva from the oral cavity to the oropharynx and beyond [1]. Drooling is common in normally developed babies but subsides between the ages 15 and 36 months with the establishment of salivary continence. Sialorrhea after 4 years of age is generally considered pathologic. Pathologic sialorrhea may develop due to hypersalivation, together with numerous neurologic disorders including cerebral palsy (CP), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS), or as an adverse effect of medications. In children, the most common cause of sialorrhea is CP, which persists in 10–38% of these patients. In adults, the most common cause of sialorrhea is PD with a rate of 70–80% [2].

Whatever the cause is, drooling is bothersome, resulting in physical and psychosocial complications. Physical complications include maceration of the skin around the mouth with secondary infection, bad odor, dehydration, speech disturbance, and interference with feeding. People with drooling are also at increased risk for aspiration of saliva, food, or fluids into lungs, particularly when the normal reflex mechanisms such as gagging or coughing are impaired. The psychosocial complications include isolation, barriers to education (such as an inability to share books or computer keyboards), increased dependency and level of care, damage to electronic devices, decreased self-esteem, and difficult social interaction [3]. Sialorrhea may have a significant negative impact on quality of life for both the patient and caregiver [1].

2. Physiology of salivation

The major salivary glands include parotid, submandibular, and sublingual glands; the largest being the parotid gland. These glands secrete saliva, which has a major role in lubrication, digestion, immunity, and maintenance of homeostasis in the human body [2]. The salivary secretion of parotid, submandibular, and sublingual glands is controlled mainly by parasympathetic nervous system, although sympathetic innervation has a minor influence. The parasympathetic fibers originate in the pons and medulla, and they synapse in the otic and submandibular ganglia. Postganglionic fibers originating from the otic ganglion regulate secretory functions of the parotid gland, while the postganglionic fibers from the submandibular ganglion regulate secretory function of the submandibular and sublingual glands. Sympathetic innervation of these glands results in contraction of muscle fibers around the salivary ducts, which enhances the flow of saliva [3].

Salivary secretion is regulated through a reflex arch that produces several actions. The afferent branch contains chemoreceptors in taste buds and mechanoreceptors in the periodontal ligament. Afferent innervations of cranial nerves V, VII, IX, and X carry impulses to salivary nuclei in the medulla oblongata. Efferent impulses are mainly parasympathetic as described above; they come from the chorda tympani nerve (a branch of the cranial nerve VII) and travel to the submandibular, sublingual, and other minor glands via lingual nerve (a branch of the cranial nerve V_3). Efferent fibers to the parotid gland are supplied by lesser petrosal nerve (a branch of cranial nerve IX), which travel through the fibers of auriculotemporal nerve (a branch of the cranial nerve V_3) and reach the gland [2].

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The major salivary glands provide 90% of the nearly 1.5 L of saliva that is produced every day. If salivary secretion is not stimulated, that is in basal state, 70% of total salivary secretion comes from the submandibular and sublingual glands. When stimulated, salivary secretion increases by five times, with the parotid glands delivering the greater amount of the saliva [3]. An example of an exogenous source causing stimulation is chewing [2]. There are two main types of saliva produced by the three major salivary glands; serous saliva is produced mainly by parotid glands by stimulation, which is thin and watery, while viscous saliva is produced by sublingual and submandibular glands throughout the day, which is thicker [4]. Both forms of these secretions can be problematic. Serous saliva results in watery saliva, consistently spilling from the side of the mouth, and viscous saliva may be mucoid and sticky, which makes it harder to clear and causes a sensation of choking, associated with panic. It is important to distinguish between thin, runny saliva and thick, mucous secretions because the treatment options differ. The stimulation of cholinergic receptors produces thin, serous secretions, whereas that of beta-adrenergic receptors produces thick protein and mucus-rich secretions. Therefore, in the case of watery saliva secretions, anticholinergics can be preferred, whereas for thick mucus secretions, the addition of beta blockers may be beneficial [5].

3. Etiology of sialorrhea

Sialorrhea associated with neurologic illnesses is generally caused by impaired swallowing due to impaired neuromuscular function. Efficient coordination of various structures, namely the oral cavity, pharynx, larynx, and esophagus, is required for the neuromuscular activity of swallowing. The coordination of these structures forms three phases; the oral phase is under voluntary control, followed by the pharyngeal and esophageal phases, which are involuntary. Spontaneous swallowing is essential for the control of drooling. In children with neurologic disorders, drooling is similarly the result of inefficient tongue and/or bulbar control, thus impaired swallowing, rather than hypersalivation [2].

In children, mental retardation and CP are the most common causes of sialorrhea. Roughly, one in three children with CP is reported to have some degree of sialorrhea. Sialorrhea in CP is caused by oral motor dysfunction, dysphagia, and intraoral sensitivity disorder. Though underestimated, sialorrhea has significant clinical and social consequences concerning the overall health of these children, including dysphagia, respiratory health, and socioemotional aspects of both the children and their caregivers [4]. In adults, PD is the most common etiology. Swallowing impairment, mostly in the oropharyngeal phase, is the major contributor to the pathophysiology of sialorrhea in PD patients, while an increase in the speed of salivary excretion might be a minor contributor. No increase in salivary production was demonstrated in scintigraphic studies in PD patients with sialorrhea, while the speed of salivary excretion of parotid glands in PD patients was significantly higher than normal controls with Tc-99 m scintigraphy [6]. Similarly, in ALS, sialorrhea is not caused by increased production of saliva, but by the inability to swallow secretions because of tongue spasticity, weakness of face, mouth and pharyngeal muscles, and loss of oropharyngeal coordination and function [5]. Less common neurologic causes of sialorrhea are pseudobulbar palsy, bulbar palsy, and stroke (**Table 1**).

Systemic causes
• Neuromuscular/sensory dysfunction—cerebral palsy, Parkinson's disease, mental retardation, motor neuron disease (ALS), pseudobulbar/bulbar palsy, stroke
• Medication side effects—antipsychotics (clozapine), tranquilizers, anticonvulsants, anticholinesterases, lithium
• Toxin exposure—mercury vapor, pesticides, snake poisoning, mushrooms
• Infection—rabies
• Gastric—gastroesophageal reflux
Local causes
• Oral Inflammation—teething
• Infection—dental caries, oral cavity infection, tonsillitis, peritonsillar abscess
• Anatomic—macroglossia, nasal blockage, oral incompetence, dental malocclusion, orthodontic problems, head and neck surgical defects
Physiological causes
• Pregnancy

Table 1. Etiology of sialorrhea.

Increased secretion of saliva frequently develops due to inflammation, such as teething, dental caries, and oral cavity infections. Pregnancy is another significant cause of hypersecretion, usually related to hyperemesis gravidarum. It has an abrupt onset in the 2nd and 3rd week of conception with the rise of hormones and usually resolves during 2nd trimester [7]. Other causes of hypersecretion include side effects from medications (i.e., antipsychotics, tranquilizers, anticonvulsants, cholinergic agonists, and lithium), gastroesophageal reflux, toxin exposure (i.e., mercury vapor, poisonous spider bites, mushrooms, insecticides), and rabies [3, 8]. Clozapine, an antipsychotic used in schizophrenia, is a rather common cause of sialorrhea, which manifests in 30–80% of patients taking the drug. Hypersalivation usually develops early in the treatment course and is typically more prominent at night [9].

Anatomic abnormalities are usually not the only cause of sialorrhea; however, most of the time, they exacerbate other causative conditions. Macroglossia (enlarged tongue) and oral incompetence may cause salivary spilling. A constantly open mouth due to nasal blockage or malocclusion and other orthodontic problems may compound oral incompetence; treatment of nasal problems and orthodontic correction can alleviate sialorrhea. Surgical defects occurring after major head and neck surgeries may result in sialorrhea as well [3].

4. Assessment of sialorrhea

Assessment of the severity of sialorrhea and its impact on the quality of life for the patient and the caregivers assist in establishing a prognosis and appropriate management of the problem. History should be taken from the patient and the caregiver to understand the etiology and severity of the situation and its impact on the daily life. Use of medications, language and communication skills, cognition, respiratory health, and presence of gastroesophageal reflux disease should be questioned. In physical examination, oral cavity should be examined for sores on the lip and chin, dental problems, tongue size and movement, and tonsillar

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Drooling severity	**Points**
Dry (never drools)	1
Mild (wet lips only)	2
Moderate (wet lips and chin)	3
Severe (clothing becomes damp)	4
Profuse (clothing, hands, tray, objects become wet)	5
Drooling frequency	
Never drools	1
Occasionally drools	2
Frequently drools	3
Constantly drools	4

Table 2. Drooling frequency and severity scale.

hypertrophy; nasal blockage, malocclusion, and jaw stability should be assessed. A neurological examination should be carried out investigating the level of alertness, swallowing ability, motor skills, and sensory dysfunction of the patient. The nutrition and hydration status, head posture, and emotional state of the patient should also be evaluated [4, 10].

Objective and subjective measures have been developed to quantify sialorrhea. The objective test methods include radioisotope scanning, collection cups strapped to the patient's chin for the measurement of salivary flow, and direct observation of saliva loss such as counting the number of napkins used daily to contain excessive saliva production, measuring the weight of the towels or dental cotton rolls [4, 10]. The importance of objective methods is that they seem to be more sensitive in detecting a reduction in sialorrhea or drooling than purely subjective assessments [11].

A variety of subjective scales for sialorrhea have been described. Subjective scales such as the drooling frequency and severity scale, the drooling rating scale, the drooling impact Scale, and visual analog scales can be given to patients or their caregivers to determine the qualitative and quantitative consequences of the severity and impact of sialorrhea [4]. The drooling frequency and severity scale is an easy comprehensive scale, which rates the severity of drooling on a five-point scale and the frequency of drooling on a four-point scale (**Table 2**) [12]. Subjective scales are useful and appropriate methods to measure changes in sialorrhea, because the impact on families, caregivers, and the patients themselves is of utmost importance when assessing satisfaction with the effectiveness of any treatment [4].

5. Management of sialorrhea

The management of sialorrhea continues to be a challenge in spite of various effective treatment strategies to diminish saliva production. The flow of saliva from the oral cavity to the esophagus depends on numerous factors, such as cognitive and mental abilities, intact swallowing, oral sensibility, lip closure, and ability to keep the head upright [1].

Treatment of sialorrhea is best accomplished with a multidisciplinary team approach. The complete history and physical examination of the patient, the assessment of the impact of drooling on quality of life, and the potential for improvement can be undertaken by the primary care physicians. Speech pathologists and occupational therapists provide education for swallowing mechanics to the patients and support their posture with devices such as the head back wheelchair. Dentists and orthodontists identify and correct dental and oral diseases and malocclusion. Otolaryngologists diagnose and treat causes of aerodigestive obstruction like macroglossia and adenotonsillar hypertrophy that contribute to drooling. Neurologists assess the severity and prognosis of neurologic conditions that result in drooling [3].

The goal of the treatment of drooling is a reduction in excessive salivary flow, while maintaining a moist and healthy oral cavity. Avoidance of xerostomia (dry mouth) is essential. The two main approaches are:

1. Noninvasive modalities including positioning, improving eating and drinking skills, oral facial facilitation, speech therapy, biofeedback, positive and negative reinforcement, oral prosthetic devices, pharmacological therapy, and botulinum toxin
2. Invasive modalities including surgery and radiotherapy

Generally, no single approach is adequately effective, and usually, a combination of therapies is used. Primarily, reversible causes of drooling should be treated. Less invasive and reversible methods are preferred before surgery is undertaken [10]. Behavioral approaches and therapies employed by speech pathologists are rarely curative, while systemic medications and surgical approaches may have severe and long-term adverse effects [1].

For minimal problems, in children younger than 4 years of age or in adults with unstable neurologic function, observation may be the convenient choice. Minimal issues can be handled with a feeding program aimed at improving oral-motor control as well; nevertheless, this can rarely be helpful. Anatomical problems should be identified and treated, and adenotonsillectomy should be undertaken, if necessary. Dental malocclusion and caries should be corrected. Patients should be fitted with appropriate wheelchairs and braces, when required. A number of orthodontic appliances may be used, such as customized plates that fit the palate for improving lip closure or movable beads placed on the upper plate that stimulate tongue movement, thus helping to deflect saliva toward the pharynx [3].

Other conservative therapeutic options include positioning techniques, oral-motor, and speech therapies given by speech therapists, which improve oral awareness and motor control. Biofeedback and automatic cueing techniques may be utilized in patients with mild neurologic dysfunction and drooling. These devices are used to associate a behavior with a cue, such as swallowing or wiping the face with a beep sound. Reinforcement methods, which are suggested behaviors such as encouraging patients for swallowing and wiping their faces and discouraging open mouth, can be used as an adjunct in moderate sialorrhea [3, 10].

Whenever sialorrhea continues to affect the patient's health and quality of life in spite of these conservative measures, pharmacological therapy and other invasive therapies should be considered.

5.1. Pharmacological therapy

Oral therapy for sialorrhea encompasses the use of anticholinergic agents such as glycopyrrolate, benztropine, scopolamine, and tropicamide. Anticholinergic agents work by downregulating acetylcholine and ultimately decreasing saliva secretion through the parasympathetic autonomic nervous system. Glycopyrrolate oral solution is an anticholinergic agent that was the first drug approved in the United States for drooling in children with neurologic conditions and is generally well tolerated. However, anticholinergic agents are poorly tolerated by elderly patients. Glycopyrrolate actually has lower risk of central side effects, owing to its quaternary ammonium structure, that makes it impossible to pass the blood–brain barrier in large amounts. It is effective and safe at 1 mg, 3 times a day [2]. Studies have shown 70–90% response rates, but approximately 30–35% of patients discontinue the drug due to side effects such as excessive dry mouth, urinary retention, decreased sweating, skin flushing, irritability, and behavior changes [10]. Other undesirable adverse effects observed with such treatment include constipation, urinary retention, tiredness, and drowsiness [11]. Anticholinergics are contraindicated in patients with glaucoma, obstructive uropathy, gastrointestinal motility disorders, and myasthenia gravis.

Intraoral tropicamide films provide short-term relief of sialorrhea. One study provided evidence that 1 mg of tropicamide resulted in significant visual analog scale score decrease and reduction in saliva volume in nondemented PD patients [2]. Transdermal scopolamine, applied as a patch behind the ear, was well tolerated in short-term studies, but its use was limited by side effects of urinary retention and blurred vision [3].

A comprehensive systematic review of the use of anticholinergics in children concluded that benztropine, given 3–3.8 mg per day, could be effective. A significant decrease in the mean score for drooling was reported with benzhexol hydrochloride (2 × 2 up to 2 × 3 mg daily). There was also some evidence for a marked decrease in drooling with glycopyrrolate [13]. Benztropine was also reported to show a significant reduction in the total salivation scores compared to botulinum toxins A and B in a study of mixed treatment network meta-analysis of randomized controlled trials on pharmacological interventions for treating sialorrhea associated with neurological disorders [14].

Antireflux medication has also been suggested for use in drooling; however, there are no double-blind studies in the literature to offer evidence for this recommendation [2].

5.2. Botulinum toxin

The injection of botulinum toxin (BT) to the major salivary glands has grown in popularity because of its limited invasiveness and demonstrated effectiveness in many patients. It has been shown to improve quality of life of patients effectively with a low profile of side effects. However, it is important to take into account that the duration of the therapeutic effect is limited in time, generally lasting a few months [11].

The effect of BT in sialorrhea was first reported in PD patients [15]. This toxin is a potent neurotoxin that blocks the release of acetylcholine and a number of other neurotransmitters from synaptic vesicles; hence, it shows its effect by blocking cholinergic postganglionic parasympathetic fibers in sialorrhea [2].

Currently, three type A and one type B toxin are approved for use in the US. These are OnabotulinumtoxinA (BOTOX®), AbobotulinumtoxinA (Dysport®), IncobotulinumtoxinA (Xeomin®), and RimabotulinumtoxinB (Neurobloc®/myobloc®) [2]. Both A and B types of BT are reported to be effective in treatment of sialorrhea, and both have a low profile of side effects [1].

BT can be injected in parotid and/or submandibular glands. The dose, concentration, and volume of injectate, number of injections, injection site, rate of injection, gauge of needle, and distance of needle tip from the neuromuscular junction are among the factors that can affect the diffusion and spread of BT, thus its efficacy in sialorrhea. A broad dose range of BT has been reported in various studies, specifically from 10 to 100 U of Botox®, from 20 to 300 U of Dysport® per patient, while usually 2500 U of Neurobloc® per patient is reported to be injected. The effect of BT on salivation lasts for 1.5–6 months [11]. Older age is significantly associated with longer benefit duration [16]. Sometimes the reduction in salivary secretion and improvement in drooling may not be correlated, owing to the variability of the factors that influence the severity of drooling and reduction of saliva secretion [2]. Patients with PD showed a more favorable safety-efficacy ratio than did patients with ALS, due to lower adverse events and longer benefit duration [16].

In a recent meta-analysis, eight randomized placebo-controlled trials involving 181 patients were reviewed. The study reported that BT improved drooling severity in patients with sialorrhea significantly in both adult and pediatric populations. Increased saliva thickness (3.9%), dysphagia (3.3%), xerostomia (3.3%), and pneumonia (2.2%) were reported as common side effects [1]. Adverse effects such as chewing difficulties and recurrent mandibular luxation have been reported [11]. BT therapy is reported to have many advantages over other noninvasive and invasive treatments. It is effective and minimally invasive with few side effects and a low risk of aspiration. However, it is expensive and temporary, and the need for repeated sedation can be troublesome with children [2].

Ultrasound guidance for intraglandular injection is preferred by some of the authors. Blind puncture of the superficial lobe of the parotid gland following anatomical landmarks is easier, because the structure is relatively superficial. Since the submandibular glands are normally nonpalpable, infiltration may be more challenging. Ultrasound easily identifies the glandular structures for infiltration, while avoiding accidental damage to other anatomical structures, the facial nerve in the case of injection into the parotid gland, or the facial vessels in the case of the submandibular gland [11].

Jongerius et al. compared the efficacy of BT injections to transdermal scopolamine. They reported that even though both treatments were successful in significantly lowering drooling parameters, patients treated with BT did not experience any side effects, while 40% of patients taking scopolamine reported severe adverse effects. The wide range of side effects and potential drug–drug interactions encountered with scopolamine and glycopyrrolate suggests that BT may be a safer option compared to systemic anticholinergics [13].

BT can also be used for empirical selection of patients who would, in the future, be good candidates for surgical treatment of the major salivary glands. In this way, patients who respond

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well to BT injections can be treated more efficiently with surgery rather than receiving multiple injections. On the other hand, patients who do not respond well to BT may be considered as poor candidates for surgical treatment, because failure rates could be much higher owing to the contribution from minor salivary glands to the etiology of sialorrhea [17].

5.3. Radiation therapy

Radiation therapy to the salivary glands is a useful treatment option in elderly patients who are not candidates for surgery and cannot tolerate medications. Radiation causes xerostomia that lasts months to years. The dose may be changed to produce the desired effect, and it can be repeated if required. The main problem is that radiation can induce malignancies, but this does not happen until 10–15 years after treatment and therefore are less of a concern in patients who are elderly and debilitated [3].

5.4. Surgical treatment

While many patients are successfully treated with conservative methods and medical therapies, a number of patients are not able to tolerate the side effects of medications. BT treatment is reported to show improvement in drooling, but surgery provides a larger and longer lasting effect. Surgeons should consider more aggressive interventions for patients with chronic sialorrhea secondary to neuromuscular dysfunction with the impairment of swallowing. In these cases, sublingual or submandibular gland excision, submandibular duct ligation, parotid duct ligation, submandibular or parotid duct rerouting, or any combination of the above procedures result in higher rates of success, both short term and long term, and they may be cost-effective compared to BT injections requiring multiple visits [18]. Nevertheless, it is important to mention that surgery has a risk of permanent consequences (especially xerostomia), and that it should be preferred only in severe cases who are not responsive to nonsurgical therapies and in whom sialorrhea has great impact on the health and quality of life of the individual and caregivers [5].

Tympanic neurectomy is now regarded as a historical technique used to denervate salivary glands. This technique is performed through the middle ear, where the tympanic plexus and chorda tympani travel before entering the major salivary glands. The procedure is relatively simple and fast, but salivary function returns within 6–18 months, when nerve fibers regenerate [3, 17].

Recently, a novel procedure, transoral endoscopic submandibular ganglion neurectomy, was performed in two cases of BT-resistant drooling. Six months follow-up was successful; however, long-term results are awaiting to be warranted [19].

The most definitive treatment of sialorrhea is to excise the major salivary glands or to ligate or reroute the major salivary ducts. Surgical management can be described by a combination parotid duct ligation or rerouting with either submandibular gland excision or submandibular duct rerouting. Preservation of salivation with decrease in drooling could be accomplished by rerouting of the parotid and submandibular ducts to the posterior oropharynx with the advantage of no external scar. There may be a potential for aspiration after these procedures. Sublingual gland

excision is suggested as well when the submandibular ducts are rerouted to prevent formation of salivary retention cysts. Parotid duct ligation is a simple fast procedure without an external scar, which decreases the stimulated salivary flow. There may be a risk of sialocele development. The most definitive surgical procedure, which includes bilateral parotid duct ligation and submandibular gland excision, is highly successful, with nearly total elimination of sialorrhea, a low incidence of facial weakness, and significant patient and caregiver satisfaction [3].

The meta-analysis of surgical management using a variety of surgical procedures demonstrates significant subjective relief in 81.6% of pediatric patients with sialorrhea following surgery. Bilateral submandibular gland excision and parotid duct rerouting had the highest reported success rate of 87.8%. However, simple bilateral submandibular duct rerouting and bilateral submandibular duct rerouting with bilateral parotid duct ligation had similar levels of subjective success. Four-duct ligation had the lowest success rate at 64.1%. Although this procedure seems simpler and less invasive compared to other surgeries, it can cause significant pain and swelling, since the ligated glands continue to produce saliva for a period before atrophy occurs. Bilateral submandibular duct rerouting is a procedure that is more complex than a simple submandibular duct ligation. The reported success rates with this procedure are consistently good and similar to procedures involving submandibular gland excision. Limited data suggest that fibrosis of the gland occurs due to obstruction of the rerouted duct, ending up as an actual ligation of the duct, but in most of the patients, function is maintained in at least one gland [17].

Author details

Işıl Adadan Güvenç

Address all correspondence to: isiladadan@yahoo.com

Department of Otorhinolaryngology, Head and Neck Surgery, Cigli Regional Education Hospital, Izmir, Turkey

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