RESPIRATORY CARE Paper in Press. Published on September 16, 2014 as DOI: 10.4187/respcare.02856

A Review of Options for Treating Sialorrhea in Amyotrophic Lateral Sclerosis

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Sialorrhea or drooling represents quite a common problem in patients with amyotrophic lateral sclerosis (ALS). In this review, we describe the possible treatments for this issue. Current medical management is not always effective: anticholinergic drugs (atropine, glycopyrrolate, amitriptyline, hyoscyamine, and transdermal scopolamine) are often used, but there is very little evidence of their effectiveness in patients with ALS. More invasive treatments, such as botulinum toxin injections and/or radiation therapy in the salivary glands, can be considered when anticholinergic drugs are not effective. In this review, we also explore the possible surgical options for treatment of sialorrhea. Although no specific studies have been conducted on patients with ALS, surgical therapies might represent a valid option for treatment of sialorrhea since there is no tachyphylaxis or need for repeated therapeutic sessions. *Key words: amyotrophic lateral sclerosis; salivary glands; sialorrhea; drooling; aspiration pneumonia; botulinum toxin; radiotherapy; surgical intervention; quality of life.* [Respir Care 2015;60(3):1–•. © 2015 Daedalus Enterprises]

Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive and fatal neurodegenerative disease affecting motor neurons in the anterior horn of the spinal cord, the brainstem, and the motor cortex. It is clinically characterized by progressive weakness, usually leading to death by respiratory insufficiency within 3–5 y.[1] Bulbar symptoms at ALS onset are observed in up to 30% of patients, and almost all patients have a bulbar involvement at later stages of the disease.[1,2] Dysphagia often leads to dehydration, malnutrition, choking, and pulmonary aspiration. Malnutrition is an independent risk factor for death in ALS.[3,4] The in-

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The authors have disclosed no conflicts of interest.

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DOI: 10.4187/respcare.02856

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volvement of upper motor neurons causes a set of symptoms known as pseudobulbar palsy, which is characterized by spasticity of the bulbar muscles (which control speech, chewing, and swallowing) and emotional lability (pathologic laughing and crying). In addition, loss of motor neurons in the spinal cord causes muscular weakness and atrophy, leading in turn to progressive respiratory dysfunction, labored communication, and decreased voluntary as well as reflexive coughing.[5-8]

In ALS, sialorrhea is caused mostly by a decreased ability to swallow secretions (not by increased saliva production) due to tongue spasticity, orofacial and palatinolingual muscle control failure, facial weakness, and inability to maintain oral and buccal competence.[9,10] The progressive weakness of facial muscles and difficulty in swallowing saliva leads to drooling.[11-13] About half of all patients affected by ALS report significant sialorrhea or drooling at some point during the course of the disease, and ~20% of them have moderate-to-severe symptoms.[14] There are different scales for the assessment of sialorrhea. The revised Amyotrophic Lateral Sclerosis Functional Rating Scale, a widely used and validated instrument to monitor disease progression in ALS, contains 3 items assessing the function of bulbar muscles, including one evaluating sialorrhea.[15]

In 2013, Abdelnour-Mallet et al[16] attempted to evaluate the effectiveness of 2 other scales: the Oral Secretion Scale (designed for the evaluation of hypersialorrhea in ALS) and the Sialorrhea Scoring Scale (initially developed for Parkinson's disease). Although both scales have a high inter-rater and intra-rater reliability, there are some limitations. The Oral Secretion Scale is not designed to evaluate the effectiveness of invasive treatments for hypersialorrhea, whereas the Sialorrhea Scoring Scale does not predict tolerance to noninvasive ventilation (NIV) in ALS patients. Salivary secretion in healthy adults is ~1.2 L/d. During unstimulated salivation, 69% of saliva is contributed by the submandibular glands, 26% by the parotid gland, and 5% by the sublingual glands. During stimulated salivation, the parotid gland contribute 66% of the total flow.[17] The submandibular gland, a mixed but mostly serous gland, is responsible for stimulated and unstimulated saliva production, whereas the parotid gland, a purely serous gland, secretes saliva mainly during mastication. The sublingual gland is purely mucous. Excessive amounts of saliva significantly decrease quality of life by impairing speech production and lung function. Patients may also experience difficulties with NIV and in sleeping in a reclined position because of saliva aspiration.

The increase in mucous secretions in the throat and lungs, the inability to swallow saliva, and the cough impairment due to progressive weakness and diaphragm and respiratory muscle fatigue usually lead to an increased risk of aspiration pneumonia.[8,18-21] Drooling also causes dermatologic problems, such as facial irritation and skin excoriation.[5] Although pulmonary aspiration syndromes are often misdiagnosed in patients with ALS, they are associated with a high mortality.[8] In a cohort of 40 consecutive patients with ALS, Sorenson et al[18] observed the occurrence of aspiration pneumonia in 5 cases (13%). In an autopsy cohort of patients with ALS, Kurian et al[22] found a similar number of occurrences, with aspiration pneumonia being listed as the cause of death in 11% of cases, bronchopneumonia in 41%, and respiratory failure in 9%. Death was directly attributable to motor neuron disease in 11% of cases, cardiac causes in 14%, malignancies in 5%, and other causes in the remaining 9% of patients.[22] Excessive drooling also limits tolerance of NIV, which has been consistently shown to increase the life expectancy and quality of life of patients with ALS.[23-33] Thus, a successful management of sialorrhea may prolong NIV tolerance in ALS,[34] resulting in enhanced survival.[35]

Table 1. Inclusion Criteria for the Four Key Questions

	Question 1	Question 2	Question 3	Question 4
Study design				
Retrospective cohort	Yes	Yes	Yes	
Retrospective case control	Yes	Yes	Yes	Yes
Prospective cohort or clinical trial	Yes	Yes	Yes	Yes
Outcomes				
Clinical characteristics of range of symptoms			Yes	Yes
Duration of symptom relief			Yes	Yes

Did the studies cited answer the following questions? Question 1: Which area was treated? Question 2: What therapy was used (and at which dosage level)? Question 3: How long did the effect last? Question 4: Have side effects been reported?

Purpose of This Review

We present a systematic review of studies describing the various possible treatments for sialorrhea in subjects with ALS, attempting to assess the effectiveness of these therapies in improving quality of life and diminishing the risks due to excessive drooling and to evaluate their side effects and long-term efficacy.

Search Strategy and Selection Criteria

After defining criteria for study selection (Table 1) and for validity assessment, we searched MEDLINE for studies published from January 1994 through November 2013 using the following MeSH terms: sialorrhea, drooling, ptyalism, anticholinergic drug, neuromuscular agents, botulinum toxin (BoNT), radiotherapy, surgical intervention

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Table 2. Side Effects of Anticholinergic Drugs in Amyotrophic Lateral Sclerosis

Anticholinergic Drug	Mode of Administration	Recommended Dose	Side Effects
Atropine	Eye drops	1–2 drops 4 or 6 times/d	Sensitivity to bright light, dry mouth, blurred vision, irregular heartbeat, mental confusion, difficulty urinating
Amitriptyline	Tablet	25–450 mg at bedtime	Constipation, drowsiness, dry mouth, dizziness, tiredness or sleepiness, feeling faint when getting up, increased blood pressure, fast/racing heart, palpitation, heart attack, stroke, irregular or slow heart beats, very low blood pressure, feeling or being sick, diarrhea, increased need to urinate
Scopolamine	Transdermal patch	0.5 mg every 3 d	Pupillary dilatation, skin reaction, urinary retention
Hyoscyamine sulfate	Tablet or elixir	Tablet or elixir 4 or 6 times/d	Diarrhea, confusion, hallucinations, tachycardia or uneven heart rate, drowsiness, blurred vision, nausea, constipation, problems with urination, dry mouth
Diphenhydramine	Tablet	25–50 mg 3 times/d	Sleepiness, fatigue, dizziness, dry mouth, difficulty urinating
Oxitropium bromide	Aerosol	1.5 mg twice daily	Dry mouth, cough, hoarseness, urinating less than usual or not at all, stuffy nose, nosebleed, fast heart rate
Glycopyrrolate	Tablet	1–2 mg 3 times/d	Blurred vision, constipation, decreased sweating, dizziness, drowsiness, dry mouth, pupillary dilatation, nausea

AND parotid, submandibular glands, salivary glands, amyotrophic lateral sclerosis, motor neuron disease, and spinal cord disease. Only studies on human subjects with ALS published in English were included. Case reports, reviews, editorials, and letters were excluded.

The literature review was focused on answering the following key questions: anatomic targets and therapeutic doses of treatments for sialorrhea, long-term efficacy of treatments, and reported side effects of treatments. AN, NT and GAG independently reviewed the full texts of articles meeting eligibility criteria based on their abstracts (see Table 1).

Anticholinergic Drugs

Self-reported data from the ALS CARE Program (www.outcomes-umassmed.org/als, *accessed March 21, 2014*) suggest that > 70% of patients with ALS may benefit from treatment with anticholinergic medications (atropine eye drops [1–2 drops 4 or 6 times/d], glycopyrrolate [1–2 mg 3 times/d], amitriptyline [25–50 mg at bedtime], scopolamine transdermal patch [0.5 mg every 3 d], hyoscyamine sulfate [0.125–0.25 tablet or elixir 4 or 6 time/d], and/or diphenhydramine [25–50 mg 3 time/d]) (Table 2). There are very few clinical studies evaluating the effectiveness of these drugs on patients with ALS in a systematic fashion.[36,37] A recent study by McGeachan et al[38] suggests that scopolamine patches are the most effective anticholinergic drugs for management of sialorrhea in ALS, reporting a positive response in 85% of treated subjects. However, the authors noticed that about half of these subjects also required additional therapies and that 20% had to discontinue the scopolamine patches, mostly because of skin reactions.[38] Orally administered anticholinergic drugs are often interrupted due to systemic side effects, such as sedation and delirium, which are especially common in elderly patients.[39] Anticholinergic drugs can also cause thickening of mucous secretions in the throat and lungs, which is a far worse and more severe complication than drooling.[14] Pupillary dilatation, skin reactions, and urinary retention are also minor adverse effects of scopolamine skin patches. In a cohort of 30 subjects with chronic neurologic diseases and persistent drooling, Mato et al[40] reported a discontinuation rate for scopolamine patches of 13%. Cooper-Knock et al[23] reported a case of treatment-resistant sialorrhea in a patient with bulbar ALS. In this patient, the administration of subcutaneous glycopyrrolate (600 μg of glycopyrrolate over 12 h via a syringe driver) was proven to be effective without significant side effects, also achieving a greater tolerance for NIV at night. Notwithstanding this isolated finding, nearly one third of treated patients do not respond to anticholinergic drugs, and even in the presence of an adequate response in the earlier phases of the disease, for a majority of patients, these medications are often not a safe or sustainable therapy for drooling.[14,41] Additionally, all anticholinergic drugs are contraindicated in the presence of heart diseases, glaucoma, pyloric stenosis, prostatic hypertrophy, and hepatic and/or renal insufficiency, and particular care must be taken in elderly patients, thus limiting their widespread adoption for the treatment of sialorrhea in ALS.

BoNT (Botox)

Patients with ALS or other neurodegenerative disorders (such as Parkinson's disease) who do not improve and/or have serious side effects with anticholinergic drugs may benefit from injections of BoNT under ultrasound guidance into the parotid and submandibular glands. BoNT, commonly known as Botox, improves sialorrhea by reduc-

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Table 3. Summary of Studies Concerning Botulinum Toxin Use in Subjects With Amyotrophic Lateral Sclerosis

Reference	Study Design	No. of Cases	Botox Type	Total Dose (U)	Parotid (U)	Submandibular (U)	Duration of Effect (mo)
Jackson et al[36,41]	Prospective randomized double-blind placebo-controlled	18	B	NeuroBloc, 2,500	500	750	3
Verma and Steele[39]	Prospective open-label	8	A	Botox, 15–45	7.5–22.5	None	2.5
Gilio et al[43]	Prospective open-label	26	A	Botox, 20–40 Dysport, 60–120	10–20 30–60	None	0.5
Contarino et al[44]	Prospective open-label	9	B	NeuroBloc, 2,500	1,000	250	3
Guidubaldi et al[46]	Prospective randomized cross-over double-blind	7	A/B	Dysport, 250	100	25	2.5–3
Anagnostou et al[47]	Prospective randomized double-blind	10	A	Botox, 40	20	None	–
Costa et al[48]	Prospective open-label	15	B	NeuroBloc, 2,500	1,000	250	> 3
Scott et al[49]	Prospective open-label	6	A	Botox, 20–60	10–30	None	–
Giess et al[50]	Prospective open-label	5	A	Botox, 30–82	30–72	5	> 2.5
Møller et al[51]	Prospective open-label	7	A	Botox, 80–140	25–40	15–30	–
Manrique[52]	Prospective open-label	5	A	Botox, 100	20	30	3–4
Lipp et al[53]	Prospective double-blind placebo-controlled	12	A	Dysport, 37.5–150	18.75–75	None	3
Porta et al[54]	Prospective open-label	4	A	Botox, 50–100	15–40	10–15	4–7

ing the release of acetylcholine at the neurosecretory junction. In Table 3, we present the most relevant studies concerning the use of BoNT in the treatment of sialorrhea in ALS.[39,41-50] These studies used different BoNT serotypes (A[39,42,43,45-47,49-54] and B[23,41,44-46,48]), treatment regimens, and routes of administration (direct or transductal approach) with varying outcome measures. A typical regimen is the administration of a total dose of 250 U of BoNT-A: 100 U diluted in 0.4 mL of saline injected into 2 sites of each parotid gland and 25 U diluted in 0.1 mL of saline injected into a single site of each submandibular gland. Another common approach is the injection of total dose of 2,500 U of BoNT-B, again subdivided into 2 sites of injection for each parotid gland (1,000 U in 0.4 mL of saline) and a single site of injection for each submandibular gland (250 U in 0.1 mL of saline). Sialorrhea is reduced 3–7 d after the injections, and maximum reduction occurs ~2–4 weeks after treatment. The mean duration of the beneficial effect is usually three and half months,[39] although the relapse time is extremely variable, and inhibition of saliva production may last up to 6 months after injection.[44] BoNT serotypes A and B are considered to be equally efficacious and safe. In a study evaluating the differences between the 2 serotypes, Guidubaldi et al[46] found that BoNT-B has a shorter latency and the same duration of efficacy compared with BoNT-A. However, the costs of the 2 treatments are significantly different: at the doses used in the study, a treatment with BoNT-B costs approximately half that with BoNT-A. In the vast majority of cases, BoNT injection has no side effects.[55-57] Uncommon adverse events are increased viscosity of saliva, local pain, chewing weakness, and respiratory infections. Anaphylactic reactions are rare but often serious. In 2005, Li et al[58] reported the first case of death connected with administration of a Botox-lidocaine mixture in a patient with chronic neck and back pain. Another study reported a case of deterioration of bulbar function after botulinum treatment in a patient with ALS.[50] Four days after injection, the patient suffered rapid onset of bulbar dysfunction, resulting in severe aphagia and anarthria. A progressive cervical kyphosis connected with BoNT injection has also been reported by Hogan et al.[56]

Radiotherapy

Radiotherapy of the salivary gland has also been proposed as an effective method to reduce excessive drooling in patients with ALS.[59] Several studies on radiotherapy for the treatment of sialorrhea in ALS adopted different techniques (electron-based therapy vs photon-based therapy) and doses (Table 4). Electron-based therapy appears to be well tolerated and induces a sustained improvement compared with photon-based therapy, with no serious side effects. In a retrospective study by Guy et al,[62] a good response to radiotherapy was observed in 65% of subjects. However, 4 of 13 subjects treated with photon-based therapy experienced acute toxicity symptoms (oral pain and mucositis during or immediately after irradiation) or delayed reactions (edema or xerostomia 1 month after irradiation or oral pain 3 months after irradiation). Conversely, none of the 8 subjects treated with electron-based therapy reported side effects. The authors suggested an optimum total dose of 20 Gy administered in 5 fractions, encompassing the whole of the submandibular gland and sparing the upper part of the parotid gland. The benefits of radiation treatment persisted for 4–6 months.[19] Another study

Table 4. Summary of Studies Concerning the Use of Radiotherapy in Subjects With Amyotrophic Lateral Sclerosis

Reference	Study Design	No. of Cases	Anti-cholinergic Drugs	Radiated Gland	Doses	Photons/ Electrons	Side Effects	Follow-up	Results
Bourry et al[19]	Retrospective	21	Yes	18 subjects, parotid/ submandibular; one subject, submandibular/ one parotid; 2 subjects, both parotid glands	In 17 d, 19.1 Gy × 5 fractions (mean dose)	13 subjects, 5.5–6-MV photons; 8 subjects, 6–15 MeV	4 of 13 subjects experienced toxicity, oral pain and mucositis under irradiation, oral pain 3 mo after radiotherapy, edema resulting in an inability to lie down properly with a head mask, or xerostomia 1 m after radiotherapy.	10.4 m: one subject lost, 8 alive, and 12 dead	Results were positive for a mean of 7 mo. 13 subjects (65%) showed a positive response: 7 subjects showed a positive response at the end of radiotherapy, and 6 subjects showed a positive response 1 m after radiotherapy. 7 subjects were considered non-responders.
Kasarskis et al[10]	Retrospective case series	10	9 subjects	One parotid gland unilaterally; one subject, both parotid glands	In 3 d, 15 Gy × 3 fractions	9 MeV	None developed long-term complications.		Reduction started 2–4 wk after radiation, with a maximum improvement 6–8 wk later.
Neppelberg et al[60]		12		Submandibular and lower part of parotid glands	Single fraction of 7.5 Gy	4- or 6-MV photons	One subject developed a slight redness of the skin in the irradiated area 3–7 d after treatment. Nine of 14 subjects felt more viscous saliva after treatment. Two subjects complained about xerostomia during meals, and one subject had the feeling of a lump in the throat. One subject reported a slight temporary swelling in front of the ears 3 d post-radiotherapy. .	3 mo	The mean salivary secretion rate was significantly reduced after radiotherapy, with a 60% reduction measured after 1 wk and 51% reduction after 2 wk. After a longer time period (3 mo), the mean reduction in secretion rate was 21% compared with that before treatment.
Harriman[61]	Retrospective	9		Single-field compassing submandibular and sublingual glands and caudal lobes of parotid glands	Single fraction of 8 Gy or double equal fractions of 12.5 Gy		Subjects experienced only minor side effects: in 4 subjects, erythema and burning of skin from a few hours to 2 wk; in 2 subjects, sore throat for a few hours to 4 d; and in one subject, nausea for a few days. One subject felt that the saliva had become thicker post-treatment.	2 and 6 mo	All 5 surviving subjects noticed an improvement, with maximum improvement after 2 wk.
Andersen et al[59]	Prospective	18	Yes	Parotid glands	13 subjects, 7.0 Gy as a single dose on each side; 5 subjects, 7.5 Gy as a single dose on each side	4- or 6-MV photons	One subject complained of persistent xerostomia. A few subjects experienced transient aching pain in the cheeks the first 24 h after the treatment.	2 wk	One subject had no effect, and 17 subjects noticed a great improvement especially after 2 wk. Drooling returning after 4–6 mo.

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found similar beneficial effects by targeting under computed tomography guidance a single parotid gland unilaterally with a total dose 15 Gy delivered in 3 equal fractions.[10] Single-dose radiotherapy has also been proven to be beneficial in reducing excessive drooling in ALS. In 14 subjects treated with a single fraction of 7.5 Gy, Neppelberg et al[60] observed a 50% reduction in salivary secretion after 2 weeks and a 20% reduction after 3 months. It has been suggested that a dose of 8 Gy delivered in a single fraction may be as effective and safe as higher fractionated doses,[14] and increasing the dose did not improve initial achievement.[61] A review of published studies on BoNT and radiotherapy for sialorrhea in ALS attempted to evaluate and compare the effectiveness and side effects of the 2 treatments. However, because of the small number of published studies, the small sample sizes, and the poor quality of reporting, it was not possible to draw firm conclusions recommending one treatment over the other.[42]

Surgical Treatment

Another therapeutic option for the management of excessive drooling is surgical intervention. To our knowledge, however, there are no clinical studies focused on patients with ALS in the literature, and most of the published studies were performed on children with cerebral palsy.[63] In these particular patients, salivary duct or gland surgery is considered to be the best established treatment, especially in the most severe cases of sialorrhea. In 1996, Strauss et al[63] defined Wilkie's original operation (1967) as "the main surgical procedure" for controlling sialorrhea. The procedure consists of the retropositioning of the parotid ducts into the tonsillar fossa region along with bilateral submandibular gland resection. Several variants of the Wilkie procedure have been described: transposition, instead of resection, of the submandibular gland duct into the tonsillar fossa; ligation, instead of repositioning, of the parotid ducts, along with the usual submandibular gland resection; deviation of both submandibular and parotid ducts behind the anterior pillar of the soft palate (4-duct diversion); bilateral submandibular duct relocation with or without sublingual gland excision; a combination of ipsilateral parotid duct ligation and contralateral parotid duct repositioning; and ligation of both parotid and submandibular ducts (4-duct ligation).

Submandibular duct relocation with or without excision of the sublingual gland is currently the most common approach. By relocating the papillae of the submandibular ducts from the anterior oral cavity to the base of the tongue, saliva from the submandibular glands can flow directly into the oropharynx.[64] However, this procedure cannot be performed in patients with a history of recurrent aspiration pneumonia, as it may increase aspiration risk because it directs the saliva posteriorly.[65] The average postoperative stay in a hospital for this kind of procedure is ~2 d. In 2007, Glynn and O'Dwyer[66] studied whether the combination of sublingual gland excision and submandibular duct relocation gives better overall results in controlling drooling. They concluded that both procedures were equally effective, but the combination increased the morbidity of the procedure while not providing any better control of drooling. However, this more extensive intervention may prevent ranula formation.[66]

Studies on the efficacy of the 4-duct ligation procedure had contrasting results. In 2008, Stamataki et al[67] showed that the long-term effectiveness of the 4-duct ligation procedure in controlling anterior drooling is questionable as measured by caregiver satisfaction and need for additional medical and surgical therapies. Martin and Conley[68] reached similar conclusions. However, Chanu et al[69] obtained very different results. In fact, in their study, 4-duct ligation seemed to be a simple procedure and caused significant reduction in drooling and improved quality of life. Additionally, the procedure had few complications, which could be managed effectively. The authors concluded that 4-duct ligation is effective in controlling moderate-to-severe sialorrhea in children.[69] Three-duct ligation procedures have also been described in the literature.[47]

Unfortunately, duct ligation is not a permanent solution. In 2006, Osailan et al[70,71] published 2 works about ligation of the submandibular duct in rats. In the first study, they evaluated submandibular gland atrophy with or without chorda-lingual nerve resection and observed that, in the absence of chorda-lingual ligation, the extent of glandular atrophy was reduced.[70] In the second study, their goal was to investigate the recovery of submandibular gland function after the removal of an obstruction.[71] They ligated the submandibular glands of rats with micro-clips for 1, 4, and 8 weeks. The glands were then allowed to recover after removal of the micro-clips for 8, 16, and 26 weeks under stimulation with autonomimetic drugs. The authors concluded that following severe atrophy, the rat submandibular glands regenerated after 24 weeks and secreted normal quantities of saliva. This is true for acinar cells, but not for ductal ones.[71] In 1989, Grant et al[72] studied the effect of resection of the chorda tympani nerve on ipsilateral and contralateral salivary secretion. They studied 20 subjects undergoing exploratory ear surgery for mastoidectomy, stapedectomy, or tympanoplasty. Chorda tympani resection did not reduce salivary flow in 35% of the subjects, whereas in the remaining 65%, the submandibular flow was reduced by ~54%. These results strongly suggest that the morbidity of bilateral chorda tympani section alone outweighs the expected benefit in individuals with sialorrhea and a limited lifespan, such as patients with ALS. Therefore, it can be considered a poor method for reducing stimulated salivary flow.[72]

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In conclusion, although a surgical approach to sialorrhea is possible in children affected by cerebral palsy, nothing similar has been tested in patients with ALS. Indeed, there is currently no safe and effective surgical therapy for these patients; however, we believe that surgery may represent a valid option for the treatment of excessive drooling in ALS because there is no tachyphylaxis or need for repeated therapeutic sessions.

Conclusions

In our experience, the first-line treatment for excessive drooling in patients with ALS is represented by anticholinergic medications. Among the different possibilities, we believe the use of a scopolamine transdermal patch (1.5 mg/d) or sublingual amitriptyline (25 drops at bedtime) to be the most effective and best tolerated option. We have no personal experience with glycopyrrolate because it has not been approved for human use in Italy. In non-responders, we also used oxitropium bromide via nasal aerosol (1.5 mg twice daily) with some success. However, anticholinergic drugs are not a definitive solution for excessive drooling in ALS. For this reason, many patients have to deal with other more invasive therapies, such as botulinum injection and radiotherapy. The available data do not permit us to determine with certainty which is the better option. Radiotherapy has fewer side effects but a shorter duration of effect. Conversely, botulinum presents more side effects, but its action lasts longer. To date, there are no evidence-based guidelines for the management of sialorrhea in patients with ALS, and application of the different techniques is based on experience of only a few specialized centers. The goal of this review was to highlight the advantages and disadvantages of each method and to represent a practical tool for all physicians involved in the symptomatic treatment of sialorrhea in ALS.

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