Symptom Management and End-of-Life Care in Amyotrophic Lateral Sclerosis

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KEYWORDS

• Sialorrhea • Pseudobulbar affect • Noninvasive ventilation • Secretion management • Laryngospasm • Edema • Urinary urgency • Constipation

KEY POINTS

- Sialorrhea should initially be treated with anticholinergic medications. For patients who remain medically refractory, treatment with botulinum toxin type B (level B; recommendation by the American Academy of Neurology Practice Parameters Committee) or low-dose radiation therapy to the salivary glands (level C) should be considered.
- Pseudobulbar affect can be successfully treated with selective serotonin reuptake inhibitors, tricyclic antidepressants, and serotonin-norepinephrine reuptake inhibitors. A combination of dextromethorphan/quinidine should also be considered (level B).
- Noninvasive ventilation (NIV) should be considered to treat respiratory insufficiency, both to lengthen survival and to slow the rate of forced vital capacity decline (level B). NIV has demonstrated a positive impact on quality of life (level C). Mechanical insufflation/exsufflation may be considered to clear secretions, particularly during an acute chest infection (level C). NIV may be considered at the earliest sign of nocturnal hypoventilation in order to improve compliance (level C).
- Although enteral nutrition may help with weight stabilization, studies that have investigated possible survival benefits have provided mixed results. There are no conclusive data regarding specific diets and possible benefits in amyotrophic lateral sclerosis (ALS). Multiple studies have found that weight loss is associated with a worse prognosis.
- End-of-life discussions are difficult for patients, families, and physicians but must not be avoided. Advance directives should be addressed soon after the diagnosis. Hospice services are essential in the management of end-of-life issues in patients with ALS and optimize the likelihood of a peaceful and dignified death. Despite its advantages, it is generally underused or initiated too late in the disease course.

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SIALORRHEA

Sialorrhea is a socially embarrassing symptom related to pharyngeal muscle weakness, which can lead to aspiration pneumonia, the most common cause of death in ALS other than respiratory failure.[1] The prevalence of the sialorrhea among patients with ALS is estimated at 50%.[2] Patients frequently have to wipe their mouth with a tissue or, in extreme cases, may need to insert a paper towel or washcloth into their mouths to absorb the saliva.

The American Academy of Neurology's (AAN) practice parameter for the care of patients with ALS published in 1999 recommended both pharmacologic interventions and nonpharmacologic approaches, such as suctioning.[3] Treatment with anticholinergic medication (**Table 1**)[4] is considered first-line pharmacologic therapy; however, the benefits of this class of medication can be insufficient to completely address the symptom. In addition, common side effects associated with anticholinergic therapy include constipation, fatigue, impotence, urinary retention, blurred vision, tachycardia, orthostatic hypotension, and dizziness. These side effects occur most commonly in elderly patients. In addition, anticholinergic medications are relatively contraindicated in patients with a history of glaucoma, benign prostatic hypertrophy, or cardiac conduction disorders (especially bifascicular block, left bundle branch block, and a prolonged QT interval).

Selection of a particular medication often depends on the severity and frequency of the drooling. Sialorrhea associated with mealtimes or a particular time of day may be treated with as-needed administration of atropine, hyoscyamine, or glycopyrrolate. Transdermal scopolamine, botulinum toxin, or antidepressant medications provide a more continuous effect. Patients who have difficulty swallowing medications may prefer an agent that can be given sublingually or transdermally or is available in a liquid form that can be administered directly through a percutaneous endoscopic gastrostomy (PEG) tube.

Data from the national ALS Patient CARE database indicate that more than 70% of patients with ALS treated with atropine, glycopyrrolate, or amitriptyline reported these modalities were helpful.[2,4,5] By inference, approximately 30% of patients were not helped by these therapies. There remains, to date, no randomized trial comparing the efficacy of these different agents in the ALS population. In general, all of these medications may cause or aggravate existing problems with constipation; therefore, it is recommended that a stool softener be initiated at the same time the anticholinergic agent is prescribed.

Table 1
Medications commonly used for sialorrhea

Medication	Dosage
Amitriptyline	25–75 mg qhs
Nortriptyline	20–100 mg qhs
Atropine	0.4 mg q 4–6 h 1–2 ophthalmic drops SL q 4–6 h
Glycopyrrolate	1–2 mg tid
Scopolamine patch	Apply behind ear q3d
Hyoscyamine sulfate	0.125 mg–0.25 mg q 4–6 h (available as oral tablets, elixir, or sublingual tablets)
Botulinum toxin type A Botulinum toxin type B	—