PALLIATIVE PEARLS
BY ENCLARA PHARMACIA

Managing Excessive Secretions in Amyotrophic Lateral Sclerosis (ALS)
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Patient Case
HG, a 57-year-old male, who lives at home with his wife, has been receiving hospice care for the past 3 months for a primary diagnosis of ALS. In addition to ALS, HG has a history of HTN, placement of a PEG tube approximately 6 months earlier and pneumonia 3 months ago. HG is no longer ambulatory secondary to dysarthria and spasticity and has significant swallowing difficulties.

Recently HG's wife reports that he is experiencing gagging and choking more often despite routine suctioning with a portable suction device. He was hospitalized 3 months ago with similar symptoms and was diagnosed with pneumonia. They are concerned he is developing another lung infection. He had initial improvement in his drooling by using hyoscyamine drops 0.125mg via PEG Q.I.D. but now the secretions are thick and difficult to manage or suction. He also takes Baclofen TID, Lorazepam PRN, Ibuprofen PRN and Citalopram Daily.

What is Amyotrophic Lateral Sclerosis (ALS)?
ALS is a progressive, invariably fatal neurologic disorder in which destruction of motor neurons leads to loss of voluntary movement resulting in muscle weakness/atrophy, dysphagia, and ultimately, respiratory failure. As the disease progresses, muscles degenerate and the ability to control voluntary movement is lost. Currently, riluzole (Rilutek®) is the only FDA-approved drug to treat ALS. Although riluzole may extend survival by an average of 2 months in some patients, it does not reverse the damage already done to motor neurons and has unknown benefit in advanced-disease patients.[1] Medications are primarily used to relieve pain and control bothersome symptoms to maximize function and improve quality of life. A common symptom that affects more than half of patients with ALS is the inability to clear saliva, of which 20% rate the severity of drooling (sialorrhea) as moderate to severe.[2,3]

Why is sialorrhea so common in ALS?
Saliva is produced by the salivary glands in response to stimuli such as the sight and/or smell of food. Those with ALS continue to produce the same amount of saliva, but as ALS progresses, they lose their ability to swallow, causing saliva to pool in the mouth with resultant drooling.[4] While drooling may cause skin irritation and embarrassment, aspirating saliva could precipitate choking or pneumonia, a leading cause of death for ALS patients.[2,5] Activation of cholinergic receptors stimulates production of thin secretions, whereas activation of beta-adrenergic receptors produces thick, protein-rich mucus.[6] Management of excessive oral secretions can therefore be helped through drugs that have anti-cholinergic and anti-adrenergic properties.

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How do we treat sialorrhea in ALS?

Mild oral secretions: For mild excess saliva, a tricyclic antidepressant (TCA), such as amitriptyline (Elavil®) or nortriptyline (Pamelor®), may be helpful and should be considered in patients with concomitant depression, insomnia, or nerve pain. Because TCAs may be sedating, they should be dosed at bedtime when initiated. Note that TCAs increase level of serotonin in brain cells and when added to a medication regimen that includes other drugs with this property (SSRIs, SNRIs, fentanyl, methadone), could increase risk of Serotonin Syndrome, a potential fatal condition exhibited by rapid heart rate, high blood pressure and fever, sweating, and myoclonus. (Reference our Serotonin Syndrome case study for more information.)

Moderate to severe oral secretions: For more excessive secretions, medications with more potent anticholinergic properties can be tried. No clinical studies exist that compare these agents head-to-head, and adverse effects such as blurred vision, constipation, urinary retention, and delirium may lead to drug discontinuation, especially in the elderly who are more susceptible to these side effects.[7] Glycopyrrolate (Robinul®) is cost-effective and available generically as tablets, liquid, and solution for injection. Glycopyrrolate has a long duration of action and limited blood-brain barrier penetration, resulting in less drowsiness and confusion compared to other anticholingeric agents.[7]

Scopolamine patches [Transderm Scop®] are effective in 85% of patients with ALS, but had to be discontinued in 20% of those patients due to localized skin reactions.[8] Hyoscyamine (Levsin®) is a more cost-effective option compared to scopolamine and is available as sublingual tablets and concentrated liquid. Atropine readily crosses the blood-brain barrier and is most likely of the anticholingerics to cause confusion. The need to frequently dose atropine and the drug's recent price increase may limit utilization.

What is the best way to manage thick mucous in ALS?

Mucus can become very thick during the terminal phase of ALS due to the drying effect of anticholingeric agents, decreased intake of liquids, weakened cough, and respiratory infections.[4] Mucus pooling at the back of the throat can increase patients' anxiety and negatively impact sleep due to the feeling of choking to death, while also increasing the risk of aspiration.[9] A small study of 16 patients with ALS/MND (motor neuron disease) found that 75% had significant improvement in thick sections after a beta-blocker was started.[6] However, beta-blockers may decrease heart rate and cause fatigue, headache, dizziness, and depression.

Another treatment option for thick mucous is to attempt to thin secretions to enable patients to cough up the mucus or be more accessible with oral suctioning. Though clinical evidence is conflicting, guaifenesin is often used during terminal ALS as an expectorant to thin thickened secretions.[10] Guaifenesin has no known drug interactions, minimal side effects, and is available as both immediate and delayed release tablets and liquid. Nebulized saline and acetylcysteine [Mucomyst®] can be used as a mucolytic agent and are useful in helping to clear thick

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secretions in lower airways which home suction devices cannot reach. [11] Steam inhalation or humidifiers may also be useful to thin secretions.

Invasive therapies: If the excessive salivation persists or if side effects to medications become intolerable, invasive therapy may be considered to improve quality of life. Injection of botulinum toxin type A or B into the salivary glands is well-tolerated and effective, but must be repeated every 3 to 5 months.[12] The effects of radiating the salivary glands may last months to years and is an option for patients without concern of future potential secondary malignancies in those requiring more than one treatment.[13] Repositioning salivary ducts could be a potential option for refractory excessive secretions, but has not been extensively studied in the ALS population[3] and is unlikely to be appropriate to patients in hospice.

Patient Case Follow Up

HG's nurse was provided the summary points above to relay to HG's physician. A recommendation was provided to discontinue hyoscyamine as it may be contributing to the thickness of the secretions and to initiate sodium chloride 0.9% (saline) 3mL via nebulizer via mask every 4 hours while awake in addition to continuing routine suctioning.

For additional information on this topic, please review these references:

- Enclara Pharmacia's On Demand Educational Webinar, "Advanced Neurologic Disease". Click here to log in.
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- Scott K, Shannon R, Roche-Green A. Fast Facts and Concepts #299. Management of sialorrhea in ALS. June 2015. Available at: https://www.mypcnow.org

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