PALLIATIVE CARE NETWORK OF WISCONSIN

**FAST FACTS AND CONCEPTS #301**
**PHARMACOLOGIC MANAGEMENT STRATEGIES IN ALS**
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**Background** Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disorder which can affect the muscles involved in swallowing, speaking, breathing, and ambulation (1). This *Fast Facts* discusses pharmacologic management strategies for patients with ALS; see *Fast Fact #300* for non-pharmacologic management strategies and *Fast Fact #299* for management of sialorrhea specifically.

**Pseudobulbar Affect (PBA)** This term refers to disordered emotional expressions caused by disruption of cortico-pontine-cerebellar tracts. It typically manifests as inappropriate and uncontrollable laughing or crying inconsistent with the patient's mood and can be socially debilitating.

- The combination drug dextromethorphan/quinidine is the only FDA approved treatment of PBA. Its mechanism of action for pseudobulbar affect seems to be related to its anti-glutamatergic and anti-NMDA actions (2). The recommended dose is 20 mg dextromethorphan/10 mg quinidine twice daily. The rationale for combination therapy is that dextromethorphan is rapidly metabolized by an enzyme that is inhibited by quinidine.
- Tricyclic and SSRI anti-depressants have shown benefit, but clinical trial data is limited by small numbers of patients and poor standardization of PBA diagnostic and severity criteria (3).

**Depression** Major depressive disorder is a common in ALS. Selective serotonin reuptake inhibitors are often used; however, there are no randomized controlled trials specific to ALS (4). Although the American Academy of Neurology advocates treatment of depression in ALS, there are insufficient data to recommend any specific treatment with regard to particular SSRIs, SNRIs, etc. (5).

**Spasticity** Damage to the upper motor neurons in ALS leads to spasticity, which can be associated with cramps and incoordination of movement. There are no high-quality, controlled trials evaluating pharmacologic treatments for spasticity (6) and clinicians should be aware that some degree of spasticity can be useful for maintenance of posture. Although baclofen and tizanidine are both commonly used, experts tend to reserve tizanidine for more severe cases (4).

- Baclofen: initial dosing is 5-10 mg BID-TID; doses up to 120 mg per day may be needed (7).
- The starting dose for tizanidine is 2-4 mg BID with 24 mg as the maximum daily dose (7).
- Intrathecal baclofen pumps are considered only for patients with medically refractory spasticity.

**Pain** Spasticity, muscle spasms, joint stiffness and skin breakdown related to immobility are all potential sources of pain in ALS, which occurs in the later stages in up to 80% of patients (8). There is insufficient evidence on which to base specific recommendations for the treatment of pain in ALS. However, as in other conditions, non-opioid analgesics and anti-inflammatory medications are generally considered first-line. When these medications fail, opioids are used commonly.

**Dyspnea** Air hunger due to ventilatory failure is common in the later stages of ALS, occurring in up to 85% of patients (9). According to the American Academy of Neurology, there are insufficient data to support specific treatments for dyspnea in ALS (5). In addition to non-invasive ventilation, opioids are used commonly to relieve air hunger. One small, non-randomized prospective study demonstrated that morphine appears to be both safe and effective in this patient population (10). Furthermore, studies evaluating the safety of opioids for dyspnea in general have not demonstrated any excess mortality (11).

**Riluzole** It is the only proven disease-modifying pharmacologic agent in ALS, providing a modest survival benefit of 2-3 months and likely works via inhibition of glutamate release (12). Unfortunately, its cost can often be prohibitive and it does not palliate any ALS-associated symptoms or improve quality of life. In fact, side effects such as fatigue can be significant enough to warrant discontinuation (5). Given these factors, it is reasonable to discontinue the medication at the time of hospice enrollment (or when a patient becomes ventilator-dependent), although there are no published guidelines regarding these considerations.

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