



REVIEW ARTICLE

Overview of amyotrophic lateral sclerosis and medications for disease progression

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ABSTRACT

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that affects the nerve cells responsible for controlling voluntary muscle movement. The progression of ALS varies, but generally follows a predictable pattern. There is no cure for ALS, and treatment is focused on managing symptoms and maximizing quality of life. Medications such as riluzole and edaravone are commonly prescribed to manage symptoms and slow the disease progression. Riluzole works by reducing the release of glutamate, a neurotransmitter that can damage motor neurons, modulating voltage-gated sodium channels, and stabilizing intracellular calcium levels. Clinical trials have demonstrated that riluzole can help slow the progression of ALS, though it does not cure the disease. It is important to note that riluzole is not effective for all patients with ALS, and its benefits are modest. Therefore, it is important to discuss the potential benefits and risks of riluzole with a health-care provider before starting treatment.

KEY WORDS: Amyotrophic lateral sclerosis, Medications, Neurodegenerative disease

INTRODUCTION

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a progressive neurodegenerative disease that affects the nerve cells in the brain and spinal cord responsible for controlling voluntary muscle movement. The progression of ALS varies from person to person, but generally follows a predictable pattern (Alam *et al.*, 2021; Yadav *et al.*, 2021).^[1,2]

Bulbar symptoms such as dysarthria (93% of cases), dysphagia (86% of cases), and tongue fasciculations (64% of cases) are also indicative of ALS (Kumar *et al.*, 2022). ALS is characterized by progressive weakening in limbs, respiratory insufficiency, stiffness, hyperreflexia, and bulbar symptoms. Half of those with ALS get some form of memory loss, and 5% develop dementia 4 out of 1, 00,000 peoples. The death toll from and severity of damage caused by motor neuron disorders are disproportionate to their comparatively modest frequency and prevalence.

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The exact cause of ALS, also known as Lou Gehrig's disease, is not yet fully understood, but it is believed to be a complex interplay of genetic and environmental factors (Alam *et al.*, 2021; Yadav *et al.*, 2021).^[1,2] About 10% of cases are classified as familial, meaning that there is a genetic component involved. In these cases, mutations in specific genes, such as the C9orf72, SOD1, FUS, and TARDBP genes, have been identified as playing a role in the development of the disease.

The remaining 90% of cases are considered sporadic, which means that there is no apparent family history of the disease (Kumar *et al.*, 2022). However, it is believed that in these cases, multiple genetic and environmental factors may interact to increase the risk of developing the disease. Several environmental factors have been suggested to contribute to the development of ALS, such as exposure to

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toxic chemicals or heavy metals, viral infections, traumatic injuries, and lifestyle factors such as smoking and poor diet.

Overall, the causes of ALS are likely multifactorial and complex, and research is ongoing to better understand the underlying mechanisms of the disease and to develop effective treatments.

EARLY STAGE

In the early stages, symptoms may be subtle and easily overlooked. The initial symptoms often involve muscle weakness or stiffness, particularly in the arms or legs. The person may also experience difficulty with fine motor tasks, such as buttoning a shirt or holding a pencil. As the disease progresses, muscle weakness spreads to other parts of the body, including the face, throat, and chest (Van *et al.*, 2017; Zhou *et al.* 2018).^[3]

MIDDLE STAGE

In the middle stages, the symptoms become more pronounced and may affect the person's ability to perform daily activities independently. The person may require assistance with walking, dressing, and other tasks. Speech may become slurred, and swallowing may become difficult. The person may experience muscle cramps, twitching, and spasms, as well as increased fatigue.

LATE STAGE

In the late stages, the person becomes increasingly dependent on others for assistance with all aspects of daily living. The ability to speak and swallow may be lost entirely. Breathing may become difficult, and the person may require mechanical ventilation to support their respiratory function. The person's cognitive function is generally unaffected by the disease.

Overall, the progression of ALS is relentless and irreversible. The rate of progression varies from person to person, with some people experiencing a more rapid decline than others.

MEDICATION FOR PROGRESSION OF ALS

Riluzole (glutamate antagonist)

There is currently no cure for ALS, and treatment is focused on managing symptoms and maximizing quality of life.

Unfortunately, there is currently no cure for ALS, and no medication that can stop or reverse the progression of the disease. However, there are medications that can help manage symptoms and improve quality of life for people

with ALS (Corcia *et al.* 2021).^[4] One medication that is commonly prescribed for people with ALS is riluzole, which has been shown to slow the progression of the disease and extend survival by a few months. Riluzole works by reducing the release of glutamate, a neurotransmitter that can damage motor neurons. It is usually prescribed early in the course of the disease and is taken orally (Witzel *et al.* 2022, Jaiwal *et al.* 2019).^[5,6]

Mechanism of action of riluzole

The exact mechanism of action of riluzole is not fully understood, but it is believed to work through a few different mechanisms:

1. Inhibition of glutamate release: Riluzole is thought to reduce the release of glutamate, an excitatory neurotransmitter that can be toxic to neurons in high concentrations. By inhibiting glutamate release, riluzole may help to prevent excessive stimulation of neurons and reduce their vulnerability to damage
2. Modulation of voltage-gated sodium channels: Riluzole has been shown to modulate the activity of voltage-gated sodium channels, which play an important role in the transmission of electrical signals in neurons. By regulating the activity of these channels, riluzole may help to improve the function and survival of neurons
3. Stabilization of intracellular calcium levels: Riluzole has been shown to stabilize intracellular calcium levels, which can become dysregulated in the context of neurodegenerative diseases such as ALS. By promoting calcium homeostasis, riluzole may help to prevent the degeneration of neurons.

Overall, the precise mechanism of action of riluzole is likely to be complex and multifactorial, involving a combination of direct and indirect effects on neuronal function and survival.

Edaravone

Edaravone is another medication that is used in the treatment of ALS. It is an intravenous medication that has been shown to slow the decline in daily functioning in people with ALS. The exact mechanism of action of edaravone is not fully understood, but it is believed to work by reducing oxidative stress, which can damage neurons. Oxidative stress occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the ability of the body to neutralize them with antioxidants. ROS are molecules that can damage cells and tissues by reacting with other molecules in the body, such as proteins, lipids, and DNA (Bhandari *et al.* 2018).^[7] In neurodegenerative diseases such as ALS, oxidative stress is thought to play a role in the degeneration of neurons.

Edaravone is a free radical scavenger that can neutralize ROS and reduce oxidative stress. It is thought to work by

protecting neurons from oxidative damage and reducing inflammation (Rokade *et al.*, 2022).^[8,9] By reducing oxidative stress, edaravone may help to slow the progression of ALS and improve symptoms. Edaravone is typically given over a period of 14 days, followed by a 14-day break, and then another 14-day treatment cycle. It is important to note that while edaravone can help manage symptoms and improve quality of life, it does not cure ALS or stop its progression (Sawada *et al.* 2017, Jaiswal *et al.* 2019).^[10,6]

In addition to these medications, people with ALS may be prescribed other medications to manage symptoms such as muscle cramps, spasticity, pain, and depression.

It is important to note that while these medications can help manage symptoms and improve quality of life, they do not cure ALS or stop its progression.^[11] As such, a multidisciplinary approach to care is important, including physical and occupational therapy, speech therapy, respiratory therapy, and palliative care.

Riluzole is a medication that has been used in the treatment of ALS, a neurodegenerative disorder that affects the nerve cells responsible for controlling voluntary muscles. The exact mechanism of action of riluzole is not fully understood, but it is believed to work by reducing the release of glutamate, an excitatory neurotransmitter that can be toxic to neurons in high concentrations.

Clinical trials have demonstrated that riluzole can help slow the progression of ALS, though it does not cure the disease. In one study, patients with ALS who were treated with riluzole had a small but significant improvement in survival compared to those who received a placebo. In addition, riluzole has been shown to delay the need for mechanical ventilation and to improve functional outcomes in some patients with ALS.^[12]

It is important to note that riluzole is not effective for all patients with ALS, and its benefits are modest. Some patients may experience side effects such as nausea, fatigue, and liver function abnormalities. Therefore, it is important to discuss the potential benefits and risks of riluzole with a health-care provider before starting treatment.

CONCLUSION

Riluzole has been shown to provide modest benefits in the treatment of ALS by slowing the disease progression and delaying the need for mechanical ventilation. However, it

is not a cure for ALS and its benefits may vary from patient to patient. It is important for patients to discuss the potential benefits and risks of riluzole with their health-care provider before starting treatment. Edaravone is a free radical scavenger that can neutralize ROS and reduce oxidative stress. It is thought to work by protecting neurons from oxidative damage and reducing inflammation. Hence, it can be better option for the neutralizing the oxidative stress and inflammation.

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