



PIC QUESTION OF THE WEEK: 04/11/05

Q: What is the role of aminopyridine in the treatment of Lambert-Eaton syndrome in a patient with lung cancer?

A: Lambert-Eaton syndrome (also referred to as Lambert-Eaton Myasthenic Syndrome--LEMS) is an autoimmune disease caused by a reduction in the release of acetylcholine into the synaptic gap. Autoantibodies develop against the pre-synaptic voltage-gated calcium channels interrupting impulse transmission. This results in symptoms such as muscle weakness, paresthesia, hyporeflexia, fatigue, and dry mouth. Lambert-Eaton syndrome is often misdiagnosed as myasthenia gravis because the two disorders have similar clinical manifestations. Lambert-Eaton is a rare condition affecting only four in a million people. The prevalence is much higher in patients with small cell lung carcinoma. About sixty percent of Lambert-Eaton patients have small cell lung cancer. Other malignancies have also been associated with Lambert-Eaton patients; however, the relationship is not as well established. There is no cure for this disorder, but several treatment options are available. The initial pharmacotherapy of LEMS utilizes agents that increase the transmission of acetylcholine across the neuromuscular junction, either by increasing the release of acetylcholine or decreasing the action of acetylcholinesterase. Two forms of aminopyridine (4-aminopyridine and 3, 4-diaminopyridine) have been used in the treatment of Lambert-Eaton syndrome. 4-aminopyridine (fampridine) is available as an orphan drug. 3, 4-diaminopyridine (3, 4-DAP) is a better choice because it does not readily cross the blood brain barrier. The most common adverse effects of 3, 4 DAP include tingling of the mouth, dizziness, gait instability, and stomach upset. Seizures have also been reported. Eighty percent of Lambert-Eaton respond to treatment when treated with 3, 4-DAP. Other therapies for this disorder include guanidine, immunosuppressants (prednisone and azathioprine), pyridostimine, and intravenous gamma globulins. Response to treatment of small cell lung cancer is generally accompanied by an improvement in Lambert-Eaton symptoms.

References:

- Maddison, P; Newsome-Davis, J. Treatment for Lambert-Eaton myasthenic syndrome. Cochrane Database of Systematic Reviews 2005;1:1-27.
- www.ninds.nih.gov accessed (4/7/05)

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