Clinical Problem: A 57 year old male has typical ALS with diagnostic EMG and nerve biopsy.

Clinical Question: Do drugs such as L-Dopa and Selegiline slow disease progression and prolong life in ALS?

Clinical Bottom Lines:
1. Selegiline 10mg daily has no effect on clinical progression of ALS.
2. Selegiline adverse effects most commonly reported are insomnia (9.6%), hallucinations (5.7%), and GI symptoms (3.8%) (ref 2).
3. L-Dopa is not an effective therapy for ALS.

The Evidence:
1. A randomized double blind single cross over trial of 10 patients compares selegiline 10mg per day with placebo. Each trial period was 12 weeks in duration with a 12 week wash-out period. Primary outcome was neurological status documented using Norris, spinal, and bulbar scores.
2. An open (non-blinded) randomized clinical trial of 111 patients compares selegiline 10mg per day to a non-treated control group over a 6 month period. Outcomes included mortality, mean MRC, Norris disability scores, and FVC.
3. A 6 month, double blind, placebo controlled study of 133 patients to determine efficacy of selegiline 10mg per day measured by Appel ALS scores.
4. An uncontrolled case series of 10 patients taking an average of 6.4g L-Dopa daily for an average of 5.5 months. Outcome assessments included a disability scale, muscle strength testing, isometric and timed tests.

Data interpretation:

<table>
<thead>
<tr>
<th>Author</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jossan</td>
<td>Selegiline: NS differences from controls in: Norris, spinal, bulbar score.</td>
</tr>
<tr>
<td>Mazzini</td>
<td>Selegiline: NS differences from controls in: mortality, MRC, Norris score at 6 months.</td>
</tr>
<tr>
<td>Lange</td>
<td>Selegiline: NS differences from controls in: A-ALS scores of after 6 months.</td>
</tr>
<tr>
<td>Mendell</td>
<td>L-Dopa: 70% of the patients’ disability, isometric muscle test, and timed-task scores deteriorated over a mean of 4.5 months. No controls.</td>
</tr>
</tbody>
</table>

Comments:
Paper 1 (Class 2b):
Small number of patients. Details of randomization process, concealment, and assurance of blinding are absent. Not all patients were adequately accounted for at trial conclusion. ALS does not lend itself to a crossover clinical trial as the disease is not a stable chronic condition.

Paper 2 (Class 2b):
The control group had better bulbar scores than treatment group at baseline. Unblinded as the control group received no placebo treatment.

Paper 3 (Class 1b):
Methodologically valid therapeutic trial.

Paper 4 (Class 4):
Uncontrolled case series of a limited number of patients.

Reference:
3. Mendell DJ et al. Selegiline is ineffective in a collaborative double-blind, placebo-controlled trial for treatment of...

**Key Words:** ALS/Selegiline/Deprenyl/L-Dopa/therapy

**Appraiser:** Bart Demaerschalk and the UWO Evidence Based Neurology Group

**Date appraised:** April 1999