Intramuscular injections of gangliosides do not alter progressive deterioration of ALS

Clinical Problem: A 57-year-old male presents to your office with a combination of both upper and lower motor neuron signs. EMG studies reveal widespread fasciculations and polyphasic, high amplitude muscle potentials. Neurogenic atrophy is noted on muscle biopsy. You make a diagnosis of ALS and discuss prognosis. The patient indicates that he has read about ganglioside therapy and wishes to pursue this avenue.

Clinical Question: Do gangliosides alter the clinical progression of ALS?

Clinical Bottom Lines:

1. Intramuscular brain gangliosides at low (40mg) and high (300mg) doses do not alter progressive deterioration of ALS.
2. No toxic effects of the drugs were noted apart from local erythema at injection site.

The Evidence:

Paper 1
A double-blind placebo-controlled 3 month trial of high dose gangliosides (300mg IM per day) in 40 patients using Norris and subjective scores as outcomes.

Paper 2
A double-blind, placebo-controlled 6 month trial of bovine brain gangliosides (40mg IM per day) in 40 patients with measures including neuro exam, PFTs, bulbar function, limb function, timed motor tasks, isometric strength, EMG, and subjective ratings.

Paper 3
A 6 month, 40 patient, double-blind placebo-controlled trial of IM gangliosides 40mg/day with assessments of objective strength and PFTs.

Data interpretation:

<table>
<thead>
<tr>
<th>Author</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lacomblez</td>
<td>No significant differences from placebo</td>
</tr>
<tr>
<td>Bradley</td>
<td>No significant differences from placebo</td>
</tr>
<tr>
<td>Harrington</td>
<td>No significant differences from placebo</td>
</tr>
</tbody>
</table>

Comments:

Paper 1 (Class 2b)
No mention whatsoever of randomization scheme.

Paper 2 (Class 1b)
Methodologically valid therapeutic trial. Possibly inadequate numbers to show effect. Dose use was lower than that shown effective in animal studies.

Paper 3 (Class 1b)
Suggestion that ganglioside group was stronger at start of trial which should have biased toward finding a positive effect of therapy. Otherwise a methodologically valid trial.
No control group. Outcomes compared to baseline values. Very small patient numbers and inappropriate use of cross-over design.

References:

Key Words: ALS/gangliosides/therapy

Appraiser: Bart Demaerschalk and the UWO Evidence Based Neurology Group

Date appraised: April 1999

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