Cannabinoids did not reduce muscle spasticity in stable multiple sclerosis


**Question**
In patients with stable multiple sclerosis (MS), are cannabinoids (oral cannabis extract [OCE] or synthetic Δ9-tetrahydrocannabinol [SAΔ9-THC]) effective for reducing MS-related muscle spasticity?

**Design**
15-week randomized (allocation concealed*), blinded (clinicians, patients, data collectors, outcome assessors, and monitoring committee)* placebo-controlled trial.

**Setting**
33 neurology and rehabilitation centers in the United Kingdom.

**Patients**
657 patients 18 to 64 years of age who had had clinically definite or laboratory-supported MS with problematic spasticity (Ashworth score ≥ 2) for the previous 6 months. Exclusion criteria included ischemic heart disease, infection or use of medication that could exacerbate spasticity, fixed-tendon contractures, and severe cognitive impairment. 630 patients (mean age 51 y, 66% women) were included in the intention-to-treat analysis.

**Intervention**
Patients were allocated to an OCE containing Δ9-THC and cannabidiol as the main cannabinoids (n = 219), SAΔ9-THC (n = 216), OCE placebo (n = 108), or SAΔ9-THC placebo (n = 114), taken twice daily after food for 14 weeks. Study medication was titrated to a maximum possible dose of 25 mg daily. The 2 placebo groups were combined into 1 group for data analysis purposes.

**Main Outcome Measures**
Change from baseline in MS-related muscle spasticity (0 to 4 Ashworth score of spasticity [0 = normal, 1 = slight catch when the limb is moved, 2 = anything more than a catch but not restricting movement, 3 = considerable increase in tone limiting passive flexion, and 4 = limb rigidity in flexion or extension] assessed before treatment, and during weeks 1, 6, 10, and 13 of treatment).

**Main Results**
Analysis was by intention to treat. The OCE and SAΔ9-THC groups did not differ from placebo for change from baseline to the 13th week of treatment in MS-related muscle spasticity (Table).

**Conclusion**
In patients with stable multiple sclerosis (MS), cannabinoids (oral cannabis extract or synthetic Δ9-tetrahydrocannabinol) were not effective for reducing MS-related muscle spasticity.

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*See Glossary.

**Table**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Comparisons</th>
<th>Mean</th>
<th>Difference between groups (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change from baseline in muscle spasticity (0 to 4 Ashworth scale scores)</td>
<td>OCE vs placebo</td>
<td>1.24 vs 0.92</td>
<td>0.32 (−1.04 to 1.67)‡</td>
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<tr>
<td></td>
<td>SAΔ9-THC vs placebo</td>
<td>1.86 vs 0.92</td>
<td>0.94 (−0.44 to 2.31)‡</td>
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</table>

‡CI defined in Glossary.

Insensitivity of the Ashworth score as a measure of spasticity may have contributed to the negative result. An analgesic effect of the cannabinoids may have contributed to the improved gait, but a strong placebo effect with a 35% improvement in pain in the placebo group was also reported. Much of the benefit may actually be related to treatment or placebo effects on the psyche of patients rather than an effect on spasticity. Pharmacodynamics of the active interventions were not assessed. Whether serum levels achieved in this study are similar to those achieved by patients who smoke marijuana has yet to be determined (such studies are in progress). This study does not give much support to the use of marijuana for its effects on spasticity resulting from MS.

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**Reference**