Short-Term Effects of Medicinal Cannabis on Spasticity in Multiple Sclerosis

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Objective
- To assess the short-term safety and efficacy of smoked medicinal cannabis vs. placebo in multiple sclerosis (MS) patients with spasticity.

Background
- Evidence that cannabis relieves MS-related spasticity is largely anecdotal; potential therapeutic effects, plus risk and safety issues remain unclear.

Methods
- Single-center, prospective, randomized, placebo-controlled crossover trial in adults with MS and spasticity. Subjects were randomly assigned to smoke either cannabis (approximately 4% THC) or identical placebo cigarettes once daily for three consecutive days, with assessments before and after treatment. Following a washout period of 11 days, subjects crossed over to the opposite condition.

Statistical analyses:
- Primary analysis was a mixed effects regression model with Ashworth Spasticity scale as the outcome, and phase (active vs. placebo), time (before vs. after treatment) and visit (1, 2 or 3 in either phase) as random effects.
- Difference in Ashworth Scores, VAS, and PASAT before and after smoking for each of the two phases was compared with paired t-test; change in this (after-before) difference in the two phases (placebo and active) was compared with paired t-test.
- Other secondary variables were analyzed as appropriate given the schedule of measurements.

Results
- Treatment order did not have a statistically significant effect on outcome (p=0.8).
- Active treatment reduced Pain VAS scores by an average of 5.3 points (p<0.01) (Table 2 and Fig 2).
- Active treatment reduced PASAT scores by an average of 8.6 points more than placebo (p<0.01) (Table 2 and Fig 2).
- Although active treatment increased BSI, PDQ, and mFIS total scores by an average of 2.9, 1.7, and 1.8 points more than placebo, respectively, none of these differences were significant (Table 3).
- Active treatment increased the SHRS-R Question 1 ("How high do you feel?") score by an average of 5.0 points (p<0.0001) more than placebo. Despite this, only 17/30 subjects correctly and consistently guessed their treatment phase (data not presented).
- Although generally well-tolerated, side effects were higher in patients during the active phase as compared to the placebo phase (Table 4). Five subjects withdrew from the study because of adverse events, including "uncomfortably high" 2 (dizziness), and 1 (fatigue). There were no episodes of hypertension, hypotension, tachycardia, or bradycardia requiring medical intervention.

Conclusions
- Smoked cannabis was superior to placebo in reducing spasticity and pain in patients with MS and, although generally well tolerated, resulted in statistically significant cognitive effects.
- Larger, long-term studies will be needed to confirm and extend these findings.

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