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

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Objective

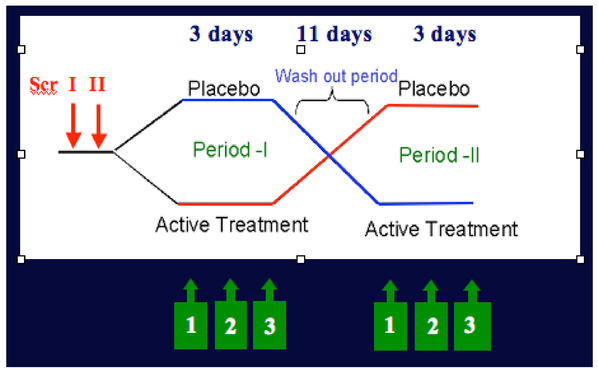
•To assess the short-term safety and efficacy of smoked medicinal cannabis vs. placebo in multiple sclerosis (MS) patients with spasticity.

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.



• The primary outcome measure was the Ashworth Spasticity Scale. Secondary outcome measures included effects on cognition (Paced Auditory Serial Addition Task [PASAT]) and pain (Visual Analog Scale [VAS]); in addition to the Perceived Deficits Questionnaire (PDQ), modified Fatigue Impact Scale (mFIS), and Brief Symptom Inventory (BSI).

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 scheduleof measurements.

Table 1. Patient characteristics

Female gender, n (%)	19 (63)
Age, y, mean	51
Education, y, mean	15
Beck Depression Inventory, mean	8.5
EDSS, mean	5
Ashworth, mean	9.3
Requiring mobility aids, n (%)	24 (80)
On DMT, n (%)	21 (70)
Previous cannabis exposure, n (%)	24 (80)
Cannabis use within year, n (%)	10 (33)

Table 2. Changes in spasticity, pain and cognition by treatment

	Baseline	Final treatment	Mean treatment difference
Ashworth			
Cannabis	9.1	6.2	2.9
Placebo	8.9	8.7	0.2
VAS			
Cannabis	16.6	8.3	8.3
Placebo	14.5	11.52	3.0
PASAT			
Cannabis	140.8	132.5	8.3
Placebo	138.1	138.4	-0.3

Table 3. Additional secondary efficacy measures: Phase summary of means

	Day 1	Day 3	Day 1	Day 3
PDQ	20.0	19.1	20.3	21.2
mFIS	32.8	35.0	34.3	34.6
BSI	17.4	9.4	19.1	14.0

Table 4. Frequency of side effects during treatment by group

	ACTIVE	PLACEBO
Dizziness	23%	3%
Headache	20%	17%
Fatigue	20%	7%
Nausea	10%	3%
“Too high”	7%	0%
Throat irritation	3%	3%

Figure 1. Mean Ashworth Total Scores, before and after treatment, on each day of each phase

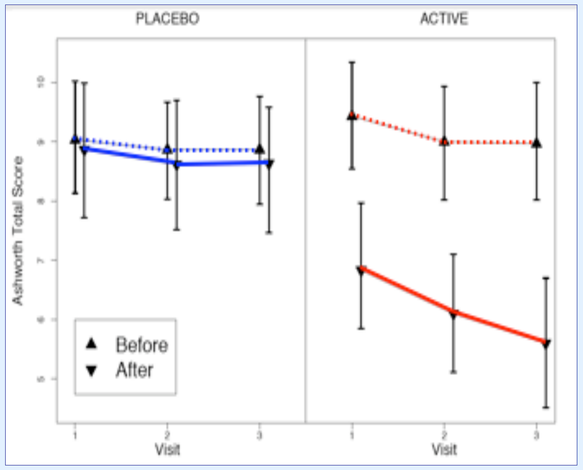


Figure 2. Mean VAS Scores, before and after treatment, on each day of each phase

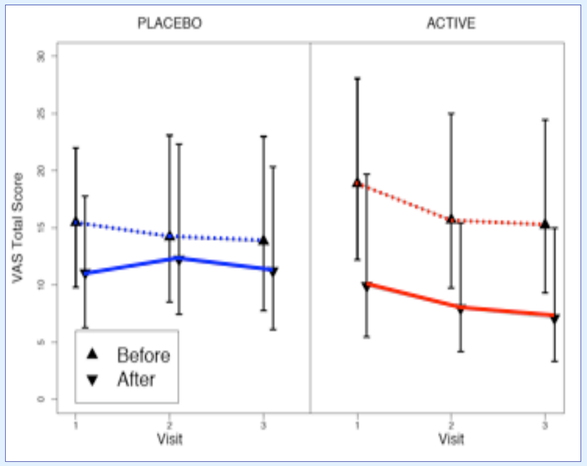
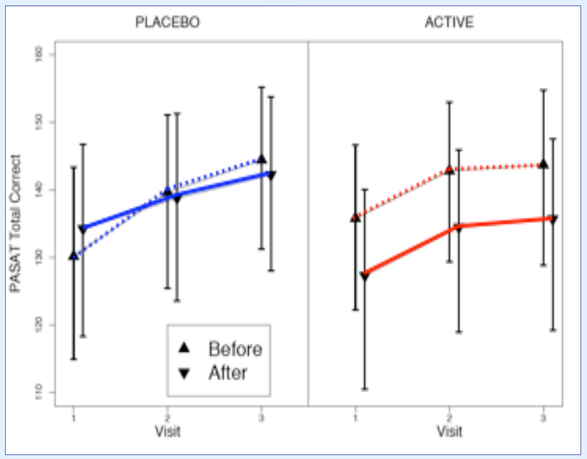


Figure 3. Mean PASAT Scores, before and after treatment, on each day of each phase of the trial



Results

- Active treatment reduced Ashworth Spasticity Total Scores by an average of 2.7 points (p<0.0001) (Table 2 and Fig 1). 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 3).
- 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 ratings 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 (2) and fatigue (1). 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.

Acknowledgements

•Study was supported by the University of California Center for Medicinal Cannabis Research. It was approved by the Human Research Protections Program (HRPP) at the University of California, San Diego, the Research Advisory Panel of California (RAPC), the Drug Enforcement Administration (DEA), the U.S. Food and Drug Administration (FDA), and the National Institute on Drug Abuse (NIDA).