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Treatment of resistant MS spasticity with THC:CBD spray and effects on driving ability

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Background

Although spasticity is one of the most common symptoms of multiple sclerosis (MS), only a limited number of treatment options can be applied in accordance with the German guidelines [1].

THC:CBD oromucosal spray (Sativex®) is a newer treatment option for patients with moderate to severe spasticity who have not responded adequately to conventional oral antispasticity medications.

Because some of the signs and symptoms of MS itself can impose restrictions on driving, it is important that medications do not impose additional restrictions on patients who are still able to drive [2,3].

Given the nature of the active ingredients in THC:CBD oromucosal spray, namely tetrahydrocannabinol and cannabidiol, German health authorities have expressed interest about possible effects of the medication on users' driving abilities; this has led to specific recommendations in the Sativex German patients' information leaflet.

Purpose

The purpose of this study was to explore whether THC:CBD oromucosal spray might impair the driving ability of MS patients starting treatment under approved and everyday conditions. A secondary objective was to provide data on the safety and tolerability of THC:CBD oromucosal spray.

Methods

This was a prospective observational pilot study conducted at MS specialist centres in Germany.

A computerised test battery was used to assess driving ability in still-driving adult MS patients starting treatment with THC:CBD oromucosal spray for moderate to severe resistant MS-related spasticity.

The validated computer tests covered 5 specific driving-related ability dimensions:

- Visual orientation (Visual Pursuit Test)
- Attention and concentration (Concentration Cognitrone Test)
- Reactive stress tolerance (Stress Tolerance Determination Test)
- Attention and reaction speed (Reaction Speed: Motor Speed Reaction)
- Observational ability and skill in gaining an overview (Adaptive Tachistoscopic Traffic Perception Test).

Test results were recorded as percentile ranks: 0 = poorest performance; 100 = optimal performance. Scores <16% in one or more driving tests (i.e. worse than bottom sixth of common population, independent of age) not compensated by stable performance in other tests would render a subject 'unfit for driving' (German Federal norms, *FeV*).

Effectiveness of THC:CBD oromucosal spray was recorded by use of the spasticity 0-10 numerical rating scale (NRS) and spasms count. Tolerability was assessed by reporting of adverse events.

Evaluations were performed at baseline (study enrollment) and after 4-6 weeks' treatment with THC:CBD oromucosal spray (final visit).

Results

Study population

A total of 33 patients were enrolled at three specialist centres in Germany (Table 1). In all patients, the medical decision to start treatment with THC:CBD oromucosal spray was taken prior to study enrolment. All patients were driving (at least once weekly) at the time of enrolment.

During the course of the study, THC:CBD oromucosal spray was used in conjunction with mainly tolperisone (n=8) and baclofen (n=5).

Two patients discontinued treatment prior to final visit because of lack of efficacy (n=1) or lack of tolerability (n=1). The mean dose of THC:CBD oromucosal spray at final visit in the remaining 31 patients was 5 sprays/day.

Table 1. Patients' demographic and clinical characteristics at baseline.

Number of patients (M:F)	33 (13:20)
Mean age (range)	48.1 (33–68)
MS type	Secondary Progressive: 26 Relapsing-Remitting: 4 Primary Progressive: 3
Mean duration of MS, years (range)	11.5 (0.33–29)
Mean duration of MS spasticity, years (range)	6.6 (0.13–17)
Spasticity severity (patient assessed)	Mild 3; Moderate 23; Severe 7
Mean EDSS score (range)	4.5 (1.0–7.5)

MS, multiple sclerosis; EDSS, expanded disability status scale.

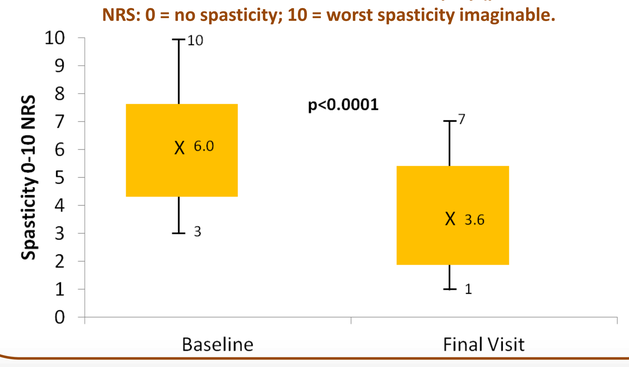
Effectiveness

At baseline, 3, 23 and 7 patients, respectively, rated their spasticity severity as mild, moderate or severe; corresponding values at final visit were 9, 23 and 1, respectively.

The spasticity 0-10 NRS score decreased from 6.0 (±1.76) at baseline to 3.6 (±1.73) at final visit (p<0.0001) (Figure 1).

In patients reporting spasms (n=20), the mean number of spasms/day decreased from 38.3 (range: 1-100) at baseline to 17.4 (range: 1-60) at final visit.

Figure 1. Mean spasticity 0-10 numerical rating scale (NRS) scores at baseline and after 4-6 weeks' treatment with THC-CBD oromucosal spray (p<0.0001 *vs* baseline). NRS: 0 = no spasticity; 10 = worst spasticity imaginable.



Effects on driving ability

At baseline, 19/33 enrolled patients scored <16% in one or more driving tests (mean: 2 tests), including 3 patients who had an overall mean score <16% in 5 tests. At final visit, 20/31 patients scored <16% in one or more driving tests (mean 1.7 tests). Compared with baseline, no new patients fell under the <16% threshold in the 5-test mean score. There was no change in the number of patients judged fit or unfit for driving between baseline and final visit.

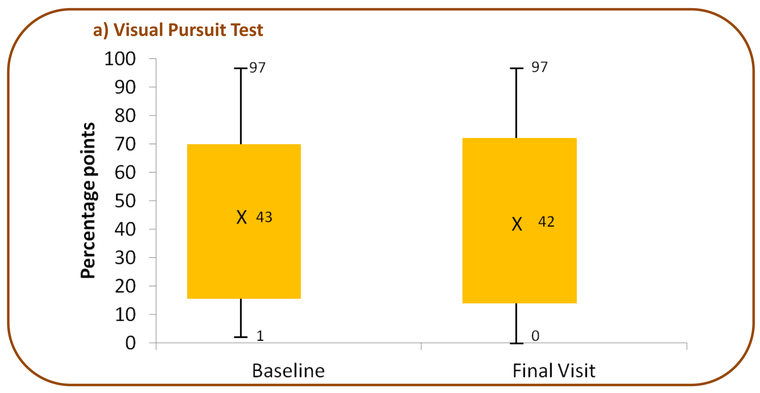
At final visit, there were no statistically significant changes versus baseline in median percent values for 5 of the 5 driving tests (Table 2).

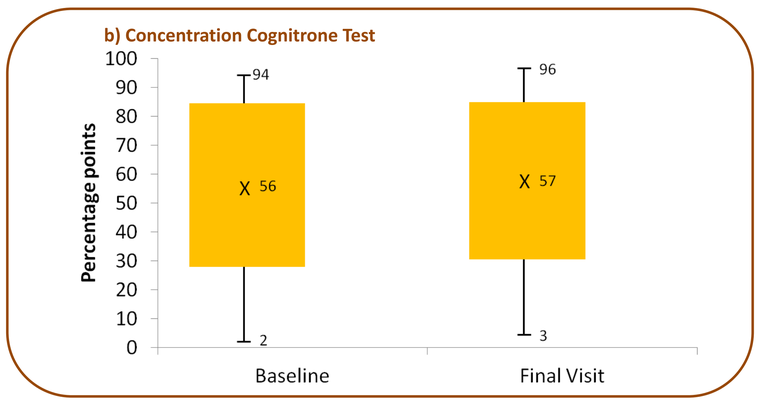
Table 2. Median percent values (interquartile range) in driving ability tests at baseline and at final visit.

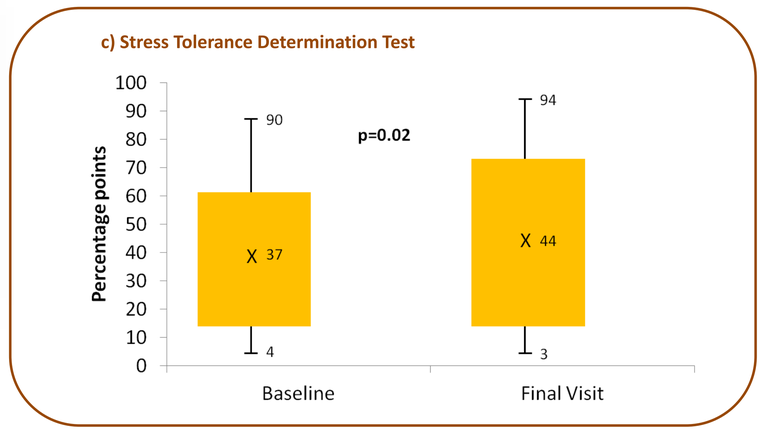
	Baseline	Final visit
Visual Pursuit Test	39 (42)	39 (52)
Concentration Cognitrone Test	61 (42)	64 (41)
Stress Tolerance Determination Test	41 (36)	40 (42)
Reaction Speed: Motor Speed Reaction	33 (54)	26 (43)
Adaptive Tachistoscopic Traffic Perception Test	34 (55)	39 (37)

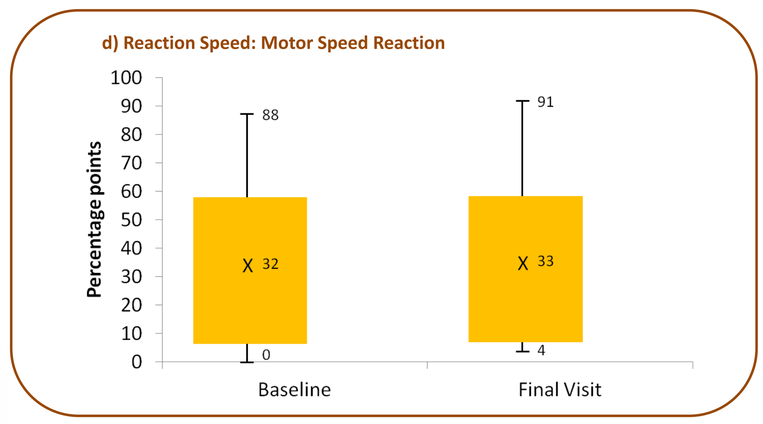
At final visit, the overall mean score for 5 driving tests improved by +2.1% (NS). There were no statistically significant changes versus baseline in mean scores for 4 of the 5 driving tests (Figure 2): Visual Pursuit Test -1.5%; Concentration Cognitrone Test +1.2%; Reaction Speed: Motor Speed Reaction +1.6%; Adaptive Tachistoscopic Traffic Perception Test +3.0%. A statistically significant improvement versus baseline in favor of THC:CBD oromucosal spray was recorded for the Stress Tolerance Determination Test (+6.1%; p=0.02) (Figure 2).

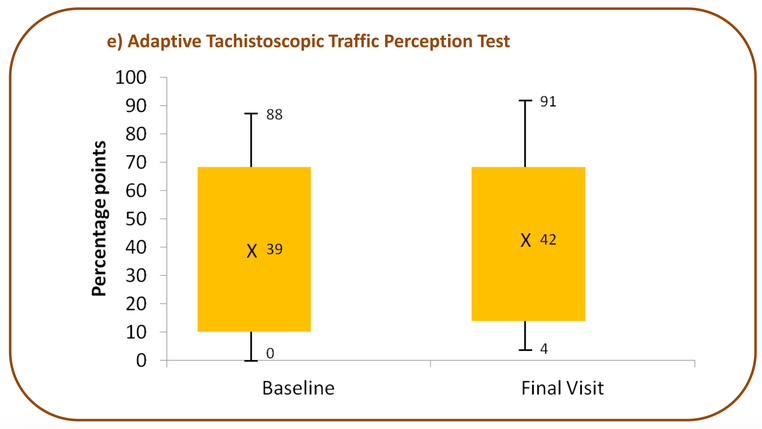
Figure 2. Mean scores on driving ability tests at baseline and after 4-6 weeks' treatment with THC:CBD oromucosal spray: a) Visual Pursuit Test; b) Concentration Cognitrone Test; c) Stress Tolerance Determination Test; d) Reaction Speed: Motor Speed Reaction; e) Adaptive Tachistoscopic Traffic Perception Test.











Tolerability

A total of 5 non-serious adverse events were reported in 4 patients: dizziness (2 events), ligament sprain (1), thrombosis (1) and vertigo (1). Only dizziness and vertigo were considered treatment related. All adverse events were considered mild or moderate in intensity.

Conclusions

Treatment with THC:CBD oromucosal spray for 4 to 6 weeks caused no significant overall deterioration from baseline in driving ability tests performed by still-driving MS patients receiving the medication for the first time.

Significant improvement was noted in a motor reaction task to multimodal stimulus processing (Stress Tolerance Determination Test) which may have been related to a positive evolution in spasticity symptoms.

Between baseline and final visit, 2 patients switched from fit to unfit for driving, and 2 patients switched from unfit to fit for driving, but the overall number of MS patients considered fit or unfit for driving did not change (24 patients fit; 7 patients unfit).

THC:CBD oromucosal spray was well tolerated in this study.

Overall, the results indicate that THC:CBD oromucosal spray as add-on therapy for MS patients with resistant spasticity presents no additional limitations to driving and is well tolerated.

Larger studies are welcomed to confirm the results of this pilot study and to detect potentially basic differences in driving ability between MS patients and a normal healthy population.

References

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