Real-life efficacy and tolerability of a cannabinoid-based oromucosal spray in Multiple Sclerosis-related spasticity: a retrospective observational multicenter study

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BACKGROUND

A cannabinoid-based oromucosal spray has been approved in Italy for the treatment of moderate to severe spasticity in Multiple Sclerosis (MS) patients, who have not responded adequately to other anti-spasticity drugs. Randomized, placebo-controlled trials suggest that 35-40% of subjects will see a 30% or more improvement in spasticity during treatment and that approximately 10% of patients will discontinue the drug due to adverse events.1

OBJECTIVE

Aim was to carry out a retrospective observational study on the drug efficacy and tolerability in a real-life multicenter study, involving nine MS centres in the Emilia-Romagna region (Italy).

METHODS

Data collected from medical records of MS patients who were prescribed the medication between October 2013 and April 2015 were summarized and analyzed using Wilcoxon's signed rank sum test.

RESULTS

We included 198 patients in the study (102M, 96F, mean age: 51 years±10). Briefly, mean disease duration was 18 years (range: 1-55), mean EDSS was 6.5 (range: 3.5-9) and mean ten-meter walking test value (carried out by 88 patients) was 20 seconds (range: 4-180). Patients' baseline characteristics are shown in Table 1.

At re-evaluation of 139 patients, after a mean period of 90 days, there was a significant reduction in the spasticity numeric rating scale (NRS) score (from 7.7 to 5; $p<0.001$), and in the mean ambulatory index (from 6 to 5.8; $p=0.002$). Analysis on intention-to-treat (ITT) population showed that 87 patients (44%) showed a 30% or greater improvement in NRS scores (Table 2)

Treatment was discontinued after a mean period of 89 days (range: 2-347) in 74 patients (37%), primarily due to inefficacy (55 patients, 28%). Adverse events led to discontinuation in 13 patients (7%) and were reported by a total of 49 patients (25%) in a mild-moderate form, the most frequent being drowsiness (21 patients, 11%), followed by dizziness (18 patients, 9%), weakness/fatigue (11 patients, 5%), and nausea (7 patients, 3%) (Figure 1). Four serious adverse events occurred (2 deaths, 2 hospitalizations).

Twenty-three patients (12%) spontaneously reported additional beneficial effects such as improvement of pain (12 patients, 6%), bladder dysfunction (7 patients, 4%), sleep pattern (7 patients, 4%) and tremor (2 patients, 1%).

Table 1 Patient characteristics and safety data

Sex (M/F)	102/96
Disease duration in months (mean ± SD)	214 ±115
Antispastic agents used in combination with cannabinoid spray (nr,%) Baclofen Tizanidine Others	 179 (90) 13 (7) 6 (3)
Treatment confirmed after follow-up (yes/no)	134/27
Daily puffs (mean ± SD)	6.3 ± 2.2
Treatment discontinuation (nr, %)	74 (37)
Reason for treatment discontinuation (nr, %) Lack of efficacy Tolerability issues Lost to follow-up Death Others	 55 (74.3) 13 (17.6) 2 (2.7) 2 (2.7) 2 (2.7)
Number of patients with adverse events	49(25)
Number of patients with serious adverse events (nr,%)	4(2%)

Table 2 Response to treatment

Baseline NRS value (mean ± SD)	7.7 ± 1.2	Follow-up NRS	5.1 ± 1.4	p = 0.000
Baseline EDSS	6.5 ± 1.1	**Follow-up EDSS**	6.5 ± 1.1	p = 0.366
Baseline Ambulation Index	6 ± 2.2	**Follow-up Ambulation Index**	5.8 ±2.2	p = 0.002
Baseline 10-meter walking test (88 patients)	20.7 ± 20.7	**Follow-up 10-meter walking test**	24 ± 31	p = 0.003

Figure 1 Reported adverse events (49 patients)

Other: dysarthria, skin rash, epigastric pain

CONCLUSION

In a real-life clinical setting, despite the relatively high percentage of patients (37%) who discontinued the drug, mainly due to inefficacy, the cannabinoid-based oromucosal spray produced clinically relevant improvements in spasticity in 42% of patients, while discontinuation due to adverse events occurred in 7% of patients, thus confirming data from clinical trials.

REFERENCES

1Meta-analysis of the efficacy and safety of Sativex (nabiximols), on spasticity in people with multiple sclerosis. Wade DT, Collin C, Stott C, Duncombe P. Mult Scler. 2010 Jun16(6):707-14.

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