MUltiple Sclerosis and Extract of Cannabis: Results of the MUSEC trial

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Introduction

Multiple sclerosis (MS) patients may experience a range of **chronic symptoms**, including muscle stiffness, spasms, pain and insomnia.

Muscle stiffness is a common symptom of MS, occurring in 90% of patients. It considerably impacts the quality of life for patients, causing pain, reduced mobility and sleep disturbances.

Current treatments for MS symptoms are limited and provide inadequate relief for patients, leading some people **to seek alternative therapies** to ease their symptoms. The efficacy of medical cannabis for the management of MS symptoms has shown promise in preclinical studies. A small number of MS patients already self-medicate with cannabis, but there is a need for clinical studies suitably designed to investigate its efficacy for muscle stiffness.

This phase III clinical trial **investigated the relief of muscle stiffness** and pain in adult MS patients using a standardised oral cannabis extract for stable disease with ongoing muscle stiffness.

Aim of the study

To investigate the symptomatic relief of muscle stiffness and pain in adults with MS using oral cannabis extract compared to placebo.

Methods and materials

A phase III, double-blinded, randomised, placebo-controlled, multicentre clinical trial of **279 MS patients** aged 18-64. Patients were diagnosed according to the McDonald criteria and had stable disease for 6 months with ongoing muscle stiffness for at least 3 months prior to enrolment.

An extract from Cannabis sativa, Tetrahydrocannabinol (THC), was administered twice daily with an initial total daily dosage of 2.5mg for 2 days and increased by 5mg every 3 days over a period of 12 days to a maximum of 25mg. In the event of intolerable side effects during the titration phase, the daily dose was reduced by 2.5mg until the side effects resolved, with one further rechallenge. Individual maximum doses were continued for the 10-week maintenance phase.

An 11-point numerical category rating scale (CRS) measured changes in muscle stiffness, body pain, muscle spasm and sleep quality.

Further patient-reported measures included validated disease-specific scales measuring spasticity in MS (MS Spasticity Scale (MSSS-88)), the physical and psychological impact of MS (MS Impact Scale (MSIS-29)) and walking ability (MS Walking Scale (MSWS-12)).

Primary and secondary outcomes

The primary outcome measured patients' perceived change in muscle stiffness after 12 weeks of treatment compared with baseline as assessed by an 11-point CRS.

Secondary outcomes measured patients' perceived relief of pain, muscle spasms and sleep disturbance at 4, 8 and 12 weeks compared with baseline as assessed by 11-point CRSs.

Results

This study achieved the primary outcome of a **significantly greater improvement in muscle stiffness at 12 weeks of treatment with oral cannabis extract** compared to placebo on an 11-point CRS scale (-1.8 ± 2.4 vs.-0.7 ± 2.4; p<0.025).

The proportion of **patients experiencing relief of muscle stiffness was almost twice as high when treated with oral cannabis** extract vs. placebo (OR 2.26, 95% CI 1.24 to 4.13, p.0.004, one-sided).

Patients treated with oral cannabis extract had consistently higher symptom relief for secondary outcomes of body pain, muscle spasms and sleep disturbance at 4, 8 and 12 weeks of treatment compared to placebo. (p < 0.025).

Improvements in MSSS-88, MSIS-29 and MSWS-12 scores at 12 weeks from baseline further supported the positive primary endpoint outcome.

Adverse events

The adverse events experienced by patients treated with cannabis extract were consistent with known side effects of cannabis and most events were mild to moderate in severity.

75.7% of patients treated with oral cannabis extract completed the study compared to 85.2% of patients treated with placebo, which may suggest treatment was tolerable for the majority of participants.

Serious AEs (SAES) were reported for seven participants in the CE group (4.9%) and for three participants in the placebo group (2.2%).

Although the rate of adverse events was higher in the cannabis extract group than placebo, there was a continuous decrease in frequency observed throughout the duration of the study.

Discussion

This phase III randomised controlled clinical trial demonstrated the efficacy of standardised cannabis extract in treating the highly complex phenomenon of muscle spasticity in MS.
Similar results were also observed in the relief of pain, muscle spasms and sleep quality.

While a higher rate of adverse events was observed in patients treated with oral cannabis compared to oral placebo, this clinical trial does not reflect the real-world flexibility of treatment where dose titration can be performed slowly and continually adjusted for optimal outcomes.

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