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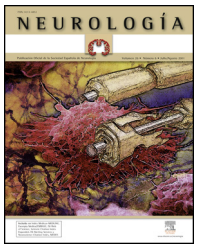

ORIGINAL ARTICLE

# Clinical experiences with cannabinoids in spasticity management in multiple sclerosis☆,☆☆

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**KEYWORDS**
Cannabidiol;
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Effectiveness;
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**Abstract**
*Introduction:* Spasticity is a common symptom among patients with multiple sclerosis (MS).

This study aims to assess the effectiveness and safety of the combination of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) in clinical practice for the treatment of spasticity in MS.

*Methods:* Retrospective observational study with patients treated with inhaled THC/CBD between April 2008 and March 2012. Descriptive patient and treatment variables were collected. Therapeutic response was evaluated based on the doctor's analysis and overall impression.

*Results:* Of the 56 patients who started treatment with THC/CBD, 6 were excluded because of missing data. We evaluated 50 patients (42% male) with a median age of 47.8 years (25.6—76.8); 38% were diagnosed with primary progressive MS, 44% with secondary progressive MS, and 18% with relapsing-remitting MS. The reason for prescribing the drug was spasticity (44%), pain (10%), or both (46%). Treatment was discontinued in 16 patients because of ineffectiveness (7 patients), withdrawal (4), and adverse effects (5). The median exposure time in patients whose treatment was discontinued was 30 days vs 174 days in those whose treatment continued at the end of the study. THC/CBD was effective in 80% of the patients at a median dose of 5 (2-10) inhalations/day. The adverse event profile consisted of dizziness (11 patients), somnolence (6), muscle weakness (7), oral discomfort (2), diarrhoea (3), dry mouth (2), blurred vision (2), agitation (1), nausea (1), and paranoid ideation (1).

*Conclusions:* THC/CBD appears to be a good alternative to standard treatment as it improves refractory spasticity in MS and has an acceptable toxicity profile.


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**PALABRAS CLAVE**
Cannabidiol;
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Esclerosis múltiple;
Espasticidad

**Experiencia clínica con los cannabinoides en la terapia de la espasticidad en la esclerosis múltiple**

**Resumen**
*Introducción:* La espasticidad es un síntoma muy frecuente entre los pacientes con esclerosis múltiple (EM). El objetivo del presente estudio es evaluar la efectividad y la seguridad de la combinación de delta-9-tetrahidrocannabinol (THC) y cannabidiol (CBD) en la práctica clínica del tratamiento de la espasticidad en EM.
*Métodos:* Estudio observacional retrospectivo con los pacientes tratados con THC/CBD inhalado de abril del 2008 a marzo del 2012. Se recogieron variables descriptivas de paciente y tratamiento. La respuesta se evaluó mediante impresión global de respuesta terapéutica analizada por el médico.
*Resultados:* Cincuenta y seis pacientes iniciaron tratamiento, 6 fueron excluidos por falta de datos. Se evaluó a 50 pacientes (42% hombres), mediana de edad 47,8 años, el 38% de ellos diagnosticados de EM primaria progresiva, el 44% de EM secundaria progresiva y el 18% de EM remitente recurrente. El motivo de prescripción fue espasticidad (44%), dolor (10%) o ambos (46%). Se suspendió tratamiento en 16 pacientes por inefectividad (7 pacientes), abandono (4) y efectos adversos (5). La mediana de tiempo de exposición de los pacientes que suspendieron tratamiento fue 30 días y 174 días para los que continuaban tratamiento al final del estudio. THC/CBD fue efectivo en un 80% de pacientes, con dosis mediana de 5 (2-10) pulverizaciones/día. El perfil de efectos adversos fue: mareo (11 pacientes), somnolencia (6), debilidad muscular (7), molestias bucales (2), diarrea (3), sequedad de boca (2), visión borrosa (2), agitación (1), náuseas (1), ideas paranoides (1).
*Conclusiones:* THC/CBD se muestra como una buena alternativa al tratamiento habitual mejorando la espasticidad refractaria en la EM con perfil de toxicidad aceptable.


## Introduction

Spasticity is a very frequent symptom in patients with multiple sclerosis (MS) and may appear at some point in up to 85% of all patients.[1] In Spain, results from the recently published 6E study show that in a population of 2029 MS patients, two-thirds experience spasticity. Symptoms range from moderate to very severe in 40% of the cases.[2] Spasticity often affects quality of life not only in patients, but also their family and caregivers to a great extent.[3] Currently available drugs used to treat spasticity and associated symptoms (pain, rigidity, spasms, etc.) generally present limited effectiveness and are poorly tolerated.[4,5] In fact, actual use of these treatments is quite low. In the 6E study, 57% of the patients with spasticity were not treated with any drugs.[2]

Activation of the endocannabinoid system has been shown to have therapeutic utility in motor disorders associated with MS, including spasticity. It has also shown utility as treatment for different forms of pain of neuropathic or inflammatory origin.[6,7] Recent years have brought advances in the development of drugs extracted from *Cannabis sativa* or synthetic molecules with a similar effect. In 2010, Spanish drug authorities approved the marketing of a standard combination of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) in a 1-to-1 proportion. This drug, administered as an oral spray, is indicated as an additional treatment for symptoms of moderate to severe spasticity in MS patients that have not responded correctly to other antispasmodic drugs.[8] THC/CBD is a drug listed for hospital use only, meaning that it can only be dispensed by hospital pharmacy departments.

As described by Oreja-Guevara in her recent review,[9] both clinical trials and longer-term extension studies have shown that THC/CBD is well-tolerated, safe, and effective for reducing spasticity refractory to other treatments. The purpose of this study is to evaluate the effectiveness and safety profile of the THC/CBD combination in clinical practice as treatment for refractory spasticity in MS.

## Patients and methods

This retrospective observational study evaluated all patients diagnosed with MS and treated with THC/CBD in our hospital from the first time the treatment was used in April 2008 up to March 2012. All patients with refractory spasticity who began treatment with vaporised THC/CBD (Sativex® oral spray, 2.7 mg THC/2.5 mg CBD) attended at least one session with the nurse educator at the MS unit. Dosing and any side effects were monitored by monthly telephone calls. The drug was dispensed monthly by the pharmacy unit for outpatients at the hospital pharmacy department. Study variables were sex, age, diagnosis, reason for prescription, concomitant medications, exposure time to THC/CBD, response, effective dose, and adverse effects. A dichotomous (yes/no) answer was given for 'response' based on the prescribing doctor's analysis and the overall impression of the patient's response to treatment. A univariate analysis was also performed to study the relationship