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Multiple Sclerosis, Spasticity and Nabiximols: A User Experience

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ABSTRACT

This clinical case concerns a 54-year-old woman with onset of multiple sclerosis at the age of 21 years, a long remission for 12 years and a subsequent resumption of disease activity partially contained by therapies. Not surprisingly, the increased burden of disability and impairment of quality of life is related not so much to the severity of the neurological damage as to the spasticity associated with the disease, which is responsible for severe alterations to posture control and trunk instability.

A complex therapeutic strategy pathway started combining physical and pharmacological treatment, which reached a delicate balance with the introduction of nabiximols.

KEYWORDS

Multiple sclerosis, spasticity, pain, nabiximols, case report

LEARNING POINTS

- Relevance of symptomatic treatment for quality of life in multiple sclerosis.
- Nabiximols is effective in the treatment of spasticity and pain in multiple sclerosis.
- Therapeutic introduction of nabiximols may require a careful assessment of the clinical picture and patient characteristics.

INTRODUCTION

Based on randomized, placebo-controlled, double-blind trials, nabiximols has been approved as an add-on therapy to treat symptoms of spasticity in patients with multiple sclerosis (MS). However, the occurrence of side effects, such as cognitive and psychiatric disorders, has burdened physicians with doubts and uncertainties. In this clinical case, the use of the drug within an appropriate framework led to increased physical and social activities for the patient and improved the quality of life.

CASE DESCRIPTION

A 54-year-old woman was diagnosed with relapsing-remitting MS according to the Poser criteria[1] in 1987, after her first pregnancy. The disease remained in clinical and paraclinical remission until 1999, and in 2000 the patient began therapy with interferon beta-1a. However, acute events persisted and clinical recovery between the relapses was incomplete until it stabilized on an Expanded Disability Status Scale (EDSS) of 4.0.

In 2009, after the patient's second pregnancy, she experienced a further worsening of the disease, with a partial recovery with intravenous corticosteroids (EDSS 4.5) and began therapy with natalizumab, which she had to suspend in 2011 due to a positive serology result for JC virus. Since then, she has been in therapy with fingolimod. In recent years, the patient showed mild spastic hypertonia in both legs and dysaesthesias, which were initially responsive to baclofen.

Despite extended treatment (baclofen 75 mg daily and gabapentin 1,200 mg daily), the patient experienced gradual worsening of painful spasticity of the lower limbs of a moderate/severe degree with posture control disorder. As a consequence, in 2020 the patient developed remarkable anteversion of the hips, lumbar hyperlordosis compensation, cervical lordosis flattening and then entered into a vicious cycle of exacerbation of symptoms, which led to worsening spasticity and shortening of iliopsoas, quadriceps and piriformis muscles. This in turn resulted in a severe increase in painful rigidity of paravertebral muscles with trunk instability.

The worsening of spasticity produced daily living impairment, decreased the patient's quality of life and remarkably reduced her walking ability, beyond what would be expected from an EDSS of 4.5.

Nabiximols, a phytocannabinoid combination of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) in a 1:1 ratio, was added as a therapy in March 2020, but after 1 week, at a dose of 5 puffs per day, the intolerable appearance of side effects (sleepiness, dizziness, confusion and disorientation) led to suspension of this medication.

The patient complained of pain and disabling rigidity of paravertebral muscles, which could not be counteracted with intramuscular steroids. Bilateral infiltrations of the paravertebral muscles with triamcinolone and lidocaine were initially effective, but the beneficial effect had a progressively shorter duration.

Physical therapy with treatment of vertebral decompression by

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the use of appropriate postures, reduction of lumbar lordosis and lumbosacral pompage and decontraction of the paravertebral masses was proposed in addition to therapy with baclofen 75 mg daily and gabapentin 1,200 mg daily.

The patient experienced quick pain relief, improved posture and gained motor movement and autonomy. However, these positive results were unstable, with unpredictable fluctuations, and gradually not lasting.

Nabiximols therapy was reintroduced at a dose of 1 puff per day with an increase in dose every 10 days up to 3 puffs per day.

With a slow titration of the drug side effects, dizziness and confusion were mild and resolved in a month. Pain and spasticity reduced in frequency and intensity and were controlled further with better fatigue management by planning of activities with day/week plans and control of energy reserves with rest breaks.

With the introduction of these articulated pharmacological, physiotherapeutic and deconditioning strategies, the patient improved her motor skills and autonomy with a considerable gain with respect to daily living and quality of life.

DISCUSSION

MS is a progressive, chronic disease with variable evolution and low predictivity of prognosis, frequently associated with even severe disability. To this broad biological spectrum of disease phenotypes, the consolidated use of immunomodulating/immunosuppressive therapies further expands the heterogeneity and stratification in the patient population, especially through the lengthening of the progression times towards disabilities.

In this scenario, for patients the degree of disability is not the only element of impairment of the quality of life and limitation of their daily activities.

Patients with mild/moderate spasticity and pain, especially if associated, experience withdrawal from social life and limitations in habitual physical activities, falling into distress and depression[2].

Extensive empirical experience suggested that Cannabis preparations have medical benefits. The characterization of products derived from Cannabis plant flowers (the psychotropic THC and the non-euphoric CBD) and the identification of the cannabinoid receptors (CB1, expressed abundantly in the brain and CB2, expressed especially in the immune system) created the conditions for the development of cannabinoid-based drugs[3,4]. Endogenous ligand lipids were subsequently identified for CB1 and CB2 receptors and for enzymes related to their metabolism. Together, the 2 receptors, the endogenous ligands and the metabolic enzymes constitute the endocannabinoid system. The discovery of this system paved the way for new therapy studies to investigate the activity, efficacy and safety of cannabinoids. In this context, the approval of nabiximols for the treatment of spasticity in MS highlights the relationship between the endocannabinoid system and neurological diseases and is an important starting point for the development of Cannabis research. In fact, the horizon is currently being further enriched with the discovery of an expanded endocannabinoid system, the endocannabinoidome, a wider endocannabinoid-related network, in overlap with other pathways and alternative metabolic processes[4,5]. This complex system projects towards the development of drugs that act selectively on the endocannabinoid system.

It is likely, from studies in animals and on patients with MS, that the modulation of endocannabinoid signalling represents an adaptive response to counteract the symptoms of the disease.

The existence of an endocannabinoidome may explain the effectiveness of reduced doses of nabiximols in this clinical case, such as a supra-additive therapeutic effect in the modulation of unidentified receptor targets and sites of action[6]. These clinical observations are a stimulus to understand the complex mechanism of action of cannabinoids. The challenge becomes the identification of specific pathways in neurological disorders within an expanded and redundant system.

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