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Improved Walking Ability in Early Treatment with Nabiximols

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ABSTRACT

We describe the case of a 46-year-old man with a 16-year history of relapsing- remitting multiple sclerosis, who, after a long period of clinical stability, manifested reduced walking ability and nocturnal painful spasm. Different therapeutic approaches were tried, such as baclofen and 4-aminopyridine, with an unsatisfactory response and a negative impact on the patient's quality of life. After introduction of nabiximols therapy, the patient showed improvement in walking with less fatigue in longer distances and a subsequent improvement in quality of life.

KEYWORDS

Multiple sclerosis, gait impairment, early treatment

LEARNING POINTS

- Efficacy of nabiximols in improving walking ability and reducing leg spasms.
- Slow titration reduces nabiximols side effects.
- Efficacy of nabiximols in improving quality of life.

INTRODUCTION

Multiple sclerosis (MS) is a chronic, predominantly immune-mediated disease of the central nervous system (CNS), and 1 of the most common causes of neurological disability in young adults globally. MS is characterized by clinical symptoms resulting from lesions in the brain, spinal cord or optic nerves, which can affect balance, gait and fall risk. Lesions accumulate over time and occur in different areas of the CNS causing symptoms including weakness, spasticity and fatigue, as well as changes in sensation, coordination, vision, cognition and bladder function. Thus, it is not surprising that imbalance, gait dysfunction and falls are common in people with MS[1]. The majority of patients have abnormalities of postural control and gait even early in the disease course. Patients with MS represent a diverse and heterogeneous population varying in terms of disease type, its severity and progression and with regard to the wide range ofpresenting symptoms. Consequently, detailed experience with individual patients is important to provide examples of therapy to specific patient types.

CASE DESCRIPTION

A 46-year-old man with a history of relapsing-remitting MS manifested reduced walking ability and nocturnal painful spasms. The first symptoms of the disease appeared in 2004 with acute onset of dizziness and visual disturbances. A diagnosis of MS was made in 2005, when he was admitted to a neurological clinic. Magnetic resonance imaging (MRI) of the brain and spinal cord revealed multiple white matter lesions disseminated in periventricular, infratentorial, juxtacortical and spinal regions (C2-C3). Cerebrospinal fluid analysis showed the presence of oligoclonal bands. The patient started treatment with IFN-β1a therapy (3/week), and he had been treated for 8 years when he experienced a disease relapse with brain MRI demonstrating 3 new enhancing lesions. Therefore, in 2013, treatment with the monoclonal antibody natalizumab was started and clinical and neuroradiological stability was achieved. This was later suspended in 2015 due to detection of John Cunningham virus (JCV) positivity. Therapy with dimethyl fumarate was then started. Over the years, the patient presented with a progressive reduction in his walking ability, nocturnal painful spasms and he showed a mild spasticity in the right leg. Different therapeutic approaches were tried, such as baclofen 12.5 mg twice a day and 4-aminopyridine 4 mg twice a day, with a poor response.

In February 2016, his Expanded Disability Status Scale (EDSS) was 4. The Ambulation Index (AI) was 3, the Modified Ashworth Scale was 2 and the Numeric Rating Scale (NRS) was 5. Walking ability was tested by the 6-Minute Walk Test (6MWT), evaluating walking endurance: he walked for 340 metres during the 6MWT.

Due to these clinical manifestations, we decided to start treatment with the tetrahydrocannabinol (THC):cannabidiol (CBD) oromucosal spray (nabiximols, Sativex®). Nabiximols was added with gradual titration, in order to avoid side effects. After 1 month, the patient's treatment response was evaluated, and he reported an improvement in his ability to walk and a reduction of painful spasms with a dosage of 4–5 puffs a day. His EDSS was 4, AI was 2, Modified Ashworth Scale was 1, NRS was 3 and he walked for 380 metres in the 6MWT. After 6 months, the patient reported reduced fatigue, improved mobility and autonomy in walking for a longer distance without stopping.

In addition, his mood and quality of life were improved. At present, the patient is settled at a dose of 4–5 puffs daily with clinical stability.

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DISCUSSION

This case shows the efficacy of early nabiximols treatment in improving walking ability in a patient with initial gait disturbance. Sativex® is an endocannabinoid system modulator containing THC and CBD in a near 1:1 ratio. THC interacts with human cannabinoid receptors that play a key role in the modulation of muscle tone, while CBD at higher than natural concentrations may limit the psychoactive effects of THC. Dizziness and fatigue are amongst the most common side effects; optimal up-titration strategies can, however, minimize side effects. Nabiximols is an option for use as an add-on medication for the management of moderate to severe generalized spasticity and related symptoms, such as spasms, pain, poor sleep quality and urinary dysfunction, in patients with MS resistant to common antispastic drugs.

The efficacy and safety of nabiximols is supported by data from phase III clinical trials[2] and has been further supplemented by a growing database of real-world experiences in patients with MS-related spasticity[3].

A small Italian study showed that nabiximols is able to improve stride speed, cadence and length[4].

Moreover, as observed in some clinical trials, relevant improvements in quality of life and in activities of daily living can be achieved using the THC:CBD spray in patients with MS spasticity, allowing them to engage in everyday activities.

REFERENCES

1. Cameron MH, Nilsagard Y. Balance, gait, and falls in multiple sclerosis. *Handb Clin Neurol* 2018;**159**:237–250.
2. Novotna A, Mares J, Ratcliffe S, Novakova I, Vachova M, Zapletalova O, et al. A randomized, double-blind, placebo-controlled, parallel-group, enriched-design study of nabiximols* (Sativex®), as add-on therapy, in subjects with refractory spasticity caused by multiple sclerosis. *Eur J Neurol* 2011;**18**:1122–1131.
3. Patti F, Chisari CG, Solaro C, Benedetti MD, Berra E, Bianco A, et al. Effects of THC/CBD oromucosal spray on spasticity-related symptoms in people with multiple sclerosis: results from a retrospective multicenter study. *Neurol Sci* 2020;**41**(10):2905–2913.
4. Coghe G, Pau M, Corona F, Frau J, Lorefice L, Fenu G, et al. Walking improvements with nabiximols in patients with multiple sclerosis. *J Neurol* 2015;**262**:2472–2477.