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Efficacy of Nabiximols in Reducing Pain and Spasticity in Primary Progressive Multiple Sclerosis

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ABSTRACT

Spasticity and its related symptoms, such as muscle stiffness, spasms and pain, are present in 60% of multiple sclerosis patients. We present the case of a 66-year-old woman with a benign form of primary progressive multiple sclerosis who had symptoms of spasticity, leg weakness and pain at disease onset. After 10 years of disease and insufficient response to antispastic and pain drugs, she was started on nabiximols oromucosal spray with good efficacy, safety and tolerability. The patient is now treated with 4 puffs per day and, after 6 years, the drug is still effective in relieving pain and improving sleep.

KEYWORDS

Nabiximols, multiple sclerosis, pain, spasticity, case report

LEARNING POINTS

- Nabiximols can represent a valid treatment option for spasticity and related pain, and is safe and well tolerated.
- Nabiximols also has a positive impact on mobility, mood, sleep and quality of life.
- The efficacy of nabiximols is maintained over time.
- The role of nabiximols in reducing pain can be extended to other clinical conditions including non-cancer pain or neuropathic pain.

INTRODUCTION

Spasticity and its related symptoms, such as muscle stiffness, spasms and pain, are present in 60% of multiple sclerosis (MS) patients, but are frequently undertreated and not properly monitored[1]. Pain was recently found to be the most common comorbidity in MS patients who are older than 60 years[2]. A recent Italian consensus study concluded that, based on available data, a strong recommendation for spasticity treatment can be given only to the use of nabiximols, intrathecal baclofen and intramuscular injection of botulinum toxin (BT)[3].

CASE DESCRIPTION

We describe the case of a 66-year-old woman with a diagnosis of primary progressive MS, which started in April 2004 at 50 years of age with the progressive onset of lower limb weakness, spasticity with muscle stiffness and systemic pain associated with back pain. In June 2005, she was admitted to the Neurological Department at Policlinico San Donato in Milan, where she underwent brain and spinal cord MRI showing the presence of T2 hyperintense lesions in periventricular and juxtacortical regions. No lesions were visible in the spinal cord, while cerebrospinal fluid examination showed the presence of specific oligoclonal bands absent in serum (pattern II), and she was diagnosed with MS.

A few months later, she experienced urinary urgency and worsening of spasticity and pain in the lower limbs, which was more evident on the right side, causing difficulty in walking and climbing stairs. She started tizanidine 1 mg daily and lorazepam 1 mg prior to bedtime. In September 2005, she also developed Lhermitte's sign; therefore, she started lamotrigine 200 mg twice a day with partial efficacy.

She was periodically readmitted to Policlinico San Donato from 2009 to 2014 for high-dose steroid treatments (methylprednisolone 1 g for 5 days) for periodic subacute worsening of the usual symptomatology. Pain was described as chronic, a sense of tightness in the lower limbs associated with occasional muscle spasms and exacerbated by physical exercise. In November 2013, gabapentin 400 mg 3 times per day was added to her prescription without efficacy. Repeated brain and spinal cord MRI results did not show any change.

Neurological examination in November 2013 showed diplopia in the bilateral extreme gaze, lower right facial nerve palsy, mild drift and difficulty in performing fine movements on the right side, drift of lower limbs with weakness more evident at proximal than distal muscles, low dysmetria in the right upper limb, difficulty in performing tandem walk, symmetric increase of reflexes in the 4 limbs, bilateral Babinski sign, Lhermitte's sign and hypoaesthesia at lower limbs (right>left). The Expanded Disability Status Scale (EDSS) was 3.5 (functional systems: pyramidal (P): 3; cerebellar (C): 2; sensory (S): 2; sphincteric (Sf): 1).

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In June 2014, the patient started treatment with nabiximols with acute improvement in pain and spasticity. In addition, sleep and mood were improved according to the patient. The drug was also safe and well tolerated by the patient. The Numerical Rating Scale (NRS) for spasticity was reduced from 8 to 1. The dosage was increased up to 8 puffs daily (times: 8, 10, 12 AM, 2, 6, 8, 10 and 12 PM). Neurological examination in September 2014 showed a reduction in spasticity in the lower limbs, weakness and reflexes, with an EDSS lowered to 2.5. The patient also suffered from spondyloarthrotic myelopathy, and spinal cord MRI demonstrated intervertebral disc herniation at C5–C6 and L3–L4. In June 2015, she had a surgical intervention for anterior and posterior vertebral arthrodesis at L3–L3 with a mild impact on pain.

In July 2019, the patient reduced nabiximols to 6 puffs and, eventually, to 4 puffs per day (1 in the morning and 3 in the afternoon/evening). From September 2020 to October 2020, she was given a daily diary on nabiximols efficacy: NRS for spasticity was 1, and clinical improvement was assigned to pain and sleep quality. She underwent new brain and spinal cord MRI in February 2020, which was also unchanged. At the last neurological visit in November 2020, she had an EDSS of 2.5.

DISCUSSION

A recent trial, SAVANT, compared nabiximols as an add-on therapy to optimized standard spasticity treatment in patients with moderate to severe MS spasticity, showing that the proportion of clinically relevant responders after 12 weeks was significantly greater with nabiximols than with placebo (77.4 vs 32.1%; $p<0.0001$)[4]. Moreover, a study on almost 2,000 MS patients found that the strongest predictors for quality of life in MS were depression, pain and walking difficulties, irrespective of MS phenotype[5], further supporting the importance of reducing pain and spasticity for quality-of-life improvement. It is worthwhile to mention that nabiximols is not the only drug that can improve spasticity; for example, a recent Italian multicentre cross-sectional study on 386 MS patients confirmed the safety of BT injections[6]. In addition, a multidisciplinary approach to spasticity and pain is warranted, combining pharmacological and non-pharmacological strategies including physiotherapy, for example.

It is difficult to assess at which level in this patient the efficacy of the drug on pain was mediated by its efficacy in reducing spasticity. This issue is particularly relevant since in most cases spasticity and pain have important implications with respect to difficulties in motion, impaired activities of daily living or problems with hygiene and daily assistance in later phases of the disease, which need to be considered as a whole.

In conclusion, the clinical case of this patient with a late-onset benign course of primary progressive MS supports the efficacy of nabiximols in reducing pain-related spasticity, weakness and impaired walking ability and in improving the sleep and quality of life of MS patients with no concerns regarding safety and tolerability. It also supports the persistence of efficacy over time, which was 6 years in this patient.

As a conclusion, it needs to be mentioned that the efficacy of nabiximols in pain relief can be extended to other clinical conditions, including chronic non-cancer pain[7] or neuropathic pain[8].

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