

## Effectiveness of Cannabinoids in Treating Symptoms of Bladder Dysfunction Associated with Spasticity in Multiple Sclerosis

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### ABSTRACT

Nabiximols is an approved add-on therapy for multiple sclerosis (MS)-related spasticity for patients non-responsive to common therapies. It is also more effective in treating bladder dysfunction with more moderate side effects compared with conventional drugs. We present the case of a 48-year-old woman with secondary progressive MS who was treated with nabiximols and who showed significant improvement in bladder complaints. This case focuses on the possibility of prescribing this treatment to patients with symptoms other than spasticity. In addition, it highlights the crucial role of bladder dysfunction improvement in controlling the physiopathological mechanisms related to urinary tract infections frequently reported by patients with MS.

### KEYWORDS

Case report, multiple sclerosis, nabiximols, bladder dysfunction, spasticity

### LEARNING POINTS

- Nabiximols therapy can be used to treat other symptoms associated with spasticity in multiple sclerosis.
- Nabiximols therapy has a positive effect on bladder dysfunction.
- The sudden suspension of nabiximols treatment may cause worsening of bladder complaints.

### INTRODUCTION

Nabiximols (Sativex®) is a Cannabis-based medicine approved in Italy by the Agenzia Italiana del Farmaco (AIFA) for adult patients with multiple sclerosis (MS) with moderate to severe spasticity. However, this treatment may be prescribed for many other symptoms as it is reported to improve bladder dysfunction caused by the reduction in muscle stiffness.

Several studies have tested the effectiveness of Cannabis in reducing some MS symptoms, and some of these analyzed its effects on bladder-related symptoms, with contrasting outcomes. A recent review reports the effects of Cannabis treatment on the bladder<sup>[1]</sup>.

The use of nabiximols can reduce the dose of other oral antispastic drugs that cause urinary function worsening, controlling or avoiding their side effects.

### CASE DESCRIPTION

We describe the case of a 48-year-old woman with secondary progressive MS and persistent radiological activity. She was diagnosed with MS at the age of 18 years and started different treatments, including interferon 1a/1b, natalizumab and cyclophosphamide. She is currently being treated with dimethyl fumarate (Tecfidera®), with no evidence, since starting the treatment, of clinical or radiological activity but with disability progression.

The patient presented a spastic paraparesis with a significant stiffness in the lower limbs, particularly on the left side, which caused walking difficulties with a tendency to foot drop. She could walk for a few steps without help and for approximately 20 m with assistance.

In the previous 5 years, the patient had also reported progressive bladder complaints characterized by vesical tenesmus, difficulty to urinate, urinary urgency with incomplete voiding, frequent urination and recurrent infections to the lower urinary tract.

Considering her significant stiffness, she started treatment with the oral antispastic baclofen up to 25 mg/3 times a day (75 mg/day), but she did not tolerate it. She reported 2 typical complaints of oral myorelaxant therapy: increasing sleepiness during the day together with asthenia (conditioning a progressive reduction in walking abilities) and the onset of incontinence episodes. For this reason, in November 2017, the patient started nabiximols treatment, gradually increasing the dose up to 10–12 puffs/day. A month later, the patient showed a gradual reduction in spastic symptoms in the lower limbs, followed by increasing walking abilities, such as being able to walk up to 100 m with a walker. Considering the good response to the treatment, the oral antispastic dose was reduced to half of a 25 mg pill 3 times a day. The therapy significantly reduced the side effects, with a reduction in asthenia and sleepiness during the day and increased cognitive performance. Bladder complaints were also improved thanks to the positive effects of nabiximols on an overactive bladder and to the reduction in the myorelaxant effect of baclofen on bladder muscles. The patient showed an improvement in bladder function with no incontinence episodes, vesical tenesmus improvement and complete voiding.

For 8 months, the patient received half of a 25 mg pill of baclofen 3 times a day plus nabiximols 10–12 puffs/day (6 + 6). After this time,

a sudden reduction of the nabiximols dosage to 6 puffs/day was needed due to some supply difficulties.

Several days after the therapeutic reduction, the patient presented a urinary blockage with severe urinary retention and stagnation of 800 cc of urine followed by catheterization during the hospitalization. For this reason, she started treatment with tamsulosin up to 4 mg/day. Over the following days, the patient showed a partial improvement in spontaneous voiding, but the bladder scan revealed post-void residual urine leading to more frequent post-void catheterizations. As the supply problems were resolved, the patient continued her treatment with 12 puffs/day. From the first day of treatment, the patient rapidly registered a gradual remission of bladder function with spontaneous voiding recovery and no post-void residual urine. The treatment with tamsulosin was suspended as the patient reported severe orthostatic hypotension and tachycardia as side effects.

Currently, she takes nabiximols (12 puffs/day), and she does not need any urinary device or specific therapy for bladder dysfunction. Together with bladder dysfunction improvement, a significant reduction in urinary infections was registered, which is the most frequent problem the patient complained about.

## DISCUSSION

This case presents some interesting insights into overactive bladder treatment for patients with MS. In MS centres, it is not always possible to evaluate bladder complaints carefully, although this should be normal practice for those patients with high disability and recurrent infections to the urinary tract<sup>[2]</sup>.

The use of common myorelaxants is often associated with many side effects, which can cause muscle strength worsening and reduction of already impaired walking ability.

Cannabis oromucosal spray acts synergically with other antispastic drugs and, in certain cases, can reduce their daily dose and the incidence and severity of side effects<sup>[3]</sup>.

Although bladder complaints result from muscle spasticity, nabiximols is not considered as a possible treatment. The regulatory authorities allow the prescribing of nabiximols only for muscle stiffness treatment.

An Italian study has tested the effectiveness of nabiximols on lower urinary tract dysfunction, showing improvement of overactive bladder symptoms due to its effects on detrusor hyperactivity<sup>[4]</sup>.

As it has been presented in this case, nabiximols should be considered not only to improve bladder dysfunction symptoms and reduce antispastic therapy side effects, but also to reduce recurrent infections in the lower urinary tract. This result is particularly significant considering that drugs with a positive effect on disease progression are now available but they still have a high impact on the immune system<sup>[5]</sup>.

Finally, the American Academy of Neurology document<sup>[6]</sup> concludes that the oromucosal spray is likely to be effective in terms of urinary

frequency improvement (Class I), but it has no effect on incontinence episode reduction (Class I), as it has been demonstrated in randomized controlled studies on detrusor hyperactivity<sup>[7]</sup>.

In conclusion, it would be interesting to conduct further studies on a more mixed and wider population to prescribe the drug more extensively so that vesical complaints could be finally included in the therapeutic criteria.

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