

## Case Report

# Effects of intrathecal Baclofen in reducing tremors in patients with multiple sclerosis

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### ABSTRACT

يعد علاج أعراض مرض التصلب اللوحي أمراً بالغ الأهمية، فهو يساعد على تقليل القيود التي تؤثر على روتين الحياة اليومية للمرضى. الرعشات تعد من الأعراض الهامة والمتكررة لدى مرضى التصلب اللوحي، ومع ذلك يوجد نقص بالأدلة العلمية التي تدعم منهجاً علاجياً محدداً. بهذه الدراسة نقدم حالة مريض يبلغ من العمر 41 عاماً لديه تاريخ مرضي بالتصلب اللوحي. خلال متابعاته بالعيادة كان يعاني من تيبس بالعضلات ورعشات أثرت على نشاطاته اليومية. أعطي المريض للتبيسات علاج الباكلوفين عن طريق حقنه بسائل النخاع الشوكي فاستجابت التبيسات العضلية للعلاج وبشكل غير متوقع أدى العلاج إلى تقليل الرعشات وتحسنها.

Symptomatic treatment of Multiple Sclerosis (MS) is crucial, since it helps to lessen the limitations that affect patients' daily lives. Tremors are a significant and frequent symptom in MS patients. However, there is still a lack of evidence supporting a specific therapeutic approach for MS patients' tremors. A 41-year-old man with a history of MS is presented in this study. He exhibited stiffness and tremors at the follow-up clinic, which affected his daily activities. For his spasticity, he received intrathecal baclofen (ITB). The patient's symptoms responded well to this treatment, as both stiffness and tremors decreased. In an MS patient, ITB therapy thus unexpectedly reduced and improved tremor symptoms.

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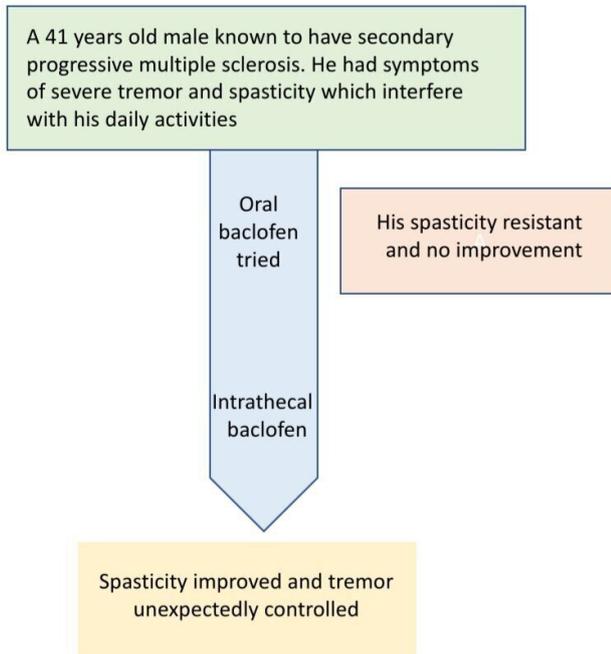
Multiple Sclerosis (MS) is a demyelinating disease that affects the brain and spinal cord. The symptomatic treatment of MS is as important as immunotherapy, because it contributes to the reduction of disabilities which impact daily life. Tremors are a

serious and frequent symptom in MS patients.<sup>1</sup> Along with nystagmus and scanning speech, French neurologist Charcot (1825–1893) identified tremors as one of the three hallmark symptoms of MS. Tremors in MS patients are caused by lesions in either the motor and sensory tract or cerebello-thalamo-cortical circuits.<sup>2,3</sup> From 25% to 58% of MS patients experience tremors, which are in turn linked to a poor prognosis and higher disability.<sup>4,5</sup> Tremors are challenging to control since they resist symptomatic treatment.

**Case Report. Patient Information.** A 41-year-old Saudi male who was diagnosed with MS in 2005, after an attack of blindness and ataxia. A follow-up visit found that he had continued to deteriorate clinically and radiologically, so he was therefore diagnosed as secondary progressive MS. During the follow-up visit, he experienced symptoms of spasticity, tremor, and dysarthria. His spasticity was severe; he could not sit or stand up, and his spasticity did not improve with oral medications. Moreover, his bilateral hand tremor affected his fine movement. The patient was referred to a rehabilitation clinic, as well as for physical and occupational therapy (Figure 1).

**Clinical findings.** The patient had bilateral lower limb spasticity. His spasticity was severe and impacted his daily activities. Initially, he could not flex his knee; he also he had difficulties in wearing shoes or socks, as he could not move his feet. The patient's spasticity increased in severity over time. Consequently, he could not sit properly in a wheelchair and his care givers had difficulty moving and turning him. As the spasticity was worse at night, he had fragmented sleep, waking multiple times because of the pain.

The patient also had a bilateral hand action tremor (postural and kinetic tremor). This was rhythmic, with a low frequency (2-4Hz). The patient already had an upper extremity weakness which limits his activities. His tremor meant activities became even more difficult. He could not hold objects such as a spoon or cup of water and had difficulty in his fine movement, too. His postural tremor was reported during physical



**Figure 1** - Timeline of a 41-year-old Saudi male who was diagnosed with MS in 2005, after an attack of blindness and ataxia.

examination.

Spasticity was recorded as 3/4 in severity when the patient was seen by rehabilitation and began with intrathecal baclofen. The first dose was 50mcg; thereafter, spasticity decreased to 2/4. After one month the dose increased to 100mcg and the patient's spasticity improved to 0/4. After that he planned for the insertion of a baclofen pump. Following intrathecal baclofen, his tremors were controlled and not noticed any more.

**Neurological examination.** Normal mental function, scanning speech with nasal tone, dysarthria.

**Cranial nerve.** Normal pupillary reaction to light. Fundus examination showed bilateral optic disc pallor. Patient has nystagmus and bilateral internuclear ophthalmoplegia. Left upper motor neuron facial weakness.

**Motor Examination:** Bilateral lower limbs spasticity, with weakness predominantly in the flexors of the lower limbs and extensors of the upper limbs. Tendon reflexes were exaggerated on both sides. Planter was mute bilaterally.

**Sensory Examination.** Impaired position and vibration in both sides.

**Coordination.** He has bilateral ataxia in both hands and feet. He also has truncal ataxia.

**Diagnostic assessment.** Brain and spine MRI showed multiple new enhancing lesions despite trying multiple

disease modifying therapies. After one year of continue progression, the patient was diagnosed with secondary progressive MS.

**Therapeutic intervention.** After failure of oral baclofen (GABA agonist) for the treatment of severe spasticity, the patient was referred to a rehabilitation clinic to decide if he was a suitable candidate for intrathecal baclofen (ITB) therapy.

The ITB was performed with a spinal tab. A small dose of baclofen was injected into the spinal fluid. Then, after a few hours, spasticity was evaluated via the Modified Ashworth Scale. The muscle tone assessment scale ranged from 0 ("normal tone") to 4 ("affected part rigid in flexion/extension"). The effect of ITB is temporary. If there is significant improvement a few hours post injection, the patient is referred to neurosurgery for baclofen pump insertion.

**Follow-up and outcomes.** After an intrathecal injection of baclofen, the patient's spasticity improved from 3/4 to 0/4. He can sit at the edge of a bed. At the same time, his tremors decreased and were better controlled, such that he can hold objects without difficulty, with no more tremors reported. The patient therefore planned for a baclofen pump to be inserted.

**Discussion.** In this case report, we presented a patient with MS, who had kinetic and postural tremors which unexpectedly improved after he received an intrathecal baclofen for his spasticity. Tremors are a common symptom in MS patients, with an estimated prevalence in the literature of around 25-58%. No clinical trial has evaluated specific treatments for tremors in MS patients. There is however one old case report by Nirit Weiss, published in 2003, about a patient with a bilateral upper-extremity tremor that improved unexpectedly after placement of an intrathecal baclofen pump for lower-extremity spasticity.

The estimated prevalence of MS tremors is around 60%, with severe disabling tremors in 3-15% of patients. The most common form of tremor in MS patients are a combination of postural and intention tremors.<sup>2</sup> The pathophysiology of tremors in MS patients is poorly understood, however lesions in cerebello-thalamocortical pathways and/or central sensory and motor pathways could contribute to the pathogenesis of either tremors or dysmetria.<sup>3</sup> In turn, therapeutic options for MS tremors include pharmacological agents, botulinum toxin A injections, along with deep brain stimulation or thalamotomy for drug resistant or severe, disabling tremors, but the evidence remains inconclusive regarding a definite approach.<sup>1,4</sup>

William Meado<sup>5</sup> undertook a survey using the North American Research Committee on Multiple Sclerosis (NARCOMS) patient registry. The study found a total of 777 respondents had tremors which were either mild or greater, while 238 (46.9%) reported tremor reduction after symptomatic treatment. The most used treatments were anticonvulsants (gabapentin 50.8%) and benzodiazepines (clonazepam 46.2%). Less than half of participants reported a benefit from symptomatic treatment. Thus, in many cases MS tremors remain poorly treated.

Meanwhile, a literature review by Mousa Hamad<sup>6</sup> found that essential tremors are caused by decreased activity in GABA receptors and that administration of oral baclofen in mice results in delayed onset and intensity of tremors. The review concludes that more clinical trials and research need to be carried out on intrathecal baclofen as a potential treatment option.

Moreover, a systemic review conducted by Ahmad Pourmohammadi<sup>7</sup> in 2022 evaluated 26 articles and concluded that well-designed clinical trials can improve clinical management of MS tremors.

Most commentaries nevertheless note there remains a gap in the understanding of how to treat tremors in MS patients, which means there is a need to conduct more research and clinical trials in this area. Moreover, up to date treatment of MS tremors is multidisciplinary, incorporating pharmacological, surgical, and physical therapies.

**Conclusion.** Tremors are a common symptom in MS patients. As of now, however, there remains no approved symptomatic treatment for tremors in MS patients. However, intrathecal baclofen, which is used as a symptomatic treatment for spasticity in MS patients, may also help to reduce and control tremors.

From this case report and accompanying literature review, we conclude there is a need to conduct more clinical trials and research on ITB as a potential symptomatic treatment for tremors in MS patients. The pathophysiology and mechanisms of tremors in MS patients also need to be studied more. It is crucial to

note that, given the current state of the evidence, there must be a means to guide future research, possibly by delegating aspects to notable MS societies to help fill in any gaps.

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