LETTER TO THE EDITOR

Misoprostol as a Therapeutic Option for Trigeminal Neuralgia in Patients with Multiple Sclerosis

Dear Editor,

Trigeminal neuralgia (TN) is characterized by attacks of recurring, paroxysmal, shock-like pain within the distribution of one or more branches of the trigeminal nerve [1]. About 2% of all TN patients have multiple sclerosis (MS); similarly, about 2% of all MS patients present with TN symptoms [2]. The combination of TN and MS is one of the rare, so-called “symptomatic” forms of TN.

We present three cases of “therapy-resistant MS-related” TN, in which misoprostol therapy was successful.

Case 1 reports of a 65-year-old female patient with a 32-year history of MS and a 4-year history of TN (V2 only). Further findings were a hemiparesis and hemiplegia lasting 1 year and a history of hypertension. She was suffering from pain attacks with a visual analog scale (VAS) of 10/10, which made eating impossible. The bouts appeared 20 times per day and lasted approximately 10 minutes. During the neurological follow-up, she received carbamazepine (CBZ) and nutrients parenterally. Increasing the doses of CBZ caused complications such as intermittent hyponatremia and hypocalcemia. She received additional administrations of 3–4 × 10 mg/day morphine subcutaneously. As the pain attacks persist, the medication was broadened to baclofen 4 × 5 mg/day, morphine retard 3 × 10 mg/day, and gabapentin at a target dose of 2,100 mg/day. By the start of our follow-up, we discontinued the morphine, began the administration of misoprostol 3 × 200 µg/day, and reduced the gabapentin dose to 3 × 600 mg/day. After the third administration of misoprostol, the bouts stopped abruptly. The patient was discharged free of pain. Oral food intake was again possible without problems. She is still under routine control of her family physician due to MS but reports of no pain at all.

Case 2 was a 69-year-old patient with a 22-year history of MS. She had been receiving immunoglobulins (Octagam®, Octapharma AG, Lachen, Switzerland) due to increasing immobility. With this therapy, she could cope with longer distances on foot. She was also suffering from a left-sided TN (V2 + V3) for which she had been treated for 7 years with CBZ 750 mg/day and gabapentin 3 × 800 mg/day. The upward titration of the CBZ dose was carried out up to the side-effect-free, tolerable level. The main problem was that the patient was again confined to the wheelchair under these high doses of anticonvulsants. An increasing shooting pain (VAS 8/10), which occurred especially when chewing and drinking, appeared. An additional acupuncture treatment performed by the treating neurologist provided no relief. We started with the administration of misoprostol 3 × 200 µg/day and slowly reduced the gabapentin dose. After the second dose of misoprostol, a significant reduction in severity of pain to 3/10 was observed. With this pain intensity, food intake was possible again without further difficulties. Our aim was not only the pain reduction but also to reduce the walking impairment which presented as a side effect of the anticonvulsive therapy. A reduction of the gabapentin dose down to 3 × 600 mg/day was tolerated well. We subsequently increased the misoprostol dose first to 3 × 400 µg/day and afterwards up to the unusual dose of 3 × 600 µg/day. Under this therapy, a reduction of CBZ down to 300 mg/day and that of gabapentin down to 1,200 mg/day were possible with maintained pain reduction. Regarding the ongoing follow-up by her family physician, the patient can walk longer distances with forearm crutches and does not complain of any pain.

Case 3 was a 61-year-old female patient who has been suffering from MS for 25 years, diagnosed with a right-sided TN (V2 + V3) 6 years ago. She suffered from shooting pain triggered by eating and speaking. The medication at initial presentation in our outpatient clinic consisted of CBZ 600 mg/day (the individual, side-effect-free, tolerable dose), gabapentin 2,400 mg/day, and the administration of tilidin/naloxone 3 × 200 mg/day. The patient reported the severity of pain as 7/10. In a first attempt, we changed the gabapentin to pregabalin (2 × 75 mg/day). Under this medication, there was a short-term reduction in severity of pain to 5/10. Subsequently, the dose of pregabalin has been increased from 75/0/75 to 150/0/300 mg. The addition of misoprostol 3 × 200 µg/day led to a further reduction in severity of pain to 3/10. Regarding the reports of the family doctor, she does not complain of having any pain.

The presented cases in this report have several common characteristics:

First, they had all been treated with antiepileptics, the so-called “first line” treatment. Later, however, the success of this strategy diminished, and the patients often had bouts of pain, leading to suicidal ideation. Misoprostol has been effective in treatment of all three patients.

Second, all patients suffered from side effects of the treatment prior to the consultation. As a matter of fact, “pain...
related to the treatment of MS is considered as another important challenge in MS [3]. In this manner, misoprostol is a treatment that is associated with less general and less intense unwarranted effects compared with the “first line” drugs.

Previously, Reder and Arnason have reported the successful use of misoprostol in MS-related TN in six out of seven patients [4]. The rationale was that misoprostol can inhibit the T-lymphocyte functions and consequently decrease their inflammatory activity in MS plaques by increasing intracellular levels of cyclic adenosine monophosphate. In another study, 14 of the 18 patients with refractory TN showed a reduction in attack frequency and intensity of pain [5].

However, the use of misoprostol cannot be found in the majority of evidence-based algorithms: The evidence has been found to be insufficient to support the effectiveness of any medication, including misoprostol, in treating pain of MS-related TN [6]. Because of the rare incidence of MS-related TN, it is almost impossible to organize a randomized, controlled trial to evaluate or increase the evidence of any alternative treatment method including misoprostol. Therefore, we believe that case series should be collected until a multicenter comparative study on this topic is performed.

For now, we conclude that treatment of patients suffering from MS-related TN with misoprostol can be a beneficial option in the long-term treatment of this specific type of pain and is associated with fewer side effects.

**References**


