



Letter to the Editor

Dalfampridine is associated with de novo occurrence or reoccurrence of positive sensory symptoms in MS



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Dear Editor,

Oral extended release dalfampridine (FA) is a recently approved medication that blocks voltage-dependent potassium channels inhibiting functioning of axonal membranes. It results in improved conduction affecting ambulation in a subgroup of patients with multiple sclerosis (MS) [1–2].

Paroxysmal symptoms are due to abnormal electrical discharges due to demyelinated nerve fibers and include sensory paroxysms such as trigeminal neuropathy associated with MS (TN) and motor paroxysms such as painful tonic spasms. These symptoms are present in approximately 10% of subjects with MS [3]. The hypothesis is that if FA enhances sensory fiber conduction it may simultaneously incite action potential conduction in damaged sensory nerves, resulting in new positive sensory symptoms such as parasthesia or pain.

Two retrospective reviews have reported the occurrence of new or worsened symptoms in MS patients treated with FA. In a review of 76 patients, 4 developed positive sensory symptoms (2 patients reported recurrence of TN, 1 dysesthesia and 1 bilateral leg pain), within one month of starting FA and 1 subject had a new-onset seizure. Cessation of FA was insufficient to resolve symptoms in 2 patients with recurrent TN, while subjects with de novo pain improved with therapy discontinuation [4]. In a second report of 71 subjects, 3 out of 5 subjects with a history of TN experienced recurrence of pain within 4 weeks of therapy with FA [5]. Subjects with TN showed no improvement in pain after discontinuing treatment.

We report on the occurrence of new painful symptoms in patients treated with FA prospectively, observed over 18 months. A battery of tests was performed at baseline (T0), at the end of treatment (T1) and 2 weeks later (T2). Responders had been defined by the literature as subjects with an improvement at on the Δ Timed 25-foot Walk (T25FW) greater than 20%. A total of 44 patients with a mean age of 51 years (range 35–76) were included: 22 (50%) were female mean EDSS was 5.87 (range 3–7) with a mean disease duration of 14.2 years (range 3–30). Fourteen patients reported a significant improvement (> 20%) in walking speed (Δ T25FW), 3 patients were “partial responders” with a subjective improvement in walking, 22 were “non responders” and 5 subjects withdrew from the study due to adverse effects. Out of 5 subjects who reported adverse effects, 2 reported experience difficulty with balance, 2 patients experienced generalized

painful parasthesia and one exacerbation of TN. The onset of TN and generalized parasthesia occurred within 3 days of initiating treatment with FA and pain resolved within 24–48 h of discontinuing treatment. No subjects experienced de novo TN during FA therapy.

In the current sample the frequency of painful sensory symptoms was around 7% and it represents the principal adverse effect leading to FA discontinuation. In comparison with other reports, the relationship between the onset of pain and FA treatment initiation (3 days), as well as and the rapid resolution of painful symptoms within 24–48 h from discontinuation suggests a causal relationship. Worsening of or ex novo painful symptoms presents a limitation to the use of FA.

FA should be used with caution particularly in subjects with a history of TN (approximately 2% of patients) until there is a clearer understanding of the relationship. This is important given that in some cases TN related to FA may be drug-resistant, although in our sample the subject who experienced worsening of pain related to TN recovered after FA discontinuation. A prospective study specifically assessing pain history and the occurrence of pain related to treatment would help to better understand possible predictors of de novo or reoccurring pain with the use of FA.

Author's contributions

- Dr. Solaro: substantial contributions to conception and design; final approval of the version to be published
- Dr. Trabucco: substantial contributions to acquisition of data
- Dr. Messmer Uccelli: drafting the article and revising it critically for important intellectual content and; final approval of the version to be published

Disclosure

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- Dr. Trabucco reports no disclosures.
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