

[EDITORIAL]

Naratriptan May Become an Alternative Prophylactic Option for Patients with Cluster Headache

Shoji Kikui and Takao Takeshima

Key words: cluster headache, naratriptan, prophylactic treatment

(Intern Med 56: 2547-2548, 2017)

(DOI: 10.2169/internalmedicine.9091-17)

Cluster headache (CH), the most common of the trigeminal autonomic cephalalgias and one of the most painful primary headache disorders. It is characterized by attacks of severe, strictly unilateral pain that is commonly retro-orbital, lasting 15-180 minutes, and occurring from once every other day to 8 times a day (1). CH pain is associated with ipsilateral conjunctival injection, lacrimation, nasal congestion, rhinorrhea, forehead and facial sweating, miosis, ptosis and/or eyelid edema, and/or restlessness or agitation (1). CH attacks have both circadian and circannual rhythmicity. A strong predilection for attacks during sleep is well recognized. In the episodic form (ECH), bouts of attacks alternate with periods of remission of varying duration. In the chronic form, there tends to be an absence of remissions within one year, or the presence of remission period lasting less than 1 month (1).

The management of CH includes (i) patient education about the nature of the disorder; (ii) advice on lifestyle changes (e.g. avoiding alcohol during an active cluster period); (iii) prompt treatment of the acute attack; and (iv) prophylactic treatment (2). The brief duration and severity of the CH attacks necessitate the use of rapid-acting pain relievers. Subcutaneous sumatriptan and inhalation of pure oxygen are the two most effective acute treatment options for patients with CH. Prophylactic treatment of CH is classified into maintenance prophylaxis and transitional prophylaxis. When treating ECH, maintenance prophylactics are generally continued through the cluster period and restarted at the onset of the next cluster period (2). For maintenance prophylactics, verapamil is considered to have the best balance of efficacy and tolerability (3). Due to its delayed onset of efficacy of usually 10 to 14 days and the required slow titration of the dose to increase tolerability, transitional prophylactics (e.g. corticosteroids) are administered for short durations as adjunctive therapies to maintenance prophylactics to abort the cluster period or to further reduce the fre-

quency and severity of CH attacks (3). The common reported side effects of verapamil are heart failure, low blood pressure, increased liver enzyme levels, atrioventricular block (a condition where heart impulses are delayed), changes in heart rate, constipation, and shortness of breath. Although the combination of verapamil and corticosteroids is effective in treating most patients with CH, these medications may not always be used because of their side effects. Other maintenance prophylaxes (e.g. lithium, topiramate, valproic acid, gabapentin, and baclofen) are not always effective for all patients and may have side effects of their own.

Naratriptan, a 5-hydroxytryptamine_{1B/D} (5-HT_{1B/D}) agonist, is an effective and well-tolerated abortive anti-migraine medication (4) and has been used preventively in transformed and menstruation-related migraines (5, 6). Naratriptan has also been reported to reduce the frequency of CH attacks (7-9). It has been suggested for the preventive treatment of CH because of its long half-life. In this issue of *Internal Medicine*, Itoh et al. (10) report that the administration of naratriptan 2 hours before attacks appeared to achieve a good response in patients with CH in Japan. In their study, among the 43 cases, 37 (86.0%) showed improvement in CH with naratriptan. Twenty-two patients received other preventive treatments (51.2%) in addition to naratriptan, whereas 21 received only naratriptan (48.8%). Nineteen patients (44.2%) showed effective improvement in CH with the use of naratriptan alone.

Provided that safety issues with daily usage are resolved, naratriptan may become an alternative option for prophylactic treatment in patients with CH. Its application for the treatment of refractory CH and chronic CH is anticipated. Because spontaneous remission is possible in CH, a double-blind placebo-controlled study using naratriptan as a preventive treatment for CH is needed to provide further insight regarding this treatment modality in the near future.

Department of Neurology and Headache Center, Tominaga Hospital, Japan

Received: February 24, 2017; Accepted: March 1, 2017; Advance Publication by J-STAGE: September 6, 2017

Correspondence to Dr. Shoji Kikui, kikui@tominaga.or.jp

The authors state that they have no Conflict of Interest (COI).

References

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia* **33**: 629-808, 2013.
2. Ashkenazi A, Schwedt T. Cluster headache-acute and prophylactic therapy. *Headache* **51**: 272-285, 2011.
3. May A, Leone M, Afra J, et al; EFNS Task Force. EFNS guidelines on the treatment of cluster headache and other trigeminal-autonomic cephalalgias. *Eur J Neurol* **13**: 1066-1077, 2006.
4. Mathew N, Asgharnejad M, Peykamian M, Laurenza A, on behalf of the Naratriptan S2WA3003 Study Group. Naratriptan is effective and well tolerated in the acute treatment of migraine. *Neurology* **49**: 1485-1490, 1997.
5. Sheftell FD, Rapoport AM, Coddon DR. Naratriptan in the prophylaxis of transformed migraine. *Headache* **39**: 506-510, 1999.
6. Mannix LK, Savani N, Landy S, et al. Efficacy and tolerability of naratriptan for short-term prevention of menstrually related migraine: data from two randomized, double-blind, placebo-controlled studies. *Headache* **47**: 1037-1049, 2007.
7. Eekers PJ, Koehler PJ. Naratriptan prophylactic treatment in cluster headache. *Cephalalgia* **21**: 75-76, 2001.
8. Loder E. Naratriptan in the prophylaxis of cluster headache. *Headache* **42**: 56-57, 2002.
9. Mulder LJ, Spierings EL. Naratriptan in the preventive treatment of cluster headache. *Cephalalgia* **22**: 815-817, 2002.
10. Ito Y, Mitsufuji T, Asano Y, et al. Naratriptan in the prophylactic treatment of cluster headache. *Intern Med* **56**: 2579-2582, 2017.

The Internal Medicine is an Open Access article distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).

© 2017 The Japanese Society of Internal Medicine
Intern Med 56: 2547-2548, 2017