

Pharmacological therapy of Trigeminal Neuralgia in the presence of raised liver function tests

A 40 yr. /o man referred to our department with the complaint of severe episodic strictly unilateral stabbing pain in the left side of the face since 4 months ago without any autonomic features. Duration of the pain doesn't exceed 1 minute with the mean duration of several seconds and frequency of 10-15 times in a day. He noted that the pain gets worse while eating, touching his face, chewing and clenching his teeth.

The patient was painfree between the attacks.

His medical history was not remarkable.

He didn't take any drug.

Systemic examination was normal except extracted left permanent molars on the left side in hope of alleviating the relevant dental problem and pain.

On neurologic examination we didn't find any abnormal findings including hypoesthesia or hypoalgesia in the affected trigeminal region which always indicates axonal damage and therefore a trigeminal neuropathy.

Our patient fulfilled the diagnostic criteria of trigeminal neuralgia according to the International Classification of Headache Disorders, 3rd edition (ICHD-3) diagnostic criteria which are as follows:

- A) At least three attacks of unilateral facial pain fulfilling criteria B and C
- B) Occurring in one or more divisions of the trigeminal nerve, with no radiation beyond the trigeminal distribution
- C) Pain has at least three of the following four characteristics:
 - Recurring in paroxysmal attacks lasting from a fraction of a second to two minutes
 - Severe intensity
 - Electric shock-like, shooting, stabbing, or sharp in quality
 - At least three attacks precipitated by innocuous stimuli to the affected side of the face (some attacks may be, or appear to be, spontaneous)

- D) No clinically evident neurologic deficit
- E) Not better accounted for by another ICHD-3 diagnosis

To rule out the secondary causes, we obtain the Brain MRI with and without contrast which was normal.

As medical therapy is the initial treatment of most patients with classic TN (i.e., TN that is idiopathic or caused by neurovascular compression), So Carbamazepine is started and gradually titrated up to the 800 mg/D.

To evaluate baseline laboratory tests, CBC diff and liver function tests were performed, all being normal.

In the second visit, after one month, the patient came to our office with raised liver function test up to 400 and he mentioned to the new onset purities and mild skin rashes. The patient precisely examined. He was not ill or toxic and the vital signs were in normal limit. lymphadenopathy was not detected. Although drug induced raise in LFT was the first diagnosis, He referred to an internist for further evaluation of concurrent baseline hepatic problem.

CBC.diff was normal.

Hepatotoxicity ranging from slight elevations in liver enzymes to rare hepatic failure has been reported with Carbamazepine use and may occur concomitantly with other immunoallergenic syndromes such as multiorgan hypersensitivity (DRESS syndrome) and serious dermatologic reactions including SJS.

This severe raise in liver function testes made us, discontinue the drug immediately.

A systematic review and practice parameter published in 2008 from the American Academy of Neurology (AAN) and the European Federation of Neurological Societies (EFNS) concluded that [carbamazepine](#) is effective for controlling pain in patients with classic TN, [oxcarbazepine](#) is probably effective, and [baclofen](#), [lamotrigine](#), and [pimozide](#) are possibly effective . There are limited data and uncertain effectiveness regarding other drugs that have been used for TN, including botulinum toxin injections, [clonazepam](#), [gabapentin](#), [phenytoin](#), tocinide, [tizanidine](#), topiramate and [valproate](#).

Severe increased liver function teases made many of the mentioned drugs contraindicated due to their metabolization in the liver.

In different studies with TN that was refractory to [carbamazepine](#) or [phenytoin](#), adjunct therapy with [lamotrigine](#) (400 mg daily) was beneficial, but increased liver function testes and mild dermatologic complication of the patient had us exclude it as the first line replacement.

[Pimozide](#), a dopamine receptor antagonist, was more effective than [carbamazepine](#) in a randomized, double-blind crossover trial of 48 patients with refractory TN. However, pimozide is seldom used for TN because it has many potentially serious side effects, including sedation, arrhythmias, anticholinergic effects, acute extrapyramidal symptoms, and parkinsonism so we didn't use it as the first line replacement. \

Gabapentin was selected due to its renal metabolization and titrated up to 900mg gradually.

The patient monitored for liver function tests and dermatologic complication which were decreased slowly. All the gastrointestinal evaluation was normal.

Unfortunately the frequency and severity of attacks didn't decrease with Gabapentin and the patient started to complaint of drug induced intolerable drowsiness. So the dose gradually tapered down, then Baclofen and Topiramate started and titrated up to 50 mg/D and 100mg/D respectively but again intolerable drowsiness of the patient made us taper the Baclofen to 20 mg/D.

As reaching Topiramate dose to 100mg/D, the severity and frequency of the attacks were decreased dramatically and the patient got pain free after 5 weeks following Topiramate initiation.

Since the medical therapies are the first and the best treatment of Trigeminal neuralgia, choosing the drug of choice in case of abnormal liver function tests or hepatitis especially in the presence of dermatologic problems could be a challenging issue.

We will discuss all nonpharmacologic treatment of Trigeminal neuralgia in the next few days which could be good replacement in these circumstances.