Two Cases of Multiple Sclerosis with Painful Tonic Seizures and Dysesthesia Ameliorated by the Administration of Mexiletine

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Mexiletine was administered in two patients suffering from multiple sclerosis with severe dysesthesia and painful tonic seizures. In both patients the painful tonic seizures disappeared and dysesthesia improved as well. The effects of mexiletine on painful symptoms have been previously reported in diabetic neuropathy, but not in diseases of the central nervous system.

Key words: Sensory disturbance, Therapy, Central nervous system

Severe pain or dysesthesia occurs in some patients with multiple sclerosis. Anti-convulsants, anti-depressants or vasodilator agents are usually used to treat these symptoms, but these treatments all have some side effects. Recently, Dejgard et al reported that oral mexiletine relieves the symptoms of chronic painful diabetic neuropathy with few side effects (1).

Here, the amelioration of both the painful tonic seizures and dysesthesia in two cases of multiple sclerosis with mexiletine administration is reported.

CASE REPORT

Case 1. A 46-year-old female suddenly began to feel chill sensations in her extremities. One month later, painful tonic seizures appeared in the right extremities. Four months later, she experienced weakness in the right extremities, and complained of dysesthesia. The weakness spread to all extremities. When she was admitted to a hospital, she exhibited quadriaparesis, hypoalgesia, anesthesia and dysesthesia throughout the area below the second cervical cord level. A diagnosis of multiple sclerosis was made. Prednisolone was administered orally at an initial dosage of 60 mg, and then was gradually tapered. Although the weakness of her upper extremities improved, dysesthesia remained unchanged. Painful tonic seizures and dysesthesia were then reduced by administration of carbamazepine (600 mg/day).

Seven months later, she was transferred to our hospital. On administration the patient had bilateral horizontal nystagmus, quadriaparesis and spasticity, which was prominent in the lower extremities. The deep reflexes were generally hyperactive, including jaw jerk. Sensory examination disclosed tactus and pinprick loss below the C2 level, and the patient complained of dysesthesia throughout the same area. Complete blood cell count and urinalysis results were normal. Blood chemical examinations revealed the following liver dysfunctions: SGOT 27 U (5–25 U), SGPT 28 U (0–20 U), γ-GTP 103 U (3–31 U) and LAP 62 U (30–51 U). CSF examination showed 2 oligoclonal Ig G bands. Cell counts, protein, sugar and myelin basic protein levels were normal. The NMR-CT brain scan (T2 weighted) revealed high intensity areas in the white matter near the bilateral lateral ventricles. The conduction velocities of the
median, ulnar and sural nerves were normal. As she was found to suffer from drug-induced hepatitis due to carbamazepine, the administration of carbamazepine was discontinued. Although SGOT, SGPT, \( \gamma \)-GTP and LAP levels decreased to normal ranges, painful tonic seizures and dysesthesia appeared in the extremities. Therefore, mexiletine was given at an initial dosage of 150 mg and then increased to 300 mg. At a mexiletine of dosage 300 mg, the painful tonic seizures disappeared and dysesthesia was reduced. Administration of mexiletine was discontinued in order to confirm that the effects obtained were indeed due to the mexiletine administration, and subsequently the dysesthesia in the extremities worsened.

**Case 2.** A 29-year-old female felt weakness in the left lower extremity, accompanied by dysesthesia of the left upper and lower extremities at the age of 17. Although the weakness improved, dysesthesia of the left extremities remained. At the age of 21, her visual acuity became poor. From 23 yr of age she began to frequently experience pain in the left side of her face. At the age of 28 she suffered dysesthesia in the bilateral lower extremities and dysuria. When she was admitted to our hospital, neurological examinations revealed left quadrant-anopsia, atrophy of both optics, dysesthesia and paresthesia in her extremities. Painful tonic seizures were frequently observed. Complete blood cell count, blood chemistry and urinalysis were normal. SEP study revealed that a central conduction time (N 19–N 13) was extended in the left side. The CSF examination results were normal. Predonisolone was administered orally at an initial dosage of 40 mg, and then was gradually reduced. Although she exhibited improvement of the dysuria, painful tonic seizures and dysesthesia continued. After mexiletine was given at a dosage of 150 mg, the painful tonic seizures disappeared and improvement of her dysesthesia was recognized.

**DISCUSSION**

Dejgard et al (1) showed that oral mexiletine relieves the symptoms of chronic painful diabetic neuropathy, especially pain, paresthesia and dysesthesia. In the present two cases, the painful tonic seizures disappeared and dysesthesia was improved by the administration of mexiletine. Therefore, it was considered that mexiletine is effective in ameliorating painful tonic seizures and dysesthesia, especially the former. It is thought that painful tonic seizures result from spinal cord or brain stem lesions (2). In the light of the case histories, neurological findings and laboratory data, the present cases were definitely diagnosed as multiple sclerosis. It is suggested that mexiletine is effective for dysesthesia, not only in peripheral neuropathy, but in other diseases of the central nervous system as well. This is the first report which shows the efficacy of mexiletine for painful tonic seizures and dysesthesia of central nervous system origin.

It has been suggested that neuropathic pain is due to spontaneous activity in the regenerating primary nociceptive small afferent myelinated fibers (3). This activity requires a flow of sodium ions into the nerve in response to depolarization of the nerve membrane (4). Mexiletine has a sodium-channel blocking effect and neuropathic pain could be inhibited (1). Furthermore, as shown by Bach et al, lignocaine has a beneficial effect on the spinal-mediated nociceptive flexor reflex in diabetic patients with neuropathy (5). Their reports support our finding that mexiletine is effective for dysesthesia of central nervous system origin. At present, we do not as yet know how mexiletine abolishes painful tonic seizures. The sodium-channel blocking property of mexiletine may play a role in the improvement of painful tonic seizures. Anti-convulsants, anti-depressants and vasodilator agents are usually used for dysesthesia.
Mexiletine on PTS and Dysesthesia

Carbamazepine and phenytoin are remarkably effective for painful tonic seizures (6, 7). But in some cases the administration of these drugs must be discontinued because of their side effects. Mexiletine, however, is safe, with few side effects; among these side effects, nausea and tremor are most common. These side effects are dose dependent and can be minimized by an increase in the interval between doses, or by administration of the drug with food that can delay absorption, thereby decreasing peak plasma concentrations (8). It is considered mexiletine can be useful for the treatment of painful tonic seizures or sensory disturbance of central nervous system origin.

REFERENCES