which recirculation can be introduced in the ischemic area. Jpn J Stroke 1986; 8:1–8 (Japanese)

Management of Phantom Limb Pain and Sensation with Milnacipran

To the Editor: Phantom limb pain is classified as neuropathic pain that develops after nerve injury. It is an aftereffect of amputation occurring in up to 85% of patients who have undergone such surgery.[1] Tricyclic antidepressants have shown effectiveness in reducing phantom limb pain. Analgesic effects have been reported for venlafaxine, a novel serotonin (5-HT) and noradrenaline reuptake inhibitor (SNRI), against various types of neuropathic pain;[2] however, there are still no reports of a successful treatment for phantom limb pain. As far as we know, this is the first report of the successful management of phantom limb pain and sensation with milnacipran, which is another SNRI.

Case Report

A 77-year-old man with an above-knee amputation on his right leg for arteriosclerosis obliterans was transferred to the department of orthopedics for the purpose of right hip disarticulation due to osteomyelitis in the amputation stump. On the 11th day after the operation, he was referred to the department of psychiatry because he developed paroxysmal phantom limb pain "squeezed" in the absent right knee and ankle joint. Simultaneously, the patient experienced a phantom limb sensation as if the "amputated right lower extremity was actually present." He was not depressive, anxious, or hypochondriacal. He was administered 100 mg/day of fluvoxamine for 3 years after the first operation to treat depressive symptoms. Other therapy included 25 mg/day of quetiapine for delirium and 0.5 mg/day of etizolam for sleep disturbances after the last operation. Milnacipran, 30 mg/day, was added to the regimen. The abnormal pain and sensation were reduced after 1 week but did not vanish. The dosage of milnacipran was increased to 50 mg/day in order to reach remission. After 3 weeks of milnacipran therapy, the phantom limb pain and sensation completely disappeared without adverse events. He continued to take 50 mg/day of milnacipran and was discharged without relapse.

Discussion

In our case, milnacipran rather than fluvoxamine was likely successful in the management of phantom limb pain and sensation because these phenomena developed abruptly during the long-term administration of fluvoxamine and there was rapid dose-dependent improvement following administration of milnacipran. There is a significant amount of evidence to show that tricyclic antidepressants have analgesic efficacy against different kinds of pain due to their action on noradrenergic and serotonergic systems in descending inhibitory pain pathways.[3] Although several reports suggest that selective serotonin reuptake inhibitors (SSRIs) are also capable of alleviating neuropathic pain, meta-analysis found that tricyclic antidepressants showed outstanding analgesic efficacy as compared with SSRIs.[4] Therefore, reuptake inhibition of both 5-HT and noradrenaline arguably play an important role in analgesic efficacy. Milnacipran would reveal a prominent analgesic effect by selectively inhibiting the reuptake of both 5-HT and noradrenaline.[5] In addition, our patient experienced no adverse events. Milnacipran is devoid of affinity for various neuroreceptors associated with numerous adverse events.[5] From a clinical point of view, with respect to pharmacodynamic characteristics, milnacipran could be expected to have tolerability and a therapeutic effect for phantom limb pain and sensation.

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Alcoholic Optic Neuropathy: Another Complication of Alcohol Abuse

To the Editor: Alcohol affects both the central and the peripheral nervous system; hence, cognitive dysfunction as well as sensory and mo-

tor peripheral neuropathy are frequent complications of chronic abuse.[1] However, symptoms of cranial nerve neuropathy are not routinely examined in alcohol abusing patients. To emphasize the necessity of such an assessment, we report on a man who abused alcohol and presented with progressive visual loss attributed to optic nerve neuropathy.

Case Report

A 55-year-old man was admitted to the clinic for alcohol detoxification. He smoked one pack of cigarettes per day for many years and heavily abused alcohol for 15 years, which he had reduced over the last 2 years. Clinical examination revealed numbness and weakness, particularly of the lower limbs, diminished tendon reflexes, and progressive painless blurring of central vision bilaterally; these symptoms, developed over the last 2 years and had seriously compromised his daily functioning. A motor and sensory nerve conduction study showed slowed motor conduction and low-amplitude response to sensory stimuli, mostly on the right. Visual fields testing revealed an inferotemporal and central defect in the right eye and a superonasal, inferior, and central defect in the left. Humphrey 10–2 static perimetry showed bilateral caecocentral scotomas. Visual acuity was 8/10 in the right and 5/10 in the left eye. Color vision was normal. Intraocular pressure was 15 mmHg in both eyes and anterior segments were normal. Funduscopy findings were unremarkable. Blood count, serum vitamin B_{12} and folate levels were normal, but macrocytosis was present (MCV: 104fl.); also, transaminases were elevated. Following alcohol withdrawal and a 6-month vitamin supplementation (vitamins C, E, B complex, folate, taken both orally and intramuscularly), peripheral neuropathy considerably improved but optic neuropathy remained refractory to treatment.

Discussion

Tobacco-alcohol amblyopia was often described prior to World War II in patients with heavy tobacco and ethanol consumption. At the present time, tobacco-alcohol amblyopia is either far less common or is seldom checked for and reported.[2–3] It is characterized by subacute or gradual loss of central vision, decreased visual acuity, and dyschromatopsia. Fundi may appear normal, with few abnormalities on detailed examination; temporal atrophy of the optic disk may become evident at later stages. Metabolic optic neuropathies are characterized by specific loss of the nerve fiber layer in the papillomacular bundle.[2–4] They are etiologically distinguished from hereditary-degenerative neuropathies, neuropathies due to nutritional deficiencies (e.g., thiamine, vitamin B_{12} and folic acid deficiency), and neuropathies caused by various toxic agents (e.g., ethambutol and cyanide). Impairment of mitochondrial oxidative phosphorylation has been proposed as the common underlying pathophysiological mechanism.[5]

In tobacco-alcohol amblyopia, gradual accumulation of formic acid, malnutrition, thiamine depletion, poor B_{12} absorption in the presence of ethanol, and a number of toxic tobacco ingredients, particularly cyanide, act synergistically to the development of neuropathy. Vitamin and nutritional deficiencies are considered especially important factors for its development and recovery is purportedly complete with abstinence from alcohol and smoking and vitamin supplementation.[3–5]

The present case, the first reported in the literature, does not fulfill the characteristic tobacco-alcohol amblyopia criteria, in that dyschromatopsia, an essential component of tobacco-alcohol amblyopia, is absent and no recovery of vision loss was recorded following sobriety from alcohol and tobacco and protracted vitamin treatment. These findings point to the possibility of a nonreversible atypical form of optic nerve neuropathy due to alcohol abuse.

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Valproate-Induced Hyperammonemic Encephalopathy without Cognitive Sequelae: A Case Report in the Psychiatric Setting

To the Editor: We report a case of reversible hyperammonemic encephalopathy induced by valproate in a patient with bipolar disorder whose cognitive abilities remained stable