Successful Treatment of Two Cases of Intention Tremor with Clonazepam

Luis Trelles, MD, PhD, J. O. Trelles, MD, PhD, Conrado Castro, MD, Juan Altamirano, MD, and Max Benzaquen, MD

We recently studied 2 patients with classic cerebellar intention tremor as defined by Marshall [2]; the conditions of both patients were dramatically improved by clonazepam. In both patients improvement has lasted until this writing, but symptoms reappeared when clonazepam was withheld briefly. Tremor in both patients had a frequency of 3 to 5 Hz and invariably accompanied purposeful movement but was not present at rest or while maintaining quiet posture. Tremor was so severe that it confined both patients to bed, and rendered them incapable of feeding or washing themselves. Simultaneous electric recording of agonist and antagonist muscles during tremor showed oscillating activity with a frequency of 3 to 5 Hz. Activities sometimes involved an alternating contraction of agonists and antagonists, while in other activities both groups of muscles contracted simultaneously and synchronously.

A 25-year-old man experienced the insidious onset of sporadic olivopontocerebellar atrophy in June 1981. By June 1983 he was bedridden with intention tremor in all four limbs and a generalized cerebellar syndrome. Computed tomographic scan showed dilatation of the prepontine and mesencephalic cisterns and mild cerebellar and cerebral atrophy. Treatment with clonazepam was started in May 1983. At a daily dose of 8 mg, the tremor disappeared.

Multiple sclerosis began in a 26-year-old man in October 1981. In August 1983, he had intention tremor in both arms, more on the left, cerebellar ataxia in all four limbs, bilateral corticospinal tract signs, and paresis of the left sixth and seventh cranial nerves. Cerebrospinal fluid examination showed 6 lymphocytes per cubic millimeter and 19.1% gamma globulins. Clonazepam was started in September 1983. At a daily dose of 9 mg, tremor disappeared in the right arm. With 15 mg per day only a mild tremor persists in the left arm.

The mechanism by which clonazepam abolished intention tremor is unknown. Possibly it could be through a γ-aminobutyric acid (GABA) liberating action on the dentate nucleus, since therapeutic effects of the benzodiazepines are attributed to a potentiation of GABA across the synapses [1]. There must be more treatment trials, however, before definite conclusions can be drawn.

Department of Neurology
Santo Toribio Neurological Hospital
Lima, Peru

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Amantadine in Essential Tremor

William C. Koller, MD, PhD

Propranolol is the drug of choice in essential tremor, but it is ineffective in some patients and contraindicated in others. Alternate therapy for these patients is lacking. Manyam [9] treated 8 patients with amantadine and using a subjective evaluation found that 5 improved, 2 worsened, and 1 was unchanged, suggesting that this drug be considered for treatment of essential tremor. We gave amantadine (100 mg twice a day) for one month to 6 males (average age, 59.2 years; 4 previously unresponsive to propranolol, 2 with bronchospastic disease) with essential tremor (average duration, 19.6 years). Tremorgrams were recorded with an accelerometer attached to the index finger, with polygraphic recordings from which frequency and the "visual mean" amplitude of tremors were measured. Three patients stated that the drug worsened their tremors. Two patients discontinued therapy after one week, one indicating that his tremor severity doubled and another noting spread of the tremor to his legs. Three patients reported no change. Mean tremor amplitude before treatment was 165 ± 38 (SD) mV, compared with 181 ± 43 mV after amantadine treatment ($n = 5$; $p > 0.05$). There was no change in tremor frequency (6 to 9 Hz). Mechanisms by which amantadine may exacerbate essential tremor are unclear. Amantadine potentiates dopaminergic transmission and has anticholinergic properties. Levodopa and anticholinergics usually do not alter essential tremor, however, although levodopa may occasionally exacerbate the tremors [2]. It appears that amantadine is not a useful alternate drug in the treatment of essential tremor.

Department of Neurology
Loyola University Stritch School of Medicine
2160 S First Ave
Maywood, IL 60153

Reply

Bala V. Manyam, MD

The therapeutic benefits of amantadine seem to be limited to about 60% of patients with essential tremor [6, 9] in unselected populations. It appears that Dr Koller's patients were selected (those unresponsive to propranolol and with bronchospastic disease), and none of the 6 patients responded to amantadine. It is not known if any of them were concurrently receiving β-adrenergic stimulants. As suggested earlier, amantadine is of limited value but should be considered when propranolol is contraindicated or ineffective [9]. Dr Koller's observation that amantadine was of no benefit in patients in whom propranolol was contraindicated or ineffective, even though therapeutically disappointing, is of consid-