In an open-labeled trial, piracetam was effective and safe in reducing myoclonus, both as mono or add-on therapy, in patients with myoclonus.

**Clinical Problem:** A 50 year old male with myoclonus is seen in the neurology clinic. The diagnosis is unknown. The myoclonus is slowly progressive and disabling. He is seeking treatment for it.

**Clinical Question:** What evidence exists for the treatment of myoclonus?

**Search Strategy:** Pubmed search of “myoclonus” and “clinical trials” (limited to adults, English language, and humans) revealed 117 papers. No further papers were identified using SumSearch with “myoclonus” and focus on therapy. Other Pubmed searches with “myoclonus” and “randomized controlled trial”, “metanalysis” or “clinical practice guidelines” did not reveal any further papers.

There were 2 small RCTs of piracetam and one of 5-hydroxy-L-tryptophan (5-HT). One piracetam trial (*J Neurol Neurosurg Psychiatry* 1998;64:344-348) included 20 patients with Unverricht-Lundborg disease from Finland and was not used due to the small size and the fact that a single, rare disorder was studied. The other piracetam trial (*Mov Disord* 1993;8(1):63-38) studied 21 patients with cortical myoclonus only and thus was excluded. The trial of 5-HT included 6 patients and was excluded due to the small size.

The search identified 7 open-label trials of levetiracetam, milacemide, sodium oxybate, and piracetam. The piracetam trial (*Mov Disord* 1996; 11(6):691-700) was chosen for review since it was the largest with 60 patients, included patients with disabling myoclonus of any etiology, and had thorough myoclonus rating scales.

**Clinical Bottom Lines:**

1. In this open-label trial without placebo controls, piracetam lowered all scores of myoclonus, including subjective evaluation (p<0.0001), stimulus sensitivity (p<0.01), resting myoclonus (p<0.001), postural myoclonus (p<0.001), action myoclonus frequency (p<0.0001) and intensity (p<0.0001), global impression of disability (p<0.0001), and video analysis (p<0.0001).

2. Functional disability scores (ADLs, ataxia, and dysarthria) were improved by piracetam (p<0.0001).

3. Piracetam was well tolerated with side effects such as gastric discomfort and diarrhea occurring during the dose-finding period only in 13 (24.5%) of patients. Leukopenia occurred in 3 patients and thrombocytopenia in 1 patient.

4. The clinical significance of piracetam treatment is unknown because this was an open-labeled trial without a placebo group for comparison.

**The Evidence:** An open-labeled study of piracetam (range 9-24g per day) in 60 patients from 1992 to 1994 with disabling myoclonus of any etiology from multiple institutions across Japan. Patients with spinal myoclonus, pregnancy, age<15, and renal failure were excluded. Patients were evaluated with a thorough rating scale, including resting myoclonus (0-32), stimulus-sensitive myoclonus (0-40), postural myoclonus (0-10), action myoclonus frequency (0-32) and intensity (0-32), global
impression of disability (0-4), subjective self assessment (0-4), and video analysis (0-4). Other outcomes included severity of other neurological symptoms such as generalized seizures, gait ataxia and dysarthria (0-4), disability with feeding, eating, dressing, hygiene, and writing (0-20) and psychological state (9 items). Assessments occurred prior to the trial, during the dose finding period, and at the end of the trial/termination of treatment. Scores were compared before and at the end of the trial with the paired t test and the Wilcoxon two-sample sign-rank test.

Electrophysiological studies including EEG, somatosensory evoked potentials, and jerk-locked back averaging were done on each patient to help classify myoclonus as of cortical or subcortical origin (undetermined was the other option).

For safety, physical exam, urinalysis, CBC, electrolytes, glucose and LFTs were assessed before the trial, at the start of maintenance dosage, and at the end of the trial. Intention to treat analysis was used.

**Data:** Myoclonus was classified as cortical in 37 patients (61.7%) or subcortical in 6 (10%). 34(57.6%) patients were categorized as progressive myoclonic epilepsy. 49 patients were on combinations of other anti-myoclonic drugs (clonazepam, valproic acid, primidone, diazepam, phenobarbital, and zonisamide).

In 53 patients, piracetam was effective in lowering all scores of myoclonus, including subjective evaluation, stimulus sensitivity, resting myoclonus, postural myoclonus, action myoclonus frequency and intensity, global impression of disability, and video analysis. Piracetam was also effective in reducing myoclonus in all scores for subgroups with cortical myoclonus (35 patients) or progressive myoclonic epilepsy (34 patients).

Generalized convulsions (p<0.01), gait ataxia (p<0.0001), and dysarthria (p<0.05) were reduced with piracetam treatment. Decreased motivation (p<0.001), sleep disturbance (p<0.01), attention deficit (p<0.05), and depression (p<0.05) were the only improved psychological symptoms.

**Comments:**
1. Although clonazepam and valproic acid are widely used for myoclonus treatment, no randomized clinical trials were identified with these medications.
2. There was no explanation of how patients were enrolled in the study.
3. Seven patients were excluded from the final efficacy analysis if they were too ill for the global assessment of myoclonus or if they had involuntary movements other than myoclonus.
4. The mean myoclonus scores were improved; however there were wide, overlapping standard deviations.
5. For 29 patients with cortical myoclonus, there was no difference in the size of SSEP amplitudes before (17.3+/−12.0uV) and after treatment (14.0+/−7.8uV). Further, 4 patients had larger SSEP amplitudes despite an improved myoclonus score.
6. Piracetam was effective in both patient groups with or without other anti-myoclonus drugs.

**References:**

**Key Words:** myoclonus, treatment, piracetam

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