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Study finds superior drug combo for difficult-to-control epilepsy

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A combination of two common drugs, lamotrigine and valproate, is more effective in treating difficult-to control epilepsy than other anti-epileptic regimens, according to a University of Washington report to be published online this week in *Neurology,* the journal of the American Academy of Neurology.

More than 3 million Americans have epilepsy, and about one million of these have a difficult-to-treat form.

In a large-scale, retrospective study of a population of patients with very difficult-to-control epilepsy, researchers discovered that only the lamotrigine/valproate treatment regimen, out of the 32 drug combinations studied, significantly decreased seizure frequency in this group.

This specific combination reduced seizure frequency by about half, on average, compared to other regimens. Although it rarely produced complete freedom from seizures, the combination was superior to others in reducing the number of convulsive seizures patients experienced.

Dr. Nicholas P. Poolos, a University of Washington associate professor of neurology who practices at the UW Medicine Regional Epilepsy Center in Seattle, led the project team of pharmacists and a neurobiologist.

Poolos explained that most people with epilepsy have good control of

seizures, which means that they have been seizure-free for at least 12 consecutive months. About one third of people with epilepsy are "medically refractory." They continue to have seizures, despite trying several drug combinations prescribed by their physicians.

Physicians have had little evidence to guide them on which drugs or drug combinations, from a multitude of possibilities, might be of most help for patients with difficult-to-treat epilepsy.

This long-standing clinical challenge was the impetus for Poolos and his team to conduct a major study, the first of its size and kind to look retrospectively at patients treated for refractory epilepsy. They went into the project with no assumptions about which regimens to test.

"Identifying any anti-epileptic drug regimen with superior efficacy in patients with refractory epilepsy would be a substantial advance," the researchers believed.

What made this study possible was the discovery of 30 years of epilepsy treatment records at two Washington state institutions for the developmentally disabled. At these institutions, the Fircrest Habilitation Center in Shoreline, Wash., and the Rainier Residential Habilitation Center in Buckley, Wash., nursing staff had been recording the occurrence of each convulsive seizure in their patients with epilepsy, along with records of each patient's dosing of anti-epileptic medications.

The researchers determined that out of 32 most frequently used combinations of anti-epileptic drugs, only the lamotrigine and valproate combination had superior efficacy, compared to an aggregate measure of other drug regimens to which the patients had been exposed, as well as head-to-head comparisons with other anti-epileptic drug combinations. The researchers looked at both older and newer generation drugs.

"The study results dispel the dogma that all drug treatments are equally ineffective for this patient population," Poolos said, "and provide evidence for future, prospective drug trials."

The researchers said that their findings reported this week on the superior efficacy of the combination should ideally be confirmed in a prospective study of patients with refractory epilepsy, preferably from the general population.

The researchers also were surprised to find that while concurrent use of two anti-epileptic drugs was more effective than a single drug alone, three drugs at a time offered no additional benefits. Limiting the combination to two may lessen side effects from taking more kinds of anti-epileptic drugs, without sacrificing efficacy.

Provided by University of Washington