64th Annual Meeting of the American Academy of Neurology (AAN)

New Migraine Guidelines Sort Through Vast Number of Therapies to Grade Evidence of Efficacy

New Orleans - Of the vast number of medications that have been studied in the prevention of migraine, only six have been identified as definitely effective in new guidelines issued jointly by the American Academy of Neurology (AAN) and the American Headache Society (AHS). These included three anticonvulsants, two beta blockers, and one triptan. This is not to say that other medications are not effective, but these were the only agents from a rigorous literature search that had been found effective in at least two multicenter controlled trials.

The three anticonvulsants identified as effective in the newly-released guidelines (Silberstein SD et al. *Neurology* 2012;78:1337-1345) were divalproex sodium, sodium valproate, and topiramate. The beta blockers cited are propranolol and metoprolol. The triptan is frovatriptan. However, these guidelines included long lists of therapies in additional categories, including one for probable efficacy, one for possible efficacy, and one for inadequate or conflicting data. Only one agent, the anticonvulsant lamitrogene, was declared as being ineffective based on two or more multicenter, controlled trials. However, there are trial data to suggest that clomipramine is probably not effective and several agents were listed as possibly ineffective based on small but negative studies.

One of the goals of the rigorous literature review and the development of guidelines is to bolster confidence in the use of preventative strategies, which appear to be underutilized. As migraines for many individuals are debilitating, prevention rather than treatment is often the best strategy, according to Dr. Stephen D. Silberstein, Jefferson Headache Center, Thomas Jefferson University, Philadelphia, PA. He cited data that nearly 40% of patients with recurrent migraines should consider prevention strategies, although it is estimated that only about a third of those who qualify do.

"If patients have attacks that are persistent which are associated with weakness or other neurologic symptoms that can be a risk or a danger, those are candidates for migraine prevention," Dr. Silberstein said. While he suggested that other reasons, including patient preference, might also warrant the use of preventative therapies, he emphasized that these guidelines are not meant to discourage use of medications which are not listed as having proven efficacy. Rather, by grading the evidence, physicians and patients are given a more organized evaluation of the data. "We are talking about how good the evidence is for a drug, not whether or not the drug works," Dr. Silberstein maintained. This is particularly relevant because of the heterogeneous response that may make a drug highly effective for one individual even when it has little benefit in another. In addition, the clinical context is important. Not the least of these is using medications in women of child-bearing age that have not been established as safe during pregnancy. While Dr. Silberstein acknowledged that "there may be many drugs out there that work" other than those listed in the guidelines, these evidence-based guidelines summarize the current state of the migraine literature.

TABLE 1 | Classification of Preventive Therapies for Migraine Based on Quality of Data

Effective >2 multicenter, controlled trials	Probably Effective >2 controlled trials	Possibly Effective 1 controlled trial	Inadequate Data	Ineffective Probably Ineffective Possibly Ineffective
Anticonvulsants Divalproex Valproate Topiramate	**Antidepressants** Amitriptyline Venlafaxine	**Anticonvulsants** Carbamazepine	**Anticonvulsants** Gabapentin	**Anticonvulsants** Lamotrigine
Beta Blockers Metoprolol Propranolol	**Beta Blockers** Atenolol Nadolol	**Beta Blockers** Nebivolol Pindolol	**Antidepressants** Fluvoxamine Fluoxetine	**RAS Inhibitors** Telmisartan
Triptans Frovatriptan	**Triptans** Naratriptan Zolmitriptan	**RAS Inhibitors** Lisinopril Candesartan	**Beta Blockers** Bisoprolol	**Antidepressants** Clomipramine
		Alpha Agonists Clonidine Guanfacine	**Others** Antithrombotics CCBs	**Benzodiazepine** Clonazepam
		Antihistamines Cyproheptadine		

Adapted from Silberstein et al. *Neurology* 2012;78:1337-1345.

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