Lamotrigine or gabapentin was better tolerated than carbamazepine in new-onset geriatric epilepsy

Rowan AJ, Ramsay RE, Collins JF, et al. **New onset geriatric epilepsy: a randomized study of gabapentin, lamotrigine, and carbamazepine.** Neurology. 2005;64:1868-73.

Clinical impact ratings: GIM/FP/GP ★★★★★☆☆ Geriatrics ★★★★★★☆ Neurology ★★★★★★☆

QUESTION

In older patients with newly diagnosed epilepsy, how tolerable and effective are lamotrigine (LTG), gabapentin (GBP), and carbamazepine (CBZ)?

METHODS

Design: Randomized controlled trial.
Allocation: Concealed.*
Blinding: Blinded (clinicians and patients).*
Follow-up period: 12 months.
Setting: 18 Veterans Affairs Medical Centers in the United States.
Patients: 593 patients ≥ 65 years of age (mean age 72 y, 96% men) with newly diagnosed epilepsy (≥ 1 seizure in the preceding 3 mo) who were untreated, treated only acutely (< 4 wk), or treated but at subtherapeutic levels. Exclusion criteria included life expectancy < 12 months, conditions that would affect the response to treatment, progressive neurologic disease, severe psychiatric disorders, current alcoholism, illicit drug use, and a history of noncompliance.
Intervention: LTG titrated at 25 mg/d for 2 weeks, 50 mg/d for 2 weeks, 100 mg/d for 1 week, and then 150 mg/d (n = 200); GBP started at 300 mg/d and then increased by 300 mg/d every 3 days to 1500 mg/d (n = 195); or CBZ titrated by 200 mg every 2 weeks to 600 mg/d (n = 198).
Outcomes: Tolerability and efficacy (retention in the trial) of GBP, LTG, and CBZ at 12 months.
Patient follow-up: 99%.

MAIN RESULTS

Fewer patients terminated therapy early with LTG or GBP than with CBZ (Table). Fewer patients who received LTG stopped therapy for adverse reactions than did patients who received CBZ (12% vs 22%, {relative risk reduction [RRR] 44%, 95% CI 12 to 65}†) or GBP (12% vs 31%, {RRR 61%, CI 41 to 75}†). LTG, GBP, and CBZ groups did not differ for seizure-free rates at 12 months (LTG 51%, GBP 47%, and CBZ 64%; P = 0.09).

CONCLUSION

In older patients with newly diagnosed epilepsy, lamotrigine or gabapentin was better tolerated than carbamazepine.

Source of funding: Department of Veterans Affairs.

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*See Glossary.

†Numbers calculated from data in article.

Lamotrigine (LTG) or gabapentin (GBP) vs carbamazepine (CBZ) for tolerability in geriatric epilepsy at 12 months‡

Outcome	Comparisons	Event rates	RRR (95% CI)	NNT (CI)
Early termination	LTG vs CBZ	44% vs 64%	31% (17 to 43)	5 (4 to 10)
	GBP vs CBZ	51% vs 64%	21% (6 to 34)	8 (5 to 28)

‡Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data at www.neurology.org.

COMMENTARY

Older patients have a high incidence of new-onset epilepsy, which often responds to moderate doses of an appropriate anticonvulsant in monotherapy. However, choosing an appropriate anticonvulsant for older patients can be complicated (1). For example, they often take other medications (an average of 7 co-medications), which makes drug interactions more likely. Furthermore, given their typically reduced hepatic and renal function and baseline neurologic impairments, older patients are especially susceptible to systemic and neurotoxic adverse effects. Rowan and colleagues provided valuable evidence that gabapentin and lamotrigine in monotherapy were effective for new-onset seizures in older patients and were better tolerated than carbamazepine.

Note, however, that while all 3 anticonvulsants seemed equally effective, these patients had seizures relatively infrequently. That is, differences in early termination largely reflect differences in tolerability rather than uncontrolled seizures; Rowan and colleagues did not rule out significant differences in efficacy for less tractable epilepsy.

An earlier randomized controlled trial in the same age group also clearly documented better tolerability for lamotrigine than carbamazepine (2), but use of an extended-release formulation of carbamazepine might improve tolerability (3). Furthermore, compared with the target dose, the incremental doses available for titrating carbamazepine were relatively large—one third that of the target dose—than for either gabapentin (with increments of one fifth the target dose) or lamotrigine (one sixth the target dose). Titration with proportionately larger increments would tend to make a drug seem less well tolerated in this study, because the dose that best balances toxicity and adverse effects might fall between the available increments.

Clearly, the newer anticonvulsants deserve strong consideration as first choices for monotherapy in older patients, but differences in seizure frequency and specific comorbid conditions will continue to influence the choice of anticonvulsants in individual patients.

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