

ANTICONVULSANT DRUG TREATMENT IN THE ELDERLY

Comparative Cognitive Effects of Carbamazepine and Gabapentin in Healthy Senior Adults

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Purpose: This study compared the cognitive effects of carbamazepine (CBZ) and gabapentin (GBP) in healthy senior adults by using a randomized, double-blind crossover design.

Methods: Thirty-four senior adults were randomized to receive one of the two drugs followed by a five-week treatment period. A four-week washout phase preceded initiation of the second drug. Antiepileptic drugs (AEDs) were titrated to target doses of either CBZ (800 mg/day) or GBP (2,400 mg/day). Primary outcome measures were standardized neuropsychological tests of attention/vigilance, psychomotor speed, motor speed, verbal and visual memory, and the Profile of Mood State (POMS), yielding a total of 17 variables. Each subject received cognitive testing at predrug baseline, end of first drug phase, end of second drug phase, and four weeks after completion of the second drug phase.

Results: Fifteen senior adults (mean age, 66.5 years; range, 59–76 years) completed the study. Seniors completing the study did not differ significantly from noncompleting seniors in terms of demographic features or baseline cognitive performances. Fifteen of the 19 seniors not completing the study dropped out while receiving CBZ. Adverse events were frequently reported for both AEDs, although they were more common for CBZ. Mean serum levels for the completers were within midrange clinical doses (CBZ, 6.8 mg/ml; GBP, 7.1 mg/ml). Significant differences between CBZ and GBP were found for only one of 11 cognitive variables, with better attention/vigilance for GBP, although the effect was modest. Performances on the nondrug average were significantly better on 45% of cognitive variables compared with CBZ and 36% compared with GBP. The over-

all pattern of means favored GBP over CBZ on 15 of 17 ($p < 0.001$), nondrug over CBZ on 17 of 17 ($p < 0.0000$), and nondrug over GBP on eight of 17 (NS).

Conclusions: Mild cognitive effects were found for both AEDs compared with the nondrug average condition. The magnitude of difference between the two AEDs across the cognitive variables was modest. Self-reported mood was not significantly affected by either AED. However, overall tolerability and side-effect profile of CBZ were poorer than those of GBP in senior adults at doses and titration rates reported in this study.

COMMENTARY

The cognitive effects of antiepileptic drugs (AEDs) is a controversial topic which is incompletely understood. Effects in the elderly are of particular interest as this group is particularly sensitive to these effects and relatively understudied. Many cognitive studies in patients with epilepsy are difficult to interpret, however, as variables such as seizure improvement may be the actual source of differences. This study has the advantage of using healthy volunteers and a crossover design, eliminating confounding factors of unrecognized seizures and polytherapy and limiting influences of interindividual variability. Doses were reasonable (target 800 mg carbamazepine and 2400 mg/day gabapentin), and treatment was long enough to overcome acute effects although relatively brief (six weeks). It should be remembered that AEDs could have different effects in epilepsy patients independent of seizures, perhaps due to influences on interictal discharges. Nevertheless, this represents a well designed, rigorous study utilizing a number of neuropsychological effects and a reasonable approximation of chronic therapy.

The study has three major points, which are important clinically. First, adverse effects of AEDs are common in the elderly population, particularly with carbamazepine. Seventy three percent of completers reported tiredness with this drug, as opposed to 33% with gabapentin. Many of these effects would likely improve with chronic treatment but probably would not completely resolve. Secondly, gabapentin was favored overall versus carbamazepine in both cognitive and

mood tests. It may be that an extended release carbamazepine would be slightly better tolerated, but given the consistency of results this is likely a clinically significant difference. Finally, both drugs were inferior to the nondrug condition.

Although this study is relatively small, the results support the clinical impression that elderly individuals are more sensi-

tive to the sedative and cognitive effects of AEDs, and that gabapentin may be somewhat better tolerated than carbamazepine at the doses studied.

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