Adverse drug effects in epileptic patients not correlated with number of prescribed medications

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Researchers have found that polytherapy with multiple anti-epileptic drugs (AEDs) did not result in greater adverse effects than monotherapy for patients with refractory epilepsy. This observational study also found AED load was not a factor in causing adverse effects, but suggests that individual susceptibility, type of AEDs used, and physicians' skills determine which patients suffer adverse effects. Results of this study are available today in *Epilepsia*, a journal published by Wiley-Blackwell on behalf of the International League Against Epilepsy.

There are more than 20 different AEDs used to treat epilepsy. However, only about one-half of patients become seizure-free with the first prescribed AED; an additional 20% of patients may find complete relief from seizures through a polytherapy AED regimen. The medical community has extensively debated the value of monotherapy versus polytherapy, not only for relative efficacy in reducing frequency of seizures, but also for impact on health-related quality of life (HRQOL).

Past studies have indicated that polypharmacy treatment provides only modest advantages in controlling seizures, with the added burden of potentially increasing adverse effects. In contrast, other studies suggest AED toxicity may be better correlated with 'drug load' (the sum of ratios between actual prescribed daily doses and the average therapeutic dose of each drug) than with the number of AEDs administered.

In the current study, 809 epileptic patients were enrolled at 11 tertiary referral centers with 709 participants (344 men and 465 women) having localization-related epilepsy. Mean duration of epilepsy in the study group was over 20 years and the median seizure frequency was 2.5 seizures per month. The most common AEDs prescribed for single AED therapy were carbamazepine, oxcarbazepine, or lamotrigine; one-fourth of participants were treated with monotherapy. In the 627 subjects (77.7%) subjects on polytherapy, levetiracetam was the most commonly co-prescribed drug.

Adverse effects were assessed using the Adverse Event Profile (AEP) questionnaire and through unstructured interviews with participants. Nervousness and/or agitation, tiredness, sleepiness, and memory problems were the most commonly reported adverse effects in the AEP questionnaire. At the unstructured interviews, about one-third of participants reported at least one adverse effect, and 13.6% reported two or more adverse effects.

"There was no major difference in frequency of the recorded adverse effects between patients on monotherapy and patients on polytherapy," confirmed Emilio Perucca, M.D., of the University of Pavia and lead author of the SOPHIE (Study of Outcome of PHarmacoresistance In Epilepsy) study. This finding differs from prior studies that suggest poorer HRQOL is associated with polytherapy and improved HRQOL after conversion from multi-AED treatment to monotherapy.

Results also showed that polytherapy patients had higher drug loads than monotherapy patients. However, researchers did not find a correlation between the AED drug load and the number of adverse effects in individual patients. "Our findings suggest that adverse effects can be attributed to individual reaction to the treatment regimen, the type of AED or combination prescribed, and the physicians' skills at treatment," concluded Dr. Perucca. "Further studies of AED therapies and

associated adverse effects are needed to uncover fundamental factors such as gender, mood status, treatment duration, and other co-morbidities that influence HRQOL."

More information: " Relationship between adverse effects of antiepileptic drugs, number of coprescribed drugs, and drug load in a large cohort of consecutive patients with drug-refractory epilepsy." Maria Paola Canevini, et al. Epilepsia; Published Online: April 20, 2010. DOI:10.1111/j.1528-1167.2010.02520.x

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