POLYTHERAPY RARELY PROVIDES BENEFIT IN PATIENTS WHO HAVE NOT RESPONDED TO MONOTHERAPY: YES

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Appropriate pharmacological management of epilepsy can result in seizure freedom for 60–70% of patients, with more than 90% of these being controlled on monotherapy. In Mohanraj and Brodie's series of newly-diagnosed patients followed longitudinally, of the 504 patients responding to treatment, 462 (92%) did so on monotherapy, usually with the first (*n* = 393) or second (*n* = 57) AED. Only 12 patients became seizure free with subsequent monotherapies. Forty patients responded to duotherapy. Combinations of three and four drugs produced seizure freedom in just one patient each. Thus, just 8% of responders (5.4% of total population) were controlled with more than one AED.

On the other hand, there are clear disadvantages to AED polytherapy:

The potential for adverse effects is substantially increased. Although the added efficacy value is often infra-additive, the adverse effects are additive, and therefore the net balance is often unfavorable.

Polytherapy implies a greater potential for drug-drug interactions, both between AEDs themselves and between AEDs and other drugs. Pharmacokinetic interactions may cause failure of one AED (or both) to achieve therapeutic serum levels, or may contribute to the occurrence of dose-related toxicity. Pharmacodynamic interactions may cause side effects such as somnolence and dizziness, which adversely affect quality of life.

Polytherapy is also associated with increased direct costs, increasing the economic burden of epilepsy.

In conclusion, taking into consideration the low likelihood of achieving seizure freedom with polytherapy, the additional side effects, drug interactions and increased costs, one can conclude that polytherapy infrequently provides real benefit to patients who have not responded to sequential monotherapy regimens.