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Title **Clinical Effectiveness, Tolerability, and Cost Effectiveness of Newer Drugs for Epilepsy in Adults: A Systematic Review and Economic Evaluation**

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Aim

To examine the clinical effectiveness, tolerability, and cost effectiveness of gabapentin (GBP), lamotrigine (LTG), levetiracetam (LEV), oxcarbazepine (OXC), tiagabine (TGB), topiramate (TPM), and vigabatrin (VGB) for epilepsy in adults.

Conclusions and results

The included systematic review reported that newer antiepileptic drugs (AEDs) were effective as adjunctive therapy compared to placebo. For newer versus older drugs, data were available for all 3 monotherapy AEDs, although data for OXC and TPM were limited. Sixty-seven RCTs compared adjunctive therapy with placebo, older AEDs, or other newer AEDs. For newer AEDs versus placebo, a trend was observed in favor of newer drugs, and there was evidence of statistically significant differences in proportion of responders favoring newer drugs. However, there was little good-quality evidence from clinical trials to support the use of newer monotherapy or adjunctive therapy AEDs over older drugs, or to support the use of one newer AED in preference to another. In general, data relating to clinical effectiveness, safety, and tolerability failed to demonstrate consistent and statistically significant differences between the drugs. The exception was comparisons between newer adjunctive AEDs and placebo, where significant differences favored newer AEDs. However, trials often had relatively short-term treatment durations and often failed to limit recruitment to either partial or generalized onset seizures, thus limiting the applicability of the data. Newer AEDs, used as monotherapy, may be cost effective in treating patients who have experienced adverse events with older AEDs, who have failed to respond to the older drugs, or where such drugs are contraindicated. The integrated economic analysis also suggested that newer AEDs used as adjunctive therapy may be cost effective compared to the current treatment alone given a QALY of about GBP 20 000.

Methods

Over 36 electronic databases and Internet resources were searched from inception to May/September 2002. Bibliographies of retrieved articles were searched and pharmaceutical company submissions examined for further studies. Two reviewers independently screened all titles and abstracts and decided on the inclusion/exclusion of studies based on fulltext articles. Data were extracted by one reviewer and checked by another. Two reviewers, using specified criteria, independently assessed the quality of included studies. Disagreements were resolved by discussion. Clinical effectiveness, adverse events, and cost effectiveness were assessed in separate analyses. An integrated economic analysis on the costs and effects of newer and older AEDs allowed direct comparisons of long-term costs and benefits.

Further research/reviews required

There is a need for more direct comparisons of AEDs in clinical trials, considering different treatment sequences in monotherapy and adjunctive therapy. Length of followup needs to be considered. Trials are needed that recruit patients with either partial or generalized seizures; that investigate effectiveness and cost effectiveness in patients with generalized onset seizures; and that investigate effectiveness in specific populations of epilepsy patients, and studies evaluating cognitive outcomes to use more stringent testing protocols and a more consistent approach in assessing outcomes. Further research is required to assess the quality of life in trials of epilepsy therapy using preference-based measures of outcomes that generate cost-effectiveness data. Future RCTs should use CONSORT guidelines and observational data to provide information on AEDs in actual practice, including details of treatment sequences and doses.

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