Cost-effectiveness of antiepileptic drugs in migraine prophylaxis
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Three antiepileptic drugs for the prevention of migraine were examined. These were gabapentin (GAB, 2,400 mg/day), topiramate (TOP, 200 mg/day), and divalproex sodium (DIV-Na, 1,000 mg/day). Two alternative formulations, an extended-release version of DIV- Na (1,000 mg/day) and metoprofol (MET, 200 mg/day), were also considered. Different doses per tablet were also considered.

Type of intervention
Primary prevention and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients with 2 to 8 migraines per month.

Setting
The setting was primary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered from studies published between 1997 and 2001. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies.

Outcomes assessed in the review
The outcomes estimated were the efficacy of each medication. The number of headaches per month (before and during treatment), the reduction in headaches per month, the therapeutic gain, and the final efficacy rates were reported.

Study designs and other criteria for inclusion in the review
The literature was reviewed to identify the most recent trials evaluating the study drugs. All the primary studies were double-blind, placebo-controlled clinical trials.

Sources searched to identify primary studies
Not stated.
Criteria used to ensure the validity of primary studies
The validity of the primary studies was ensured by selecting only randomised, double-blind clinical trials.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Five primary studies were included in the review.

Methods of combining primary studies
The primary estimates were not combined since a single study provided the evidence for each drug.

Investigation of differences between primary studies
Not stated.

Results of the review
With GAB, the number of headaches per month was 4.2 before treatment and 2.7 during treatment. The reduction in headaches per month was 1.5, the therapeutic gain was 0.9, and the final efficacy rate was 35.7%.

With TOP, the number of headaches per month was 4.7 before treatment and 3.2 during treatment. The reduction in headaches per month was 1.5, the therapeutic gain was 1.0, and the final efficacy rate was 31.9%.

With DIV-Na, the number of headaches per month was 4.7 before treatment and 2.7 during treatment. The reduction in headaches per month was 2.0, the therapeutic gain was 1.5, and the final efficacy rate was 42.6%.

With extended-release DIV-Na, the number of headaches per month was 4.4 before treatment and 3.2 during treatment. The reduction in headaches per month was 1.2, the therapeutic gain was 0.6, and the final efficacy rate was 27.3%.

With MET, the number of headaches per month was 3.6 before treatment and 1.8 during treatment. The reduction in headaches per month was 1.7 and the final efficacy rate was 48.7%.

Measure of benefits used in the economic analysis
The summary benefit measure used was the number of headaches prevented with each drug. This was derived from the review of the literature.

Direct costs
Discounting was not relevant since the costs were incurred during a short time. The unit costs and the quantities of resources used were not reported separately as only daily doses were reported. The health services included in the economic evaluation were study drugs and sumatriptan (50 mg), which was used as acute care treatment. The cost/resource boundary of the study was unclear. Resource use was estimated from trial data. The costs came from retail pharmacy prices estimated from "drugstore.com". The price year was 2001.

Statistical analysis of costs
The costs were treated deterministically.
Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not conducted.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
Depending on the dose per tablet, the monthly cost was $207 to $302 with GAB, $101 to $293 with TOP, $96 to $101 with DIV-Na, $96 with extended-release DIV-Na, and $14 with MET.

In general, the least expensive prescription of a monthly supply of each antiepileptic drug was the use of higher doses. For example, the monthly cost for GAB was lower when using three tablets of 800 mg than when using 24 tablets of 100 mg.

Synthesis of costs and benefits
The costs and benefits were combined using two approaches, the average cost per headache prevented and the cost-equivalent number (CEN). The CEN was defined as the number of headaches per month at which the cost of preventive medication equalled the cost-savings in acute care treatment realised by using the preventive medication. This appears to have been a type of threshold analysis.

Depending on the dose per tablet, the cost per headache prevented ranged from $138 to $202 with GAB, from $67 to $195 with TOP, from $48 to $50 with DIV-Na, and was $80 with extended-release DIV-Na and $8 with MET.

Depending on the dose per tablet, the CEN ranged from 24.1 to 35.3 with GAB, from 13.7 to 38.2 with TOP, from 9.4 to 9.9 with DIV-Na, and was 14.6 with extended-release DIV-Na and 1.2 with MET.

Authors' conclusions
Prophylaxis with antiepileptic drugs for migraine was not a cost-effective strategy unless the effectiveness of preventive therapy reached at least 50%. Therefore, antiepileptic drugs should not be recommended in patients responding to their acute care medications, in those with a low frequency of migraine, or in patients with co-morbid diseases.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. The three most widely used antiepileptic drugs were selected as basic alternative treatments. Cheaper formulations, in terms of both different dosages and alternative drugs (e.g. MET), were also considered to cover all possible strategies of migraine prevention. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used evidence derived from robust and valid sources since all the primary studies were randomised trials. However, no head-to-head comparison studies were used as the trials were all placebo-controlled. In
fact, each study provided evidence for a single drug. Therefore, the primary estimates were not combined. Average values were derived from each trial. The information on the primary studies was limited. The use of confidence intervals around mean values would have been helpful for addressing the issue of uncertainty around the effectiveness estimates. The primary studies were identified from the literature, but it was unclear whether a systematic review of the literature had been undertaken. The authors noted that the patient population on which the trials were conducted might not reflect the patient population in which the medications should be used in clinical practice. Therefore, caution should be required when interpreting the results of the analysis.

**Validity of estimate of measure of benefit**
The summary benefit measure was specific to the disease considered in the study and was derived directly from the effectiveness analysis. Therefore, it will be difficult to compare it with the benefits of other health care interventions.

**Validity of estimate of costs**
The perspective of the study was somewhat limited as only the drug costs were considered. The resource use data were reported, but the drug costs were not, thus limiting the possibility of replicating the study in other settings. It should be noted, however, that the unit costs could easily be obtained from the source used by the authors. Alternative doses per tables were considered and the costs were calculated for each dosage. The price year was reported, thus facilitating reflation exercises in other settings. However, the costs were treated deterministically and the estimates were specific to the study setting as sensitivity analyses were not conducted. The adoption of a wider perspective, with the subsequent inclusion of other interesting categories of costs, would have been interesting.

**Other issues**
The authors did not make extensive comparisons of their findings with those from other studies. They also did not address the issue of the generalisability of their results to other settings. As all estimates were specific to the study setting and sensitivity analyses were not conducted, the external validity of the analysis is low. The study involved patients suffering at least 2 headaches per month and this was reflected in the conclusions of the analysis. The authors noted that the use of the CEN to assess the cost-effectiveness of migraine prophylaxis ignored some relevant aspects. For example, the inclusion of other relevant direct and indirect costs, and the use of triptans for the concomitant treatment of other disorders.

**Implications of the study**
The authors suggested that future trials should be conducted in patients suffering from at least 10 headaches per month.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
12453029

**Other publications of related interest**


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