A pharmacoeconomic evaluation of intravenous fosphenytoin (Cerebyx) versus intravenous phenytoin (Dilantin) in hospital emergency departments
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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
Intravenous (IV) fosphenytoin (Cerebyx) versus IV phenytoin (Dilantin) in patients needing an IV loading dose of phenytoin for the treatment or prevention of seizures in acute care settings.

Type of intervention

Economic study type
Cost-effectiveness analysis.

Study population
Patients needing an IV loading dose of phenytoin for the treatment or prevention of seizures.

Setting
Hospital. The economic study was carried out in Illinois, the USA.

Dates to which data relate
The effectiveness analysis was based on data extracted from a multicentre clinical study published in 1996. The cost data corresponded to the fiscal year 1994. The prices used were those prevailing in the fiscal year 1994.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was not undertaken on the same patient sample as that used in the effectiveness analysis and was carried out retrospectively.

Study sample
No power calculations were reported. 52 patients were included in the study. Thirty-nine patients were randomly allocated to the intervention (fosphenytoin) group, and 13 patients were allocated to the control (phenytoin) group.

Study design
This was a randomised controlled trial, carried out as a multicentre study. The duration of follow-up was 2 hours post-treatment. Double blinding was used. No loss to follow up was reported.
Analysis of effectiveness
The analysis was based on the 'intention to treat' principle. The primary health outcomes reported were time expended in treatment (length of hospital stay) and the rates of five types of complications viz:

(1) significant neurologic toxicity,
(2) severe IV site reaction requiring a change in the site of administration,
(3) symptomatic decrease in blood pressure (>20 mm Hg systolic),
(4) moderate-to-severe neurologic symptoms without ataxia or vertigo, and
(5) infusion-related adverse event requiring a reduction in the infusion rate.

These categories were defined by the authors and others working on the final study. The groups were shown to be comparable in terms of age, gender, race, body weight, and medical history.

Effectiveness results
The mean administration time was 38.3 minutes for the intervention and 11.5 minutes for the comparator. However, it was assumed that these data did not reflect standard care and the "total time expended for standard care was considered to be similar for both treatment groups". The rates of 'significant neurologic toxicity' complications were 0.0% and 7.69% for the intervention and comparator, respectively. The rate of 'severe IV site reaction...' was 0.0% for the intervention and 15.38% for the comparator. The rates of 'symptomatic decrease in blood...' were 7.69% and 15.38% for the intervention and comparator, respectively. The rates of 'moderate-to-severe neurologic symptoms...' were 0.0% for both strategies. The rates of 'infusion-related adverse event ...' were 10.26% and 23.08% for the intervention and the comparator, respectively.

Clinical conclusions
Not reported.

Modelling
A modified activity-based cost-accounting model was developed and applied in order to estimate costs.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic study, and only separate clinical and health outcomes were reported.

Direct costs
Quantities were not reported separately from the costs but cost items were reported separately. The costs measured were operating costs, (drug acquisition costs, etc.), costs of complications and overhead costs. The perspective adopted in the cost analysis was not explicitly reported. The quantities and costs were based on actual data. The data were collected for the fiscal year 1994.

Indirect Costs
Not included.

Currency
US dollars ($).

**Sensitivity analysis**
Rank order stability analysis (identification of break-even points) was carried out on drug acquisition cost, adverse-event management, cost per minute and time in the emergency department for adverse-event management.

**Estimated benefits used in the economic analysis**
Not applicable.

**Cost results**
The average cost per patient for the intervention was $156.68, and for the comparator was $543.57. The incremental cost for the intervention with respect to the comparator was, therefore, -$386.89. The duration of costs was for 2 hours post-treatment.

**Synthesis of costs and benefits**
The costs and benefits were not combined since a cost minimisation analysis was performed based on the assumption of equal effectiveness for the two strategies involved. The sensitivity analysis revealed that "a significant increase (or decrease, in the case of cost per minute) in the variables tested is required before the total cost of a regimen of fosphenytoin is equivalent to phenytoin".

**Authors' conclusions**
The authors concluded that: "Additional economic studies are needed to evaluate the impact of fosphenytoin on hospital length of stay. In addition, fosphenytoin can be administered intramuscularly and, thus, has the potential of being used by emergency medical services personnel in alternative settings. This potential could possibly result in overall savings to the health care system by reducing the burden on emergency departments. Again, additional studies are needed."

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of comparator is clear. The comparator was reported as consisting of IV phenytoin (Dilantin) infused at a target rate of 50 mg/min. - as for the intervention, this dose could be lowered to a minimum of 10 mg/min. depending on the patient's health status. You, as a database user, should consider whether this is a widely used health technology in your setting.

**Validity of estimate of measure of benefit**
The clinical benefit comparison was apparently based on the time expended in treatment between strategies, which was assumed to be equal for both options. The complication rate would have been a better outcome measure, however as the study used a small sample size the authors preferred to assume equal clinical benefit and carry out a cost minimisation analysis.

**Validity of estimate of costs**
The resource quantities were not reported separately from the prices, however, adequate details of methods of cost estimation were given. The cost data were collected from a different sample of patients from that in the effectiveness analysis. No important cost items appear to have been omitted.

**Other issues**
The issue of generalisability to other settings or countries was not addressed and no appropriate comparisons were made with other studies. The results were not presented selectively.
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