Substitution of immediate-release valproic acid for divalproex sodium for adult psychiatric inpatients

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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
Immediate-release valproic acid and divalproex sodium for adult psychiatric inpatients.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Adult psychiatric inpatients.

Setting
The practice setting was a hospital chronic care ward. The economic analysis appears to have been carried out at the University of Maryland, Baltimore, USA.

Dates to which data relate
Effectiveness and resource data were collected between 1996 and 1997. No price year was given.

Source of effectiveness data
The effectiveness data on the substitution of immediate-release valproic acid for divalproex sodium in the treatment of adult psychiatric inpatients were derived from a single study.

Link between effectiveness and cost data
Costing appears to have been conducted prospectively alongside the effectiveness study sample.

Study sample
47 subjects were included in the study with a mean age of 38.9 years (range: 18 - 73).53% were Caucasian and 43% were African-Americans. 62% were male. Indications for valproic were found for mood disorders (53.2%), behavioural dyscontrol (42.6%) and seizures (14.9%). 98% of patients completed the two-week study. There was a follow-up after 6 months. No power calculations were stated for the determination of the study sample size.

Study design
This was a prospective cohort study. 1 patient failed to complete the study due to the discontinuation of valproic acid.
this was unrelated to the treatment substitution.

**Analysis of effectiveness**
The analysis of the clinical study appears to have been based on treatment completers only of which there was a 98% completion rate. The primary health outcome was patients’ reactions to valproic acid in terms of side-effects (developed checklist), patient responses (i.e. mild, moderate, severe on the Clinical Global Impressions (CGI) scale), and seizure frequency (measured by event occurrence). Morning trough serum evaluations were drawn two weeks after switching.

**Effectiveness results**
No change in seizure occurrence or CGI scores was recorded (mean baseline 4.44). 4 indicates moderate severity whereas 5 indicates marked severity. The mean CGI change score was 4.02 and 4.08 at one and two weeks, respectively. 10.6% of subjects had gastrointestinal complaints during the study compared with 31.9% in the period prior to the study initiation. 80% of these complaints were of mild to moderate in severity. At 6 months 53.2% of study subjects had been discharged and 40.4% remained on valproic acid treatment. For these hospitalised patients the mean baseline CGI severity score was 4.76 and at 6 months this fell to 4.41, (p=0.055).

**Clinical conclusions**
Many chronic psychiatric inpatients stabilised on divalproex may be safely moved to valproic acid.

**Measure of benefits used in the economic analysis**
Benefits were measured in terms of primary outcome improvements such as CGI scores.

**Direct costs**
No price dates were specified. The hospital medication costs of valproic acid and divalproex were computed. No other cost information was recorded.

**Statistical analysis of costs**
Not performed.

**Currency**
US dollars ($).

**Sensitivity analysis**
Not performed.

**Estimated benefits used in the economic analysis**
See effectiveness results above.

**Cost results**
The total intervention costs for both medications were not reported but it was stated that valproic acid was $905 cheaper than the comparator per annum.

**Synthesis of costs and benefits**
Not performed.
Authors' conclusions
The preliminary outcome and costing results suggest that many chronic psychiatric inpatients stabilised on divalproex may be safely moved to valproic acid.

CRD COMMENTARY - Selection of comparators
The selection of comparators, divalproex and valproic acid, was justified. However, no direct comparison of 2 concurrent subject groups receiving either treatment was carried out, only one assessing the effectiveness or otherwise of valproic acid. In addition there was no (blinded) randomisation in subject selection, which, as the authors stated, may have introduced (selection) bias into the analysis.

Validity of estimate of measure of benefit
The only benefits expressed in the study were primary health outcomes which negatively affects the overall validity of the benefit results.

Validity of estimate of costs
Mal (treatment) costings were provided with no price years or sources. The costs of increased or reduced staff time were not computed.

Other issues
Over calculations were stated. The authors acknowledged that the CGI scale may not have been sensitive enough to detect the range of clinical changes that may have occurred. No inter-rater reliability was performed (although the same raters followed individual patients throughout). It was also conceded that the sample size was probably too small.

Implications of the study
The authors recommend future studies be undertaken with larger sample sizes and with a fuller assessment of whether such findings can be applied to other settings such as outpatient care.

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