Pregabalin and gabapentin in matched patients with peripheral neuropathic pain in routine medical practice in a primary care setting: findings from a cost-consequences analysis in a nested case-control study

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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.

CRD summary
The objective was to assess the costs and benefits of pregabalin and gabapentin, for the treatment of adults with peripheral neuropathic pain, in routine medical practice. The authors concluded that pregabalin seemed to reduce the mean weekly intensity of pain more than gabapentin, with no significant difference in costs. The reporting and methods were satisfactory. The authors' conclusion appears to be appropriate, but highly uncertain.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to assess the costs and benefits of pregabalin and gabapentin, for the treatment of adults with refractory peripheral neuropathic pain, in routine medical practice.

Interventions
The intervention was gabapentin at a mean dose of 1,263mg daily, compared with pregabalin at a mean dose of 202mg daily.

Location/setting
Spain/primary care.

Methods
Analytical approach:
An ad-hoc analysis of data from two multicentre, 12-week, observational, prospective studies performed between 2005 and 2006 was undertaken. The costs and outcomes were compared by matching 44 patients treated with gabapentin, to 88 patients treated with pregabalin, on key characteristics and clinical variables. The authors did not explicitly state the perspective.

Effectiveness data:
A ratio of two patients on pregabalin to one patient on gabapentin was used for the post-hoc analysis. The effectiveness measures included pain intensity, anxiety and depression, disability, sleep, and self-perceived health. Pain intensity was measured using the Spanish version of the Short-Form McGill Pain Questionnaire (SF-MPQ) visual analogue scale (VAS), and treatment response was defined as a 50% reduction in VAS score. No pain or mild pain was defined as less than 40mm on the VAS. Other measures were the Hospital Anxiety and Depression Scale (HADS), the Sheehan Disability Scale (SDS), the Medical Outcomes Study (MOS) Sleep Scale, and the EQ-5D VAS. Measures were taken at the first visit and at 12-week follow-up, and patients completed weekly diaries on pain intensity and EQ-5D VAS scores.

Monetary benefit and utility valuations:
Quality-adjusted life-years (QALYs) gained, over 12 weeks, were calculated using the patient-reported weekly EQ-5D VAS scores.

Measure of benefit:
Health benefits were measured by the increase in the number of responders, the change in SF-MPQ VAS, HADS, MOS Sleep Scale, and SDS scores, and the QALYs gained.

Cost data:
Both direct health care costs and indirect costs were included. The direct costs included drugs, nonpharmacologic treatments, medical visits, hospitalisations, and complementary tests. The resource use was from the first study visit, the 12-month follow-up, and patient medical records. This was valued using the Spanish Pharmaceutical Drug Catalogue, reference prices, or the Soikos health care cost database. Patients were interviewed to assess the impact of pain on their productivity and attendance at work. The human capital method was used to determine the cost of a lost workday equivalent, using wages from the National Institute of Statistics. The costs were reported in 2006 Euros (EUR) and inflated, where necessary.

Analysis of uncertainty:
Variability in the results was presented as standard deviations for both the cost and effect outcomes.

Results
Patients on gabapentin had a 42.6% (SD 27.1) reduction in SF-MPQ VAS score, and 53% (SD 40.5) of patients responded. Patients on pregabalin had a 54.6% (SD 27.2) reduction in SF-MPQ VAS score, and 17% (SD 60.9) of patients responded.

With pregabalin, significantly greater reductions in pain intensity were observed, than with gabapentin (p<0.05). Most other measures indicated that both drugs produced statistically significant improvements, compared with baseline, but non-significant differences between the drugs. In the gabapentin group 0.30 QALYs (SD 0.34) were gained, compared with 0.33 QALYs (SD 0.39) in the pregabalin group (p=0.652).

Both drugs increased their costs, compared with baseline, but they reduced other costs, which reduced the total costs. The total costs reduced by EUR 1,384 (SD 2,874) with gabapentin, and EUR 1,254 (SD 1,479) with pregabalin (p=0.593).

Authors' conclusions
The authors concluded that pregabalin seemed to reduce the mean weekly intensity of pain more than gabapentin, with no significant difference in costs.

CRD commentary
Interventions:
The intervention and comparator were clearly reported. The two drugs were considered to be the first choices of anticonvulsant treatment for peripheral neuropathic pain, implying that they were the usual care. There were other anticonvulsants, and other forms of treatment, such as opiates, that were used in practice. It is likely that the analysis did not include all the relevant options.

Effectiveness/benefits:
The key details of the two trial designs and patient baseline characteristics were reported. The two trials were identical, except for the conditions that induced neuropathic pain: one focused on pain secondary to diabetic neuropathy, postherpetic neuralgia, or trigeminal neuralgia, whereas the other focused on pain secondary to radiculopathy at axial rotation. A ratio of 2:1 was used to identify the sample rather than a power calculation, so it was not clear that the analysis was powered to detect significant differences in all of the outcomes. The patients were matched and the limitations of this process, despite appropriate methods, were highlighted. The effect and benefit outcomes were clearly reported.

Costs:
The costs were clearly reported and were appropriate for a societal perspective (productivity costs were included). The sources used to cost the resource use were appropriate for the population, and were specific to Spain. The method used to derive the productivity costs was clearly reported and appropriate. The costs appear to have been very uncertain (large standard deviations), which the authors indicated was a result of the small sample. The reporting was clear and comprehensive.
Analysis and results:
Results of the analysis were clearly reported. The authors justified the short time horizon, stating that 12 weeks was routine practice when treating this type of condition, and was in line with regulatory body recommendations. They acknowledged the limitations of the observational designs and small samples. They tried to control for potential confounding variables, using matching techniques and regression analysis, but selection bias could not be eliminated. The small sample meant that the study could not detect potentially relevant differences, created large standard deviations, and limited the generalisability of the results. The authors stated that there were no prospective head-to-head trials of the clinical differences between gabapentin and pregabalin, and the results in the literature were contradictory. This supports the uncertainty in the effectiveness and costs of the two drugs.

Concluding remarks:
The study reporting and methods were satisfactory. The authors’ conclusion appears to be appropriate, but highly uncertain.

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