Cost effectiveness analysis of dopamine agonists in the treatment of Parkinson's disease in Japan

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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
The study examined dopamine agonists for the treatment of Parkinson's disease. Dopamine agonists such as bromocriptine or pergolide added to levodopa were compared with levodopa alone.

Type of intervention
Treatment.

Economic study type
Cost utility analysis.

Study population
The study population comprised hypothetical 60 year old men with Parkinson's disease in Hoehn Yahr (HY) Stages 2 to 5 who were taking levodopa.

Setting
It was unclear whether the setting was primary, secondary or tertiary care. The economic study was conducted in Japan.

Dates to which data relate
A literature search covering the period 1966 to December 1999 was undertaken. The effectiveness data appear to have been taken from studies published between 1983 and 1995. The resource use data were derived from studies published between 1996 and 1999. The price year was 1998.

Source of effectiveness data
The effectiveness data were drawn from published studies.

Modelling
A Markov model was used to simulate the course of Parkinson's disease, and to compare the cost-effectiveness of dopamine agonists added to levodopa versus levodopa alone, in Japan. The model assumed that 60 year old men with Parkinson's disease in HY Stages 2 to 5, who were using levodopa, were administered dopamine agonists or continued on levodopa alone. The time horizon was 10 years.

Outcomes assessed in the review
The outcomes assessed were the rate of improving the HY stage by one stage for dopamine agonists and levodopa, and utility by HY stage.
Study designs and other criteria for inclusion in the review
For information on the dosage of dopamine agonists, Japanese domestic studies were included. For information on the benefits of co-therapy with dopamine agonists and levodopa, studies on 20 or more patients who reported improvement in HY stage were reviewed.

Sources searched to identify primary studies
MEDLINE was searched from 1966 to December 1999 for primary information. The keywords used included "Parkinson's disease", "randomised controlled trial", "bromocriptine" or "pergolide", and "Japan". Secondary information was obtained from a database of the Japanese literature and manual searches without restrictions to randomised controlled trials.

Criteria used to ensure the validity of primary studies
Not stated.

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

Number of primary studies included
Not stated.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
The initial therapeutic effect, expressed as the rate of improving the HY stage by one for treatment with bromocriptine was:

0.214 (range: 0.1 0.329) for HY Stage 2;
0.321 (range: 0.15 0.493) for HY Stage 3;
0.429 (range: 0.2 0.657) for HY Stage 4; and
0.536 (range: 0.25 0.821) for HY Stage 5.

The initial therapeutic effect, expressed as the rate of improving the HY stage by one for treatment with pergolide, was:

0.357 (range: 0.229 0.443) for HY Stage 2;
0.536 (range: 0.343 0.729) for HY Stage 3;
0.714 (range: 0.457 0.971) for HY Stage 4; and
0.893 (range: 0.571 1) for HY Stage 5.

Bromocriptine and pergolide improved the average HY stage of patients compared with treatment with levodopa alone,
Pergolide resulted in significantly more patients experiencing improvements in comparison with bromocriptine, although the difference in average HY stage after treatment between bromocriptine and pergolide did not reach statistical significance.

The utility in each HY stage decreased along with the progression of the disease, from:

- 0.719 in HY Stage 0,
- 0.708 in HY Stage 1,
- 0.678 in HY Stage 2,
- 0.622 in HY Stage 3,
- 0.547 in HY Stage 4,
- 0.451 in HY Stage 5.

A range of +/- 0.07 was assumed for each utility by HY stage.

**Measure of benefits used in the economic analysis**
The summary measure of benefit used was the quality adjusted life-years (QALYs). A total of 1,200 patients with Parkinson's disease in Japan were randomly selected and sent a questionnaire. The questionnaire asked about their personal characteristics, health status and utility by means of a visual analogue scale and the time trade off method.

**Direct costs**
The direct costs included the costs of drugs, hospitalisation and long-term care at home. Other costs (e.g. visiting physicians at the outpatient clinic, transportation, or house alterations) were assumed to be similar, irrespective of treatment, and were not taken into consideration. The costs were discounted at a rate of 5% per annum. The price year was 1998.

**Statistical analysis of costs**
No statistical analysis of the costs was undertaken.

**Indirect Costs**
The indirect costs arising from the inability of the patient to work were not considered.

**Currency**
Japanese yen (Y). These were converted to US dollars ($) at 1998 values.

**Sensitivity analysis**
A one dimensional sensitivity analysis was conducted to investigate variability in the data for key variables, such as the rate of progression, utility and the costs. The ranges of variables used in the sensitivity analysis were the 95% confidence intervals for progression rate and utility, and +/- 25% for the costs. The effects of gender, age at the start of treatment, and duration of treatment were also examined in the sensitivity analysis.

**Estimated benefits used in the economic analysis**
For HY Stage 2 patients, the benefit from treatment was 4.618 QALYs with levodopa, 4.697 QALYs with levodopa-bromocriptine and 4.750 QALYs with levodopa-pergolide.
For HY Stage 3 patients, the benefit from treatment was 4.150 QALYs with levodopa, 4.300 QALYs with levodopa-
bromocriptine and 4.401 QALYs with levodopa-pergolide.

For HY Stage 4 patients, the benefit from treatment was 3.681 QALYs with levodopa, 3.883 QALYs with levodopa-
bromocriptine and 4.016 QALYs with levodopa-pergolide.

For HY Stage 5 patients, the benefit from treatment was 3.373 QALYs with levodopa, 3.538 QALYs with levodopa-
bromocriptine and 3.648 QALYs with levodopa-pergolide.

Cost results
For HY Stage 2 patients, the cost of treatment was $98,800 with levodopa, $112,400 with levodopa-bromocriptine and
$122,400 with levodopa-pergolide.

For HY Stage 3 patients, the cost of treatment was $188,300 with levodopa, $184,300 with levodopa-bromocriptine and
$183,000 with levodopa-pergolide.

For HY Stage 4 patients, the cost of treatment was $266,700 with levodopa, $257,100 with levodopa-bromocriptine and
$251,600 with levodopa-pergolide.

For HY Stage 5 patients, the cost of treatment was $312,900 with levodopa, $312,100 with levodopa-bromocriptine and
$312,600 with levodopa-pergolide.

Synthesis of costs and benefits
Incremental cost effectiveness ratios were calculated to combine the costs and benefits of the treatments.

For HY Stage 2 patients, the incremental cost-effectiveness ratio was $172,300/QALY for levodopa-bromocriptine
over levodopa alone, and $178,900/QALY for levodopa-pergolide over levodopa alone.

In HY Stages 3 to 5, co-therapy with bromocriptine or pergolide was less costly and more effective than levodopa alone,
making it dominant.

In HY Stage 3, the cost-effectiveness of co-therapy with dopamine agonists was better over the wide range of variables.
Cost-effectiveness declined when bromocriptine or pergolide was marginally effective: the incremental cost-
effectiveness was approximately $160,000/QALY for bromocriptine and approximately $71,000/QALY for pergolide.
A similar trend was observed in the sensitivity analysis for HY Stages 4 or 5.

The cost and effectiveness of bromocriptine and pergolide had a great influence on cost-effectiveness within the range
of variables studied. In particular, the use of generic bromocriptine exerted the strongest influence on cost-
effectiveness. Other factors (including gender, age at start of treatment, duration of treatment, annual rate of
progression, cost of hospitalisation, and care according to HY stage and utility) had no appreciable effect on the cost-
effectiveness.

Authors' conclusions
Dopamine agonists would appear to be cost-effective in advanced Parkinson's disease, although their use is sensitive to
the costs and effectiveness of dopamine agonists. If factors discouraging the prescription of generic drugs in Japan were
removed, the treatment of Parkinson's disease would become more cost-effective.

CRD COMMENTARY - Selection of comparators
The comparator used was justified on the grounds that it represented the main treatment for Parkinson's disease in
Japan.
Validity of estimate of measure of effectiveness
The effectiveness evidence used in the study was taken from the literature. However, the methods and conduct of the review were not reported. No information on the primary studies was provided. The authors also made some simplified assumptions on the model parameters, and many of them do not appear to have been validated.

Validity of measure of benefit
The summary benefit measure (i.e. the QALY) was appropriate as it detected the impact of the treatment on quality of life. Utility was discounted, which was appropriate because the time horizon was 10 years.

Validity of estimate of costs
Although the authors reported explicitly that a societal perspective was adopted, no indirect costs were included. The unit costs and resource use were not reported separately. The costs were discounted at a rate of 5% per annum. The price year was reported.

Other issues
The issue of the generalisability of the results to other settings was addressed. The authors reported several limitations of the study. More specifically, their simplified assumptions on HY severity classification, the constant yearly rate of progression of HY stage, and the constant effectiveness of dopamine agonists over 10 years. In addition, adverse reactions associated with drug therapy were not considered.

Implications of the study
The authors suggested that the lower cost-effectiveness of dopamine agonists in HY Stage 2 should not discourage the use of dopamine agonists in selected patients. The generic form of bromocriptine proved to be dominant in comparison with levodopa alone, even in HY Stage 2. Thus, if similar effectiveness is guaranteed, the use of generic drugs should be strongly recommended. The authors recommended that, in Japan, factors discouraging the use of generic drugs should be removed to control rising health care costs.

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Other publications of related interest


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Subject indexing assigned by NLM

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