Analisis coste-efectividad de olanzapina frente a haloperidol en el tratamiento de la esquizofrenia en España [Cost effectiveness analysis of olanzapine versus haloperidol in the treatment of schizophrenia in Spain]

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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 use of olanzapine, a new drug for the treatment of patients with schizophrenia. Olanzapine has a pharmacologic profile similar to clozapine, the efficacy of which has been demonstrated in reducing both the positive (for example, delirium and hallucinations) and negative (for example, lack of motivation and social isolation) symptoms of schizophrenia, and reducing the incidence of extrapyramidal symptoms (EPS).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who experienced multiple episodes of acute schizophrenia. Patients who had only a single episode were excluded, as were those who were treatment-resistant.

Setting
The setting of the study was unclear, but appears to have been that of the community. The economic study was conducted in Spain.

Dates to which data relate
The effectiveness data were derived from studies published between 1990 and 1997. The quantities of resource use were derived from studies published in 1995 and 1996. The price year was 1995.

Source of effectiveness data
The effectiveness evidence was derived from published studies and from experts' opinions.

Modelling
A decision analytic model based on Markov cycles was constructed to simulate the natural history and medical treatment of the disease. The cycle length was equal to 3 months. The time horizon of the model was 5 years. Each patient starting the process had the same chance of receiving one of the two drug treatments.

Outcomes assessed in the review
The health outcomes used as inputs in the model were the suicide and attempted suicide rates, the renouncing rate, the
relapse rate, and the rate of EPS. Other health outcomes were the scores obtained with haloperidol and olanzapine, measured according to different scales. The scales used included the Brief Psychiatric Rating Scale (BPRS), the positive and negative syndrome scale (PANSS), the Montgomery-Asberg depression rating scale (MADRAS), and Clinical Global Impression (CGI).

**Study designs and other criteria for inclusion in the review**
One of the main sources of the effectiveness evidence was an international, multi-centre, randomised, double-blind, parallel clinical trial. This used the intention to treat principle and included 1,996 schizophrenic patients.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

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

**Number of primary studies included**
The effectiveness data were obtained from three primary studies.

**Methods of combining primary studies**
The primary studies were not combined since each was used to estimate different variables.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
In a 3-month interval, the suicide rates were 0.2% with both drug therapies during the first cycle. The corresponding attempted suicide rates were 2.0%. During cycles 2 to 20, the suicide rates were 0.2% for both haloperidol and olanzapine. However, the attempted suicide rate was 2.0% with haloperidol but only 1% with olanzapine.

In a 3-month interval, the renouncing rates with haloperidol were and 49.2% during cycle 1, 17.0% during cycle 2, 8.4% during cycle 3, and 8.6% during cycle 4. The corresponding rates with olanzapine were 27.2% during cycle 1, 12.3% during cycle 2, 6.7% during cycle 3, and 5.1% during cycle 4.

The relapse rates with haloperidol were 7% during cycle 1, 27.8% during the first year, and 3.29% for each cycle from the second to the fifth years. The corresponding rates with olanzapine were 4.4% during cycle 1, 19.2% during the first year, and 2.35% for each cycle from the second to the fifth years.

The rates of EPS were 45% with haloperidol and 19% with olanzapine in each cycle.

Haloperidol scored 8 on the BPRS while olanzapine scored 11, (p<0.05).

Haloperidol scored 13 on the PANSS while olanzapine scored 18, (p=0.051).

Haloperidol scored 4 on the PANSS for positive symptoms only while olanzapine scored 5, (p=0.056).
Haloperidol scored 3 on the PANSS for negative symptoms only while olanzapine scored 5, (p<0.05).

Haloperidol scored 3 on the MADRAS while olanzapine scored 6, (p<0.05).

Haloperidol scored 1 on the CGI while olanzapine scored 2, (p<0.05).

**Methods used to derive estimates of effectiveness**
The results of a study on schizophrenia and an expert panel were used to overcome the lack of data in the decision model relating to the rates of attempted suicide. Also, to make assumptions concerning the medical treatment of the patients. The international panel consisted of 12 experts (psychiatrists and health economists) from 9 countries including Spain.

**Estimates of effectiveness and key assumptions**
The attempted suicide rates reported in the effectiveness results were estimated using assumptions made by the experts. All data relating to resource consumption were derived from the panel estimates.

**Measure of benefits used in the economic analysis**
The primary benefit measure used in the economic analysis was the partial or total recovery. This was defined as the number of months during which the patient reached a BPRS score of less than 18. Since the time horizon of the study was 5 years, the maximum possible value of the benefit measure was 60. This was obtained from the decision model. A 6% discount rate was used for benefits incurred in the future. A secondary benefit measure was the percentage of patients without relapse.

**Direct costs**
A 6% discount rate was used because the time horizon of the study was 5 years. The quantities of resource use and the unit costs were reported. The cost/resource boundary appears to have been that of the community. The cost items included in the analysis were for the first and second psychiatric visits, the day cost for acute general hospital, group therapy, partial and outpatient treatment, laboratory tests, treatment of EPS, attempted suicide, and drug acquisition. The costs were estimated from data published in 1995 and 1996, relating to the Spanish setting. The resources were estimated from the expert panel. The price year was 1995.

**Statistical analysis of costs**
Statistical analyses of costs were not conducted.

**Indirect Costs**
The indirect costs were not included.

**Currency**
Spanish pesetas (Pta).

**Sensitivity analysis**
Since the data were generally estimated from different sources, sensitivity analyses were conducted to assess the robustness of the study's results to variations in the model inputs. The model inputs investigated were the discount rate (0%), the length and cost of hospitalisation, the cost of suicide, use of the outpatient care programme, and the duration of partial or total recovery with olanzapine.
Estimated benefits used in the economic analysis
Partial or total recovery was 30.7 months with haloperidol and 37.4 months with olanzapine, giving a difference of 6.7 months. The proportion of patients without relapse was 32.2% with olanzapine and 19% with haloperidol.

Cost results
The total costs of the treatments were Pta 4,143,135 for haloperidol and Pta 4,360,861 for olanzapine. The cost-saving associated with haloperidol was Pta 217,726.

Synthesis of costs and benefits
Average and incremental cost-effectiveness analyses were performed. The average per-patient cost, per month of partial or total recovery, was Pta 134,726 for haloperidol and Pta 116,476 for olanzapine.

The incremental cost per month of partial or total recovery for olanzapine over haloperidol was Pta 32,516.

When the percentage of patients without relapse was considered as the benefit measure, the average cost-effectiveness ratio was Pta 135,078 for olanzapine and Pta 219,801 for haloperidol. The incremental cost per month of partial or total recovery for olanzapine over haloperidol was Pta 14,043.

The results of the analysis were quite robust to the variations performed in the sensitivity analyses.

Authors’ conclusions
Compared with haloperidol, olanzapine was a cost-effective treatment for Spanish schizophrenic patients.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparator. Haloperidol was selected for two reasons. First, it was the most common drug therapy used in Spain for schizophrenic patients. Second, it was also the comparator used in many of the primary studies from which the effectiveness evidence was obtained. In addition, data relating to other drug therapies were not available from prospective studies. You should assess whether this represents a commonly used therapy in your own setting.

Validity of estimate of measure of effectiveness
The authors noted that the effectiveness analysis was conducted by mixing data from several sources. However, the main source was a large, international, randomised, double-blind clinical trial, which should, to some extent, ensure the internal validity of the study. Further, several sensitivity analyses were conducted and conservative scenarios were adopted for olanzapine.

Validity of estimate of measure of benefit
The benefit measure was obtained from a decision model, which appears to have been appropriate for simulating the medical treatment of the disease.

Validity of estimate of costs
The perspective of the study was unclear. The unit costs and the quantities of resources used were reported separately. Statistical analyses of the costs were not conducted. The estimated costs appear to have been fairly specific to the study setting.

Other issues
The issue of the generalisability of the study results was not specifically addressed. However, several sensitivity analyses
were conducted. The findings of the study were not compared with those from other studies, because no similar analyses had been carried out in Spain.

**Implications of the study**
The authors suggest that further research should be conducted considering other drug therapies, once the effectiveness data become available.

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