A cost-effectiveness analysis of the orphan drug cysteamine in the treatment of infantile cystinosis

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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 a drug, cysteamine, to prevent the accumulation of cystine in both muscle and liver, in patients previously diagnosed with cystinosis.

Type of intervention
Secondary prevention; Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Hypothetical cohort of children with cystinosis for whom renal failure would be delayed by five years by using cysteamine.

Setting
Hospital. The economic analysis was conducted in San Diego, California, USA.

Dates to which data relate
Effectiveness data were collected from literature published between 1983 and 1993. Resource data were collected from literature published between 1990 and 1991, as well from data collected by the authors in 1992. The base price year used in the analysis was not stated, although drug cost data were based on current charges at the authors’ hospital at the time the manuscript was being prepared.

Source of effectiveness data
Effectiveness data were derived from a review of the literature.

Modelling
A decision tree analysis model was used to synthesise data identified on expected lifetime patient outcomes and associated costs for treating renal failure. There were two arms in the decision tree: patients treated with or without cysteamine. The difference in subsequent time to renal failure as a result of initial treatment, was the only difference in the model, all ensuing treatment options, dialysis, transplant, second renal failure and further treatment were identical in the two treatment arms. Individuals were assumed to undergo a maximum of two renal transplants only. In the base case scenario cysteamine treatment was received up until initial renal failure only.

Outcomes assessed in the review
The review assessed initial renal survival time in patients with cystinosis who received, or did not receive, cysteamine therapy were identified. Pre-operative waiting mortality rates and operative mortality rates during renal transplantation; graft and maintenance dialysis survival rates were also used.

Study designs and other criteria for inclusion in the review
Not stated.

Sources searched to identify primary studies
Not stated.

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
Three published primary studies were used to estimate initial renal survival time. One of these was a 1982 observational study in which patients with cystinosis never received cysteamine. The other two more recent studies examined the impact of cysteamine on renal function in children with cystinosis. European registry data were used to identify mortality during the waiting period for transplant, and operative mortality rates associated with renal transplantation. Data from a 1990 publication of the US Renal Data Systems were used to approximate graft and maintenance survival times.

Methods of combining primary studies
Not combined.

Investigation of differences between primary studies
Not stated.

Results of the review
Life tables were constructed using data from the 1982 study. It was estimated that there was a 50% renal survival time of 15 years for patients treated with cysteamine compared with 9.5 years for patients who did not receive cysteamine. The mortality rate for patients awaiting transplant was estimated to be 0% and the operative mortality rate during transplantation was reported to be 5%. The time to graft failure with renal transplant was estimated to be 7 years and time to death on maintenance therapy was estimated to be 15 years.

Measure of benefits used in the economic analysis
The measure of benefit used was life years gained.

Direct costs
It is not clear whether costs were determined separately from quantities of resources used. Drug treatment costs were based on current charges at the authors' institution. These included costs of therapy, cystine level measurements, outpatient visits and blood chemistry panels. It is not clear whether hospital charges were converted to costs. Renal transplantation and maintenance dialysis costs were taken from Medicare cost data. The base price year used was not
stated. Costs were discounted at a rate of 5% per annum and costs were estimated from the perspective of a third party insurer. The time spent waiting on maintenance therapy for renal transplantation was taken from a published study in the literature.

**Indirect Costs**
No indirect costs were included.

**Currency**
US dollars ($).

**Sensitivity analysis**
A threshold analysis was conducted to identify the level of drug costs at which lifetime treatment costs were greater than those for patients who did not receive cysteamine therapy. There is uncertainty over the possible commercial price of cysteamine. The additional delay before renal failure due to cysteamine was also varied between high and low levels, ranging from 10 years to 1 year.

**Estimated benefits used in the economic analysis**
In the base case scenario patients treated with cysteamine gained an additional 5 years of life compared with those who did not receive treatment.

**Cost results**
Lifetime treatment costs for patients were estimated to be $234,000 in the cysteamine group and $238,000 in the non-treatment group.

**Synthesis of costs and benefits**
Costs and benefits were not combined since the intervention was the dominant strategy.

**Authors’ conclusions**
Cysteamine delays the need for expensive renal transplantation and dialysis for patients, increasing life expectancy whilst reducing overall costs. Quality of life considerations associated with the use of cysteamine have not been considered, although the authors believed that quality of life may also be improved. The drug may also prevent the development of additional problems of organ and nervous system deterioration, which may advocate its continued use in patients following renal transplantation.

**CRD COMMENTARY - Selection of comparators**
The choice of comparator (no treatment) was implicitly justified as this appears to be the only alternative therapy option currently in use for patients with cystinosis.

**Validity of estimate of measure of benefit**
Effectiveness data were obtained from a review of published studies. The authors did not state that a systematic review of the literature had been undertaken, and data were not combined in the analysis. However, in the case of effectiveness data for patients who received no treatment, only one study was available. No differences between the two studies that examined the use of cysteamine were reported, and it is unclear how these two estimates of time until renal failure were combined. Estimates of effectiveness were based on the time until renal failure. This choice of estimate was justified.
Validity of estimate of costs
The authors reported that costs were estimated from a societal perspective, however costs appear actually to have been estimated from the perspective of a third party payer. Costs associated with providing additional care for children and with lost productivity could be significant and may be worth including in future analyses. It is unclear whether resources and costs were estimated separately as only information on costs is reported in the paper. Costs were obtained from published sources and from charges at the authors’ institution. It is unclear, however, whether charges were converted to costs or were used to proxy costs. No date was provided for the price years used in the analysis. Sensitivity analysis was used to vary the costs of therapy administration and costs were discounted at a rate of 5% per annum. It is unclear whether benefits were also discounted, and it would be helpful to clarify this in any future analysis.

Other issues
The authors did not make any comparisons of their findings with those from other studies; this was to be expected given the lack of previous economic analyses of the therapy and disease as well as limited access to long term data. However the authors did cite another study which suggested that patients treated with cysteamine for more than 10 years showed no signs of developing renal failure, indicating that the effectiveness assumptions in the model may be conservative. The issue of generalisability of the results of the analysis to other settings was not addressed. The results of the study were not reported selectively and the scope of the conclusions reflected the scope of the analysis. The authors acknowledged that their study did not consider quality of life issues, although they contend that these are likely to be positive. They did report adverse effects such as nausea associated with taking cysteamine.

Implications of the study
Further clinical and economic analyses are required to consider the impact of taking cysteamine following renal transplantation and also to determine whether there is any additional health related benefits such as a reduction in additional organ and nervous system deterioration. Quality of life associated with the intervention should also be elicited. Economic analyses in other settings and from other perspectives should also be conducted further to test the conclusions of this study.

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