Electron microscopic examination of skin biopsy as a cost-effective tool in the diagnosis of lysosomal storage diseases

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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
Using electron microscopic evaluation of skin biopsies versus multiple lysosomal enzyme assays in cases of lysosomal storage disease.

Type of intervention
Screening and diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with lysosomal storage disorders.

Setting
Hospital. The economic study was carried out in Boston, Massachusetts, USA.

Dates to which data relate
The effectiveness data were from the period 1986-1995. The dates related to resource use and cost data were not reported.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing for the comparator was obtained from separate sources. The cost of the intervention was, apparently, a standard charge from the institution hosting the study. It was not stated whether the costing was performed prospectively or retrospectively.

Study sample
No power calculations were carried out to determine the sample size. The electron group consisted of a total of 100 proven cases representing more than 35 different lysosomal storage diseases. The cases included in the study constituted only 5 to 10% of all the skin biopsies submitted. The effectiveness study lacked a control group.

Study design
The study was a case series, carried out mainly in a single centre (with some biopsies being performed in other institutions).

**Analysis of effectiveness**
The analysis was based on treatment completers only (this was a sub-sample from a group of patients known to have, or suspected of having, lysosomal storage disorders and undergoing evaluation using ultrastructural examination of skin biopsies). The outcomes used were sensitivity and false negative rates. The proof of lysosomal storage disorders was obtained biochemically.

**Effectiveness results**
Electron microscopic evaluation of skin biopsies was not able to show storage material in two cases of biochemically confirmed storage disease. There were three cases of positive results not confirmed by a standard battery of enzyme assays.

**Clinical conclusions**
Electron microscopic evaluation of skin biopsies provided an effective screening tool for more than 35 lysosomal storage disorders. No summary benefit measure was identified in the economic analysis and only separate clinical outcomes were reported.

**Direct costs**
Quantities were reported in the detailed description of the protocol. The costs measured (per procedure) were operating costs (procedural and processing costs). The boundary adopted was the hospital. The source of quantities was based on the institution’s protocol whereas costs were based on standard prices. For the comparator, the costs from three separate regional referral laboratories were obtained. The study data collection took place from 1986 to 1995 and there was no report of change of protocol during the period. The price data was not dated.

**Indirect Costs**
Not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was performed.

**Estimated benefits used in the economic analysis**
Not applicable.

**Cost results**
The total cost per skin biopsy was $680. The total costs of WBC/serum/plasma assay per beta-galactosidase, beta-hexosaminidase and glucosylceramide beta-glucosidase were $140 (range: $105 - 175), $120 (range: $70 - 175) and $140 (range: $105 - 175), respectively. The cost of fibroblast assay per procedure for each of the enzyme assays mentioned was $275.

**Synthesis of costs and benefits**
No formal synthesis was performed but the authors claimed that, in spite of being more expensive, skin biopsies were more cost-effective since they allowed screening for 35 different diseases simultaneously, whereas the individual enzyme assays generally permitted the assessment of only one disease.

**Authors' conclusions**
"Ultrastructure examination of skin biopsy is a quick and relatively inexpensive method to screen for lysosomal storage disease. It is the only method to confirm the diagnosis of neuronal ceroid lipofuscinosis and mucolipidosis IV and for the identification of new phenotypic variants of known and unknown lysosomal storage disorders. Furthermore, morphologic characterisation of the type of cell affected, their surrounding matrix and the ultrastructural appearance of stored material improves our understanding of the pathogenesis of these disorders. In addition, it reduces the cost of diagnosis by decreasing the number of enzyme assays needed to establish a specific diagnosis."

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator is clear.

**Validity of estimate of measure of benefit**
The internal validity of the effectiveness results may be weakened by the lack of randomisation and a proper control group.

**Validity of estimate of costs**
Insufficient details were provided of the methods of cost estimation.

**Other issues**
Given the lack of randomisation, sensitivity analysis, and statistical analysis, the results need to be treated with some caution. The issue of generalisability to other settings or countries was not addressed.

**Implications of the study**
The authors argue that "In the future, the skin biopsy may prove a useful tool for monitoring novel therapies in lysosomal storage disorders."

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
8807420

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Biopsy /economics; Child; Cost-Benefit Analysis; Humans; Immunoenzyme Techniques /economics; Lysosomal Storage Diseases /economics /genetics /pathology; Microscopy, Electron /economics; Skin /pathology

**AccessionNumber**
21996000746

**Date bibliographic record published**
31/07/1999

**Date abstract record published**

31/07/1999