Replacement of routine liver biopsy by procollagen III aminopeptide for monitoring patients with psoriasis receiving long-term methotrexate: a multicentre audit and health economic analysis

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 serum procollagen III aminopeptide (PIIINP) measurement for the monitoring of patients receiving long-term methotrexate for psoriasis was examined.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with psoriasis who were receiving long-term methotrexate.

Setting
The setting was secondary care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness and resource use data were gathered from 1985 to 1990 for the historical control group, and from June 1998 to May 2000 for the other groups. The prices were estimated using 2000/2001 values.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively for the historic control, and prospectively for the other groups, on the same sample of patients as that used in the clinical study.

Study sample
Power calculations were not reported. The following patient groups were considered:

PIIINP intervention group 1 (Manchester), which included patients seen in clinics in Greater Manchester and managed according to the Manchester protocol;

PIIINP intervention group 2 (London), which included patients from the St. John's Institute of Dermatology (London)
managed according to the Manchester protocol with the exception that they were also recommended to have a baseline pre-treatment or early liver biopsy;

liver biopsy control groups 1 (Dublin) and 2 (Essex), which included patients from Dublin (Ireland) and from Basildon and Chelmsford (Essex), managed by serial liver biopsy as recommended in the AAD guidelines;

liver biopsy control group 3 (historical controls), which included patients managed in Manchester between 1985 and 1990 according to the AAD guidelines who served as a historical control group.

The mean age was 38.3 years (range: 28 - 82) in the PIIINP intervention group 1, 35.6 years (range: 32 - 69) in the PIIINP intervention group 2, 44.6 years (range: 25 - 72) in the liver biopsy control group 1, and 42.4 years (range: 20 - 76) in the liver biopsy control group 2. The mean duration of psoriasis ranged from 24 years for control group 2 to 26.8 years for control group 1. The mean duration of methotrexate therapy ranged from 66.3 months for intervention group 2 to 87.9 months for control group 2.

**Study design**

This was a prospective cohort study with historical controls that was carried out at several centres in the UK. The length of follow-up was not reported. It would appear that no patient was loss to the follow-up assessment.

**Analysis of effectiveness**

All of the patients included in the initial study sample appear to have been included in the analysis of the clinical study. The outcome measures used were the number of liver biopsies performed in each group and the biopsy rate per patient per year. An audit of Manchester guidelines for PIIINP during the period 1996 - 2004 was also undertaken to assess the validity of the new protocol. Patient preferences for PIIINP and biopsy were also examined in the PIIINP intervention group 1 and liver biopsy control group 2 using a questionnaire. The baseline comparability of the study groups was not discussed.

**Effectiveness results**

The number of liver biopsies performed was 10 in the PIIINP intervention group 1, 1 in the PIIINP intervention group 2, 21 in the liver biopsy control group 1, 26 in the liver biopsy control group 2, and 39 in the historical control group.

The biopsy rate per patient per year was 0.04 in the PIIINP intervention group 1, 0.02 in the PIIINP intervention group 2, 0.26 in the liver biopsy control group 1, 0.30 in the liver biopsy control group 2, and 0.34 in the historical control group.

Abnormalities of sufficient severity to influence management were identified in one in 5 patients subjected to liver biopsy in the PIIINP intervention group 1, compared with one in 16 in the control groups.

Ninety-five per cent of patients in the PIIINP intervention group 1 stated that they would prefer serum PIIINP measurement, 2% preferred liver biopsy and 3% did not express a preference. Only 3 of the 32 patients contacted in the liver biopsy control group 2 stated that they would prefer serological monitoring with PIIINP to liver biopsy.

The audit of patient charts revealed that changing the threshold for PIIINP would have reduced the number of false positives, but at the expense of possibly increasing the risk of failing to detect significant liver damage.

**Clinical conclusions**

The effectiveness analysis showed that fewer liver biopsies were required among patients managed using serological monitoring with PIIINP, without evidence that important liver toxicity was missed. Further, patients preferred serological monitoring with PIIINP to liver biopsy.

**Measure of benefits used in the economic analysis**

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The health outcomes were left disaggregated and no summary benefit measure was used in the economic analysis. In effect, a cost-consequences analysis was carried out.

**Direct costs**

The economic evaluation was carried out from the perspective of the health care system (i.e. the NHS). The categories of costs included in the analysis were liver biopsy and serum PIIINP test. The items associated with liver biopsy were overnight stay, ultrasound-guided biopsy, and histopathology. Resource use was estimated using patient-level data that were derived from the sample of patients included in the effectiveness study. It was assumed that the PIIINP assay was performed according to the guidelines, that is, four times per year. The costs came from NHS references prices. Several unit costs for biopsy were used, as such estimates varied depending on the medical centre. The unit costs were presented separately from the quantities of resources used. Discounting was not relevant since the costs per patient were incurred during a short timeframe. The costs were evaluated using 2000/2001 prices.

**Statistical analysis of costs**

The costs were treated deterministically.

**Indirect Costs**

The indirect costs were not included in the economic evaluation.

**Currency**

UK pounds sterling (£). The exchange rate at 31 May 2000 between pounds sterling and Euros (Euro) was 1 = Euro 1.61.

**Sensitivity analysis**

Sensitivity analyses were not carried out.

**Estimated benefits used in the economic analysis**

See the 'Effectiveness Results' section.

**Cost results**

The authors calculated the costs of switching from AAD guidelines to the new Manchester guidelines.

Using the costs of liver biopsy at the Essex hospitals (270), then the annual cost per patient of monitoring for hepatic fibrosis using PIIINP and selective liver biopsy would be 100.80, compared with 75.60 for following AAD guidelines using liver biopsy alone.

If Manchester costing were applied (577), then the annual cost of monitoring each patient using Manchester guidelines would be 113.08, compared with 161.56 for using liver biopsy alone. This would represent an annual cost-saving of 48.48 per patient monitored.

A change to the cheaper option of day-case liver biopsy would reduce the financial gains to be achieved from using Manchester rather than AAD guidelines for monitoring patients for hepatic fibrosis.

**Synthesis of costs and benefits**

A synthesis of the costs and benefits was not relevant since a cost-consequences analysis was performed.

**Authors' conclusions**
Patients managed by the Manchester protocol using serial procollagen III aminopeptide (PIIINP) measurement and selective liver biopsy were subjected to 7-fold fewer liver biopsies without evidence that important liver toxicity was missed in the process. Significant savings to the health care budget were also observed.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparators, which was appropriate to the study question. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a cohort study that was carried out at several centres across the UK. The baseline comparability of the study groups was not discussed and details on patient follow-up were not reported. Further, owing to the design of the analysis, the impact of selection bias and confounding factors might not have been excluded. Differences in treatment patterns between study centres were not investigated. Since the patients were identified at different medical centres, the study sample might have been representative of the patient population. Power calculations were not reported and there was no evidence that the sample size was appropriate. No statistical analyses were performed to address the issue of comparability among the study groups, or the significance of differences in the effectiveness results. These issues tend to limit the validity of the effectiveness estimates.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The inclusion of costs was consistent with the perspective selected for the analysis. The unit costs were reported, and alternative sources of data were used to reflect variability within the NHS. Reference prices, which represent a typical NHS source of costs, were used. Resource use reflected treatment patterns suggested in the two guidelines under examination. The unit costs and the quantities of resources used were presented separately, thus allowing the cost analysis to be replicated in other settings. The cost estimates were treated deterministically. The price year was reported, which aids reflation exercises in other time periods.

Other issues
The authors reported the results of other published studies but did not make extensive comparisons of their findings with those from such analyses. The issue of the generalisability of the study results to other settings was not explicitly addressed and sensitivity analyses were not performed. This reduces the external validity of the study. The analysis referred to patients with psoriasis receiving methotrexate and this was reflected in the authors’ conclusions.

Implications of the study
The authors stated that the complete abandonment of AAD guidelines cannot be recommended, although they suggested that liver biopsies should be restricted to patients with repeatedly abnormal PIIINP levels.

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Bibliographic details