Protein A immunoadsorption column versus splenectomy in the treatment of steroid-resistant immune thrombocytopenic purpura

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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
New treatment for immune thrombocytopenic purpura (ITP): the protein A immunoadsorption column (the column).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
A hypothetical cohort of 30-year-old women with chronic ITP who had failed corticosteroid treatment.

Setting
Hospital. The economic study was carried out in the USA.

Dates to which data relate
The main effectiveness data were taken from sources dated 1958-1993. Some resource use data were taken from 1991 sources, whilst most of the remaining data were derived from the experience of practising physicians. Costs were expressed in 1993 prices.

Source of effectiveness data
Effectiveness data were derived from previously completed studies and opinions.

Modelling
A decision-analytic approach with Markov processes for each of the four strategies considered in the study was used to estimate the corresponding costs and benefits. This was due to the lack of studies directly comparing the two main health technologies under scrutiny.

Outcomes assessed in the review
The review assessed the overall estimated response rate to treatment with the column and with splenectomy, and probability of death from use of the column and splenectomy. Bleeding rates in the ITP state were also estimated.

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
For the response rate estimates, the estimate for the column was based on two studies, whilst the rate for splenectomy was based on 4 studies. The estimate of the probability of death was based on 2 studies and a Delphi panel of 5 haematologists, for the column, and on one (review) study, for splenectomy. Bleeding rates were based on 2, 1 and 2 studies, respectively, for serious, temporary and no bleeding.

Methods of combining primary studies
Average values from those found in the literature.

Investigation of differences between primary studies
Not stated even though it would have been applicable.

Results of the review
The overall response rate to treatment with the column was estimated to be 36% (range: 34 - 42) and the overall response rate to splenectomy was estimated to be 64% (range: 50 - 92). The probability of death from the use of the column was 0.01% (range: 0.01 - 1.94). These same values were used for the corresponding figures for splenectomy. It was also estimated that 2% of ITP patients bleed seriously, 41% bleed on a temporary basis, and 57% do not bleed.

Methods used to derive estimates of effectiveness
Assumptions based on experts' opinion were used to derive the frequency and timing of the occurrence of complications, relapses, and differential response rates and relapses in patients with a previously observed treatment failure.

Estimates of effectiveness and key assumptions
The following assumptions were made:

(1) postoperative complications occurred within 1 year after primary splenectomy;

(2) the rate of relapse was highest in the first year after treatment for ITP, with a lower, constant rate in subsequent years;

(3) the rate of relapse from remission was the same regardless of the previous treatment;

(4) the rate of spontaneous remission was the same in patients who had failed to respond to either of the treatments but was lower for those who had failed both treatments; the rate of response to splenectomy was lower in patients who had failed previous treatment with the column, and vice versa.
Measure of benefits used in the economic analysis
Quality-adjusted life years (QALYs) gained was the measure of benefits used in the analysis and incorporated utility values from the literature and from the opinion of the Delphi panel which provided effectiveness and resource use data for the study.

Direct costs
Unit charges were used as proxies for costs in this analysis. Costs were discounted over a 10 year period. Few quantities were reported separately from the costs. The quantity/cost boundary adopted was the hospital. Resource use data were mainly derived from average responses of a Delphi panel of five haematologists practising at University hospitals in different geographic regions in the USA. The remaining data were taken from the California Office of Statewide Health Planning and Development(OSHPD) database of all hospital discharges in 1991. Government publications dated 1991 and the 1993 Medicare Physician Fee Schedule provided some unit cost (charge) data and, when necessary, data were reflated using the medical component of the CPI so that costs were expressed in 1993 prices. Total costs were calculated using a model.

Currency
US dollars ($).

Sensitivity analysis
The main costs variables were investigated using a one-way simple sensitivity analysis and best-worst case scenarios, as were the baseline probabilities and utilities.

Estimated benefits used in the economic analysis
In the base-case the sequential treatment with the column first, followed by splenectomy if necessary was estimated to produce 0.03 QALYs (11 quality-adjusted days) more than performing splenectomy first followed by the column if needed (7.22 versus 7.19 QALYs). The 'column alone' strategy was associated with 7.00 QALYs, whilst the 'splenectomy alone' option yielded 7.19 QALYs. All the above figures were discounted at a 5% annual rate.

Cost results
The column-first strategy cost $1,036 less than the splenectomy-first strategy: $59,815 (range: $36,154 - 64,094) versus $60,851 (range: $25,449 - 70,766)). The corresponding total cost figures for the 'column alone' and 'splenectomy alone' options were $33,421 (range: $24,455 - 34,520) and $60,899 (range: $26,620 - 70,618), respectively. All the figures above were discounted at a 5% annual discount rate.

Synthesis of costs and benefits
Costs and benefits were not combined since the base case showed the column first strategy to be dominant over all strategies except 'column alone' which was disregarded after being observed to be less effective (producing lower QALYs than all the other strategies). However, it seems that an incremental analysis comparing 'column followed by splenectomy' with 'column alone' would be relevant to the study question. Sensitivity analyses showed that a response rate of 34% or more (the lowest reported in the literature) for 'column' treatment with the column first was dominant over splenectomy first. On the other hand, a response rate of 69% or more rendered the former strategy dominated. The threshold cost for initial (one-time) splenectomy costs was $23,835, below which ('splenectomy first') it was a less costly option although a less effective one than 'column first'. Other parameter variations (e.g. discount rate and utilities) did not affect the qualitative results in general.

Authors' conclusions
The preferred strategy in terms of both QALYs and cost was sequential treatment with the column, followed by splenectomy if necessary. This was a robust result over all parameters under uncertainty.
CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used.

Validity of estimate of measure of benefit
Adequate details about the source of QALY data were not given. In particular, it is questionable whether the range of values included true patient preferences. Incomplete information was provided on the methodology used in the literature search and review. Nevertheless, as the authors noted there was a lack of evidence of effectiveness data (long term safety and efficacy) for 'the column', further evidence seems necessary to obtain a clear, valid result on the benefits associated with such an intervention.

Validity of estimate of costs
Few data on resource use quantities were reported in the study.

Other issues
Appropriate comparisons were made with other studies and the issue of generalisability to other countries was addressed. The 'column alone' option appears to have been disregarded based on a purely effectiveness criterion. Incremental analysis of the 'column first' relative to the 'column alone' would appear to be appropriate to the issue of defining the most efficient use of scarce resources in the treatment of steroid-resistant immune thrombocytopenic purpura.

Implications of the study
Further research evidence is needed in order to reduce the high level of uncertainty in the data which formed the basis of the economic model reviewed above.

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