Analysis of the use of digoxin immune fab for the treatment of non-life-threatening digoxin toxicity

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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
This study evaluated the use of digoxin immune Fab (FAB) in the treatment of patients with non-life-threatening digoxin toxicity. The use of FAB was compared to standard therapy. Standard therapy consisted of supportive care aimed at correcting electrolyte abnormalities, treating arrhythmias and correcting any precipitating causes of digoxin toxicity such as acute renal failure, drug-drug interactions, and excessive dosage.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised hypothetical patients with non-life-threatening digoxin toxicity with serum digoxin concentration of 3.8 ng/ml, creatinine clearance of 30 ml/min and lean body weight of 70 kg. Patients were over 18 years old.

Setting
The setting was modelled around tertiary care. The economic study was conducted in a hospital in Chicago, USA.

Dates to which data relate
The effectiveness evidence was based on studies published in 1990 and 1991. Resource use and cost data were from 1991, but were adjusted to 1997 costs.

Source of effectiveness data
Effectiveness estimates were based on a review of the literature.

Modelling
A decision-analytic model was constructed to estimate the average cost of the treatment strategy of using FAB versus standard therapy.

Outcomes assessed in the review
The outcomes assessed were complete response, partial response and no response to the immune Fab. Furthermore, complications associated with the digoxin immune Fab were incorporated in the model.
Study designs and other criteria for inclusion in the review
Not reported.

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
Two studies provided data on the effectiveness of the digoxin immune Fab.

Methods of combining primary studies
It is not clear how the results from the primary studies were combined.

Investigation of differences between primary studies
The authors did not discuss any details of previous clinical studies or the differences between them.

Results of the review
Complete response to immune FAB was estimated at 69% (range: 58 - 80), partial response was 19% (range: 10 - 28) and no response was 12% (range: 10 - 14).

A total of 9% of patients were estimated to experience complications from the immune Fab. Of these, 22% were for hypokalemia, 4% for hypersensitivity, 17% for loss of inotropic support, and 13% for recrudescent digoxin toxicity.

Methods used to derive estimates of effectiveness
The authors also made estimates/assumptions about effectiveness.

Estimates of effectiveness and key assumptions
The authors assumed that all patients would survive the episode of digoxin toxicity without sequelae.

Measure of benefits used in the economic analysis
No summary measure of health benefits was used in this cost-consequences analysis, although length of stay was a primary end point used in the economic analysis and as a proxy for health benefits.

Direct costs
The analysis was conducted from the perspective of the health care service (hospital only). Therefore, only inpatient medical care costs were included. Costs included daily hospital bed costs, ancillary services such as electrocardiogram and blood tests, acquisition costs of the drug and costs of the complications associated with FAB. The resource use quantities were modelled. The resource use was costed using hospital accountancy data, hospital charges, drug acquisition costs from producer, and costs of complications were derived from DRG costs.
Statistical analysis of costs
A statistical comparison of cost differences was not carried out.

Indirect Costs
Indirect costs were not included in this analysis.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was conducted to explore which values had most impact on the cost estimates. In this analysis, the authors varied serum digoxin concentration, creatinine clearance, and body weight across a range of plausible values reported in the two trials that were used as the basis for the effect estimate. Furthermore, length of stay, drug costs and daily hospital costs were also varied in one-way and multi-way sensitivity analyses.

Estimated benefits used in the economic analysis
The authors stated that the use of FAB was associated with a decrease in length of stay by 1.5 days compared to standard therapy, as length of stay was on average 1.5 days for patients using FAB and 3.0 days for patients not receiving FAB.

Cost results
The overall total costs associated with the use of FAB were $54 more than the total cost of standard therapy ($2,784 versus $2,730). The costs associated with the use of FAB ranged from $2,324 in patients who responded completely and did not suffer complications to $7,416 in patients responding partially to FAB but who also suffered congestive heart failure. Monte-Carlo simulation indicated an incremental increase in costs of $303 (standard deviation $1,242), and that the use of FAB would reduce the costs in 37% of the cases, but would reduce the length of stay in 72% of the cases. Variation in body weight, acquisition costs of FAB, and the probability of complete response to FAB resulted in minor changes in total costs. The estimates were sensitive to the assumption about length of stay in patients given FAB, serum digoxin concentration, and creatinine clearance.

Synthesis of costs and benefits
Costs and benefits were not combined in this cost-consequences analysis.

Authors' conclusions
Based on this study, the authors concluded that the use of FAB in patients with non-life-threatening digoxin toxicity can be a cost saving alternative to not using FAB.

CRD COMMENTARY - Selection of comparators
The authors stated that FAB is rarely used in routine treatment of non-life-threatening digoxin toxicity. Therefore, the use of FAB seems an appropriate comparator to standard practice in this evaluation.

Validity of estimate of measure of effectiveness
The measure of effectiveness was based on response rates from clinical trials. The authors did not state whether these were identified in a comprehensive literature review, and it is difficult to assess whether evidence was presented selectively. Furthermore, the authors provided no information about these trials with which to inform a judgement of
the validity of the estimates. Sensitivity analyses, to assess variability in the estimates, were undertaken, which may compensate for limitations in the validity of the effectiveness results.

**Validity of estimate of measure of benefit**
Not applicable.

**Validity of estimate of costs**
The scope of the study was somewhat limited, including, as it did, only costs incurred at the institution in which patients were treated. The authors did not report resource use or unit costs in a disaggregated fashion, and it is therefore difficult to assess how resource consumption was estimated, and the validity of these estimates. A good range of sensitivity analyses was, however, performed on the cost data.

**Other issues**
The authors made appropriate comparisons with other studies. The authors did not explicitly address the issue of generalisability. However, the study was based on resource use estimates from one institution in the USA, and lack of transparency of costing methodology makes extrapolation of the results to other settings difficult. The authors pointed out that the frequency of events might differ between patients with severe toxicity and those assessed in the model (mild-to-moderate toxicity). Additionally, the response to FAB may differ according to toxicity levels.

**Implications of the study**
Although not approved by the American Food and Drug Administration, the authors suggest that FAB is underused in patients with non-life-threatening digoxin toxicity. However a prospective study is needed to confirm these findings.

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None given.

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