Declining value of alanine aminotransferase in screening of blood donors to prevent post-transfusion hepatitis B and C virus infection


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
Alanine aminotransferase (ALT) screening of blood donors.

Type of intervention
Screening and secondary prevention.

Economic study type
Cost-utility analysis.

Study population
Blood donors (with normal, slightly elevated or highly elevated ALT) who made two or more donations over a 3-year period and patients undergoing transfusion with units of blood tested according to different protocols (ALT testing only, anti-HCV EIA-2 (second generation enzyme-linked immunoassay), or both tests).

Setting
Primary care. The economic study was carried out in the USA.

Dates to which data relate
The data for the effectiveness analysis were collected for the most part between 1 January 1991 and 31 December 1993. The remainder of the data were obtained from studies published in 1993-1995. The data for the resource use and costs were based mainly on studies published in 1993 and 1994. 1994 prices were used.

Source of effectiveness data
Effectiveness data were derived from a single study combined with a review of previously completed studies.

Link between effectiveness and cost data
Costing was not undertaken on the same patient sample as that used in the effectiveness analysis and appears to have been carried out retrospectively.

Study sample
Power calculations were not used to determine the sample size. A total of 2,962,229 units of allogeneic blood were gathered during the three-year study period of which 2,318,356 were given by 586,507 multiple-time donors. There were 1,731,849 intervals for evaluation of seroconversion rates. The relative frequency of the three ALT groups (normal, slightly elevated, and highly elevated) in the total REDS database of allogeneic donations were 98.4%, 1.4%, and 0.2%, respectively.
Study design
This was a retrospective cohort study using the database of the National Heart, Lung, and Blood Institute Retrovirus Epidemiology Donor Study (REDS), and involving blood centres in five separate geographical regions of the USA. The duration of the follow-up corresponded to a set of intervals produced for each donor on the basis of consecutive pairs of donation dates and test results for a period of three years. Loss to follow-up was not reported.

Analysis of effectiveness
The principle (intention to treat or treatment completers only) used in the analysis of effectiveness was not explicitly specified.

The following data were collected:
- incidence of HbsAg (hepatitis B surface antigen) and anti-HBc (hepatitis B core antigen);
- HCV incidence in EIA-1-screened and EIA-2 screened donors (incidence rates = seroconversion to marker positivity per 100,000 person-years);
- positive predictive value of ALT in detection of HBV- and HCV-infected donations before and after anti-HCV screening.

Effectiveness results
The incidence of HbsAg was 4.12 (95% CI: 2.8 - 5.6) for the normal group and 0% (95% CI: 0 - 34.1) for the slightly elevated group, with a total rate of 4.07 (95% CI: 2.8 - 5.6). The corresponding rates for anti-HBc were 522 (95% CI: 506 - 538) and 514 (95% CI: 374 - 675), with a total rate of 522 (95% CI: 506 - 537). HCV incidence in EIA-1-screened donors was 69.9 (95% CI: 59.5 - 81.2) for the normal group and 606.3 (95% CI: 352.3 - 928.7) for the slightly elevated group, with a total rate of 76.5 (95% CI: 65.6 - 88.2). The corresponding values for the EIA-1-screened donors were 4.3 (95% CI: 2.4 - 6.9) and 63.0 (95% CI: 5.9 - 180.5), with a total rate of 4.9 (95% CI: 2.8 - 7.6). The ALT screening resulted in no value for early detection of HBV infection in donors.

The positive predictive values of ALT screening for the identification of HCV-infected donors was:
- no anti-HCV screening, 6.98%;
- donors screened as nonreactive after anti-HCV EIA-1, 0.785%; and
- donors screened as nonreactive after anti-HCV EIA-2, 0.082%

Clinical conclusions
The present study documents a marked decline in the yield of ALT as a screening test for post-transfusion hepatitis and in the detection of HIV-infected flood donations in particular.

Modelling
A decision tree model was used to estimate costs and benefits.

Outcomes assessed in the review
The review assessed the duration of the HCV seroconversion window period, mean survival after transfusion (with discounting) for all patients, and excess mortality rate for patients with chronic post-transfusion hepatitis.

Study designs and other criteria for inclusion in the review
Two cases series including a total of 34 well-documented cases of post-transfusion HBV and HCV were identified and were used to determine the duration of ALT elevation prior to HBV and HCV seroconversion. The designs of other studies included in the review were 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**
The methods used to judge relevance and validity were not reported. The data were extracted by means of summary statistics.

**Number of primary studies included**
A total of 6 primary studies (including two cases series) were included.

**Methods of combining primary studies**
The primary studies were not combined; results were extracted and combined within the model used in the final analysis.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The outcome values adopted from the literature were as follows:

- duration of the HCV seroconversion window period, 81.9 days (0.2242 years);
- mean survival after transfusion (with discounting) for all patients, 10.7 years;
- excess mortality rate in patients with chronic post-transfusion hepatitis, 0.35% per year.

**Measure of benefits used in the economic analysis**
The measures of benefit were HCV cases detected (per million units), and the corresponding quality-adjusted life-years (QALYs) saved by each strategy. A decision tree was used to deal with uncertainty in the outcomes. The QALY measures were obtained from a previously completed study and were adjusted for morbidity results.

**Direct costs**
The costs were discounted. The quantity measures were not reported separately from the prices. The costs measured were testing costs (costs of testing which covered the costs for notification of deferred donors, recruitment of replacement donors, publicity on testing decisions, and defence of associated litigation) and costs of treating patients with transfusion-related hepatitis and its complications. The costs of treating post-transfusion hepatitis during a lifetime were obtained from studies published in 1993 and 1994. The sources of costs of testing data were not reported. 1994 prices were used.
Indirect Costs
Not considered.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was carried out using total testing-related costs ($0-10 range (per unit)), transmission probabilities, projected longevity, and others (not reported). A one-way simple sensitivity analysis was used.

Estimated benefits used in the economic analysis
Transmission probabilities were:

- 0.00448 (1/223) for the strategy of no testing;
- 0.00278 (1/359) for the strategy of testing for ALT alone;
- 0.0000125 (1/80,257) for the strategy of testing for anti-HCV EIA-2 alone;
- 0.0000097 (1/103,306) for the strategy of testing for both ALT and anti-HCV EIA-2.

The probability of an infection leading to clinical disease was estimated to be 0.5%. 1,698 HCV cases were detected per million units for ALT alone, 4,470 for anti-HCV (EIA-2) alone, 2,775 for anti-HCV in addition to ALT and 2.8 for ALT in addition to anti-HCV (EIA-2). The QALY outcome measure results were not reported. A 5% discount rate was used to discount benefits.

Cost results
A 5% discount rate was used. The total incremental cost of ALT testing was $2.50 per unit. The costs of public relations and legal cost of a decision not to test were $0.25 per unit and the total incremental costs of anti-HCV testing compared to the costs of ALT testing were $2.50. The total costs associated with each strategy were not reported.

Synthesis of costs and benefits
The cost per QALY saved was used as a cost-utility measure to combine costs and benefits. The ALT-alone strategy resulted in -$91,800 cost (saving) per QALY saved, whereas the anti-HCV (EIA-2)-alone strategy had a cost of -$94,400 (saving) per QALY saved. The anti-HCV in addition to ALT strategy had a cost of -$87,900 (saving) per QALY saved and the ALT after anti-HCV (EIA-2) figure was $7,931,000. The results were reported as most sensitive to the probability of disease transmission, with the cost-utility ratio of ALT remaining above $100,000 per QALY for parameter values nine times greater than the estimates obtained in the study.

Authors' conclusions
The authors concluded that the study "analysis shows a dramatic decline in the yield, predictive value, and cost-effectiveness of ALT screening of blood donors".

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

Validity of estimate of measure of benefit
The estimate of measure of benefit may not be internally valid given the restricted number of primary studies included.

**Validity of estimate of costs**
The resource quantities were not reported separately from the prices. Adequate details of the methods of cost estimation were not given.

**Other issues**
The authors' conclusions were justified based on the sensitivity analysis performed. The issue of generalisability to other settings was not fully addressed. Some brief comparisons were made with other studies. The results were not presented selectively.

**Implications of the study**
The authors report that, based on the results of the data used in this study, "a National Institutes of Health consensus conference and a Food and Drug Administration advisory committee recently recommended the discontinuation of ALT screening". The blood organisations were also by then "finalizing plans and procedures for discontinuing the test".

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