I sostituti di volume plasmatico: strategie di impiego in terapia intensiva per il mantenimento di un corretto rapporto tra efficacia terapeutica e costi [Plasma substitutes: strategies for use in intensive therapy to maintain a correct ratio between therapeutic efficacy and costs]

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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
Two products used in plasma replacement therapy were studied. A solution of hydroxyethylamide (HES) 6% with an intermediate molecular weight (MW 200 kDa SD 0.5) was compared with a solution of modified fluid gelatine (MFG) at 4% (MW 30 kDa). Both solutions were administered at the start of the first postoperative day in order to maintain a mean arterial pressure greater than 60 mmHg and central venous pressure between 10 and 14 mmHg.

Type of intervention
Intensive therapy treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population included patients undergoing major abdominal surgery and requiring postoperative plasma replacement therapy.

Setting
The study setting was a hospital. The economic study was carried out at the ACO San Filippo Neri in Rome, Italy.

Dates to which data relate
The dates for the effectiveness and resource use data were not reported, and neither was the price year.

Source of effectiveness data
The effectiveness estimates were derived from a single study.

Link between effectiveness and cost data
The costing was conducted prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
A sample of 126 patients was enrolled in the study, of which 63 were in the HES group and 63 in the MFG group. The patients in the HES group were aged 61 (+/- 15) years (range: 37 - 79) and 29 were men. The patients in the MFG group were aged 59 (+/- 13) years (range: 30 - 75) and 30 were men. No patient was excluded from the initial sample for any reason. Power calculations to determine the sample size were not reported.
Study design
This was a prospective randomised controlled trial, which was conducted at the ACO San Filippo Neri in Rome, Italy. The method of randomisation and the length of follow-up were not reported. No patient was lost to follow-up. The study was single-blinded since the study doctors were unaware of the treatments allocated, but did not know the study objectives.

Analysis of effectiveness
The basis of the analysis of effectiveness was intention to treat. The health outcomes used in the analyses were:

- patients in intensive therapy,
- patients requiring assisted ventilation,
- time under assisted ventilation,
- patients requiring dopamine or epinephrine,
- survival,
- adverse reaction, and
- several haemodynamic parameters such as PAM, PVC, Hgb, aPTT, fibrinogen, plasmatic creatinine, cholinesterase, paO2/FIO2, colloids, crystalloids, concentrated blood products, frozen plasma, blood loss, and urinary output.

The study groups were comparable at baseline in terms of demographics conditions and clinical characteristics.

Effectiveness results
The number of patients in intensive therapy was 56 in the HES group and 54 in the MFG group.

The number of patients requiring assisted ventilation was 26 in the HES group and 28 in the MFG group.

The time under assisted ventilation was 629 (+/- 245) minutes in the HES group and 668 (+/- 298) minutes in the MFG group.

Six patients in the HES group and 8 in the MFG group required dopamine, while 2 (HES) and 4 (MFG) patients, respectively, required epinephrine.

No patients died during the study period and no adverse effects were reported.

All haemodynamic parameters were similar in the study groups.

Only the total quantity of MFG used after the intervention (2,690 +/- 500 mL) was significantly higher than the total quantity of HES used after the intervention (1,673 +/- 435 mL).

Clinical conclusions
The effectiveness analysis showed that both plasma replacement therapies were safe and performed similarly in patients undergoing major abdominal surgery. The quantity of MFG required was significantly greater than that of HES.

Measure of benefits used in the economic analysis
The health outcomes were not statistically different in the two study groups. Thus, a cost-minimisation analysis was conducted.
Direct costs
The health service costs included in the analysis were for crystalloids, colloids, frozen plasma and concentrated blood products. Materials (e.g. syringes) and personnel were assumed to be similar in the two study groups, and thus were excluded from the analysis. The costs were estimated using actual data derived from the pharmacy of the study hospital. The cost/resource boundary adopted in the study was that of the hospital. The quantities of resources used were obtained from trial data. The unit costs were reported separately from the quantities of resources. Discounting was not performed since the costs were incurred over a short time period. No price year was reported.

Statistical analysis of costs
Standard statistical analyses of the costs were conducted.

Indirect Costs
No indirect costs were included.

Currency
The costs were estimated in Italian lira (L), then converted into Euros and US dollars ($). The exchange rates were L 1,936.27 = Euro 1 = $0.96.

Sensitivity analysis
No sensitivity analyses were performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The total costs per patient were Euro 89.54 ($85.95) in the HES group and Euro 96.24 ($92.39) in the MFG group. The total costs per study group were Euro 5,641.20 ($5,415.55) in the HES group and Euro 6,063.60 ($5,821.05) in the MFG group. The difference in costs did not reach statistical significance.

Synthesis of costs and benefits
Not relevant.

Authors' conclusions
Both plasma replacement therapies were safe and effective, and no statistically significant difference was found in terms of the estimated costs. The authors also stated that the costs of albumin were far greater than those of hydroxyethylamide (HES) and modified fluid gelatine (MFG) and recent studies demonstrated that albumin might lead to severe side effects.

CRD COMMENTARY - Selection of comparators
HES and MFG solutions were selected as both were widely used in plasma replacement therapy. The authors also discussed the comparison of the two therapies with albumin, which, for a long time, represented the gold standard. You should decide whether they represent valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The internal validity of the analysis is likely to have been high, as a randomised controlled trial was conducted to derive the effectiveness evidence. The study groups were shown to be perfectly comparable at baseline in terms of several characteristics. The study sample was representative of the study population. However, it appears that power calculations were not performed and there was no evidence that the initial study sample was appropriate for the study question. The method of randomisation was not described.

**Validity of estimate of measure of benefit**
A summary benefit measure was not used as a cost-minimisation analysis was conducted.

**Validity of estimate of costs**
The perspective adopted in the study was implicitly that of the hospital. It appears that all the relevant categories of costs have been included in the analysis. Some costs that were common to both therapies were not included, but these exclusions should not have affected the conclusions of the analysis. The unit costs and the quantities of resources were reported separately. Standard statistical analyses of the costs were performed. The price year was not reported, thus making reflation exercises in other settings difficult. The costs were fairly specific to the study setting and no sensitivity analyses were conducted, although the authors acknowledged that variability exists across Italian regions in terms of drug prices.

**Other issues**
The authors made some comparisons of their findings with those from other studies. They did not, however, address the issue of the generalisability of the study results to other settings. Sensitivity analyses were not conducted, thus the external validity of the analysis was low. The study enrolled patients undergoing major abdominal surgery, but the conclusions of the study were generalised to all patients requiring plasma replacement therapy.

**Implications of the study**
The authors highlight the fact that the more expensive HES proved to be as safe, effective and costly as MFG in plasma replacement therapy.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
11533544

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Aged; Cost-Benefit Analysis; Critical Care /economics /methods; Female; Humans; Male; Middle Aged; Plasma Substitutes /economics /therapeutic use

**AccessionNumber**
22002006590