Cytoprotective effect of amifostine in the treatment of childhood neoplastic diseases: a clinical study including the pharmacoeconomic analysis

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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
The authors assessed amifostine (Ethylol, Schering-Plough) administered as a short intravenous infusion before alkylating agents (cyclophosphamide, ifosfamide), carboplatin and/or anthracyclins as a cytoprotector in the treatment of children with neoplastic diseases. The dose used was 910 mg/m².

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children treated for solid tumours and acute nonlymphoblastic leukaemias (ANLL).

Setting
The setting was secondary care. The economic study was carried out in Lodz, Sporna (Poland).

Dates to which data relate
The effectiveness and resource use evidence related to patients treated between 1998 and 2001. A price year was not reported.

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

Link between effectiveness and cost data
The costing appears to have been carried out retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The study sample comprised 18 children who received 57 courses of chemotherapy for solid tumours and ANLL. There was no report that power calculations were carried out. The very small sample size suggested that chance may play a role in the results obtained. The sample was selected by including all children treated in the study setting between the dates of the study. Eighteen of the treatment courses were included in study group A (with amifostine) and each course was compared with at least two similar courses without amifostine, group C. The mean age of the children was 7.1 (+/- 1.9) years. There were 13 girls and 5 boys. There was no evidence that the study sample was representative of the study population.
population.

**Study design**
The authors designed a retrospective cohort study with groups being defined by whether or not their course of treatment included amifostine. The study was conducted at a single centre, the Department of Paediatrics, University of Medicine in Lodz, Poland. The patients were followed for the duration of their stay in hospital, which extended to just over 2 weeks in some cases.

**Analysis of effectiveness**
The analysis was conducted on the basis of the treatment received. The primary outcomes were early adverse effects of treatment and their severity (according to the World Health Organization scale of toxicity), such as:

- the mean degree of myelotoxicity,
- the mean duration of neutropenia,
- the duration and severity of thrombocytopenias and need for platelet transfusion, and
- the duration of hospitalisation.

Significant differences between the treatment groups were determined using the Mann-Whitney and Wilcoxon tests (p<0.05 was considered statistically significant). The authors did not report the comparability of the groups, in terms of the patients, at analysis.

**Effectiveness results**
The mean degree of myelotoxicity was 2.54 in group A and 2.71 in group C, (p>0.05).

The mean duration of neutropenia was 6.5 days in group A (requiring 4.1 days of granulocyte-colony stimulating factor, G-CSF) and 6.8 days in group C (requiring 5.7 days of G-CSF), (p>0.05).

The severity of neutropenia was significantly lower in group A (0.72 versus 1.02 degrees according to the World Health Organization scale; p=0.049).

Patients in group A required fewer erythrocyte transfusions (0.8 versus 1.1).

The duration of thrombocytopenias was 8.2 days in group A (requiring, on average, 1.5 platelet transfusions per course of chemotherapy) and 6.6 days in group C (requiring 0.5 platelet transfusions per course), (p>0.05).

The duration of hospitalisation was 11.6 days in group A and 14.3 days in group C, (p=0.049).

**Clinical conclusions**
There was a tendency to shorter duration of neutropenia, better reaction to G-CSF, lower number of transfusions required and reduced hospitalisation, with a significantly lower severity of neutropenia, with chemotherapy involving amifostine. However, thrombocytopenias tended to last longer in this group than in the group receiving chemotherapy without amifostine.

**Measure of benefits used in the economic analysis**
The authors did not estimate a summary measure of health benefit. The study was therefore categorised as a cost-consequences analysis.
Direct costs
The authors presented very few details of the cost analysis, for instance, the perspective adopted was not reported although it might have been that of the hospital. The cost categories considered were intravenous antibiotics, blood preparations, immunoglobulins, G-CSF, GM-CSF and hospitalisation costs. The source of the unit costs was not reported and it was unclear whether capital costs, overhead costs, or salaries were taken into account. The quantities seem to have been taken from the effectiveness study, although this was not explicitly stated. Discounting was not required given the very short time horizon of the study as a whole. The price year was not reported.

Statistical analysis of costs
The costs of groups A and C were compared statistically.

Indirect Costs
Indirect costs exploring the impact on society in terms of lost or gained productive capability were not estimated.

Currency
Polish zlotych (PLN).

Sensitivity analysis
There was no report that sensitivity analyses were carried out.

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

Cost results
The authors reported that the costs of other elements such as blood preparations, immunoglobulins, G-CSF and GM-CSF were similar and not statistically significantly different between the groups. Therefore, the analysis focused on the difference in cost of antibiotic therapy between the two groups.

The mean cost of one course of intravenous antibiotics was PLN 242 with amifostine and PLN 896 without amifostine, (p=0.037).

Antibiotics comprised 3.6% of the total costs in group A (with amifostine) and 9.9% of the total costs in group C (without amifostine).

The mean cost of one course of chemotherapy was PLN 8,650 in group A and PLN 8,977 in group C, (p>0.05).

The authors reported that significant differences were only visible when the cost of amifostine was excluded from the mean cost of the chemotherapy course (i.e. PLN 7,000 in the group with amifostine and PLN 8,977 in the group without amifostine; p=0.048).

Synthesis of costs and benefits
Not relevant since a cost-consequences approach was used.

Authors' conclusions
The use of amifostine during chemotherapy in children reduced the number of infectious complications and limited the costs of treatment (since it decreased the costs of antibiotics). However, overall reductions in costs were not achieved because of the high cost of amifostine.
CRD COMMENTARY - Selection of comparators
The authors compared amifostine as a cytoprotector with standard chemotherapy without amifostine. This choice of comparators was justified with a discussion of the potential benefits of amifostine. You should decide if this is an appropriate comparator for your own setting.

Validity of estimate of measure of effectiveness
The authors designed a retrospective cohort study that analysed courses of chemotherapy received in the study sample at the study setting. This design was appropriate for considering differences in the outcomes between patients treated using the two alternatives, but it does not help minimise potential systematic differences between the patient groups that might otherwise explain differences in key outcomes. Moreover, the authors did not report summary statistics and a comparison between the groups at baseline in order to establish whether potentially confounding factors were present. The study sample was not shown to be representative of the study population. Statistical analyses were carried out to explore whether differences between the groups were statistically different, although lack of significance for most of the comparisons might have been due to the small sample size considered at analysis. As a limitation, the authors highlighted the fact that the study accounted only for the short-term side effects of chemotherapy and not, for instance, for protection against nephrotoxicity.

Validity of estimate of measure of benefit
The authors did not estimate a summary measure of benefit. The study was therefore categorised as a cost-consequences analysis. The reader is thus referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above), given that the health benefits are reflected in the disaggregated effectiveness outcomes.

Validity of estimate of costs
Despite a key objective of the study being to analyse cost-effectiveness, the authors conducted only a very basic cost analysis. In addition, they did not report key information, such as the perspective from which the analysis was carried out, the source of the unit costs, and the exact scope of the analysis. The authors might have improved their analysis by providing a full breakdown of the cost components. For instance, they reported that antibiotics comprised only a small percentage of the total costs but did not consider which elements made up the remaining proportion of total costs. The price year was not reported, which would limit reflation exercises in other settings.

Other issues
The authors were able to draw some comparisons between their own results and those already published, citing primarily effectiveness results with different levels of agreement across studies. The issue of generalisability to other settings was limited by the lack of a perspective and narrow reporting of the cost analysis. Generalisability of the effectiveness results would be limited to children because of the very specific nature of the study population. The conclusions drawn were an accurate reflection of the results presented and related well to the scope of the study.

Implications of the study
The authors did not make any recommendations for policy or practice relating to their study. However, they suggested further work, in terms of larger randomised studies, to confirm the clinical and economic benefits of amifostine.

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Bibliographic details
Other publications of related interest


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MeSH
Amifostine /administration & dosage /economics /pharmacology; Antineoplastic Agents /toxicity; Child; Cytoprotection /drug effects; Drug Evaluation; Drug-Related Side Effects and Adverse Reactions /drug therapy; Economics, Pharmaceutical; Female; Humans; Male; Neoplasms /complications /drug therapy; Radiation-Protective Agents /economics /therapeutic use /toxicity; Retrospective Studies

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