Cost-effectiveness of ceftriaxone and amikacin as single daily dose for the empirical management of febrile granulocytopenic children with cancer

Pession A, Prete A, Paolucci G

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
Ceftriaxone and amikacin in the empirical management of febrile granulocytopenic children with cancer.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study focused on children undergoing anticancer chemotherapy.

Setting
The practice setting was a pediatric clinic at the University of Bologna, Italy. The economic analysis was carried out in the same institution.

Dates to which data relate
Effectiveness data were collected between June 1994 and August 1996. It was not clear when resource data were obtained. No prices were stated.

Source of effectiveness data
Estimates for the effectiveness of single daily doses of ceftriaxone and amikacin were obtained from a single study.

Link between effectiveness and cost data
Costing appears to have been undertaken on the effectiveness study population. It was not clear whether costings were obtained retrospectively or prospectively.

Study sample
183 children were empirically treated with ceftriaxone and amikacin in a single daily dose, with 96 (52%) having absolute granulocyte count less than 100/mm3 at the onset, 68 (37%) were affected by acute leukemia or lymphoma, 3 (1%) by chronic leukemia, 94 (51%) by solid tumours and 21 (11%) patients underwent bone marrow transplantation. The mean age of study subjects was 6.5 years (1-17). There were 105 males (57.4%) and 78 females (42.6%) involved in the study. The mean weight was 24.8kg (3.9-68).
Study design
The study was a retrospective cohort study.

Analysis of effectiveness
The analysis of the clinical study was based on the whole sample. Primary health outcomes were based around response rates for:

1) bacteremic patients (n=20),
   (a) single gram-positive patients (n=14),
   (b) single gram-negative patients (n=11),
   (c) polymicrobial patients (n=1); and

2) non-bacteremic patients (n=6).

Further, assessments of effectiveness were carried out on patients with peripheral polymorphonucleates (PMN) count cells/mm³ <100 (n=88), and 100-500 (n=77).

Effectiveness results
Response rates were:

1) bacteremic patients, 60%;
   (a) single gram-positive patients, 57%;
   (b) single gram-negative patients, 55%;
   (c) polymicrobial patients, 100%; and

2) non-bacteremic patients, 50%.

Ceftriaxone plus amikacin was effective in 135/183 (74%) patients with a median time defervescence of 3 days (1-11). 70% of subjects with a PMN cell count/mm³ <100 responded to the therapy, and 77% of those subjects with a PMN cell count/mm³ 100-500 also responded to the therapy.

Note: The initial antibiotic regimen was discontinued due to side-effects (cutaneous eruption allergic reactions) experienced by 3 patients.

Clinical conclusions
Once daily ceftriaxone plus amikacin should remain as the standard regimen for the empirical treatment of febrile granulocytopenic children suffering from cancer.

Measure of benefits used in the economic analysis
Benefits were expressed in costs.

Direct costs
No discounting was required. Quantities and costs were not analysed separately. The cost boundary adopted appears to be that of a health service provider. No prices were stated.
Statistical analysis of costs
Not performed.

Indirect Costs
Not considered.

Currency
US dollars ($) alongside a conversion for Italian lira (L).

Sensitivity analysis
Not performed.

Estimated benefits used in the economic analysis
Benefits were expressed in costs (i.e. cost-minimisation).

Cost results
For ceftriaxone (every 24 hours) plus amikacin (every 24 hours) the daily costs were estimated at $23.5 (L37,650), and the 6-day period at $141 (L225,900). Conversely, for ceftriaxone (every 8 hours) plus amikacin (every 24 hours) the daily costs were estimated at $34.5 (L55,150), and the 6-day period costs at $207 (L330,900).

Synthesis of costs and benefits
Benefits and costs were not synthesised. Instead, for a child of 30kg body weight, cost savings of $11 (L17,500) for daily costs, and $65.6 (L105000) for 6-day treatment costs, were found in favour of the single daily dosage regimen.

Authors’ conclusions
Ceftriaxone plus amikacin should remain as the standard regimen for the empirical treatment of febrile granulocytopenic cancer suffering children. The single daily dose regimen has the potential to be cost saving (i.e. nursing time) as well as improving the quality of life of the patients that receive this treatment.

CRD COMMENTARY - Selection of comparators
The selection of comparator appears to be justified (ceftriaxone was selected because of its prolonged half-life of 8 hours, allowing for once daily dosage).

Validity of estimate of measure of benefit
Apart from primary health outcomes, the benefits expressed in the study were relative treatment costings.

Validity of estimate of costs
Costs were poorly referenced and sourced, and were analysed together with quantities, thus making the issue of generalisability difficult to judge.

Other issues
No power calculations were stated in determining the study sample size. No proper synthesis of costs with effectiveness was carried out. The authors cite the justification for maintaining the study treatment regimen (ceftriaxone plus amikacin) as being due to the results found as well as the potential for further cost reductions and improvements in
patient quality of life, however, they do not substantiate these claims.

**Implications of the study**
Further comprehensive economic analyses are required in order to substantiate the claims and recommendation of the authors.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
9309370

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adolescent; Agranulocytosis /chemically induced /drug therapy; Amikacin /administration & dosage /economics /therapeutic use; Anti-Bacterial Agents /administration & dosage /economics /therapeutic use; Antineoplastic Agents /adverse effects; Ceftriaxone /administration & dosage /economics /therapeutic use; Cephalosporins /administration & dosage /economics /therapeutic use; Child; Child, Preschool; Cost-Benefit Analysis; Drug Therapy, Combination /administration & dosage /economics /therapeutic use; Female; Fever /drug therapy; Humans; Infant; Male; Neoplasms /drug therapy; Retrospective Studies; Treatment Outcome

**AccessionNumber**
21997001197

**Date bibliographic record published**
28/02/1999

**Date abstract record published**
28/02/1999