Assessment of the efficacy and cost efficiency of two strategies in the treatment of acute pyelonephritis in children: oral cefixime or parenteral ceftriaxone after an initial IV combination therapy

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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
Support therapy strategies suitable for the treatment of acute pyelonephritis in children.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of child in-patients diagnosed as having APN. The study population was required to comply with the following selection criteria: aged between 6 months and 10 years; body weight >=5 kg; no history of abnormal urinary tract; fever >= 38 degrees C; significant bacteriuria; and an abnormal C reactive protein (CRP) value.

Setting
The setting was secondary care. The economic study was conducted in France.

Dates to which data relate
The effectiveness data were gathered between November 1993 and January 1995. The price year was 1995.

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

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient group as that used in the effectiveness study, except for indirect costs which were collected through a specific questionnaire addressed to the parents.

Study sample
The study sample consisted of two groups of children: 63 in the group treated with cefixime and 65 children in the group treated with ceftriaxone. Both groups had males and females (in favour of female). The mean age of patients was 4 years, and mean weight was 17 kg. The mean fever was 39.3 degrees C and E. coli was 93%. 90.6% had no history of urinary tract infection and 39.8% had abnormal cystography. Initially, 169 children were included in the study sample but 12 were excluded because of the absence of bacteriuria data. Power calculations were not used to determine the sample size. Children were randomly assigned to the cefixime or ceftriaxone groups.
Study design
The study was a randomised, multi-centre trial (28 French centres were included in the trial), using the French software MINITEL (phone numbers) to randomise support treatment allocation. The period of treatment was divided into four stages:

during day 1 (D1) to day 4 (D4) all children received intravenous therapy ceftriaxone-netilmicin;

between day 5 (D5) and day 10 (D10) children received either cefixime (8mg/kg/day) or ceftriaxone (50mg/kg/day).

between day 13 (D13) and day 15 (D15), treatment was evaluated; and

after this period and until days20 to 30 (D20-D30), children received prophylactic treatment (nitroxoline 20mg/kg/day) to prevent relapses.

Analysis of effectiveness
The basis for the analysis of the clinical study was not specifically stated but is likely to have been intention to treat. The effectiveness of support treatments was measured at the end of the treatment (D12) and at D20-D30 in terms of success rate, as the main health outcome, and side effects. The clinical definition of the success rate was not stated. The groups were comparable in terms of the baseline characteristics defined earlier.

Effectiveness results
A test for difference in effectiveness was carried out using the two one-sided test. Both treatments were equivalent at D12 and D30 with a success rate of 98% (62/63) and 100% (65/65), (p<0.0001) for cefixime and 100% (49/49) and 96% (51/53) (p<0.0001) for ceftriaxone at D12 and D30 respectively. Side effects were reported for 13% (9/67) of patients receiving cefixime and 11% (8/72) of patients in the ceftriaxone group. Only one severe side effect was reported in each group and one patient stopped treatment in the ceftriaxone group. E. coli was the most common pathogen isolated in both groups (93%) with a resistance rate to amoxicillin and amoxicillin/clavulanate reaching 45% and 24% respectively. No strain exhibited resistance to third generation cephalosporins.

Clinical conclusions
There is no statistically significant difference in success rate between cefixime and ceftriaxone.

Measure of benefits used in the economic analysis
Since the effectiveness analysis showed that there was no difference in effectiveness between cefixime and ceftriaxone, the economic analysis was based on the difference in costs only. As such it is appropriate to classify the economic analysis as cost-minimisation according to the clinical outcomes reported in the effectiveness results.

Direct costs
Treatment costs, hospitalisation and ambulatory costs, and associated drugs costs were estimated. 1995 prices were used. In-patient costs were calculated, based on the number of hospitalisation days and the average full-time hospitalisation cost. In-patient costs were obtained from hospital data. Ambulatory costs were based on parents’ estimates using data collected by questionnaire. Costs and quantities were reported separately for hospitalisation costs only. Only average costs per child were estimated. Discounting was not applied because the period of analysis was less than one year.

Statistical analysis of costs
Tests for statistical differences in costs were carried out using the two one-sided test.
**Indirect Costs**
The loss of income from work and nursing home costs were estimated, based on 53 questionnaires administered to parents (22 from cefixime group, 31 from ceftriaxone group). Discounting was not applied because the period of analysis was less than one year. Costs and quantities were not reported separately.

**Currency**
French francs (Ffr).

**Sensitivity analysis**
No sensitivity analysis was performed.

**Estimated benefits used in the economic analysis**
Not applicable to the cost-minimisation approach.

**Cost results**
The average direct cost of the support treatment strategy was Ffr512.9 (95% CI: 176.4 - 896.5; p<0.05) for cefixime and Ffr3,544.7 (95% CI: 2,477.7 - 4,673.3; p<0.05) for ceftriaxone.

The average indirect cost was Ffr636 (95% CI: 417 - 845; NS) for the cost of the loss of income from work and Ffr-28 for the modification in the cost of nursing home in the cefixime group. These costs were Ffr690 (95% CI: 523 - 857; NS) and Ffr+32 in the ceftriaxone group.

In-patient costs represented the largest share of the total direct cost: Ffr361.7 (95% CI: 83.5 - 612.2; p<0.05) for cefixime and Ffr2,782.5 (95% CI: 2,114.7 - 3,450.3; p<0.05) for ceftriaxone.

The lower costs of the cefixime strategy were due to lower treatment costs, lower in-patient costs and absence of outpatient costs. Associated drugs costs and indirect costs were not statistically different between the two groups.

**Synthesis of costs and benefits**
Not relevant.

**Authors' conclusions**
The authors concluded that the use of cefixime may confer the same clinical benefits as ceftriaxone treatment and lead to a drop in global direct costs per patient by reducing the number of days of full-time hospitalisation and removing ambulatory costs.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the comparator used, namely that it was standard practice. You, as a user of this database, should decide if this is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness analysis was based on a randomised, multi-centre trial that was appropriate for the study question. The measure of effectiveness is likely to be valid. However, the definition of success rate was not reported. The study sample was representative of the study population, and patient groups were shown to be comparable at analysis. Appropriate statistical analyses were not undertaken to take into account of potential biases and confounding factors.
Validity of estimate of measure of benefit
The analysis of benefits was based upon the effectiveness equivalence of treatment alternatives. The economic analysis therefore included only costs.

Validity of estimate of costs
Although the authors did not report clearly that costs were estimated from a societal perspective, direct and indirect costs were included. For each category of costs, all relevant costs were included in the analysis. Costs and quantities, however, were not reported separately which tends to limit the generalisability of the cost results. A statistical analysis of quantities was appropriately performed. A sensitivity analysis of prices might have been useful but none was provided. Since all costs were incurred over one year, discounting was unnecessary.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, but the issue of generalisability to other settings was not addressed. The authors did not report their results selectively. The authors' conclusions reflected the scope of the analysis. The study considered children with APN and this was reflected in the authors' conclusions. The authors reported one limitation to their study, namely the non-inclusion of DMSA kidney scintigraphy, recently advocated but not recommended.

Implications of the study
The data presented here support the use of cefixime in the treatment of acute pyelonephritis in children.

Source of funding
None stated.

Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by CRD

MeSH
Acute Disease; Cefixime /administration & dosage; Ceftriaxone /administration & dosage; Cephalosporins /administration & dosage; Child; Child, Preschool; Cost-Benefit Analysis; Drug Administration Schedule; Infant; Infusions, Parenteral; Injections, Intravenous; Kidney Diseases; Pyelonephritis /drug therapy /complications; Treatment Outcome
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