Comparison of 7 versus 10 days of antibiotic therapy for hospitalized patients with uncomplicated community-acquired pneumonia: a prospective, randomized, double-blind study

Siegel R E, Alicea M, Lee A, Blaiklock R

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 health technologies studied were the use of two alternative strategies for the treatment of hospitalised patients with uncomplicated community-acquired pneumonia (CAP):

A 10-day treatment course comprising intravenous (IV) administration of cefuroxime (Zinacef; Glaxo Wellcome Inc, Research Triangle Park, NC; 750mg every 8 hours) during the two first days, and followed by 8 days of oral cefuroxime axetil (Ceftin; Glaxo Wellcome Inc; 500 mg every 12 hours).

A 7-day treatment, comprising two days of IV cefuroxime, followed by 5 days of cefuroxime axetil (using the same doses as for the 10 day treatment).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised hospitalised patients who had new pulmonary infiltrate on chest radiograph, and either a clinical history consistent with pneumonia (fever, chills, cough, sputum, or chest pain) or physical findings suggestive of pneumonia (localised crackles or bronchial breath sounds). Patients were excluded if they had empyema, septic shock, or respiratory failure, an allergy or hypersensitivity to cephalosporins, or had received systemic antibiotics in the past 72 hours.

Setting
The setting was secondary care. The study was carried out in New York, USA.

Dates to which data relate
The effectiveness data were collected between December 1995 and June 1997. The cost data were collected from studies published in 1993 and 1997, and from hospital data from the Centers for Disease Control (1992). The price year was not reported.

Source of effectiveness data
The source of the effectiveness data was a single study.
Link between effectiveness and cost data
It is not clear whether the costing was estimated from the same sample population used in the effectiveness analysis.

Study sample
No power calculations appear to have been performed in the planning phase of the study in order to assure a certain power. Patients admitted to an inpatient medical ward at the Bronx Veterans Affairs Medical Center were selected for randomisation if they met the inclusion criteria reported above. Patients who had been admitted to the study in the past were excluded. The final study sample comprised 52 patients (all male). 25 were assigned to the 10-day treatment group, and 27 to the 7-day treatment group. The authors did not provide evidence that the study sample was representative of the study population.

Study design
This was a randomised, double-blind study, performed at a single centre. A computer-generated randomisation method, performed by the Pharmacy service at the hospital, was used to randomly allocate patients to one of the treatment strategies, keeping both patients and investigators blinded. The masking of patients appeared to be appropriately performed by administering a placebo to patients in the 7-day treatment group. Patients were followed up for a period of 42-44 days, approximately. In total, six patients withdrew from the study, three from each study arm.

Analysis of effectiveness
The clinical study was based on a 'treatment completers only' (TCO) analysis. Patients were excluded from the analysis if (1) they had organisms resistant to cefuroxime that were isolated, (2) 15% or more of the antibiotic doses were not administered, (3) they were unable to tolerate oral medication or (4) morbidity or mortality unrelated to pneumonia prevented the continuation of the study protocol. The TCO study sample comprised 46 patients: 22 in the 10-day treatment group, and 24 in the 7-day treatment group. Additionally, an intention-to-treat (ITT) analysis was also carried out for some of the health outcomes considered. The health outcomes reported for both study arms were the rates of cure, late recurrences, length of hospital stay, and number (and %) of treatment failures. The study groups were comparable in terms of age, the number of lobes involved, the presence of pleural effusion, smoking history, white blood cell count (WBC), the proportion of patients with WBC elevation, the maximum temperature on admission, the number of patients with fever, serum creatinine, and the number of comorbidities. The entry oxygen saturation was significantly higher for patients in the 7-day treatment arm, which may indicate a less severe condition for these patients when compared to the 10-day treatment arm.

Effectiveness results
The groups had similar cure rates: 90.9% (20/22) of patients in the 10-day group versus 87.5% (21/24) of patients in the 7-day group (the 95% CI for the difference between the study arms was -14.5% to 21.3%).

Similar results were found when an ITT analysis was carried out.

No late recurrences occurred after antibiotics had been completed.

The study arms did not show significant differences in terms of the length of hospital stay.

There were two failures (9.1%) in the 10-day treatment arm, versus 3 (12.5%) in the 7-day treatment arm and one of the patients in this arm died.

Clinical conclusions
The 10-day treatment strategy did not show significant health improvements when compared to the 7-day treatment strategy.
Measure of benefits used in the economic analysis
The effectiveness results showed no significant differences between the alternative treatment strategies, and therefore the economic analysis was based on a cost-minimisation approach.

Direct costs
The direct costs considered in the economic analysis were not clearly reported, and the only costs that were undoubtedly included were the antibiotic costs. The sources of the cost estimation were published studies and hospital data from the Centers for Disease Control. The estimation of costs seemed to be based on actual data. Adjustments were performed to approximate costs by retail pharmacists, adding a 20% increase to the average wholesale cost. Therefore, the perspective adopted appeared to be that of the third party payer. The authors estimated the incremental costs of administering a 10-day treatment course rather than a 7-day treatment. Moreover, the authors estimated the potential cost saving per year in the USA in case a 7-day treatment, instead of a 10-day treatment course, was administered for patients with CPA hospitalised in private centres. Discounting was not performed, and it was not necessary because of the short study period considered at analysis (i.e. less than 2 years). The price year was not reported, and resource quantities were not reported separately from the costs.

Statistical analysis of costs
No statistical analyses of costs were reported.

Indirect Costs
No indirect costs were reported.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analyses were reported.

Estimated benefits used in the economic analysis
The reader is referred to the 'Effectiveness Results' section, reported above.

Cost results
The total incremental costs of administering a 10-day treatment course instead of a 7-day treatment course were estimated to be $30.37 for the additional 3 days of therapy.

The authors estimated that $27,242,000 per year could be saved in the USA if a 7-day treatment course for hospitalised patients with CAP were administered, instead of the 10-day treatment strategy currently delivered.

Synthesis of costs and benefits
Not applicable since a cost-minimisation analysis was performed.

Authors' conclusions
The authors concluded that a 7-day antibiotic treatment is safe and sufficient for the treatment of inpatients with uncomplicated CAP, when compared to a 10-day treatment strategy, since the longer treatment did not show improvements in terms of cure rates or recurrences, but did incur higher costs.
**CRD COMMENTARY - Selection of comparators**

Although none of the treatment strategies was explicitly reported to be the comparator, the authors commented that the 10-day treatment course was the current practice in their setting for the treatment of inpatients with uncomplicated CAP, while the 7-day treatment course was one of the alternative clinical practices used outside the USA. You should decide which health technology is the most commonly used in your own setting.

**Validity of estimate of measure of effectiveness**

The study design (double-blind randomised controlled trial) was appropriate for the study question, since it reduces potential biases affecting the study results. The authors based the clinical study on a TCO analysis, but they also performed an ITT analysis, showing no differences between the results obtained. Statistical analyses were performed, although it must be highlighted that the conclusions about the effectiveness analysis relied on the fact that no differences in effectiveness were found between the treatments compared. However, the small sample size considered at analysis may have limited the power of the study to detect significant differences between the study groups. Furthermore, the fact that patients in the 7-day treatment arm may have had less severe illness compared to patients in the 10-day treatment arm introduces uncertainty into the internal validity of the effectiveness results. Additionally, the study sample was not representative of the study population, since it was recruited from a single centre and included only men.

**Validity of estimate of measure of benefit**

Since the effectiveness analysis did not show significant differences between the treatment alternatives, the authors did not derive a summary measure of benefit but performed a cost-minimisation analysis.

**Validity of estimate of costs**

The perspective adopted appeared to be that of the third party payer, since cost adjustments were performed to consider the cost increments because of the retail prices. Resource quantities were not reported separately from the costs, and the price year was not reported. Moreover, the costs considered in the economic analysis were not appropriately described and no statistical or sensitivity analyses were performed. All these issues introduce uncertainty into the reliability of the conclusions and hinder reflation exercises to other settings. Discounting was not performed, and was not required, since the period considered at analysis was shorter than 2 years. The authors reported a further limitation of the cost analysis in that the period of treatment differs depending on the patient, and a short-course treatment may not be appropriate for some patients.

**Other issues**

The authors compared the cure rates of this study with those from similar studies, which showed similar or even better cure rates. Since the study considered only inpatients with uncomplicated CAP, the authors recommended that the reader should not generalise the results obtained to the outpatient population. The authors do not appear to have presented their results selectively, and their conclusions reflected the scope of the analysis. No further limitations were reported by the authors.

**Implications of the study**

The authors recommended that further large multi-centre studies, including women and non-veterans, be undertaken before recommending the routine use of 7-day course antibiotic treatment for CAP. Moreover, they suggested that a similar study should be carried out, considering outpatients with CAP treated only with oral antibiotics, in order to determine whether the results of the study apply also to this patient population.

**Source of funding**

Supported in part by grant from Glaxo Wellcome Inc.
Bibliographic details

PubMedID
11329100

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Aged; Anti-Bacterial Agents /administration & dosage /therapeutic use; Community-Acquired Infections /drug therapy; Costs and Cost Analysis; Double-Blind Method; Hospitalization; Humans; Male; Middle Aged; Pneumonia, Bacterial /drug therapy; Prospective Studies; Time Factors

AccessionNumber
22001006394

Date bibliographic record published
30/04/2005

Date abstract record published
30/04/2005