Pharmacoeconomic considerations associated with the use of intravenous-to-oral moxifloxacin for community-acquired pneumonia

Davis S L, Delgado G, McKinnon P S

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 present study compared three pharmacy intervention (PI) strategies for patients with community-acquired pneumonia (CAP):

- intravenous (IV) beta-lactam plus a macrolide (no PI strategy);
- IV beta-lactam, with or without a macrolide, switched to an oral (PO) PI (PI switch strategy); and
- IV moxifloxacin with pharmacist-initiated automatic PO moxifloxacin conversion (PI sequential strategy).

In the PI switch strategy, the IV therapy recommendation was a combination of ceftriaxone and erythromycin, and patients were targeted to attempt early conversion to PO levofloxacin.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Adult patients admitted to a university hospital with a diagnosis of CAP were considered for enrolment. Patients were excluded if they were pregnant, had been transferred from a nursing home or long-term care facility, or had been hospitalised within the past 30 days. They were also excluded if they had received antibiotics within 48 hours of presentation to the emergency department.

Setting
The setting was tertiary care, specifically, a university-affiliated urban hospital and Level I trauma centre for adult patients. The economic study was carried out in Detroit (MI), USA.

Dates to which data relate
The effectiveness evidence and resource use data were collected from January to March of 2001, 2002 and 2004. The 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 was undertaken on the same patient sample as that used in the effectiveness study.

Study sample
The sample size and power calculations were not reported. The method of sample selection was stated to be sequential. Clinically evaluable results were available for 251 patients recruited during three study periods. There were 79 patients in the no PI group (year 2001), 81 in the PI switch group (year 2002) and 91 in the PI sequential group (year 2004).

Study design
This was a single-centre, prospective, comparative study with historical controls. Consecutive adults patients admitted with a diagnosis of CAP over a 3-month period in 2004 were targeted by an intervention to initiate IV moxifloxacin, with conversion to PO moxifloxacin recommended by an infectious diseases pharmacist when specific criteria for conversion were met. The conversion criteria were reported in a detailed appendix. This group was compared with two groups of historical controls from the same time period in 2001 and 2002.

Clinical status was evaluated in a blinded fashion by two independent reviewers on each day of antibacterial treatment, and outcomes were assessed on days 3 and 7 of therapy and at the end of therapy. During the prospective study periods, physician interventions included both educational presentations and direct interaction.

Analysis of effectiveness
The patients in the three groups were similar in terms of their age, gender, severity of illness, most co-morbid conditions, and organisms isolated. Significantly more patients treated in 2004 were found to have chronic obstructive pulmonary disease: 33% of patients in the PI sequential group versus 16.5% of patients in the no PI group and 9.9% of patients in the PI switch group, (p<0.001). The primary end point of the study was the rate of "clinical success”. This was defined as an improvement in temperature, white blood cell (WBC) count, and mechanical status. "Clinical deterioration and/or failure" was defined as an increase in temperature, WBC count, and/or decline in mechanical ventilation status. The outcomes were assessed on days 3 and 7 of therapy and at the end of therapy. The detection of adverse events was not a primary end point of the study. Student's t test was used for continuous variables for independent samples, while the Mann-Whitney U-test was used for non-parametric data. The chi-squared test and Fisher's exact test were used for categorical variables.

Effectiveness results
Clinical success rates on day 7 of therapy and at the end of therapy were similar in all three groups. However, the success rate at day 3 of therapy was significantly improved in the PI sequential group. The clinical success rates on day 3 of therapy were 83.4% for the no PI group, 84% for the PI switch group, and 94.5% for the PI sequential group, (p=0.045). The clinical success rates on day 7 of therapy were 96.2% (no PI group), 92.6% (PI switch group) and 95.6% (PI sequential group), respectively, (p non significant). At the end of therapy, the clinical success rates were 98.7%, 98.8% and 97.8%, respectively, (p non significant).

Patients who met criteria for oral antibacterial use had treatment converted to PO therapy sooner in both PI groups. In the no IP group, patients received IV therapy for an average of 2.14 days after meeting criteria for PO therapy, compared with 0.96 days for the PI switch group and 0.35 days for the PI sequential group, (p<0.001). No significant differences in length of stay were observed across the three study periods.

Rates of infection-related readmission to the hospital within 30 days after discharge were similar among all groups. Specifically, 3.8% for the no PI group, 4.9% for the PI switch group, and 4.4% for the PI sequential group.

No adverse events were attributed to treatment for CAP.

Clinical conclusions
Sequential therapy with a fluoroquinolone offered the advantage of enhanced potency, while using the same drug facilitated physician acceptance of early IV/PO conversion. No differences in clinical outcomes were noted when pharmacists were responsible for IV/PO conversion of antibacterials. The clinical outcomes in the automatically converted group were at least as successful as those in the other study groups.

**Measure of benefits used in the economic analysis**
There was no summary measure of benefit. In effect, a cost-consequences analysis was performed.

**Direct costs**
The direct costs included were antibacterial acquisition costs, the ancillary costs of drug preparation, administration, and monitoring, and hospitalisation costs. The costs were analysed in three levels. The first level included drug acquisition costs only. The second level included level 1 costs and other antibacterial-related costs. The third level included level 2 costs plus hospitalisation costs. Data on medications or procedures not directly related to treatment for CAP were not included. The costs for all medications were obtained from the average wholesale prices listed in the Drug Topics Red Book. Although they were relevant, adjustment for inflation and discounting were not carried out. The quantities and the costs were not reported separately. Estimations of the quantities and the costs were based on actual data. The price year was not reported.

**Statistical analysis of costs**
The costs were treated stochastically. The costs were compared among the three groups using a Kruskal-Wallis one-way analysis of variance. Outliers were removed from comparisons of costs and length of stay by deleting extreme values that were more than twice the standard deviation of the mean.

**Indirect Costs**
No indirect costs were reported.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were carried out to determine whether antibacterial prices (+/- 50%) would change the economic outcome, and to account for the variance in antibacterial prices between institutions. The method used to select the ranges was not reported.

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

**Cost results**
The total costs by treatment protocol were $3,409 for the no PI group, $3,631 for the PI switch group, and $3,547 for the PI sequential group.

For the first level cost analysis, the drug acquisition costs during the PI sequential period were significantly lower than during both prior periods, (p<0.0001). The difference accounted for cost-savings of almost $110 per patient. Similar results were obtained in level 2 of the cost analysis.

A graphical representation of the sensitivity analysis of level 1 costs showed that under the assumption that the success rates were similar, antibacterial costs during the PI sequential period would have to be increased to 135% and costs...
during the no PI or PI switch periods would have to be decreased 65% for the cost-effectiveness to favour no PI or PI switch options.

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

**Authors' conclusions**
Although no differences in overall efficacy were observed between the three study periods, the patients in the pharmacy intervention (PI) sequential group improved at a faster rate. Also, pharmacist-initiated intravenous (IV) to oral (PO) conversion of moxifloxacin resulted in significantly reduced drug costs. Although patients in the PI sequential group did have reduced level 1 and level 2 costs, the level 3 cost was the same as that for the no PI and PI switch groups. Conversion from IV to PO therapy was accomplished most efficiently in the PI sequential group, with 80% of patients in this group receiving IV therapy for 3 days or less. Therefore, automatic IV/PO conversion of antibacterials facilitated by an infectious diseases pharmacist was clinically reasonable and economically advantageous.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator was explicitly justified. The justification given was based on the fact that it was a usual and current practice in the authors' setting. You should judge whether these drug regimens are relevant in your own setting, or whether other comparators from other treatments or drug classes could have been relevant as well.

**Validity of estimate of measure of effectiveness**
The analysis was based on a comparative study with historical control groups, with all the inherent potential problems of using non-randomised designs to derive comparative measures of effectiveness between treatments, which the authors acknowledged. Two independent reviewers assessed the outcomes blinded, which could help to reduce bias. The sample size and power were not reported. The comparability of the study groups was reasonable. Statistical analyses were performed, but sensitivity analyses to explore uncertainty in the outcomes were not reported.

**Validity of estimate of measure of benefit**
No summary measure of benefit was used. In effect, a cost-consequences analysis was performed. Please see the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**
There was insufficient detail on the quantities and resources used for the cost estimation. Although it was not stated, some relevant costs could have been omitted from the analysis since the only costs considered were those of drugs, drug administration and hospitalisation. Also, outliers were deleted but not reported. This might have affected the authors' conclusions. The costs and the quantities were not reported separately, thus the analysis could not be easily extrapolated to other settings. The sources of the cost data were not fully reported. A statistical analysis of the costs was reported, but only a sensitivity analysis of drug price was performed and the method used to select the range studied was not given. Discounting and adjustment for inflation were not carried out, even though the costs were incurred in three different years. The price year was not reported, which will not help any future reflation exercises.

**Other issues**
The authors' findings were compared with other relevant studies and the results found to be similar. The authors addressed the limited generalisability of the results to other settings, owing to the important proportion of patients with risk class I or II measured by the clinical pulmonary infection score. Further limitations reported included the exclusion of the indirect costs (which should be equivalent since length of stay was not different among groups) and the possibility that the IV/PO conversion rates were influenced by outside factors such as physician behaviour.
Implications of the study
The switch from IV to PO therapy is becoming more frequently used in all settings. It is possible that the faster rate of conversion seen in the present study was the result of physicians becoming more comfortable with IV/PO conversion over time and choosing to independently switch patients to oral medication.

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