Critical steps in fluoroquinolones and carbapenems prescriptions: results from a prospective clinical audit


Introduction

Antibiotic usage has emerged in the last decades as a main concern in hospital settings throughout the world (1–10). Emergence of resistant bacteria and multiplication of costs are added as new and more expensive drugs are used. Therefore, implementation of strategies for a more judicious use of antimicrobial agents has become mandatory.

In most hospitals in low resources settings, the inappropriate use of antibiotics can range from 20% to 60% (5). Data from developed countries show similar percentage of inappropriateness (7,11). Fluoroquinolones (FQ) and carbapenems (CP) are antibiotics with good activity against many resistant pathogens, but they also have great capacity of inducing further resistance (6,7,12,13). They should be preserved for treatment of severe infections and special situations in which other agents are contraindicated or ineffective (1,6,7,12,13). However, FQ are largely used empirically (10,14).

Antibiotics account for a significant per cent of total health-care expenses (7,15). Rational prescribing of these drugs can minimise costs, still providing the best care for the patient. Hospital settings have been implementing infection control policies to prevent the emergence of resistant organisms and decrease costs (1,3–5,7–10,14,15). In this context, we undertook a clinical audit in order to evaluate the critical pathways on FQ and CP orders in a teaching hospital, where electronic resources of infection control are available.

Methods

This investigation was conducted in Hospital de Clínicas de Porto Alegre, a 730 bed university hospital with 26,854 admissions per year in southern Brazil. A restrictive antimicrobial policy has been established since 1992. Glycopeptides and all broad-spectrum antibiotics are included in this policy. These antimicrobial prescriptions are electronically reviewed by two Infection Control (IC) physicians. They evaluated clinical information provided by assistant doctors, as well as information about examinations (e.g. cultures, imaging, blood chemistry), previous antimicrobial use and risk factors for infection, which are also electronically available. Although this is a powerful method for antimicrobial prescription control (16), the lack of more detailed bedside information led our group to undertake a clinical audit. We characterised six different critical pathways on antimicrobial prescription.
During a 30-day period, from 10 March 2003 to 9 April 2003, we evaluated all new prescriptions of FQ and CP through a prospective, multistep clinical audit. Whenever a new order of these drugs was submitted for IC approval the patient was included in the study. After informed consent, patients’ data were collected within the first 24 h after prescription through a standardised data abstraction instrument, which was fulfilled by research assistants (medical students) trained by the IC team. Antibiotic orders were analysed by two physicians, which were blinded to initial electronic antimicrobial evaluation performed by IC physician. This was carried out in order to judge steps considered to be cornerstones of an adequate prescription (Table 1). The hospital’s institutional review board approved the study protocol.

Critical steps evaluated
Absence of demand to antimicrobial usage was defined as treatment of colonisation or futile therapy (use of a restricted antibiotic to treat a terminal patient already allocated to a Do Not Resuscitate (DNR) order with fever and no other signs of an infectious disease) (17). Initial choice was considered inappropriate when it had a low probability to cover the most commonly involved microorganisms in the case appraised – based on standard guidelines (17,18) or principles for diagnosis and treatment of infectious diseases – or when second-line drugs were used empirically. Inadequate monotherapy and unnecessary multiple antibiotics were also considered inappropriate initial choice. Mismatch between culture results and antibiotic used was also judged inappropriate. Adequacy of dose was evaluated according to standard guidelines (18,19), creatinine clearance, age and weight. Intravenous (i.v.) route was considered inadequate if the patient had availability of oral route and stable vital signs for more than 24 h (heart rate <100 bpm, respiratory rate <24 rpm, axilar temperature <38°C and systolic arterial pressure >90 mmHg) according to our hospital guidelines.

### Statistical analysis
All data collected were inputted in an Epiinfo 6.04 database. Analysed variables included the six steps listed below. Process measurement among each setting (clinical, surgical and paediatric) was also compared. Direct costs related to prescriptions were evaluated. Categorical variables were compared with Fisher exact test. A two-tailed p-value of less than 0.05 was considered significant.

### Results
A total of 202 FQ were prescribed. Ten patients died and 13 were discharged before signing informed consent; eight patients refused to participate in the study. Ciprofloxacin comprised 71% of the 171 evaluated prescriptions, the remaining were of levofloxacin. Of 64 CP prescribed, 46 were meropenem and 18 imipenem. One patient died before signing the informed consent. Ciprofloxacin was used mostly for urinary tract infection (UTI) – 26 patients due to lower tract infection and 10 with symptoms consistent with pyelonephritis/urinary sepsis – and diabetic foot ulcer (17 patients). Pneumonia was the leading cause for levofloxacin order, accounting for 42.9% (21) of prescriptions. CP was more often prescribed for sepsis (30.2%), lower UTI (23.8%) and febrile neutropenia (9.5%). Infections treated with FQ were classified as nosocomial in 31% of cases, community-acquired in 42.7% and indeterminate in the remaining. Within CP, 65% were hospital-acquired, 9.5% community-acquired and indeterminate in the remaining. Twenty-four patients (38.7%) in the CP group and 36 patients (21.1%) in the FQ group were immunosuppressed.

The six steps evaluated are described below. Figures 1 and 2 summarise the overall evaluation.

Step 1 – Was there a clear justification for antibiotic prescription? In the FQ, lack of a clear indication for treatment with antibiotics occurred in 14 cases (8.9%), while in the CP group, it occurred once (1.5%, p = 0.076 comparing groups).

<table>
<thead>
<tr>
<th>Table 1 Multistep approach to antibiotic evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step</strong></td>
</tr>
<tr>
<td>1. Was there a clear reason for antibiotics prescription?</td>
</tr>
<tr>
<td>2. Was initial antibiotic choice appropriate?</td>
</tr>
<tr>
<td>3. Were there microbiological examinations collected prior to therapy?</td>
</tr>
<tr>
<td>4. Were the initial dosage and route adequate?</td>
</tr>
<tr>
<td>5. Were culture results appropriately used?</td>
</tr>
<tr>
<td>6. Was therapy switched to the oral route when possible?</td>
</tr>
</tbody>
</table>
Step 2 – Was initial antibiotic choice appropriate? Within the 157 FQ prescriptions judged as correct in step 1, 33 were considered as inappropriate scheme (21%). Ten patients were treated in monotherapy, although they had infections demanding multiple antibiotics regimen; six patients received multiple drugs without indication; eight cases had a second-line scheme chosen empirically; five patients had initial empiric choice with insufficient coverage for the most likely involved microorganisms; four cases were judged incorrect because of miscellaneous causes. In the CP group, 16 prescriptions were appraised as inappropriate (25.8%). Two patients received multiple drugs unnecessarily, two cases had meropenem as initial empirical regimen, seven patients could be treated with other drugs according to microbiological examinations – mostly with cefepime – and five cases had the scheme changed to CP prematurely.

Table 2 shows the proportion of adequacy in the most prevalent clinical settings.

Step 3 – Were microbiological examinations collected prior to therapy? Twenty-two cases of FQ were excluded according to our hospital diabetic foot ulcer guideline, in which cultures are not mandatory. We analysed cases separately, regarding their judgement in step 2. Among adequate prescriptions, 95.5% of the CP and 71.8% of the FQ situations had cultures collected prior to therapy, and not collected at all in 2.3% and 20.0% respectively (p = 0.005). Within the inadequate prescriptions, 100% of CP and 92.3% of the FQ cases had microbiological examinations collected before treatment.

Step 4 – Were the initial dose and route adequate? In the 124 FQ cases considered adequate in step 2, one patient received incorrect dosage, six had initial i.v. therapy despite oral route availability and one case contained both inadequacies. Within CP appraised as correct in step 2, two prescriptions had excessive dosage. The route could not be evaluated, because these drugs lack oral formulation.

Step 5 – Were culture results appropriately used? There were 47 examinations with microorganisms identified during the follow-up in the FQ group and 15 in the CP group. Twenty-seven results were adequately used in FQ group and 11 in CP. In seven FQ and in one CP patient the antimicrobial was changed.
inappropriately; whereas in 13 FQ and three CP cases, the results demanded a change, which was not carried out. Figure 3 shows frequency of the most common microorganisms identified in cultures according to drug prescribed.

Step 6 – Was therapy switched to the oral route when possible? Eighty-three FQ patients were adequately treated through i.v. route. In the follow-up period, 22 patients who could have switched to oral route did not accomplish the transition.

Considering all steps together as performance indicators, total adequacy occurred in 34.5% FQ (59) and 63.4% CP (40) prescriptions. There was no difference in performance indicators in clinical vs. surgical settings (p = 0.12).

Economical Impact
The economical impact of inappropriateness was studied by a direct cost evaluation. Within the FQ, total cost of acquisition was US$ 7546, with US$ 7167 (95%) represented by the i.v. formulations. The excessive cost accounted for step 1 was US$ 270. Availability of less expensive treatment was identified in nine cases among the 33 inadequacies...
in step 2, with an extra expenditure of US$ 355. Use of i.v. formulation was inadequate in 34 cases (US$ 1861, 24.5% of total month’s expense). Total unnecessary costs was US$ 2486 (33% of total cost), projecting annual expenses of US$ 29,832. Monthly cost of CP was US$ 31,694. Lack of clear indication for treatment accounted for US$ 80. Step 2 inadequacies responded for US$ 4316 (13.61% of total). Excessive dosage was responsible for 2.94% of the month’s total (US$ 934). Total inadequacies costs were US$ 5330 (17% of total cost).

Discussion

Despite restrictive policies, inappropriateness of antibiotic usage reaches up to 60% in some series (6). Our study audits FQ and CP prescriptions in a multistep approach in order to identify possible flaws in the antimicrobial usage and at the same time review different process indicators of our own activity. Therefore, it could provide tools to policies and educational actions within the hospital, focusing on the most problematic steps.

There is concern about the lack of a clear indication for treatment with antibiotics in 8.9% of FQ prescribed, in spite of a restriction policy and the information technology tools available. It creates a risk for emerging resistance. In fact, a case-control study of nosocomial acquisition of FQ-resistant strains of Escherichia coli or Klebsiella pneumoniae confirmed recent FQ use as an independent risk factor (16). Inadequate use was more frequent with FQ than with CP use – clinicians seem to be more aware of restriction policies to CP. Early switch to oral route is clinically effective and allows early discharge (19,20). We found that no early switch to oral route was responsible for 76% of the unnecessary costs in the FQ group. An inappropriate initial choice accounted for 13.6% of total monthly expenses with CP.

This audit provides bedside information in order to maximise the efficacy of antibiotic control when added to computer-assisted management support. As this process is resource and time consuming, it should not be used as a continuous antimicrobial surveillance. However, it can be faced as a process indicator to optimise antimicrobial usage and even evaluate infection control policies. Using a multistep approach, we can identify unique indicators of inappropriate drug use, which could be employed to evaluate all restricted drugs. Results of audits on different drugs may also provide focused interventions to improve antibiotic use by physicians.

References


*Paper received February 2006, accepted March 2006*