INTRODUCTION

Inappropriate antimicrobial use has been associated with increased morbidity, mortality and hospital costs. As antimicrobial use is considered a major determinant in the evolution of resistance, hospital antibiotic stewardship programmes has been developed for the prevention and containment of antimicrobial resistance. Determining classes of antibiotics to be restricted/cycled and optimal time intervals required for an antibiotic restriction/cycling policy is considered a key aspect, and should be informed by local epidemiology data. The objective of the presented work was to evaluate temporal relationships existing between antimicrobial drug use and the incidence of *Clostridium difficile* Infection (CDI) in Antrim Area Hospital, thus providing theoretical basis for designing efficient antibiotic stewardships. This was achieved using time-series analysis technique which considered the strongest quasi-experimental method to ascertain the longitudinal effects of healthcare interventions.

METHODS

Data: The present retrospective investigation involved collecting data on a monthly basis on the usage of antibiotics and, gastric-acid suppressive agents, and on infection control practices together with the incidence of CDI within Antrim Area Hospital over a five-year period (February 2002- March 2007). The study was ecological in design.

Pharmacy and microbiology data: The monthly quantities of each antimicrobial agent delivered to each ward of the hospital were obtained from the pharmacy information system and were converted into defined daily doses (DDDs). Similarly, monthly quantities of gastric-acid suppressive agents i.e. proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2RAs) were determined. CDI cases per month were obtained from the clinical microbiology information system over the study period. All variables were adjusted per 100 bed-days.

Infection control practices: Details on infection control practices i.e. data on usage of chlorhexidine (litters) and alcohol-based hand rub (litters), and data on staffing levels of nurses/auxiliary nurses were obtained at monthly intervals. All variables were adjusted per 100 bed-days.

Statistical methods: A multivariate autoregressive integrated moving average (ARIMA) model was built to relate CDI incidence with antibiotic use, the usage of gastric-acid suppressive agents and the level of infection control practices. Data were analysed using Eviews 6.0 (Quantitative Micro Software, Irvine, California, USA).

RESULTS

Time series analysis showed that CDI incidence had a positive relationship with the use of second-generation cephalosporins, third-generation cephalosporins, fluoroquinolones, amoxicillin-clavulanic acid, macrolides and H2RAs with various time lags (Table 1).

For example, temporal variations in CDI incidence followed temporal variations in second-generation cephalosporin use with an average delay of two months. This means that, on average, an increase (or decrease) of second-generation cephalosporin use by 1 DDD/100 bed-days resulted two months later in an increase (or decrease) of the incidence of CDI by 0.01/100 bed-days. Projections for Antrim Area Hospital on the DDDs of the implicated agents and the numbers of patients needed to be treated to cause or prevent one CDI case at the hospital are presented in Table 2.

DISCUSSION

The findings of this study confirm that the restriction of specific antibiotics could reduce the incidence of CDI, but further prospective work is required to investigate the feasibility of restricting those antibiotics and into appropriate alternatives during restriction periods.

The results of this research can help hospitals to set priorities for restricting the use of specific antibiotic classes, based on the size-effect of each class and the delay necessary to observe an effect.

Measuring the delay required to observe an effect following the restriction/use of particular antibiotics, which was possible using the time-series analysis technique, could be a possible way forward in determining the optimal time required for an antibiotic restriction policy.

REFERENCES


Table 1. Multivariate time-series analysis model for monthly CDI incidence (R² = 0.78).

<table>
<thead>
<tr>
<th>Term</th>
<th>Lag time (a)</th>
<th>Coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Second-generation cephalosporin use</td>
<td>2</td>
<td>0.010299</td>
<td>0.0038</td>
</tr>
<tr>
<td>Third-generation cephalosporin use</td>
<td>2</td>
<td>0.018226</td>
<td>0.0059</td>
</tr>
<tr>
<td>Fluoroquinolone use</td>
<td>3</td>
<td>0.003835</td>
<td>0.0016</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid use</td>
<td>1</td>
<td>0.001518</td>
<td>0.0024</td>
</tr>
<tr>
<td>Macrolide use</td>
<td>5</td>
<td>0.001835</td>
<td>0.0317</td>
</tr>
<tr>
<td>H2-receptor antagonist use</td>
<td>1</td>
<td>0.001035</td>
<td>0.0035</td>
</tr>
</tbody>
</table>

(a) Represents the delay necessary to observe the effect (in months).
(b) Indicates the size and direction of the effect.