Multifaceted intervention to optimize antibiotic use for intra-abdominal infections

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Objectives: Implementing evidence-based practice guidelines is challenging. We used a multifaceted, continuous educational approach to disseminate an up-to-date internal guideline adapted from published guidelines for management of intra-abdominal infections (IAI).

Patients and methods: The intervention consisted of continuing educational sessions, internal guideline pocket cards and posters with collaboration among all key stakeholders starting in December 2010. We emphasized risk stratification and the use of ceftriaxone/metronidazole for treatment of low-risk IAI, and discouraged the use of fluoroquinolones due to the high local resistance rates. We then compared patients with IAI before the intervention (April–November 2010) to those after implementation of the guideline (April–November 2011) in a surgical unit at a tertiary care teaching hospital in Hamilton, Ontario, Canada. Antibiotic use was measured in in-hospital days of antibiotic therapy (DOT) per 1000 patient days (PD).

Results: 152 and 145 patients with IAI were included in the pre- and post-intervention periods, respectively. There was a significant reduction in the proportion of patients who received ciprofloxacin therapy from 74% to 34% (OR 0.18, 95% CI 0.11–0.31) and in DOT/1000 PD from 221 to 74 (OR 0.3, 95% CI 0.2–0.3). Also, a reduction in the DOT/1000 PD for piperacillin/tazobactam was seen (from 116 to 67; OR 0.6, 95% CI 0.5–0.7). There was an increase in the use of ceftriaxone from 1.3% to 53% of patients (OR 85, 95% CI 20–515) and from 6 to 92 DOT/1000 PD (OR 17, 95% CI 10–25). This change in practice was sustained over >2 years since the end of the active intervention, as shown in the unit-wide antimicrobial utilization data.

Conclusions: A multifaceted intervention aimed at all key stakeholders resulted in a high adherence to evidence-based treatment guidelines for IAI and has initiated a sustained culture change in prescribing of antibiotics.

Keywords: antimicrobial stewardship, fluoroquinolones, culture, knowledge translation

Introduction

Intra-abdominal infections (IAI) are very common and are associated with high rates of morbidity and mortality.1–3 IAI often need treatment with broad-spectrum antimicrobials that can result in adverse effects including emergence of resistance, fungal infections and Clostridium difficile infections.4 In 2010, both the IDSA and the Association of Medical Microbiology and Infectious Disease Canada released evidence-based practice guidelines on IAI management.5,6 Both guidelines highlight the importance of risk stratification and local susceptibility patterns to guide empirical treatment.

The availability of clinical practice guidelines does not necessarily change practice, as demonstrated by discordance with clinical practice for decades after publication.7 Multifaceted interventions can facilitate knowledge translation of new evidence into practice.8,9 Thus, we initiated a multifaceted guideline-implementation initiative consisting of: (i) a local consensus process to develop an internal guideline; (ii) educational meetings; and (iii) educational tools.
In this single-group pre–test-post–test quasi-experimental study, we aimed to compare hospital antibiotic prescribing practices pre- and post-intervention. We hypothesized that the implementation of the internal guideline would result in a shift from fluoroquinolone to cephalosporin use and in a reduction in the treatment duration.

**Methods**

**Population**

Patients admitted to a surgical ward in a high-volume tertiary hospital in Hamilton, Ontario, Canada between 1 April and 30 November in 2010 (baseline phase) and 2011 (intervention phase) were screened for eligibility. Patients were excluded if they were being treated for an IAI (appendicitis, cholangitis, cholecystitis, diverticulitis, peritonitis, intra-abdominal abscess or perforation) or if receiving pre-emptive antibiotics for intra-abdominal trauma. Patients were excluded if they had been previously enrolled in this study. Two of the authors (K. W. and T. R.) used a piloted and standardized screening tool to assess the eligibility (with disagreements resolved by a third author (C. M.)) and to collect the data independently. This study was approved by the local Research Ethics Committee.

**Internal guideline**

A multidisciplinary team consisting of infectious diseases specialists, a medical microbiologist, a hospital epidemiologist, clinical pharmacists and general surgeons developed an internal guideline. Adapting recently published guidelines,5,6 we focused on patient risk stratification, choice of empirical antimicrobial regimen, duration of therapy and switch from intravenous (iv) to oral route. In short, IAI was stratified into either community-acquired or healthcare associated (onset of symptoms ≥5 days after admission). Community-acquired IAI was further stratified into uncomplicated (no previous antimicrobial therapy and absence of significant comorbid conditions) or complicated (previous antimicrobial therapy, comorbid diseases and/or APACHE score of ≥15).5,6

Based on local epidemiology, ceftriaxone plus metronidazole was recommended for uncomplicated community-acquired IAI and piperacillin/tazobactam for the other two groups. Ciprofloxacin plus metronidazole were selected as second-line regimens for patients with documented β-lactam allergy. Due to high rates of fluoroquinolone resistance locally (24% for *Escherichia coli* in 2011), we emphasized the importance of reserving this regimen for clinically significant allergies.

**Intervention**

The intervention was endorsed by hospital and programme leadership and included a multimodal educational and collaborative approach, implemented from December 2010 through March 2011. The intervention consisted of: (i) adapting published guidelines based on local susceptibility data; (ii) creating educational tools such as handouts, posters and pocket cards; and (iii) providing educational sessions/meetings for surgery, infectious diseases, pharmacists and nurses from the surgical ward. All rotting residents assigned to the surgical ward were provided with educational sessions at the beginning of the rotation throughout the intervention phase. The medical teams—typically the surgical residents—prescribed antibiotics; however, the other healthcare providers were provided with educational sessions and meetings to provide awareness and endorsement. During the study period, there was no dedicated clinical pharmacist on the study ward; however, the organizational aspects of this project were spearheaded by a clinical pharmacist (Z. P.) who had time dedicated to this antimicrobial stewardship project.

The internal guideline was summarized on an educational pocket card (please see the Supplementary data available at JAC Online) and posters. All potential prescribers were provided with a hard copy and pdf file of the pocket card. The surgical ward was also provided with reprints of the internal guidelines and an electronic presentation outlining key details of the published clinical practice guidelines and their local adaptation.

**Analysis plan**

The coprimary endpoints were the proportion of patients who received fluoroquinolones versus ceftriaxone and antimicrobial utilization on the individual level, which was reported in days of therapy (DOT) per 1000 patient days (PD). In a sensitivity analysis, the denominator was defined as the total number of PD of all patients on the study ward, rather than the PD of the study population only. Secondary outcomes included duration of treatment, patient outcomes (readmissions and mortality) and antibiotic utilization. Data on clinical diagnosis, DOT and outcomes were collected manually. At the ward level, antibiotic utilization was measured in DDD/1000 PD.

For comparison between the two phases, χ² and Fisher’s exact tests were used for categorical data and t-tests for continous data. Statistical significance was set at an α value of 0.05. All statistical analyses were performed using Microsoft® Excel (version 2008 for Mac OSX).

**Results**

We recorded 512 antimicrobial regimens from 152 unique patients on the study unit between 1 April and 30 November 2010 (baseline phase). A total of 484 regimens were recorded from 145 unique patients over the same period in 2011 (intervention phase). The two groups were similar with respect to demographics and clinical characteristics, with a trend to more frequent surgical procedures in the intervention group (Table 1).

There was a notable decrease in the proportion of patients in the intervention phase who received at least one course of ciprofloxacin therapy (74% versus 34%; OR 0.18, 95% CI 0.11–0.31; P<0.001). Likewise, there was a significant increase in the proportion of patients receiving at least one course of ceftriaxone therapy (1.3% versus 53%; OR 85, 95% CI 20–515; P<0.001). Only five and two patients were treated with carbapenems in the baseline and intervention periods, respectively.

In DOT/1000 PD, there was a decrease from 221 to 74 (OR 0.3, 95% CI 0.2–0.3; P<0.001) for ciprofloxacin and from 116 to 67 (OR 0.6, 95% CI 0.5–0.7; P<0.001) for piperacillin/tazobactam. Smaller, albeit significant changes were seen for cefazolin (from 49 to 38; OR 0.8, 95% CI 0.6–1.0; P=0.048) and metronidazole (from 266 to 207; OR 0.7, 95% CI 0.6–0.8; P<0.001). The rate of ceftriaxone use increased from 6 to 92 (OR 17, 95% CI 10–25; P<0.001). The sensitivity analysis yielded similar results.

The mean duration of in-hospital courses of antibiotic treatment was 6 and 5 days for the baseline and intervention phases, respectively (mean difference 1.0, 95% CI −0.82–2.82). The duration of iv treatment was 5 and 4 days (mean difference 1.0, 95% CI −0.58–2.58) and a total of 28% and 26% of patients were treated for >7 days during their hospital stay, respectively.

Overall antibiotic utilization on the study ward in DDD/1000 PD corroborated the findings in DOT/1000 PD on the patient level (Figure 1). Ciprofloxacin use was reduced by 58% (from an average of 232 DDD/1000 PD in 2009–10 to 97 DDD/1000 PD in 2011) while there was an increase in ceftriaxone use of >600% (from 11 to 72 DDD/1000 PD). Importantly, the drop in ciprofloxacin use was sustained after the active intervention (Figure 1).
We achieved a significant culture change in antibiotic prescribing for IAI through the implementation of a multifaceted intervention. Despite the availability of evidence-based practice guidelines for antimicrobial therapy for IAI, we found that these guidelines were not being adopted at baseline. This was, in part, demonstrated by the high rate of fluoroquinolone use to which key pathogens in IAI had high rates of resistance at our institution.

Table 1. Patient characteristics and antibiotic utilization during the baseline and intervention phases

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Intervention</th>
<th>Total</th>
<th>P&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>152</td>
<td>145</td>
<td>297</td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>89 (59)</td>
<td>81 (56)</td>
<td>170 (57)</td>
<td>0.64</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>51.5 (19.3)</td>
<td>53.2 (20.4)</td>
<td>52.3 (19.8)</td>
<td>0.46</td>
</tr>
<tr>
<td>Surgical procedure to achieve source control, n (%)</td>
<td>97 (64)</td>
<td>105 (72)</td>
<td>202 (68)</td>
<td>0.11</td>
</tr>
<tr>
<td>Type of IAI, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>appendicitis</td>
<td>50 (33)</td>
<td>40 (28)</td>
<td>90 (31)</td>
<td>0.38</td>
</tr>
<tr>
<td>cholangitis/cholecystitis</td>
<td>38 (25)</td>
<td>45 (31)</td>
<td>83 (28)</td>
<td>0.3</td>
</tr>
<tr>
<td>diverticulitis</td>
<td>21 (14)</td>
<td>15 (10)</td>
<td>36 (12)</td>
<td>0.38</td>
</tr>
<tr>
<td>intra-abdominal abscess/trauma/perforation</td>
<td>30 (20)</td>
<td>36 (25)</td>
<td>66 (22)</td>
<td>0.33</td>
</tr>
<tr>
<td>other</td>
<td>13 (8)</td>
<td>9 (6)</td>
<td>22 (7)</td>
<td>0.51</td>
</tr>
<tr>
<td>At least one course/patient, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cefazolin</td>
<td>45 (30)</td>
<td>35 (24)</td>
<td>80 (27)</td>
<td>0.29</td>
</tr>
<tr>
<td>ciprofloxacin</td>
<td>112 (74)</td>
<td>49 (34)</td>
<td>161 (54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>metronidazole</td>
<td>128 (84)</td>
<td>121 (83)</td>
<td>249 (84)</td>
<td>0.86</td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>2 (1.3)</td>
<td>77 (53)</td>
<td>79 (27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>piperacillin/tazobactam</td>
<td>38 (25)</td>
<td>32 (22)</td>
<td>70 (24)</td>
<td>0.55</td>
</tr>
<tr>
<td>Duration of antibiotics (days), mean (SD)</td>
<td>6.0 (9.44)</td>
<td>5.0 (6.1)</td>
<td>6.0 (7.97)</td>
<td>0.29</td>
</tr>
<tr>
<td>Outcomes, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>readmission (overall)</td>
<td>24 (16)</td>
<td>16 (11)</td>
<td>40 (13)</td>
<td>0.24</td>
</tr>
<tr>
<td>readmission (related to abdominal infection)</td>
<td>14 (9)</td>
<td>10 (7)</td>
<td>24 (8)</td>
<td>0.47</td>
</tr>
<tr>
<td>death (in-hospital)</td>
<td>1 (0.7)</td>
<td>3 (2.0)</td>
<td>4 (1.3)</td>
<td>0.36</td>
</tr>
</tbody>
</table>

<sup>a</sup>Comparing the baseline phase with the intervention phase.

Figure 1. Antibiotic utilization in DDD/1000 PD before, during and after implementation of the intervention. ‘Overall’ includes ciprofloxacin, ceftriaxone, cefazolin and piperacillin/tazobactam. The grey shaded area corresponds to the intervention phase.

**Discussion**

We achieved a significant culture change in antibiotic prescribing for IAI through the implementation of a multifaceted intervention. Despite the availability of evidence-based practice guidelines for antimicrobial therapy for IAI, we found that these guidelines were not being adopted at baseline. This was, in part, demonstrated by the high rate of fluoroquinolone use to which key pathogens in IAI had high rates of resistance at our institution.
Our intervention resulted in a significant shift from a fluoroquinolone- to a cephalosporin-based regimen in keeping with our internal guideline. There was also a reduction of piperacillin/tazobactam use, likely due to the risk stratification component of our guideline. Of interest, the decrease in ciprofloxacin use was sustained after discontinuation of the active intervention. This highlights that an intervention can trigger a sustainable change when all key stakeholders buy into this change.

A recently published study on IAI guideline implementation was only partly successful in improving antimicrobial therapy with subsequent de-escalation. While similar in study design, patient characteristics and sample size to our study, the authors were not successful in demonstrating a significant reduction in ampicillin/sublactam and fluoroquinolone use as recommended by their guideline. They concluded that additional interventions were warranted. In contrast to our study, they only distributed their internal guideline to the clinicians and posted it on their intranet, while we implemented an ongoing, multifaceted intervention occurring over an 11 month period and incorporated education in the form of guideline presentations to surgical residents at implementation and throughout the study period. In addition, educational tools in the form of pocket cards, posters and presentations to study ward nurses and pharmacists provided reinforcement of the guidelines and continuity throughout the study period.

We did not find a statistically significant reduction in either the duration of overall antibiotic treatment or of the iv treatment duration or for antibiotics that were available in an oral and iv form. This can be explained by either: (i) the duration of treatment did not change at all and patients were not switched to oral treatment significantly earlier; or (ii) a difference in overall duration could only be appreciated when taking treatment as outpatients into account. Unfortunately, we were not able to collect reliable data on the duration of outpatient treatment. Another limitation of this study is the quasi-experimental design. We did not, however, identify any other interventions during the study periods that could potentially have influenced antimicrobial use. We also utilized identical time periods in two consecutive years to eliminate any potential seasonal influence. Finally, conduct of this study in one single surgical ward may limit generalizability to other settings.

In conclusion, our study demonstrates that a multifaceted intervention involving all key stakeholders can result in a sustained culture change in antimicrobial prescribing.

Acknowledgements
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Transparency declarations
Z. P. has received honoraria from Merck and Astellas for lectures. All other authors: none to declare.

Supplementary data
Supplementary data are available at JAC Online (http://jac.oxfordjournals.org/).

References