Impact of a computer-generated alert system prompting review of antibiotic use in hospitals

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Objectives: The aim of this study was to measure the impact on antibiotic use of a computer-generated alert prompting post-prescription review and direct counselling in hospital wards.

Methods: A computer-generated alert on new prescriptions of 15 antibiotics was reviewed weekly by an infectious disease physician for 41 weeks. During the first 6 months of the study, criteria selected for potential intervention were: (i) a planned duration of treatment of ≥10 days; (ii) discordance between the spectrum of the prescribed antibiotic and available microbiological results; or (iii) prescriptions of broad-spectrum β-lactams, fluoroquinolones, glycopeptides or linezolid. During the following 5 months, the alert was restricted to any prescription of the 15 antibiotics in the 9 wards where overall antibiotic use had not decreased in the past year.

Results: We analysed 2385 prescriptions, 932 (39%) of which generated an alert for potential intervention. Among the latter, 482 (51.7%) prescriptions prompted direct counselling, mainly for shortening the planned duration of therapy (18.9%), withdrawing antibiotics (16.2%) or streamlining therapy (15.5%). The attending physicians’ compliance with the recommendations was 80%. The overall median (interquartile range) days of therapy prescribed by the attending physicians was reduced from an initial duration of 8 (7–14) to 7 (6–11) days (P<0.0001), resulting in 26.5% less antibiotic days prescribed. The time required for the intervention was 6 h per week.

Conclusions: This computer-prompted post-prescription review led physicians to modify one half of the antibiotic courses initially prescribed and was well accepted by the majority, although they had not requested counselling.

Keywords: antibiotic stewardship, prescription review, infectious disease physician

Introduction

Antimicrobial stewardship programmes have been implemented in healthcare institutions to optimize antimicrobial use, ensure cost-effective therapy and potentially reduce antimicrobial resistance and improve patient outcomes.1–3 Many strategies (not mutually exclusive) can be employed, including education and guideline implementation, formulary and restriction policies and review and feedback strategies.1,2 Among these, prospectively auditing prescriptions with intervention and feedback to the prescribers have been recommended as a core strategy to improve antimicrobial use.

At our hospital, a restrictive order form has been implemented since 1996. In February 2006, the antibiotic policy was strengthened by educational sessions and the implementation of a computer-generated listing for post-prescription review of antibiotic orders. Between March and August 2006, we first tested the potential impact of this strategy on amoxicillin/clavulanate prescriptions. Of 343 prescriptions analysed during this period, 50.4% were considered as inappropriate and prompted a recommendation to the prescriber, including changing or discontinuing this agent. When compared with the previous year, the overall use of amoxicillin/clavulanate decreased by 11% (P. Lesprit, unpublished...
results). Because of this encouraging result, we decided to extend the prescription review to 15 selected antibiotics in wards where a computerized prescription system had been implemented, with the aim of improving the use of the targeted antibiotics by reducing the duration of therapy and de-escalating therapy whenever feasible. We also assessed the impact of interventions on patients’ clinical outcomes.

Methods

Setting
Henri Mondor Hospital is a tertiary-care, 960-bed university hospital with an average of 25,000 admissions per year. There is one infectious disease (ID) specialist who provides advice on an on-call basis in all hospital wards. Twelve antimicrobial agents have been placed on restricted access using a specific order form that provides information on daily dosage and costs of treatment, but does not include suggested durations of therapy. Orders are checked upon receipt by pharmacists for adherence to indications, selection of the drug and usual daily dosage, as recommended in the hospital’s guidelines issued by the Anti-Infective Drugs Committee. These guidelines are distributed hospital-wide in a pocket format and are also available on the Intranet. Every 6 months, all staff and junior physicians of each ward are offered educational sessions about antibiotic prescribing.

Programme design
A computerized prescription system was implemented in our hospital in 2005, except in the five intensive care units (ICUs) and the haematology unit. In this system, prescribers have to specify an intended duration when initiating antibiotic therapy. Although prescribers also have computerized access to laboratory results and clinical information, the system does not include a built-in decision-support or alert to prescribers. A computer-generated alert based on a predefined list of antibiotic prescriptions was made available to the infection control department on 1 November 2006, allowing screening of all prescriptions of antibiotics targeted. Data collected by the ID physician included demographic characteristics and locations of patients, information on new prescriptions of the 15 systemic antibiotics selected for review, including the type, modalities of administration and prescribed duration of treatment (start and stop date) and microbiological results. Antibiotic prescriptions analysed included amoxicillin/clavulinate (oral and intravenous), piperacillin/tazobactam, cefotaxime, ceftriaxone, cefepime, ceftazidime, imipenem, gentamicin, ofloxacin (oral and intravenous), ciprofloxacin (oral and intravenous), levofloxacin (oral and intravenous), moxi-floxacin (oral), vancomycin (intravenous), ticloplatin and linezolid (oral and intravenous). The ID physician reviewed the prescriptions from the computer-generated list on a given day each week.

The timeline for the intervention was developed as follows: during the first 6-month period of the study (28 November 2006 to 22 May 2007), 19 medical and surgical wards where the computerized prescription system was in use were surveyed. Predefined criteria for potential intervention were: (i) an ordered prescription of >10 days for any of the 15 antibiotics targeted; (ii) a discordance between the spectrum of the ordered antibiotic and the available microbiological results (including the prescribed antibiotic being inadequate or excessively broad); or (iii) any prescription of broad-spectrum β-lactams (piperacillin/tazobactam, cefepime, ceftazidime or imipenem), of fluoroquinolones, glycopeptides or linezolid, irrespective of its duration. At the end of this period, we analysed the antibiotic consumptions of the 19 wards during the preceding year. During the following period (1 June 2007 to 16 October 2007), the computer-prompted review and intervention were restricted to any prescription of the 15 antibiotics in the 9 wards where antibiotic consumption had not decreased between 2005 and 2006.

Prescriptions fulfilling one or more criteria for further analysis prompted direct interaction with the prescribing physicians during ward visits by the ID physician. First, the relevant clinical data from medical records, bedside flow sheets and reports of microbiological studies were reviewed and complemented by clinical examination of patients when necessary. Secondly, recommendations to modify the antibiotic regimen were provided orally to the attending physicians, when appropriate. When direct interaction with the physician could not occur, recommendations were written in the medical chart. These could be overridden, and no further attempt was made if recommendations were not followed. However, compliance with recommendations was recorded, and the duration of the treatment initially ordered by the attending physician was compared with the actual duration recorded after the intervention through the computerized prescription system. The actual duration was defined as being from the start to the end of the antibiotic administered in the hospital. Prescriptions ordered on patients’ discharge were not accounted for. Comparison of initially ordered and actual durations of treatment was made for all prescriptions, whether submitted for intervention or not.

To control for the actual duration of therapy in the absence of intervention and to examine clinical outcomes of patients with and without interventions, we analysed the planned and actual durations in the group of patients for whom no intervention was performed. Clinical outcomes (length of hospital stay, in-hospital mortality and readmission during the 30 days after the antibiotic course) were compared between the two groups of patients.

Statistical analysis
Categorical variables were compared using χ² test or Fisher’s exact test when appropriate. Ordinal variables were compared using a non-parametric Mann–Whitney test. Results of ordinal variables were expressed as median and interquartile range (IQR). Initial prescribed and actual durations of antibiotic therapy were compared using the non-parametric Wilcoxon matched pairs signed-rank test. Comparisons were made with 928 prescriptions since four outliers (duration expected of 360 days) were excluded. No sample size calculation was made a priori. A P value <0.05 was considered as significant.

Results

Characteristics of antibiotic prescriptions
Among the 2385 prescriptions of the 15 antibiotics screened during the 41 week period of the study, 932 (39%) ordered for 786 patients met our criteria for further analysis and potential intervention.

The prescriptions analysed originated from medical (60%) or surgical (40%) wards. The most common types of infection treated were urinary tract infection, pneumonia and skin and soft tissue infection (Table 1). A majority of prescriptions were of amoxicillin/clavulanate, fluoroquinolones or third-generation cephalosporins (Table 2). Microbiologically documented infections accounted for 56.5% of the prescriptions. The distribution of microorganisms identified as was as follows: Enterobacteriaceae,
27.7%; polymicrobial infections, 10.6%; *Pseudomonas aeruginosa*, 6.5%; staphylococci, 5.9%; streptococci or enterococci, 2.8% and others, 2.7%.

**Intervention**

Among the 932 prescriptions that met our criteria for further analysis, 482 (51.7%) were considered inappropriate and prompted counselling. The time required for the intervention (including collection and analysis of the data and feedback of recommendations to wards physicians) was 6 hours per week. The cost of the intervention, including the antibiotics listing reviews and ward visits by the ID physician, was estimated at €9300 for the whole period of the study. Most of the interventions (85%) were based on reviews of the medical and laboratory records. Clinical examination of patients by the ID physician occurred in 15% of cases. Feedback provided to prescribers included educational messages mainly based on the rationale of de-escalating therapy and reducing duration. Specifically, standard durations of antimicrobial therapy according to the site of infection were emphasized.

In accordance with the objectives of the intervention, three main changes were suggested: stopping therapy in the absence of apparent bacterial infection (n=151, 16.2%), de-escalating therapy (n=145, 15.6%) or altering the planned duration of therapy (n=190, 20.4%), mostly by recommending shortening the antibiotic course ordered by the physicians (n=176, 18.9%). Other recommendations, such as advocating a broader spectrum antibiotic (n=9, 1.0%), switching to oral therapy (n=24, 2.6%) or changing the dosing regimen (n=4, 0.4%), were rarely made.

**Follow-up of the interventions**

The final decision to alter the prescription was left to the attending physician, and actual changes in antibiotic prescriptions were recorded on the day following the intervention, except for 30 interventions (6.2%). Physicians rarely decided not to adopt the suggestion made during the intervention (n=65, 13.5%), and most recommendations (n=387, 80.3%) were followed.

Interventions occurred more frequently in surgical than medical wards; there were also more interventions for specific infections, such as bacteraemia, sepsis or surgical site infections.
Prescription review of antibiotic use

Table 3. Effect of the interventions on the duration of antibiotic therapy for 928 prescriptions prompting intervention

<table>
<thead>
<tr>
<th></th>
<th>Duration initially prescribed</th>
<th>Duration suggested by the intervention</th>
<th>Actual duration after intervention</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQR), days</td>
<td>8 (7–14)</td>
<td>7 (5–10)</td>
<td>7 (6–11)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total number of treatment days</td>
<td>11942</td>
<td>8318</td>
<td>8789</td>
<td></td>
</tr>
</tbody>
</table>

IQR, interquartile range.

Table 4. Clinical characteristics of the 786 patients receiving antibiotics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention (n=410)</th>
<th>No intervention (n=376)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital mortality, n (%)</td>
<td>17 (4.1)</td>
<td>21 (5.6)</td>
<td>0.348</td>
</tr>
<tr>
<td>Hospital length of stay, median (IQR) days</td>
<td>19 (10–33)</td>
<td>15 (8–30)</td>
<td>0.011</td>
</tr>
<tr>
<td>Hospital readmission, n (%)</td>
<td>63 (15.4)</td>
<td>57 (15.2)</td>
<td>0.936</td>
</tr>
<tr>
<td>Presence of co-morbidity, n (%)</td>
<td>276 (67.3)</td>
<td>249 (66.2)</td>
<td>0.674</td>
</tr>
<tr>
<td>Presence of severe co-morbidity, n (%)</td>
<td>84 (20.5)</td>
<td>79 (21.0)</td>
<td>0.883</td>
</tr>
</tbody>
</table>

*Readmission during the 30 days after antibiotic treatment.

(Table 1). Interventions were more often directed at prescriptions of broad-spectrum β-lactams, fluoroquinolones or vancomycin (Table 2).

Effect of the interventions on the duration of therapy and antibiotic use

To examine whether the intervention altered the duration of therapy, we compared three types of durations: those initially ordered by the physicians, those recommended by the ID physician during the ward visit and the actual duration after this intervention (including prescriptions for which the recommendation was not followed by the physicians or could not be assessed).

As shown in Table 3, the intervention led to a significant reduction of the median duration of therapy and was associated with a 26.5% reduction of the total antibiotic days.

In contrast, among the 450 concurrent prescriptions that were not submitted to interventions, there was no significant difference between initially prescribed and actual durations of therapy (both median and IQR: 7 and 6–10 days; P = 0.31).

Patients’ clinical outcomes

To examine whether the interventions could have some clinical impact, we compared clinical characteristics and patients’ outcomes between those who were or were not submitted to the ID physician intervention (Table 4). Although the prevalence of co-morbidities was similar between the two groups, patients within the ‘intervention’ group had a significantly longer length of stay in the hospital, possibly reflecting more severe illness. Despite this finding and the reduction of the duration therapy observed in the ‘intervention’ group, no significant difference in hospital mortality or 30 day hospital readmission rates was found between the two groups. However, the power of the study to detect a significant change in hospital mortality was only 12%.

Discussion

In this study, we took advantage of the recent implementation of a computerized prescription system in most wards of our hospital to add an automatic screening module, generating an alert for all new prescriptions of antibiotics targeted for review and potentially prompting an intervention.

Several positive results were found using this strategy. First, the intervention led to altering one half of the antibiotic courses thus identified, with an acceptable workload of about 1 day per week. The relatively high rate of inappropriate antibiotic use found in this study is consistent with the literature. Secondly, the recommendation mainly consisted of stopping or shortening the duration of therapy and streamlining therapy, three steps that are advocated for improving antimicrobial use and preventing antimicrobial resistance. As a result, the overall use of the targeted antibiotics significantly decreased, with a 12% reduction of the median duration and a 25% decrease in total number of treatment days. Parenteral-to-oral switch, which is also considered as an important component of antimicrobial stewardship programmes, was not a primary target of the interventions. Consequently, it was recommended in only 2.6% of interventions. Clearly, this must be improved in our hospital, using educational measures that have shown some efficacy. Also, few interventions were made with regard to antibiotic dosing. This could be explained by the fact that most of the antibiotics targeted were on restricted access using a specific order form. This form provides information on drug dosing, and orders are checked upon receipt by pharmacists for adherence to usual daily dosage.

A formulary restriction and requirement for review of prescriptions for specific drugs—most of which are among the
15 drugs targeted in this study—had been in place in our hospital for over 10 years; however, its efficacy was questioned because of an 8% increase in antibiotic consumption in 2005, likely illustrating the physicians’ limited adherence to, and the limited efficacy of, passive and restrictive measures for controlling antibiotic use. In this context, it is noteworthy that physicians’ compliance with the recommendations made through direct interaction was high in our study. This high rate was key to the success of the intervention and may be explained by the previous experience with direct counselling by our antibiotic control team. Although this finding may not be generalizable to other settings, a high rate of physicians’ compliance with direct feedback interventions has been observed by others.

Many interventions have been employed to improve antibiotic use in hospitals, but the current literature does not allow defining the best strategy because of the paucity of randomized controlled trials. However, a proactive strategy using prospective audit with intervention and feedback is considered as the core strategy. Indeed, two randomized controlled trials have shown that this strategy resulted in a reduction of inappropriate use of antibiotics and maintained its efficacy in the long term. A computer-generated alert as implemented in our study is one way to rapidly identify prescriptions potentially needing further review and intervention with appropriate direct counselling to prescribers on the wards. The screening algorithm can be customized to specific needs or interventions and adapted to local needs and resources. For example, we found that interventions were more frequent in surgical wards, at specific infection sites or in drug classes such as broad-spectrum β-lactams or vancomycin.

However, prescription review and ID intervention occurred only once per week, meaning that some patients might have received 6 days of treatment before review. Clearly, this was not ideal. We are currently evaluating another strategy using the same alert system 5 days a week and reassessing antibiotic prescriptions at 4 days. The cost of the whole intervention was modest and mainly attributable to the ID physician’s activity. Our study was not designed to assess the positive economic impact of the interventions, but such an impact has been previously reported in the literature.

There are some other limitations to our strategy. First, our computer-generated list did not allow reviewing prescriptions in the ICUs and haematology units, where the computerized prescription system had not been implemented. Because the level of antibiotic consumption is highest in these units, our strategy will only be partially effective to improve the overall antibiotic use in our hospital. Secondly, the major limitation of this study is its uncontrolled design. We assessed the effect of the intervention on treatment duration by comparing the planned duration of therapy initially prescribed by the attending physician with that actually prescribed after interaction with the ID specialist. This outcome may be not valid if the prescribers do not really administer (in the absence of intervention by the ID) what they have planned in the first place. However, we could show that the planned and actual durations of antibiotic therapy were similar in the concurrent group of prescriptions that were not submitted to the intervention. Finally, our study was not designed to assess a correlation between changes in antibiotic prescribing and microbiological or clinical outcomes. Quantifying the microbiological efficacy of our programme on the prevalence of antibiotic-resistant bacteria or Clostridium difficile disease would require a longer follow-up, as was shown, for example, during an antibiotic management programme conducted over 7 years. In contrast to the studies aimed at improving the adequacy of antibacterial treatment, which resulted in improved clinical outcomes, interventions aiming at decreasing antibiotic use have not been associated with such effects. In fact, very few studies have monitored mortality or readmission rates. Results for mortality rates were heterogeneous, but there was a trend towards an increased risk of readmission associated with the interventions. We found no significant difference in these clinical outcomes when comparing patients receiving antibiotics submitted or not to the intervention, a finding similar to that observed by Solomon et al. However, these results should be interpreted with caution because our study lacked the power to detect a significant difference in these outcomes. Similarly, the higher length of stay of patients within the intervention group observed in our study may reflect differences in patients’ acuity, but we were not able to explore this.

In conclusion, using a customized computer-generated alert of selected antibiotic prescriptions to prompt review with direct counselling and feedback to prescribers was associated with a high rate of interventions and several potential beneficial outcomes. The high rate of physicians’ compliance suggests that this strategy might be implemented successfully in many hospitals and wards.

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Transparency declarations
None to declare.

References


