Academic Detailing to Improve Use of Broad-Spectrum Antibiotics at an Academic Medical Center

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Background: Antibiotic misuse is common and costly and may promote antibiotic resistance. We tested the efficacy of a targeted one-on-one educational program ("academic detailing") designed to improve the appropriateness of broad-spectrum antibiotic use.

Methods: A randomized controlled trial was conducted in a large US teaching hospital. During an 18-week study period, 17 general medical, oncology, and cardiology services either received academic detailing or did not. The intervention was prompted by an order for either levofloxacin or ceftazidime that led to a computer-based review of data for that patient. Orders for the 2 target antibiotics deemed unnecessary by a priori criteria were included in the study. The primary outcome examined was the number of days that unnecessary levofloxacin or ceftazidime was administered in intervention and control groups.

Results: Before the trial, intervention and control services had similar prescribing patterns for the target antibiotics; the drugs were used for similar indications throughout the study period. During the intervention, there was a reduction of 37% in days of unnecessary levofloxacin or ceftazidime use per 2-week interval on services randomized to the educational intervention vs control services ($P<.001$). In multivariable analyses controlling for baseline prescribing and study interval, the rate of unnecessary use of the 2 target antibiotics was reduced by 41% on the intervention services compared with controls (95% confidence interval, 44%-78%; $P<.001$). Length of stay, intensive care unit transfers, readmission rates, and in-hospital death rates were similar in both groups ($P \geq .10$ for all).

Conclusion: Targeted one-on-one education is a practical, effective, and safe method for reducing excessive broad-spectrum antibiotic use.

Arch Intern Med. 2001;161:1897-1902

ANTIBIOTIC MISUSE is common and costly. Approximately one third of all hospitalized patients receive an antibiotic, and several reports suggest that at least half of antibiotic orders are unnecessary, poorly chosen, or incorrectly dosed. Physicians often opt for broad-spectrum antibiotics when a narrower-spectrum agent would suffice. A review of 2 months of vancomycin hydrochloride use at one teaching hospital found that 70% of orders were inappropriate; problematic orders were as common for the medical service as they were for the surgery service.

Suboptimal use of antibiotics poses problems beyond those applicable to the individual patient so treated; overreliance on broad-spectrum agents is also thought to be an important contributor to growing worldwide antimicrobial resistance. A recent study found that as quinolone use increased more than 6-fold between 1988 and 1997, from 0.8 to 5.5 per 100 persons per year, the prevalence of pneumococci with reduced susceptibility to quinolones increased from 0% to 1.7%. Quinolone-resistant Salmonella enterica and Campylobacter jejuni infections have also been increasingly reported. New antimicrobial resistance has emerged in many different human pathogens, and rates of existing resistance have increased. At least 6 studies have suggested that rates of invasive infections with drug-resistant Streptococcus pneumoniae are related to recent antibiotic exposure, and 1 recent study suggested that local antibiotic use patterns directly affected local resistance patterns. These data have prompted a working group of the Centers for Disease Control and Prevention to focus attention on the judicious use of antibiotics as one part of the strategy to combat drug-resistant Streptococcus pneumoniae.
PARTICIPANTS AND METHODS

STUDY SITE

Brigham and Women's Hospital is a 697-bed academic medical center affiliated with Harvard Medical School in Boston, Mass. Approximately 32% of admissions are to the internal medicine department, including general medical, oncology, and cardiology services. A typical service consists of 1 attending physician, 1 second- or third-year medical resident, and 2 interns; interns and residents write all antibiotic orders.

To achieve balanced patient groups for the present study, we assigned services to intervention or control status using a blocked randomization design. Three of the general medical services were randomly assigned to intervention and 3 to control, and 2 of the oncology services were randomly assigned to intervention and 2 to control. Three additional general medical services and 4 cardiology services were added at week 3 through a similar blocked random assignment approach. In all, 9 services comprised the intervention group and 8 the control group. The study period began January 20, 1999, and ended May 19, 1999; the 4 weeks immediately preceding this period were considered the baseline period.1

TARGET ORDERS

We used the hospital's computerized pharmacy records to review all orders for levofloxacin and ceftazidime written for patients on the intervention and control teams. The hospital's Division of Infectious Diseases developed a set of guidelines for first-line antibiotic therapy, including recommendations for the proper use of these agents. We disseminated these guidelines to all house officers as pocket-sized laminated brochures (available on request) before this study. Although in any given situation many antibiotics may be effective, these guidelines recommended preferred antibiotic choices for our hospital.

Each morning, a research assistant reviewed computerized laboratory, pharmacy, and prior admission data for all patients for whom physicians ordered levofloxacin or ceftazidime in the prior 24 hours. The criteria were applied without regard to the study group assignment. All orders for levofloxacin were flagged for review unless the patient had (1) an isolate sensitive to levofloxacin, (2) a history of antibiotic resistance is substantial. A report from the US Office of Technology Assessment estimated that the extra hospital costs associated with drug-resistant nosocomial bacterial infections were $1.3 billion annually.17

In our institution, drug use evaluations have suggested that narrower-spectrum antibiotics could be safely substituted for a substantial number of broad-spectrum antibiotic orders. However, most patients are never seen by infectious disease consultants; thus, there is no routine method for such antibiotic optimization. Given increasing concern over unnecessary patient exposure to broad-spectrum antibiotics, trends in antimicrobial resistance patterns, and the costs associated with both, we undertook the present study to determine whether one-on-one education by clinical specialists on a patient-specific basis (“academic detailing”) could reduce excessive use of broad-spectrum antibiotics.

RESULTS

More than 4500 patients were admitted to the intervention and control services during the baseline and study periods. Patient characteristics on both sets of services were similar and did not differ between the baseline and study periods (Table 1). At baseline, the mean±SD number of days of unnecessary target antibiotic use was
were prescribed ceftazidime had cystic fibrosis and were
and 7.6±4.7 for the control services (P=.001) (Figure 1). During the 18-week study period, 490 patients from all study services were prescribed levofloxacin or cefta-
the target antibiotics. Computerized record re-
view indicated that 212 patients were not appropriate for
services either intern or resident after reviewing the chart. This
and duration of the intervention would be impor-
tant confounders, multivariable models were constructed in-
cluding these factors as independent variables. The dependent
variable was unnecessary prescribing of the target antibiot-
tics during each 2-week interval of the intervention period.
To estimate the relative reduction in unnecessary use of tar-
gent antibiotics in the intervention group, we used a fixed-
effects model (PROC GENMOD in SAS statistical software).20 This model used a log-linear link function, assumed a Pois-
sion distribution, and accounted for overdispersion. Experi-
mental group assignment (intervention or control) was the
independent variable of interest, the individual service was
considered a class effect, and covariates included level of base-
line prescribing and time, modeled as both a linear and cat-

gorical effect. The interaction between assignment and time
also for every patient admitted to a study service during
the hospital. We examined these secondary outcomes not
related to an intensive care unit, taken to surgery on the
study period to measure rates of death and transfer
within 30 days of discharge.

The main study end point was the average number of days
that unnecessary levofloxacin or ceftazidime was adminis-
tered per service. This outcome was compared for each
2-week interval for services in the intervention vs control
groups. The prescribing information was drawn from the hos-
pital’s computerized pharmacy records. In a subsample of
patients, we validated the computerized pharmacy data against
the manually completed medication administration rec-
ords in the patient’s hospital chart. There was complete agree-
ment in 14 (93%) of 15 patient records examined and par-
tial agreement in the 1 remaining record. Patients who were
prescribed more than one new course of levofloxacin or cefta-
zidime were counted in the analysis more than once. We also
reviewed the medical records of all patients in both the in-
tervention and control groups to determine the presumed
source of infection that prompted the target antibiotic or-
der. Next, medication orders for the day of the educational
intervention (or the comparable day on the control ser-
vice) were examined to determine whether the target drug
regimens were continued, discontinued, or changed in route or dosage. Finally, we examined computerized records for
every patient admitted to intervention or control services dur-
ing the study period to measure rates of death and transfer
to an intensive care unit, length of stay, and readmission
within 30 days of discharge.

8.5±7.8 per 2-week interval for the intervention service
and 7.6±4.7 for the control services (P=.80) (Figure 1).
During the 18-week study period, 490 patients from all study services were prescribed levofloxacin or cefta-
zidime, the target antibiotics. Computerized record re-
view indicated that 212 patients were not appropriate for
study for the following reasons: 83 were discharged, trans-
ferrred to an intensive care unit, taken to surgery on the
index date, or died; 37 had serum creatinine levels greater
than 1.5 mg/dL (>132.6 µmol/L); 23 had a known iso-
late sensitive to one of the target antibiotics; 21 had a his-
tory of a solid organ transplantation or were taking immu-
nosuppressive medications; 20 who were prescribed ceftazidime had an absolute neutrophil count less than
500/mm3; 18 had multiple antibiotic allergies; and 10 who
were prescribed ceftazidime had cystic fibrosis and were
at high risk of pseudomonal infections. The remaining
278 unnecessary prescriptions in 260 patients formed the
study cohort. Among these patients, the indications for
treatment or presumed sources of infection were similar for
those in the intervention and control groups (Table 2). There were slightly higher rates of fever and neu-

troenia among levofloxacin users on the intervention
services (P=.04).

We then examined the mean number of days of un-
necessary target antibiotic use per 2-week interval per ser-
vice for each group (Figure 1). Although baseline pre-
scribing was similar, during the intervention period, the
number of days of unnecessary use of target antibiotics
was 37% lower for the intervention services than for con-
trols (P<.001) (Figure 1). During the study period, there
were a mean±SD of 5.5±2.1 days per 2-week interval for

**ANALYSIS**

We compared the average number of days of unnecessary le-
voﬂoxacin and ceftazidime use during each 2-week interval
for the intervention and control services. To calculate the ex-
pected values and conﬁdence intervals (CIs) and to test dif-
dences, we used a linear univariate fixed-effects model (PROC
MIXED).20 Since we suspected that differences in baseline pre-
scribing and duration of the intervention would be impor-
tant confounders, multivariable models were constructed in-
cluding these factors as independent variables. The dependent
variable was unnecessary prescribing of the target antibiot-
tics during each 2-week interval of the intervention period.
To estimate the relative reduction in unnecessary use of tar-
gent antibiotics in the intervention group, we used a fixed-
effects model (PROC GENMOD in SAS statistical software).20 This model used a log-linear link function, assumed a Pois-
sion distribution, and accounted for overdispersion. Experi-
mental group assignment (intervention or control) was the
independent variable of interest, the individual service was
considered a class effect, and covariates included level of base-
line prescribing and time, modeled as both a linear and cat-

gorical effect. The interaction between assignment and time
was also assessed. We further considered a linear random-
effects model to account for variation between services (PROC
MIXED in SAS statistical software)20; the results of this analy-
sis were similar to those found in the fixed-effects models with
respect to the level of statistical significance, and only the fixed-
effects model results are presented.

All analyses were conducted on an intention-to-treat
basis. Several services had unusually heavy prescribing of
the target antibiotics during certain 2-week blocks. To ex-
amine the effect of such periods, we performed identical
analyses of the main effect after removing these outlier in-
tervals from the analyses. The results were nearly identi-
cal; thus, only the analyses using all data points will be pre-

tended. Finally, we assessed the mean length of stay for all
patients on intervention and control services and mea-
sure the proportion of patients who were transferred to
an intensive care unit, were readmitted to Brigham and
Women’s Hospital within 30 days of discharge, or died in
the hospital. We examined these secondary outcomes not
only for patients who received the target antibiotics, but
also for every patient admitted to a study service during
the baseline and intervention periods.
the intervention services vs 8.8±2.2 days for the controls; this reduction was because of 28 fewer starts and an average antibiotic course 0.8 day shorter. The multivariate analyses, accounting for repeated measures of the target antibiotics and baseline prescribing, indicated that the risk of receiving a day of unnecessary target antibiotic was reduced by 41% on the intervention services compared with controls (95% CI, 44%-78%; \( P = .001 \)) for the difference between intervention and control groups during the study period. For the study period, confidence intervals were calculated from the univariate fixed-effects model. See text for description of "unnecessary use of target antibiotics."

services, 69 patient orders (55%) for unnecessary target antibiotics had all antibiotic use discontinued. This significantly differed from the control services in which only 24 patient orders (16%) were followed by discontinuation of all antibiotic use (\( P = .001 \)). Route changes (intravenous to oral) were equal and uncommon (14%) for both intervention and control services.

The intervention had no measurable negative clinical effects. The average length of stay, proportion of patients transferred to an intensive care unit or patients readmitted within 30 days of discharge, and death rates were similar for all patients in the intervention and control services (Table 3).

### Table 1. Characteristics of Study Services*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Intervention Services (n = 9)</th>
<th>Control Services (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admissions per 2 wk per service, mean ± SD</td>
<td>26 ± 4</td>
<td>25 ± 4</td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>61 ± 4</td>
<td>60 ± 5</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>52</td>
<td>48</td>
</tr>
</tbody>
</table>

### Table 2. Presumed Source of Infection During Study Period*

<table>
<thead>
<tr>
<th>Infection Source</th>
<th>Intervention Services, %</th>
<th>Control Services, %</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genitourinary</td>
<td>23</td>
<td>20</td>
<td>.52</td>
</tr>
<tr>
<td>Respiratory</td>
<td>46</td>
<td>43</td>
<td>.53</td>
</tr>
<tr>
<td>Intra-abdominal</td>
<td>14</td>
<td>19</td>
<td>.32</td>
</tr>
<tr>
<td>Joint, bone, skin, soft tissue</td>
<td>9</td>
<td>9</td>
<td>.94</td>
</tr>
<tr>
<td>Sepsis, line or not otherwise specified</td>
<td>5</td>
<td>5</td>
<td>.91</td>
</tr>
<tr>
<td>Fever and neutropenia</td>
<td>5</td>
<td>1</td>
<td>.04</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>0</td>
<td>1</td>
<td>.23</td>
</tr>
</tbody>
</table>

* A total of 260 patients accounted for the 278 orders included in the study. There were 125 study orders in the intervention services group and 153 in the control services group. Columns do not add to 100% because of rounding. Genitourinary includes urosepsis and urinary tract infections.

Respiratory includes upper and lower tract infections.

### Table 3

<table>
<thead>
<tr>
<th>Infection Source</th>
<th>Discontinued Orders, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target Antibiotics</td>
<td>80</td>
</tr>
<tr>
<td>All Antibiotics</td>
<td>50</td>
</tr>
</tbody>
</table>

\( P = .001 \)

### Comment

Reduction of inappropriate use of antibiotics, especially broad-spectrum agents, is an important goal in acute care settings such as teaching hospitals. In a randomized controlled trial that took place in the department of medicine of a US academic medical center, we found that the risk of prescribing a day of unnecessary target antibiotic was 41% lower on services randomized to a intervention of “academic detailing” compared with controls. This significant effect of the intervention remained after adjusting for baseline prescribing, clustering of repeated mea-
sures within a given service, and duration of the intervention. Both fewer starts and shorter courses of target antibiotics account for the reduction of use of broad-spectrum antibiotics in the intervention services. This suggests that to some degree interns and residents learned not to prescribe an unnecessary antibiotic but that the daily academic detailing reminded prescribing physicians to stop the use of previously started but unnecessary antibiotics.

The intervention was based on the academic detailing approach developed by our group that has proven to be a useful method for improving behavior in a variety of prescribing situations. Academic detailing is a program of one-on-one interactive educational outreach provided by a clinician, either a pharmacist or physician, who has been trained to discuss prescribing decisions with physicians in a manner likely to induce evidence-based practice change. An academic detailing approach has been used successfully to improve outpatient antibiotic use, but not inpatient prescribing, to our knowledge.

Several limitations of the present study should be considered. Since resident physicians switched services every month, contamination occurred between intervention and control groups. This would have biased the results against finding any difference between intervention and control teams and thus may have dampened the observed effect of the intervention. One method for dealing with this potential would have been to randomize physicians; however, many of the decisions regarding antibiotic orders are made by the team and thus randomization by a physician would have allowed for substantial intrateam contamination. Fourteen orders were included in the intervention set that were not deemed appropriate for academic detailing because the antibiotics had been suggested by a prior consultation from the infectious diseases division. We kept these orders in the analysis since they were part of the original randomization set; their inclusion reduced the effect of the intervention. Finally, although we did not collect specific data from house officers about why they continued using possibly unnecessary antibiotics, possible reasons include misinformation, neglect of microbiologic laboratory information, pressure from attending physicians, and patient or family concerns.

Part of the success or failure of the academic detailing intervention rests on the ability and availability of the educators doing the one-on-one intervention. We attempted to minimize the effect of the detailer’s personal style on the study outcome by standardizing the educational encounter through the use of scripts and a common evidence-based approach. In addition, many hospitals may not have infectious disease consultants available to perform the academic detailing. Our intervention used a trained clinical pharmacist whose impact on prescribing was similar to that of the infectious disease physicians; previous interventions have likewise used pharmacist-educators with good effects.

Other than the one-time initial costs of developing and printing antibiotic guidelines for our hospital, the daily costs of conducting the intervention included approximately 1 hour of a research assistant’s time to review new orders for the target antibiotics and 1 hour from an academic detailer; thus, the estimated annual cost was $21,750. Although a formal economic analysis was not performed, we found that the length of antibiotic courses was shortened on the services randomized to the intervention: 55% of patients had all antibiotic use stopped in the 24 hours after the intervention vs 16% in the controls. In addition, there is a real but hard-to-quantify economic benefit of reducing the risk of resistance associated with overuse of broad-spectrum antibiotics. Taken together, these benefits are likely to outweigh the very modest cost of the intervention. As a result, we plan to continue and expand such antibiotic counterdetailing efforts in our institution.

Further work will be required to demonstrate the generalizability of an academic detailing approach to other settings and to define the most efficient means to conduct such programs on a larger operational scale. Although development of newer antibiotics may help address antimicrobial resistance in the short term, improving the prescribing of available antibiotics will continue to be a priority throughout the health care system for the foreseeable future.

Accepted for publication February 22, 2001.

Financial support for this work was provided by a core grant from the Brigham and Women’s Hospital to the Division of Pharmacoepidemiology and Pharmacoeconomics. Dr Solomon is a recipient of an Arthritis Foundation Investigator Award.

Gonzalo Graupera, MD, and Asra Warsi provided assistance with data collection and Nancy Keating, MD, MPH, provided helpful comments on an early draft of the manuscript.

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