MAJOR ARTICLE

Effectiveness of Education and an Antibiotic-Control Program in a Tertiary Care Hospital in Thailand

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(See the editorial commentary by Nouwen on pages 776–7)

Background. We conducted a study to evaluate the impact of education and an antibiotic-control program on antibiotic-prescribing practices, antibiotic consumption, antimicrobial resistance, and cost of antibiotics in a tertiary care hospital in Thailand.

Methods. A study of the year before and the year after the intervention was performed. Inpatient antibiotic prescriptions were prospectively observed. Demographic characteristics, hospital unit, indication for antibiotic prescription, appropriateness of antibiotic use, reasons for inappropriate antibiotic use, antibiotic consumption (i.e., the rate of antibiotic use), bacterial resistance, and antibiotic cost data were collected. Interventions included education, introduction of an antibiogram, use of antibiotic prescription forms, and prescribing controls.

Results. After the intervention, there was a 24% reduction in the rate of antibiotic prescription (640 vs. 400 prescriptions/1000 admissions; $P<.001$). The incidence of inappropriate antibiotic use was significantly reduced (42% vs. 20%; $P<.001$). A sustained reduction in antibiotic use was observed ($R^2 = 0.692$; $P<.001$). Rates of use of third-generation cephalosporins (31 vs. 18 defined daily doses [DDDs]/1000 patient-days; $P<.001$) and glycopeptides (3.2 vs. 2.4 DDDs/1000 patient-days; $P = .002$) were significantly reduced. Rates of use of cefazolin (3.5 vs. 8.2 DDDs/1000 patient-days; $P<.001$) and fluoroquinolones (0.68 vs. 1.15 DDDs/1000 patient-days; $P<.001$) increased. There were no significant changes for other antibiotic classes. Significant reductions in the incidence of infections due to methicillin-resistant *Staphylococcus aureus* (48% vs. 33.5%; $P<.001$), extended-spectrum β-lactamase–producing *Escherichia coli* (33% vs. 21%; $P<.001$), extended-spectrum β-lactamase–producing *Klebsiella pneumoniae* (30% vs. 20%; $P<.001$), and third-generation cephalosporin–resistant *Acinetobacter baumanii* (27% vs. 19%; $P<.001$) were also observed. Total costs saving were US$32,231 during the study period.

Conclusions. Education and an antibiotic-control program constituted an effective and cost-saving strategy to optimize antibiotic use in a tertiary care center in Thailand.

Overuse of antimicrobial agents occurs globally in both community and hospital settings [1–5]. Misuse of antibiotics can lead to a variety of adverse outcomes, including the development of antimicrobial resistance and increased cost of hospitalization [4, 6]. This issue has been particularly problematic in developing countries, where antibiotic-management programs rarely exist and where antibiotics can be purchased without a prescription [7]. In Thailand, the rate of antibiotic resistance among gram-positive and gram-negative organisms has increased significantly over the past decade [8–10]. These findings provide compelling evidence of the need for more-rational use of antimicrobial agents in Thailand.

Inappropriate antimicrobial use has been defined as the use of therapeutic or prophylactic antibiotics that are not appropriate. Example of these circumstances include use of antibiotics when there is no evidence of infection, administration of antibiotics to patients who are colonized with an organism, inappropriate surgical prophylaxis (including inappropriate dose, dosing

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interval, and treatment duration before and after surgery), administration of antibiotics for treatment of infection with microorganisms that are resistant to those antibiotics, administration of broad-spectrum antibiotics when narrower-spectrum antibiotics would have been effective and available, administration of multiple antibiotics that have a redundant spectrum, administration of antibiotics that are inadequate for the microorganisms that cause the disease, and administration of antibiotics with inappropriate doses and treatment durations. In Thailand, inappropriate antimicrobial use has been found to occur for 25%–91% of hospitalized patients in tertiary care centers [11].

A number of measures have been taken to influence the use of antibiotics in hospital settings. Restrictive or administrative approaches may work in the short term, but by themselves, they may meet resistance from the prescribers. Educational strategies have been used, but their effect may be short lived [12, 13]. In our institution, we identified a variety of antimicrobial use patterns among prescribers in various units. Admissions to surgery and obstetrics and gynecology units were particularly associated with inappropriate antibiotic use [11]. Limited data are available on strategies to control or improve antibiotic use practices in Thailand [14–17]. We describe the intervention and the outcomes associated with the institution of an educational program and an antibiotic-management program in a tertiary care hospital in Thailand.

METHODS

Setting. Thammasart University Hospital is a 350-bed tertiary care university hospital in central Thailand. The referral base has a ~250-km radius, and the hospital has 17 patient care departments. Each unit is staffed with 1 attending physician, residents, interns, and medical students. Antibiotics are prescribed by attending physicians (18%), residents (37%), and interns (33%) directly or by medical students (12%) under an attending physician or resident's supervision. There are 2 infectious disease specialists who evaluate patients with infectious diseases on a consultation basis. In this hospital, 88% of antibiotics are prescribed to inpatients in intravenous form, and 12% are prescribed in an oral form.

Definitions. The rate of antibiotic use by inpatients was recorded as the total number of grams of the drug, and the value was converted into defined daily doses (DDDs) per 1000 patient-days, in accordance with the World Health Organization recommendations [18]. Only expenditures for drugs that were administered intravenously were analyzed and included for cost analysis. Criteria used to define the need for antimicrobial therapy were adopted from the current edition of *Principles and Practices of Infectious Diseases* [19]. We used local hospital antibiotic guidelines developed from existing published guidelines to measure the appropriateness of antibiotic use. The antibiotic appropriateness guidelines were prepared by the antimicrobial-management program committee. The guidelines included a short description of all antibiotics available in Thammasart University Hospital together with the recommended dosage of each antibiotic, principles of antibiotic use for prophylaxis and treatment of infectious diseases, recommended antibiotics for prophylaxis, and recommended antibiotics for treatment in situations in which the infecting organisms are either known or suspected. The antibiotic guidelines were modified and agreed upon by the faculty members in the clinical departments, the Department of Pharmacology, and the Department of Microbiology and were later approved by the Faculty of Medicine Committee to be used as the guidelines for clinical practice in Thammasart University Hospital. Specific use categories were modeled after those of Kunin et al. [20] (table 1) and were modified to fit local practices by an expert panel, which consisted of 2 infectious diseases physicians. Modifications were also made to accommodate susceptibility patterns and management of some diseases that are peculiar to Southeast Asia, such as melioidosis. For patients who received surgical prophylaxis, assessment of appropriateness of antibiotic treatment also included the specific type of antibiotic and the dose and duration of prophylaxis before and after surgery, in

Table 1. Categories of judgment of antibiotic use.

Category	Judgement
I	Agree with the use of antimicrobial therapy/prophylaxis; the prescription is appropriate
II	Agree with the use of antimicrobial therapy/prophylaxis
	A potentially fatal bacterial infection cannot be ruled out, or
	Prophylaxis is probably appropriate, although advantages derived remained controversial
III	Agree with the use of antimicrobial therapy/prophylaxis, but a different (usually less expensive or less toxic) antimicrobial is preferred
IV	Agree with the use of antimicrobial therapy/prophylaxis, but a modified dose or duration is recommended
V	Disagree with the use of antimicrobial therapy/prophylaxis; administration is unjustified

NOTE. Categories are adapted from Kunin et al. [20]. Categories I and II essentially indicate appropriate therapy; categories III–V indicate that there was some major deficiency in the choice or use of antibiotics by the physician managing the problem and that antibiotic use was inappropriate.

accordance with the methodology of Bratzler et al. [21]. Data on the number of patient admissions, discharges, and patient-days were supplied by the medical record database system. Sustained reduction was defined as a persistent reduction in any outcomes of interest measured.

Program design. The timeline for these interventions was developed as follows: during period 1 (1 July 2003 to 31 June 2004), baseline data (data on bacterial resistance, antibiotic use, prescribing practice, and antibiotic costs) were collected, and data were analyzed; during period 2 (1–30 June 2004), we performed feedback activities according to the baseline findings, introduced antibiotic order forms, and transformed the antibiotic order form into an obligatory requirement for procuring the drug from the pharmacy; period 3 (1 July 2004 to 30 June 2005) was similar to period 2, but with bedside discussion among the pharmacists, clinical microbiologist, and attending physicians (except for surgical prophylaxis prescriptions, which were already standardized), and data collection was continuous. The antimicrobial-management program committee comprised an infectious disease physician, a clinical microbiologist, 4 pharmacists, 2 internists, a hospital epidemiologist, an infection-control specialist, and a computer system analyst; it convened on 1 June 2004 to design an intervention program to optimize antibiotic use within the hospital. A computerized system for data recording and analysis was implemented on 1 July 2003 in the departments of pharmacy, microbiology, and infection control to collect baseline data. Data collected included demographic characteristics and location of patients and information on systemic antibiotics that the patients received, including the type, dose, frequency, start and stop date, prescribing physician, indication for antibiotic prescription, appropriateness of antibiotic use, classification of inappropriate antibiotic use, rates of antibiotic use, pattern of antimicrobial resistance, and cost. All data were entered into computer software prepared for this project. The costs of antibiotics were calculated on the basis of the actual dosage given to the patients and were based on the purchase price to the institution after mark-up by the pharmacy, without the inclusion of the administration cost. All costs in Thai baht currency were converted to US dollars (exchange rate, 40 baht = US$1). The data derived from the preintervention period were analyzed, and the major causes of inappropriate use of antibiotics were used for information feedback and to construct the antibiotic guidelines [11].

Additional interventions for antibiotic controls included introduction of an antibiogram and antibiotic prescription forms; monthly education of medical students, residents in the departments of surgery, obstetrics and gynecology, and internal medicine; and control of specific antibiotic classes. Because most antibiotics were administered in their intravenous forms (88%), we decided to implement these interventions only for intravenous antibiotic regimens. The antibiotic prescription forms were developed for 4 major classes of antibiotics (third-generation cephalosporins, β-lactam/β-lactamase inhibitors, glycopeptides, and carbapenems). Because the potential for use of fluoroquinolones and aminoglycosides was partially limited by patients' insurance, such agents were not included in the antibiotic prescription forms. The antibiotic prescription form required physicians to state the certainty of infection diagnosis, as well as the most relevant microbiologic data. Two infectious diseases physicians reviewed and completed the form with the same data as the antibiotic prescription form, as well as with additional data, such as any interruption or modification of treatment suggested by the antimicrobial management program committee. Each infectious diseases physician reviewed and completed the form for different departments and followed explicit criteria (table 1) for prescribing appropriateness using a checklist. There were no duplicate reviews of prescriptions. At each educational session, information and feedback relevant to each specialty or clinical practice were given, and the hospital antibiotic guidelines were also introduced. Additional training sessions were performed every 4 months for all physicians in the hospital. There were no restrictions on antibiotic-prescribing habits. However, physicians were informed about the increased risk of development of bacterial resistance associated with the overuse of third-generation cephalosporins and carbapenems, as well as the potential benefits of replacing such agents with β-lactam/β-lactamase inhibitors or fourth-generation cephalosporins. There were no specific actions to control or prevent nosocomial infections, with the exception of standard precautions and contact precautions for antimicrobial-resistant organisms, such as methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum β-lactamases (ESBL)–producing microorganisms, third-generation cephalosporin–resistant *Acinetobacter baumanii,* imipenem-resistant *Pseudomonas aeruginosa,* and multidrug-resistant *A. baumanii* that were already being undertaken before the starting date. All interventions were initiated on 1 July 2004.

To evaluate the impact of changes in antibiotic use on bacterial resistance, we selected certain important and prevalent multidrug-resistant species detected in the baseline period for analysis. These included MRSA, ESBL-producing *Escherichia coli,* and *Klebsiella pneumoniae.* To date, vancomycin-resistant enterococci has not been isolated at our hospital; therefore, we did not include this microorganism in the analysis.

Statistical analysis. Categorical variables were presented as absolute values, and percentages were compared using χ^2 or Fisher's exact test, as appropriate. Continuous variables were expressed as means ± SDs. A 2-tailed Student's *t* test was performed to compare continuous variables. Trend analysis was performed to evaluate the overall pattern of changes on outcomes of interest over time using simple linear regression anal-

Table 2. Patient characteristics, principal diagnoses, and antibiotic prescribing practices during the pre- and postintervention periods.

Characteristic	Preintervention period (n = 4305)	Postintervention period (n= 2830)	P
Age, mean years ± SD	65 ± 18	66 ± 19	NS
Male sex	2066 (48)	1443 (51)	NS
Principal diagnosis[a]			
Cardiovascular disease	1033 (24)	707 (25)	NS
Infectious disease	1162 (27)	785 (28)	NS
Cerebrovascular or other neurological disease	559 (13)	368 (13)	NS
Gastrointestinal disease	516 (12)	311 (11)	NS
Lung disease	431 (10)	255 (9)	NS
Other	603 (14)	396 (14)	NS
Condition leading to prescription of antibiotics	1937 (45)	1358 (48)	NS
Respiratory tract infection	818 (19)	623 (22)	NS
Urinary tract infection	517 (12)	396 (14)	NS
Gastrointestinal tract infection	258 (6)	1358 (5)	NS
Fever and suspected bacterial infection	215 (5)	623 (3)	NS
Other[b]	129 (3)	396 (4)	NS
Pattern of antibiotic prescription			
Empirical therapy[c]	1765 (41)	1104 (39)	NS
Documented infection	1292 (30)	962 (34)	NS
Surgical prophylaxis	1249 (29)	764 (27)	NS

NOTE. Data are no. (%) of patients, unless otherwise indicated; NS, not significant (P> .05).
[a] As noted in the charts at the time of discharge from the hospital.
[b] Sepsis, meningitis, endocarditis, or prophylaxis of endocarditis.
[c] Includes community-acquired pneumonia, urinary tract infection, sepsis of unknown origin, CNS infection, skin and soft-tissue infections, and nosocomial infection.

ysis, and correlations among variables were assessed by Pearson correlation analysis performed on SPSS, version 11.0 (SPSS). All tests were 2-tailed. A P value of <.05 was considered to be statistically significant.

RESULTS

Prescribing practices. Patient characteristics, antibiotic-prescribing practices, and common reasons for inappropriate antibiotic use during the pre- and postintervention periods are presented in table 2. There were no differences in the patients' demographic characteristics, underlying diseases, and indications for antibiotic use during the pre- and postintervention periods. After the intervention, there was a 24% reduction in the rate of antibiotic prescription (640 vs. 400 prescriptions/1000 admissions; $P < .001$). The incidence of inappropriate antibiotic use was also significantly reduced overall (1808 prescriptions [42%] vs. 566 prescriptions [20%]; $P < .001$). The impact of interventions on the incidence of inappropriate antibiotic use was significantly demonstrated in the surgery service (table 3). Common reasons for inappropriate antibiotic use before the initiation of the study were observed less often after the intervention (table 3). In all, 4305 and 2830 antibiotic prescription forms (corresponding to 1 patient each) were evaluated during the pre- and postintervention periods, respectively. At baseline, a high rate of third-generation cephalosporin prescriptions (60%) was observed. Fourth-generation cephalosporins (1.4%) and β-lactam/β-lactamase inhibitors (2.1%) were seldom ordered. After the intervention, a dramatic decrease was observed in the rate of prescription of third-generation cephalosporins (41.9%) and glycopeptides (3.9%). The proportion of third-generation cephalosporins used in our hospital remained stable (ceftriaxone, 95%; ceftazidime, 5%) during the pre- and postintervention periods. Prescription rates for cefazolin and quinolones increased after the intervention (postintervention rates, 17.6% and 1.4%, respectively) (table 4).

Antibiotic use and cost savings. Variations in antibiotic use during the pre- and postintervention periods are shown in table 4. The numbers of patient-days for the pre- and postintervention periods were 75,332 and 78,905. A significant reduction in the rate of antibiotic use was observed between the pre- and postintervention periods (57 vs. 49.8 DDDs/1000 patient-days; $P < .001$). Linear regression analysis showed that this trend persisted during the study period ($R^2 = 0.69$; $P < .001$). Furthermore, linear regression analyses revealed a sustained reduction in use of third-generation cephalosporins ($R^2 = 0.61$; $P <$ .001) and glycopeptides ($R^2 = 0.47$; $P = .002$). A sustained in-

Table 3. Incidence of inappropriate antibiotic use, reasons for inappropriateness, and departments associated with inappropriate antibiotic use during the pre- and postintervention periods.

Variable	Preintervention period (n = 4305)	Postintervention period (n = 2830)	P
Inappropriate antibiotic use	1808 (42)	566 (20)	<.001
Reason for inappropriateness[a]			
Inappropriate surgical prophylaxis[b]	452 (25)	115 (20)	**.02**
Use of antibiotic without any evidence of infection	723 (40)	200 (35)	**.04**
Redundant spectrum	217 (12)	50 (9)	**.03**
Bacterial resistance[c]	235 (13)	91 (16)	.07
Narrow spectrum was available[d]	181 (10)	41 (7)	**.04**
Department[e]			
Surgery	633 (35)	170 (30)	**.01**
Obstetrics and gynecology	452 (25)	125 (22)	.17
Internal medicine	416 (23)	113 (20)	.14
Other[f]	307 (17)	113 (20)	.12

NOTE. Data are no. (%) of patients, unless otherwise indicated. P values shown in boldface are statistically significant.

[a] Analyzed using proportion of each specific reason for inappropriateness/total number of prescriptions associated with inadequate antibiotic use.

[b] Includes dose, interval, and duration of treatment before and after surgery.

[c] Administration of antibiotics for treatment of infections due to microorganisms resistant to these antibiotics.

[d] Administration of broad-spectrum antibiotics when a narrower-spectrum antibiotic would have been effective and was available.

[e] Analyzed using proportion of number of prescriptions from each department associated with inappropriate antibiotic use/total number of prescriptions associated with each department.

[f] Includes pediatrics, orthopedic, rhino-otolaryngology, general practices, and critical care units.

crease in use of cefazolin (R^2 = 0.68; $P<.001$) and quinolones (R^2 = 0.68; $P<.001$) was observed. Total cost savings from the reduction in antibiotic use were $32,231 ($84,450 − $52,219) during the study period (R^2 = 0.47; $P<.001$).

Impact of the intervention on antimicrobial-resistant microorganisms. After the intervention, there was a significant reduction in the incidence of MRSA (48% vs. 33.5%; R^2 = 0.702; $P<.001$), ESBL-producing *E. coli* (33% vs. 21%; R^2 = 0.67; $P<.001$), ESBL-producing *K. pneumoniae* (30% vs. 20%; R^2 = 0.62; $P<.001$), and third-generation cephalosporin–resistant *A. baumanii* (27% vs. 19%; R^2 = 0.55; $P<.001$). Decreased rates of ESBL-producing *E. coli* (33% vs. 21%) and *K. pneumoniae* (30% vs. 20%) as well as of third-generation cephalosporin–resistant *A. baumanii* (27% vs. 19%) were associated with the reduction in rate of third-generation cephalosporin use (table 5). The decreased prevalence of MRSA (48% vs. 33.5%) was related to a sustained reduction in the rates of use of third-generation cephalosporins and glycopeptides (table 5). No correlation was shown among other antimicrobial-resistant microorganisms and the use of any other antibiotics. During the study period, there was no evidence suggesting that outbreaks of infection with these antimicrobial-resistant microorganisms had occurred. Infection-control surveillance data for other antimicrobial-resistant microorganisms also suggested that there were no increases in the rates of other antimicrobial-resistant microorganisms. The variation in bacterial resistance rates during the study period is summarized in table 5.

DISCUSSION

Improving antimicrobial use practices in hospitals is a challenging task that raises complex issues. Various approaches taken in developed countries include educational programs, development of a restricted hospital formulary, limitations on reports of sensitivity tests, regulation of interactions between pharmaceutical representatives and physicians, controlled distribution, automatic stop-orders, and written justification for specific antimicrobial agents and/or requirement for expert approval before or after prescribing some medications [22–25]. Although several studies have focused on the reduction in antibiotic volume and cost, few have documented the effect of such interventions on the appropriateness of antibiotic use [22, 25]. Our study demonstrates that an easily applicable, inexpensive, multifaceted intervention program was highly effective in a 350-bed hospital in a developing country. The intervention had an evident impact on prescribing practices, antibiotic use rates, bacterial resistance, and cost savings within 1 year.

Previous Thai studies evaluating antimicrobial use in tertiary care hospitals revealed that up to 91% of prescriptions were

Table 4. Antibiotic use rates during the pre- and postintervention periods.

Antibiotic or antibiotic class	Preintervention period: Frequency of prescription, %	Preintervention period: Antibiotic use, DDDs/1000 patient-days	Postintervention period: Frequency of prescription, %	Postintervention period: Antibiotic use, DDDs/1000 patient-days	R^2	Slope	*P*
First-generation cephalosporins[a]	5.8	3.56	17.6	8.2	0.68	0.25	**<.001**
Second-generation cephalosporins	3.2	2.45	3.9	2.95	0.25	0.01	NS
Third-generation cephalosporins	60.42	31	41.9	18	0.61	−0.68	**<.001**
Fourth-generation cephalosporins	1.4	1.55	1.9	1.85	0.30	0.02	NS
Aminoglycosides	13.1	6.29	14.9	6.84	0.23	0.01	NS
Quinolones	0.78	0.68	1.4	1.15	0.68	0.05	**<.001**
Glycopeptides	5.4	3.20	3.9	2.40	0.47	−0.05	**.002**
β-Lactam/β-lactamase inhibitors	2.1	2.21	2.3	2.4	0.02	−0.004	NS
Carbapenems	4.1	2.93	6.4	3.13	0.8	0.02	NS
Other[b]	3.8	3.13	5.9	2.94	0.24	0.01	NS

NOTE. Data are no. (%) of patients, unless otherwise indicated; *P* values shown in boldface are statistically significant. DDD, defined daily dose; NS, not significant ($P > .05$).

[a] Cefazolin is the only first-generation cephalosporin available at the study hospital.

[b] Includes penicillin, penicillinase-resistant penicillins, aminopenicillins, clindamycin, and metronidazole.

inappropriate [1, 7, 14, 26–27]. In the past 2 decades, several interventions have been implemented to control antimicrobial use with varying degrees of success. Such interventions include educational programs and use of antibiotic order forms, with or without audit and prescriber feedback [14–17]. Factors associated with some of these successes included the active involvement of infectious diseases specialists and continuous auditing and reinforcement of antibiotic use practices. To our knowledge, our study is the first Thai study to evaluate the effect of a multifaceted intervention to specifically target antibiotic-prescribing defects identified during a baseline period of observation [11]. These interventions were also well accepted by prescribers.

Although sustained reduction in antibiotic use ($R^2 = 0.692$; $P < .001$) was observed, we found a significant increase in the use of fluoroquinolones and cefazolin. The increase in fluoroquinolone use may be explained in part by their broad-spectrum activity and favorable pharmacokinetic profile, contributing to the excessive use of these drugs. This emphasizes the need to monitor the use of fluoroquinolones, even in the settings in which access to fluoroquinolones is limited, as in this study. Not surprisingly, the increase in cefazolin use may have been the result of an increase in appropriate antimicrobial use before surgery. The correlation between decreasing rates of MRSA and a reduction in third-generation cephalosporin and glycopeptide use may be explained by the reduction in the use of third-generation cephalosporins (mostly ceftriaxone) leading to a significant reduction in MRSA rates, with subsequent reduction in glycopeptide consumption. Notably, the correlation of antimicrobial use and the observed reduction in the prevalence of certain antimicrobial-resistant microorganisms occurred within 1 year in our study (table 5). Although it is

Table 5. Bacterial resistance rates during the pre- and postintervention periods.

Microorganism	Resistance rate, %[a]: Preintervention period	Resistance rate, %[a]: Postintervention period	Associated antibiotic class	Type of variation	R^{2b}	*P*
Methicillin-resistant *Staphylococcus aureus*	48	33.5	Glycopeptides	Decrease	0.55	<.001
	…	…	Third-generation cephalosporins	Decrease	0.93	<.001
ESBL-producing *Escherichia coli*	33	21	Third-generation cephalosporins	Decrease	0.74	<.001
ESBL-producing *Klebsiella pneumoniae*	30	20	Third-generation cephalosporins	Decrease	0.69	<.001
Third-generation cephalosporin–resistant *Acinetobacter baumanii*	27	19	Third-generation cephalosporins	Decrease	0.78	<.001
Imipenem-resistant *Pseudomonas aeruginosa*	5	4	None	…	…	
Multidrug-resistant *Acinetobacter baumanii*	4	5	None	…	…	

NOTE. ESBL, extended-spectrum β-lactamase.

[a] Calculated using the total number of strains.

[b] Linear regression analysis between evolution in the resistance rate and antibiotic use throughout the study.

possible that outbreaks of infection with these antimicrobial-resistant microorganisms may have occurred during the preintervention period, our infection-control surveillance data did not reveal any evidence of such outbreaks during the entire study period.

There are several limitations to this study. This was not a randomized trial, which would have been difficult to perform within a single department because of knowledge contamination among groups. However, our study design did allow us to test the effect of the antibiotic-management program on physician prescribing behavior. Because several interventions were made simultaneously, it is difficult to know which of the specific interventions was the most effective in improving antibiotic use practices. The fact that data on oral antibiotic use were not collected prevented us from concluding that there was no shift from use of intravenous antibiotics to use of oral antibiotics. Nevertheless, a shift from intravenous to oral antibiotic use is not likely, because oral antibiotic expenditures by the study institution, including those for quinolones and metronidazole, did not increase during the study period. Quasi experimental studies are susceptible to biases, especially with regard to secular trends unrelated to the interventions. However, we did collect the data continuously for 12 months after the interventions. Therefore, it is unlikely that the changes found in the study were solely related to secular trends. Although there are nearly 200 faculty members in the clinical departments in our hospital, most of the antibiotics are prescribed by residents and interns. Therefore, we chose these clinicians and medical students as the target populations for our interventions. Because the infectious diseases physicians responsible for the implementation of this program were also reviewing and completing the form, bias may have been introduced, but this bias was conservative, given that both infectious diseases physicians were experienced and strictly followed explicit criteria using a checklist. The fact that clinical outcomes were not collected prevented us from measuring the impact of these interventions on the outcomes of nosocomial infections, as well as measuring other attributable cost savings that may have occurred from the reduction in antimicrobial-resistant microorganisms.

Our study shows that an educational program and antibiotic management program can be associated with a significant alteration of prescribing practices and reductions in antibiotic use, bacterial resistance, and costs. Substantial antibiotic misuse may still persist for some medications that may be difficult to control only through restricted access. Auditing and reinforcing practice guidelines through direct counseling appear to be warranted. Specific classes of medications that are easily and largely used empirically, such as fluoroquinolones, may also be at particularly high risk of misuse and should be targeted in antibiotic-control programs. Multifaceted interventions to reduce inappropriate antibiotic use involving infectious diseases physicians, pharmacists, infection-control specialists, and microbiologists were easily applicable, inexpensive, and highly effective in a medium-sized hospital in Thailand.

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