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CONCISE COMMUNICATION

Inappropriate Antibiotic Use in a Tertiary Care Center in Thailand: An Incidence Study and Review of Experience in Thailand

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Somwang Danchaivijitr, MD; Thomas C. Bailey, MD;
Victoria J. Fraser, MD

The incidence and patterns of and factors associated with inappropriate antibiotic use were studied in a tertiary care center in Thailand. The incidence of inappropriate antibiotic use was 25%. Admission to the surgical department (adjusted odds ratio, 2.0; $P = .02$) and to the obstetrics and gynecology department (adjusted odds ratio, 2.0; $P = .03$) were associated with inappropriate antibiotic use, whereas consultation with an infectious diseases specialist was protective against inappropriate antibiotic use (adjusted odds ratio, 0.15; $P = .01$).

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Inappropriate antibiotic use (IAU) leads to a variety of adverse outcomes, including unnecessary exposure to medications, persistent or progressive infections, superinfection, and increased costs.¹ The evolution of antibiotic resistance is also clearly related to overuse of antibiotics, especially in developing countries, where antibiotics can be purchased without a prescription.² Antibiotic resistance among gram-positive and gram-negative organisms has increased significantly in Thailand.³⁻⁵ Despite these concerns, there is a paucity of data regarding IAU in Thailand. We performed 2 period-incidence surveys to assess the incidence and patterns of and factors associated with IAU at a tertiary care hospital. We also reviewed the relevant literature regarding antibiotic use in tertiary care hospitals in Thailand.

METHODS

Thammasart University Hospital (Pratumthani, Thailand) is a level III, 350-bed, tertiary care university hospital in central Thailand. It has a 150-mile radius referral base, with 17 patient care service units and departments. Each unit is staffed with 1 attending physician and residents, interns, and medical students. Antibiotics are prescribed directly by attending physicians, residents, and interns or by medical students who are under the supervision of an attending physician. There are 2 infectious diseases specialists (one adult and one pediatric) who evaluate patients with infectious diseases on a consultation basis. At the time of this study, there were no existing policies for antibiotic use at this hospital.

Two separate period-incidence surveys were performed on May 15, 2004, and June 15, 2004, to assess the incidence and patterns of and factors associated with IAU. All patients hos-

pitalized in 17 units were surveyed. Inpatients receiving antibiotics were included in the study and were monitored until discharge. Each admitted patient for whom antibiotics were prescribed was visited 3 times: (1) at the time of the survey, to document the empirical use of antibiotics; (2) 72 hours later, when microbiologic laboratory results were available; and (3) on the day of discharge, when the final diagnosis was available. Data collected included patients' demographic characteristics, underlying diseases, severity of illness (acute physiology and chronic health evaluation II score), hospital unit, prescribing physician, antibiotic type, indication for antibiotic prescription, surgical operation, request for infectious diseases consultation, appropriateness of antibiotic use, and category of IAU. From the patient's chart, it was determined whether therapy was intended for empirical treatment of infection, surgical prophylaxis, or treatment of a documented infection. All data were collected by one investigator. Prescribing physicians were unaware of the purpose of this study at the time of chart review.

We used existing published guidelines for appropriate antibiotic use. Specific use categories were modeled after those of Kunin et al.⁶ and were modified to fit local practices by an expert panel consisting of 2 infectious diseases physicians who were not directly involved in the clinical care of the study patients. Modifications were also made to accommodate susceptibility patterns and management of some diseases peculiar to Southeast Asia, such as melioidosis. For patients who received surgical prophylaxis, assessment of appropriateness also included the specific type of antibiotic and the dose and duration of prophylaxis administered before and after surgery.⁷ The measurements were performed either once or twice. For the majority of patients, for whom the empirical and final diagnoses were similar, the measurement was undertaken only once. Measurements were performed twice for patients whose diagnosis at admission was later modified and for whom treatment was revised in response to culture results. Measurements were performed by one investigator, who was blinded to the prescriber and patient identification data.

Categorical variables were compared using the χ^2 or Fisher exact test, as appropriate, and continuous variables were compared using the Mann-Whitney U test. All tests were 2-tailed, with $P < .05$ considered to be statistically significant.

RESULTS

During the study period, 502 patients were admitted to the hospital. Antibiotics were prescribed for 319 patients (64%). Of those 319 patients, 126 (39%) received antibiotics as surgical prophylaxis, 103 (32%) received antibiotics as empirical therapy, 90 (29%) received antibiotics for documented infections, and 79 (24.8%) received inappropriate antibiotics. Patient characteristics and the incidence and patterns of and

the reasons for IAU among different units are summarized in Tables 1 and 2. In 49 (62%) of the 79 instances of IAU, the antibiotics were prescribed by interns or residents. There were no differences between the first and the second survey with respect to patients' demographic characteristics, patterns of antibiotic prescription, factors associated with IAU, duration of follow-up, and the length of hospital stay.

By univariate analysis, admission to a surgery department was associated with IAU (32% vs 22%; odds ratio [OR], 1.73; 95% confidence interval [CI], 1.2-2.9). Infectious diseases consultation was associated with a lower incidence of IAU (5% vs 28%; OR, 0.13; 95% CI, 0.03-0.58). There were no differences in other characteristics or risk factors among patients who received appropriate antibiotics, compared with those who received inappropriate antibiotics (Table 1). By multivariate analysis, admission to a surgery department (adjusted OR, 2.0; 95% CI, 1.1-3.6; $P = .02$) and admission to an obstetric and gynecology department (adjusted OR, 2.0;

95% CI, 1.1-4.1; $P = .03$) were associated with IAU, whereas infectious diseases consultations were associated with lower incidences of IAU (adjusted OR, 0.15; 95% CI, 0.03-0.65; $P = .01$). Infectious diseases consultation helped in the selection of appropriate antibiotics for empirical treatment (13 [34%] of 38 cases) and for the treatment of documented infections (10 [26%] of 38 cases), prevented the unnecessary use of broad-spectrum antibiotics (8 [21%] of 38 cases), and streamlined antibiotic use (7 [18%] of 38 cases).

DISCUSSION

Udomthavornsak and colleagues first reported the incidence of IAU to be 52.3% in a tertiary care university hospital in northeastern Thailand.⁸ The incidence of IAU was 42.3% among patients who received empirical therapy (mainly as a result of the lack of an indication for antibiotic use), 82.4%

TABLE 1. Characteristics of Patients Admitted to Thammasart University Hospital (Pratumthani, Thailand)

Characteristic	Patients in Entire Cohort (N = 502)	Patients Receiving Appropriate Antibiotics (n = 240)	Patients Receiving Inappropriate Antibiotics (n = 79)	P ^a
Demographic				
Age, years, median (range)	35 (0-94)	40 (0-75)	43 (0-94)	NS
Female sex	279 (56)	128 (53)	41 (52)	NS
Clinical				
Any underlying immunocompromised state ^b	67 (13)	36 (15)	12 (15)	NS
APACHE II score, median (range)	9 (2-25)	5 (2-23)	7 (4-25)	NS
Concurrent nosocomial infections ^c	27 (5)	21 (8)	6 (7)	NS
Previous antibiotic therapy	105 (21)	76 (32)	29 (37)	NS
Length of hospitalization, days, median (range) ^c	5 (1-55)	4 (1-25)	5 (2-55)	NS
Admission ward				
Surgery	144 (29)	65 (27)	31 (39)	.04
Obstetrics and gynecology	96 (19)	44 (18)	21 (26)	.10
Medicine	132 (26)	69 (28)	16 (20)	.19
Other ^d	130 (26)	62 (26)	11 (15)	NS
Antibiotic prescriber^e				
Attending physician ^f	127 (40)	97 (40)	30 (38)	NS
Resident	100 (31)	76 (32)	24 (30)	NS
Intern	92 (29)	67 (28)	25 (32)	NS
Other				
Received infectious diseases consultation ^e	40 (13)	38 (95)	2 (3)	.001
Duration of follow-up, days, median (range) ^g	10 (2-18)	9 (3-14)	11 (2-18)	NS
Total length of hospital stay, days, median (range)	17 (2-89)	16 (3-52)	18 (2-89)	NS

NOTE. Data are no. (%) of patients, unless otherwise noted. APACHE II = acute physiology and chronic health evaluation II;

NS = not significant.

^a Determined by use of Fisher exact test, for proportion variables, and the Wilcoxon rank sum test, for continuous variables.

^b Includes patients infected with human immunodeficiency virus, patients who underwent solid or bone-marrow transplantation, and patients who received chemotherapy, immunosuppressive medications, or long-term steroid therapy (>2 weeks).

^c Duration prior to antibiotic administration.

^d Includes pediatric, orthopedic, rhino-oto-laryngology, general practices, and critical care units.

^e There were total of 319 instances of antibiotic prescription.

^f Includes antibiotics prescribed by medical students under the supervision of an attending physician.

^g For the study incident of antibiotic prescription.

TABLE 2. Factors Associated With Inappropriate Antibiotic Use (IAU) Among Different Units at Thammasart University Hospital (Pratumthani, Thailand)

Factor	Medicine Units (n = 16)	Surgery Units (n = 31)	Obstetrics- Gynecology Units (n = 21)	Other Units ^a (n = 11)
Incidence of IAU ^b	16 (20)	31 (39)	21 (26)	11 (15)
Patterns of IAU				
Empirical therapy ^c	10 (62)	9 (29)	6 (29)	8 (72)
Documented infection	6 (38)	2 (6)	2 (9)	3 (28)
Surgical prophylaxis	...	20 (65)	13 (62)	...
Reasons for IAU ^d				
No evidence of infection	7 (45)	6 (20)	9 (43)	8 (73)
Narrow spectrum still available	2 (12)	4 (13)	2 (9)	...
Colonized patient	3 (14)	...
Resistant microorganisms	4 (25)	3 (9)	2 (9)	1 (1)
Redundant spectrum	1 (6)	3 (9)
Inappropriate dose, interval, or duration	2 (12)	...	2 (9)	...
Failure to cover likely microorganisms	...	4 (13)
Inappropriate surgical prophylaxis	...	11 (35)	3 (14)	2 (2)
Medications commonly associated with IAU ^b				
Third-generation cephalosporins	8 (50)	8 (26)	...	2 (18)
Aminopenicillin	...	1 (3)	9 (43)	1 (9)
Glycopeptides	4 (25)	3 (10)	2 (9)	2 (18)
Carbapenems	4 (25)	5 (16)	1 (5)	1 (9)
Other ^e	...	14 (45)	9 (43)	5 (46)

NOTE. Data are no. (%) of patients.

^a Includes pediatric, orthopedic, rhino-oto-laryngology, general practices, and critical care units.

^b There were 79 instances of IAU.

^c Includes community-acquired pneumonia, urinary tract infections, sepsis with unknown origin, central nervous system infections, skin and soft-tissue infections, and nosocomial infections.

^d Other common reasons for IAU include (1) use of antibiotics without any evidence of infection (30 [38%] of 79 cases); (2) inappropriate surgical prophylaxis, including dose, interval, and duration before and after surgery (16 [20%] of 79 cases); (3) administration of antibiotics for microorganisms resistant to these antibiotics (10 [13%] of 79 cases); (4) administration of broad-spectrum antibiotics when a narrower spectrum antibiotic would have been effective and was available (8 [10%] of 79 cases); (5) administration of multiple antibiotics that had redundant spectrum (4 [5%] of 79 cases); (6) administration of antibiotics that were inadequate for the microorganisms that caused the disease (4 [5%] of 79 cases); (7) administration of antibiotics with inappropriate dose and duration (4 [5%] of 79 cases); and (8) administration of antibiotics to patients who were colonized but not infected (3 [4%] of 79 cases).

^e Includes penicillin; first-, second-, and fourth-generation cephalosporins; aminoglycosides; quinolones; extended-spectrum penicillin; β -lactam/ β -lactamase inhibitors; clindamycin; and metronidazole.

among patients who received surgical prophylaxis (mainly as a result of delayed use and excessive duration [>72 hours]), and 39.6% among patients who had documented infection (mainly as a result of inappropriate antibiotic choice and redundant antibiotic spectrum). Aswapokee et al.⁹ reported a 91% incidence of IAU among medical units in a tertiary care university hospital in Bangkok, mainly as a result of the use of antibiotics without any evidence of infection. Thamlikitkul et al.¹⁰ later reported the incidence of IAU to be 50% among inpatients and outpatients at the same hospital. Inappropriate antibiotic choices, the duration of surgical prophylaxis, and the use of antibiotics prescribed for acute diarrhea and for upper respiratory tract infections were the main reasons for IAU.¹⁰ The findings of our study complement the findings of other studies and suggest that IAU occurs

quite commonly in Thailand. The variation in the incidence of IAU may be the result of different study designs, patient demographic characteristics, and definitions of IAU among published studies. The fact that third-generation cephalosporins are the most common antibiotics associated with IAU may be partially responsible for the trend of increasingly resistant gram-negative microorganisms in our hospital.⁴⁻⁵ Data on the incidence and pattern of IAU in tertiary care centers in Thailand are summarized in Table 3.

Although the cross-sectional nature and the small sample size of our study limit our capacity to identify the incidence of and other relevant factors associated with IAU, our data are the first, to our knowledge, to suggest the benefit of infectious diseases consultation in guiding appropriate antibiotic use in a developing country, as has been consistently

TABLE 3. Incidence and Patterns of Inappropriate Antibiotic Use (IAU) in Tertiary Care University Hospitals in Thailand

Reference	Type of Study	No. of Patients	Patients Receiving Antibiotics, %	Incidence of IAU, %	Reasons for IAU
Udomthavornsuk et al. ⁸	Incidence ^a	400	NA	52.3	Inappropriate surgical prophylaxis, ^b no indication of use, or redundant antibiotic spectrum
Aswapokee et al. ⁹	Prevalence	690	44	91	No indication of use, inappropriate choice of antibiotic, or inappropriate dose, interval and duration
Thamlikitkul et al. ¹⁰	Prevalence	29,929	41 ^c and 19 ^d	50	Inappropriate surgical prophylaxis, ^b inappropriate antibiotics for normal labor, inappropriate antibiotics for cataract surgery, inappropriate antibiotics for acute diarrhea, or inappropriate antibiotics for respiratory tract infections
Present study	Prevalence	502	63.5	24.8	No indication of use, inappropriate surgical prophylaxis, ^b inappropriate antibiotics for resistant microorganisms, use of broad-spectrum antibiotics where narrow spectrum antibiotic is still available and effective, or other reasons ^e

NOTE. NA = not applicable.

^a This was a prospective study to evaluate all antibiotic prescriptions written for 1 month.

^b For inpatients.

^c For outpatients.

^d Includes choices of antibiotics, dose, interval, and duration.

^e Includes inappropriate choices of antibiotics, administration of antibiotics with redundant spectrum, and inappropriate dose, interval, duration, and administration of antibiotics to colonized patients.

shown in developed countries.¹¹⁻¹⁵ Given the findings of our study, attempts to rectify IAU should be focused on educational interventions aimed at improving the clinical recognition of specific infectious diseases and at establishing antibiotic management programs with the involvement of infectious diseases specialists. Further studies of the factors associated with IAU and interventions to reduce the incidence of IAU in developing countries are needed to help identify effective strategies to control IAU and to prevent the emergence of drug-resistant microorganisms.

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