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MAJOR ARTICLE

Effectiveness of Implementing a Locally Developed Antibiotic Use Guideline for Community-Acquired Cellulitis at a Large Tertiary Care University Hospital in Thailand

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Background. To determine the effectiveness of implementing a locally developed clinical practice guideline (CPG) for antibiotic treatment in adults with community-acquired cellulitis at Siriraj Hospital in Bangkok, Thailand.

Methods. The CPG for antibiotic treatment of community-acquired cellulitis was developed based on local data during June to December 2016. The CPG was introduced by multifaceted interventions, including posters, brochures, circular letters, social media, conference, classroom training, and interactive education during January to September 2018.

Results. Among 360 patients with community-acquired cellulitis, 84.4% were ambulatory and 15.6% were hospitalized. The median age of patients was 62 years, and 59.4% were female. Antibiotic prescription according to CPG (CPG-compliant group) was observed in 251 patients (69.7%), and CPG noncompliance was found in 109 patients (30.3%) (CPG-noncompliant group). The demographics and characteristics of patients were comparable between groups. Patients in the CPG-compliant group had a significantly lower rate of intravenous antibiotics (18.7% vs 33.9%, $P = .007$), lower prescription rate of broad-spectrum antibiotics (14.7% vs 78.9%, $P < .001$) and antibiotic combination (6.4% vs 13.8%, $P = .022$), shorter median duration of antibiotic treatment (7 vs 10 days, $P < .001$), lower median cost of antibiotic treatment (US $3 vs $7, $P < .001$), and lower median hospitalization cost (US $601 vs $1587, $P = .008$) than those in the CPG-noncompliant group. Treatment outcomes were not significantly different between groups.

Conclusions. Adherence to CPG seems to reduce inappropriate prescription of broad-spectrum antibiotic or antibiotic combination and treatment costs in adults with community-acquired cellulitis without differences in favorable outcomes or adverse events.

Keywords. antibiotic; cellulitis; community-acquired; guideline; Thailand.

Cellulitis is an acute infection involving the dermis and subcutaneous tissues that is characterized by pain, swelling, erythema, and hotness at the affected area [1]. This condition is one of the most common bacterial infections observed in general clinical practice. The bacteria that most often cause cellulitis are Gram-positive cocci, primarily *Staphylococcus aureus* or *Streptococcus* spp [2–4]. Therefore, antibiotic treatment with narrow-spectrum anti-Gram-positive antibiotic monotherapy is recommended for most patients with cellulitis by several international guidelines [2–4].The majority of patients with cellulitis have favorable clinical outcome after antibiotic treatment, and the mortality in patients is low. However, many published studies showed that patients with cellulitis were frequently treated with broad-spectrum antibiotics or antibiotic combinations that have activity against Gram-positive bacteria, Gram-negative bacteria, and/or anaerobes [5]. Antibiotic overuse for therapy of cellulitis (ie, unnecessary use of broad-spectrum antibiotic or combined antibiotics) can lead to the development of antimicrobial resistance, which increases the rate of *Clostridioides difficile* infection and the cost of treatment [5, 6].

A study conducted at Siriraj Hospital in Bangkok, Thailand among 970 adult patients with cellulitis found methicillin-susceptible *S aureus* (MSSA) and β-hemolytic streptococci to be the most common causative bacteria isolated from Thai adults with community-acquired cellulitis. The responsible physicians prescribed broad-spectrum antibiotics and antibiotic combination to many patients according to their clinical judgement since the local guideline for antibiotic therapy of cellulitis was not available. The mortality and complication rates among those patients were very low [7]. These study findings suggested that the majority of patients with community-acquired cellulitis

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in Thailand could be treated with a narrow-spectrum antibiotic against Gram-positive cocci. That same study also revealed that 77% of patients with cellulitis received a broad-spectrum antibiotic or antibiotic combination, and that only 40% of those patients were prescribed appropriate antibiotic therapy [7].

Several reports on the implementation of a clinical practice guideline (CPG) for treatment of cellulitis described a decrease in the prevalence of inappropriate antibiotic treatment after implementation of the CPG [6, 8, 9]. There are differences in the epidemiology and microbiology of community-acquired cellulitis among different settings [2–4, 10]. For example, community-acquired methicillin-resistant *S aureus* (CA-MRSA) is extremely rare in Thailand [11]. Some international guidelines developed in Western countries where CA-MRSA is prevalent may not be suitably applicable in the Thai community [7, 10]. Moreover, it is hypothesized that one of the contributing factors to a high rate of broad-spectrum antibiotic or antibiotic combination used to treat cellulitis in Thailand is the lack of a local antibiotic guideline for treatment of cellulitis. Therefore, we developed a CPG for antibiotic treatment of community-acquired cellulitis based on local data from 970 adult patients that were diagnosed with and treated for cellulitis at Siriraj Hospital during June to December 2016 [7]. Management of community-acquired cellulitis remains problematic. The CPG can be useful for encouraging proper antibiotic treatment, minimizing adverse effects, reducing multidrug resistance, and lowering the cost of treatment.

The objective of the present study was to determine the effectiveness of implementing a CPG for antibiotic treatment of adult patients with community-acquired cellulitis at Siriraj Hospital in terms of the prevalence of CPG compliance and comparison of outcome of treatment, cost of antibiotic treatment, and cost of hospitalization between patient who received antibiotic treatment according to the CPG recommendations (CPG-compliant group) and patients who did not receive antibiotic therapy according to the CPG recommendations (CPG-noncompliant group).

MATERIALS AND METHODS

Patient Consent Statement

This study was approved by the Institutional Review Board of the Faculty of Medicine Siriraj Hospital, Mahidol University (Certificate of Approval [COA] no. 708/2017). The requirement for written informed consent was waived due to the retrospective anonymous nature of the study. The study was conducted at Siriraj Hospital, a 2300-bed tertiary care university hospital located in Bangkok, Thailand during the January to September 2018 study period.

The CPG was prepared as a 1-page Thai language document that was translated to English (Figure 1). The CPG contains recommendations that are divided into 3 parts. The first part focuses on choice and duration of empiric antibiotics. The second part outlines the indications for prescribing broad-spectrum antibiotics and antibiotic combinations. The third part lists the recommended dosing regimen for the recommended antibiotics. This CPG is endorsed by Division of Infectious Diseases and Tropical Medicine, Department of Medicine, Siriraj Hospital. This CPG was distributed to physicians from relevant departments, including Medicine, Surgery, and Emergency. The methods of communicating the CPG to physicians included posting the CPG in the patient care area, disseminating brochures and letters, distributing the CPG via social media, conference, and interactive training. Implementation of the CPG was conducted during January to March 2018. The responsible physicians have been reminded of using CPG every month via social media. Assessment of the impact of the CPG implementation was performed by identifying the adult patients with cellulitis who received medical care at Siriraj Hospital during April to September 2018. The list of patients with cellulitis was retrieved from the hospital's database according to the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision* (ICD-10) codes L03.0–L03.9. Patients with hospital-acquired cellulitis, nonbacterial cellulitis, or those who had insufficient data were excluded. Retrieved medical records were reviewed for demographic data, clinical features of cellulitis, microbiological results, antibiotic regimens, clinical outcomes, and cost of antibiotic treatment. The cost of hospitalization was also retrieved from our hospital's database. Data were recorded on a standardized case record form.

Fever was defined as a body temperature ≥38°C, and hypotension was defined as systolic blood pressure <90 mmHg. The severity of cellulitis was determined using the modified Dundee classification system that divides cellulitis into 4 classes based on the clinical presentation (ie, classes 1–2, mild to moderate illness; and classes 3–4, severe illness) [12]. Broad-spectrum antibiotic was defined as an antibiotic that had activity against a wide range of Gram-positive bacteria, Gram-negative bacteria, and/or anaerobes [5]. Narrow-spectrum antibiotic was defined as an antibiotic that contained activity against MSSA and β-hemolytic streptococci (ie, cloxacillin, dicloxacillin, cefazolin, cephalexin, and clindamycin). Community-acquired cellulitis was defined as cellulitis in ambulatory patients or hospitalized patients within 2 days who had no healthcare-associated conditions (ie, prior hospitalization within 3 months, prior use of antibiotic within 90 days, resident of long-term care facility, and/or undergoing chronic hemodialysis). Hospital-acquired cellulitis was defined as cellulitis in ambulatory patients with healthcare-associated conditions or hospitalized patients admitted longer than 2 days at Siriraj Hospital or at other hospitals before admission to Siriraj Hospital [7]. Nonbacterial cellulitis was defined as cellulitis caused by atypical organisms, ie, mycobacteria, fungi, or noninfectious causes (ie, deep vein thrombosis, vascular disorders, skin diseases, and drug allergy). Insufficient data was defined as the relevant data were

Clinical practice guideline for antibiotic treatment of community-acquired acute cellntilis in adult at siriraj hospital

1. Recommended empiric antibiotic

-Oral antibiotic: didoxacillin or cephalexin

-IV antibiotic: cloxacillin or cefazolin followed by oral antibiotic (dicloxacillin or cephalexin)

-Roxiffiromycin or ctindamycin should be considered in penicillin allergy patient

-Broad-spectrum antibiotic (e.g., amoxicillin-clavulanate or ceftriaxone) or combination therapy with ctindamycin is not necessary in most patients

Duration of antibiotic therapy at least 5 days

2. Indications for broad-spectrum antibiotic (e.g., amoxicillin-clavulanate or ceftriaxone) or combination of antibiotics (e.g., ceftriaxone plus clindamycin)

-Severe infection (hypotension or organ dysfunction) OR

-Rapidly progressive disease within 24 h OR

-Having risk factor for uncommon pathogen (e.g. Gram-negative bacteria):

-Severely immunocompromised (neutropenia, post-chemotherapy, post-translantation) OR

-Bite wound related infection OR

-Failure to respond to empiric antibiotic after 48 h treatment

3. Antibiotic dosing regimen

Antibiotic	Dosing
Patenteral antibiotic (intravenous)	
-Cloxacillin	1–2 g q 4–6 h
-Cefazolin	1–2 g q 6–8 h
-Clindamycin	600–900 mg q 8 h
-Amoxicillin-clavulanate	1.2 g q 8 h
-Ceftriaxone	1–2 g q 24 h
Oral antibiotic	
-Dicloxacillin	250–500 mg before meal 4 times/day
-Cephalexin	500 mg 4 times/day
-Roxithromycin	150 mg before meal 2 times/day
-Clindamycin	300–450 mg after meal 4 times/day
-Amoxicillin-clavulantate	875/125 mg after meal 2 times/day

Figure 1. Clinical practice guideline for antibiotic treatment of community-acquired acute cellulitis in adult.

not available in the medical records of the study patients with cellulitis. A patient who received antibiotic treatment according to the CPG recommendations was classified as CPG-compliant group, and patients who did not receive antibiotic therapy according to the CPG recommendations was classified as CPG-noncompliant group. Outcome of treatment was defined as the clinical outcome of patients with cellulitis after receiving complete course of antibiotic treatment, and it was classified as cure (resolution of signs and symptoms of celluliis), complication (septic shock or necrotizing fasciitis), or death (from cellulitis or other causes). Cost of antibiotic treatment was determined as the total cost of antibiotics that were used for treatment of cellulitis. Cost of hospitalization was defined as the total expenses of hospitalized patients with cellulitis from admission to discharge from the hospital.

Sample Size Estimation and Statistical Analysis

It was expected that the rate of CPG compliance for antibiotic treatment of cellulitis after implementation of the CPG would be 70.0% ± 5.0%. Using a type I error (2-sided) of 5%, a minimum sample size of 323 patients was needed. Data are presented as number and percentage, mean ± standard deviation, or median and range, as appropriate. Fisher's exact test or χ^2 test was used to compare categorical variables, and Student's *t* test

or Mann-Whitney *U* test was used to compare quantitative variables. All statistical analyses were performed using either SPSS Statistics version 18.0 (SPSS, Inc., Chicago, IL) or Microsoft Excel version 2016 (Microsoft Corporation, Redmond, WA). $P \leq .05$ was considered statistically significant.

RESULTS

There were 500 patients with the diagnosis of cellulitis retrieved from hospital database during mid-April to mid-September 2018 (5 months). Some patients were excluded from analyses due to having hospital-acquired cellulitis (48 patients), nonbacterial cellulitis (42 patients), and those who had insufficient data on clinical features, treatment outcomes, or the cost of treatment (50 patients). Therefore, the information from 360 patients with community-acquired cellulitis were analyzed.

The characteristics of all study patients are shown in Table 1. The most common underlying illnesses were diabetes mellitus, malignancy, chronic kidney disease, and vascular disorder. The majority of patients (67.5%) had cellulitis at 1 or both of their lower extremities. Cellulitis in most patients (93.4%) was classified as class 1 or class 2 in severity. Three hundred four patients (84.4%) were ambulatory patients who received outpatient care, and 56 patients (15.6%) were hospitalized patients. The patients in this study received medical care by physicians from different medical specialties, including internists (38.1%), emergency medicine physicians (25.6%), surgeons (23.3%), and other physicians (12.5%).

Antibiotic regimens and outcomes of treatment for community-acquired cellulitis are shown in Table 2. Dicloxacillin, amoxicillin-clavulanate, cephalexin, and ceftriaxone-clindamycin were the most common antibiotics used for combination therapy in all patients. Among the 56 hospitalized patients, the most frequently prescribed parenteral antibiotics were ceftriaxone-clindamycin combination (39.3%), cefazolin (32.1%), and amoxicillin-clavulanate (12.5%). Oral switch antibiotic therapy was ordered in 50.0% of hospitalized patients when their clinical condition improved. Amoxicillin-clavulanate (48.3%), cephalexin (27.6%), cefdinir-clindamycin combination (10.3%), and dicloxacillin (7.1%) were the most commonly prescribed oral antibiotics for switch treatment. Among the 304 ambulatory patients, the most common antibiotics were dicloxacillin (39.8%), amoxicillin-clavulanate (34.5%), cephalexin (9.5%), and clindamycin (8.6%). The median duration of antibiotic treatment was 7 days (range, 5 to 63 days), and most patients (99.4%) had a favorable clinical outcome. Subsequent complication of cellulitis, including necrotizing fasciitis and septic shock, was found in only 2 patients (0.6%). All patients were successfully treated with appropriate medical care without fatality. The average cost of antibiotic treatment was US $42.4/patient. For hospitalized patients, the median duration of hospitalization was 7 days, the median hospitalization cost was US $650, and the average cost of hospitalization was US $1094.1/patient.

Table 1. Characteristics of 360 Study Patients With Community-Acquired Cellulitis

Characteristics	Numbers of Patients n = 360, n (%)
Female gender	214 (59.4%)
Median age (range) (years)	62 (18–93)
Clinical Presentation	
Fever	91 (25.3%)
Hypotension	5 (1.4%)
Locations of Cellulitis	
Leg	168 (46.7%)
Foot	75 (20.8%)
Arm	35 (9.7%)
Hand	31 (8.6%)
Head and neck	28 (7.8%)
Trunk	15 (4.2%)
Unknown	8 (2.2%)
Comorbidity	
Overall comorbidity	256 (71.1%)
Diabetes mellitus	81 (22.5%)
Malignancy	43 (11.9%)
Chronic kidney disease	40 (11.1%)
Vascular disorder	40 (11.1%)
Liver disease	16 (4.4%)
Skin disease	15 (4.2%)
Rheumatic disease	11 (3.1%)
Heart disease	10 (2.8%)
Lung disease	3 (0.8%)
Immunocompromised status	2 (0.6%)
Severity of Cellulitis	
Class 1	250 (69.4%)
Class 2	86 (23.9%)
Class 3	21 (5.8%)
Class 4	3 (0.8%)
Settings	
Ambulatory patients	304 (84.4%)
Hospitalized patients	56 (15.6%)
Responsible physicians	
Medicine	137 (38.1%)
Emergency Medicine	92 (25.6%)
Surgery	84 (23.3%)
Others	47 (13.1%)

Among the 76 patients (21.1%) who had clinical specimens sent for bacterial culture (blood culture in 76 patients, pus culture in 21 patients, and both cultures in 18 patients), bacteria were isolated from 17 patients (4.7%). The most commonly isolated bacteria (82.4%) were Gram-positive bacteria, which were isolated from 14 patients (82.4%). Those bacteria were beta-hemolytic streptococci in 7 patients (41.2%), MSSA in 4 patients (23.5%), and both beta-hemolytic streptococci and MSSA in 3 patients (17.6%). Gram-negative bacteria were found in only 3 patients from the skin lesions (*Pseudomonas aeruginosa* in 2 patients, and *Escherichia coli* in 1 patient).

Table 2. Antibiotic Regimens and Outcomes of 360 Patients With Community-Acquired Cellulitis

Antibiotic Regimens for Therapy of Community-Acquired Cellulitis in All Patients	Numbers of Patients, n = 360, n (%)
Oral antibiotics	280 (77.8%)
Parenteral antibiotics	80 (22.2%)
Clindamycin combination	43 (11.9%)
Type of Parenteral and Oral Antibiotics	
Dicloxacillin	124 (34.4%)
Amoxicillin-clavulanate	123 (34.2%)
Cephalexin	38 (10.6%)
Ceftriaxone plus clindamycin	31 (8.6%)
Clindamycin	28 (7.8%)
Cefazolin	19 (5.3%)
Ceftriaxone	14 (3.9%)
Cefdinir plus clindamycin	7 (1.9%)
Ciprofloxacin	5 (1.4%)
Dicloxacillin plus clindamycin	4 (1.1%)
Amoxicillin	4 (1.1%)
Ciprofloxacin plus clindamycin	3 (0.8%)
Cloxacillin	2 (0.6%)
Piperacillin-tazobactam	2 (0.6%)
Meropenem	2 (0.6%)
Levofloxacin	1 (0.3%)
Clarithromycin	1 (0.3%)
Median duration of antibiotic therapy (range) (days)	7 (5–63)
Antibiotic Regimens for Therapy of Community-Acquired Cellulitis in Hospitalized Patients	Numbers of Patients, n = 56, n (%)
Type of Parenteral Antibiotics	
Ceftriaxone plus clindamycin	22 (39.3%)
Cefazolin	18 (32.1%)
Amoxicillin-clavulanate	7 (12.5%)
Ceftriaxone	2 (3.6%)
Piperacillin-tazobactam	2 (3.6%)
Cloxacillin	2 (3.6%)
Ciprofloxacin	2 (3.6%)
Carbapenem (meropenem)	1 (1.8%)
Oral Antibiotics After Parenteral Antibiotics	Numbers of Patients, n = 28, n (%)
Amoxicillin-clavulanate	14 (48.3%)
Cephalexin	8 (27.6%)
Cefdinir plus clindamycin	3 (10.3%)
Dicloxacillin	2 (7.1%)
Clindamycin	1 (3.4%)
Levofloxacin	1 (3.4%)
Antibiotic Regimens for Therapy of Community-Acquired Cellulitis in Ambulatory Patients	Numbers of Patients, n = 304, n (%)
Type of Parenteral and Oral Antibiotics	
Dicloxacillin	121 (39.8%)
Amoxicillin-clavulanate	105 (34.5%)
Cephalexin	29 (9.5%)
Clindamycin	26 (8.6%)
Ceftriaxone	12 (3.9%)
Ceftriaxone plus clindamycin	9 (3.0%)
Amoxicillin	4 (1.3%)
Dicloxacillin plus clindamycin	4 (1.3%)
Ciprofloxacin	3 (1.0%)
Cefdinir plus clindamycin	3 (1.0%)
Ciprofloxacin plus clindamycin	1 (0.3%)
Clarithromycin	1 (0.3%)
Cefazolin	1 (0.3%)
Carbapenems (ertapenem)	1 (0.3%)
Outcomes and Costs of Patients With Community-Acquired Cellulitis	Number of Patients n = 360, n (%)
Cure	358 (99.4%)
Complication	2 (0.6%)
Septic shock	1 (0.3%)
Necrotizing fasciitis	1 (0.3%)
Overall mortality	0 (0.0%)
Median duration of hospitalization (range) (days)	7 (3–21)
Median cost of antibiotic treatment (range)	US $4 ($2–$580)
Average cost of antibiotic treatment	US $42
Median cost of hospitalization (range)	US $650 ($173–$4601)
Average cost of hospitalization	US $1094

Of the 360 adult patients with community-acquired cellulitis, 251 patients (69.7%) received antibiotic treatment according to the CPG recommendations (CPG-compliant group), and 109 patients (30.3%) did not receive antibiotic therapy according to the CPG recommendations (CPG-noncompliant group). Demographics, clinical features, antibiotic treatment, and patient outcomes compared between the CPG-compliant group and the CPG-noncompliant group are shown in Table 3. Demographic data, clinical characteristics, and cellulitis severity were not significantly different between groups, although patients with cellulitis at the hand or trunk were more common in the CPG-compliant group than in the CPG-noncompliant group. Physicians from the Department of Medicine usually followed the CPG. Oral antibiotics were more commonly prescribed in the CPG-compliant group, whereas parenteral antibiotics were more frequently given in the CPG-noncompliant group. Clindamycin combination prescription was less in the CPG-compliant group than in the CPG-noncompliant group. The median duration of antibiotic treatment was significantly longer in the CPG-noncompliant group. Dicloxacillin, cephalexin, and cefazolin were more commonly used in the CPG-compliant group than in the CPG-noncompliant group. Amoxicillin-clavulanate and ceftriaxone-clindamycin combination was used more frequently in the CPG-noncompliant group than in the CPG-compliant group. Regarding the cellulitis associated with fight or bite, or other infections where the physician had a reason to suspect a Gram-negative bacterium, the CPG recommends using broad-spectrum antibiotic (eg, amoxicillin-clavulanate) or combination of antibiotics (eg, ceftriaxone plus clindamycin) for such cases, and these patients were also classified as CPG-compliant group.

Table 3. Demographics, Clinical Features, Antibiotic Treatments, and Outcomes Compared Between the CPG-Compliant Group and the CPG-Noncompliant Group

Characteristics	CPG-Compliant Group (n = 251)	CPG-Noncompliant Group (n = 109)	*P* Value[a]
Female gender	155 (61.8%)	59 (54.1%)	.176
Median age (range) (years)	62 (18–93)	62 (18–87)	.991
Clinical Presentations			
Fever	62 (24.7%)	29 (26.6%)	.702
Hypotension	4 (1.6%)	1 (0.9%)	.614
Locations of Cellulitis			
Leg	115 (45.8%)	53 (48.6%)	.624
Foot	50 (19.9%)	25 (22.9%)	.517
Hand	27 (10.8%)	4 (3.7%)	.028
Arm	20 (8.0%)	15 (13.8%)	.088
Head and neck	18 (7.2%)	10 (9.2%)	.514
Trunk	14 (5.6%)	1 (0.9%)	.042
Unknown	7 (2.8%)	1 (0.9%)	.268
Comorbidities			
Overall comorbidities	182 (72.5%)	74 (67.9%)	.374
Diabetes mellitus	54 (21.5%)	27 (24.8%)	.497
Malignancy	32 (12.7%)	11 (10.1%)	.475
Vascular disorder	29 (11.6%)	11 (10.1%)	.685
Chronic kidney disease	27 (10.8%)	13 (11.9%)	.745
Liver disease	9 (3.6%)	7 (6.4%)	.230
Skin disease	9 (3.6%)	6 (5.5%)	.402
Rheumatic disease	7 (2.8%)	4 (3.7%)	.655
Heart disease	7 (2.8%)	3 (2.8%)	.984
Lung disease	2 (0.8%)	1 (0.9%)	.908
Immunocompromised status	2 (0.8%)	0 (0.0%)	.350
Severity of Cellulitis			
Class 1	172 (68.5%)	78 (71.6%)	.566
Class 2	60 (23.9%)	26 (23.9%)	.992
Class 3	16 (6.4%)	5 (4.6%)	.454
Class 4	3 (1.2%)	0 (0.0%)	.252
Settings			
Ambulatory patients	207 (82.5%)	97 (89.0%)	.117
Hospitalized patients	44 (17.5%)	12 (11.0%)	.117
Responsible Physicians			
Medicine	112 (44.6%)	25 (22.9%)	<.001
Emergency medicine	58 (23.1%)	34 (31.2%)	.106
Surgery	47 (18.7%)	37 (33.9%)	.002
Others	34 (13.5%)	13 (11.9%)	.675
Antibiotic Treatment			
Oral antibiotics	205 (81.7%)	75 (68.8%)	.007
IV antibiotics	46 (18.3%)	34 (31.2%)	.007
Clindamycin combination	21 (8.4%)	22 (20.2%)	.001
Median duration of antibiotics (range) (days)	7 (5–63)	10 (5–35)	<.001
Median cost of antibiotic treatment (range)	US $3 ($2–$456)	US $7 ($3581)	<.001
Average cost of antibiotic treatment	US $35	US $60	NA
Antibiotic regimens			
Dicloxacillin	124 (49.4%)	0 (0.0%)	<.001
Amoxicillin-clavulanate	37 (14.7%)	86 (78.9%)	<.001
Cephalexin	36 (14.3%)	2 (1.8%)	<.001
Ceftriaxone plus clindamycin	16 (6.4%)	15 (13.8%)	.022
Cefazolin	18 (7.2%)	1 (0.9%)	.015
Median duration of hospitalization (range) (days)	6 (3–21)	7 (3–17)	.233
Median cost of hospitalization (range)	US $601 ($173–$3526)	US $1587 ($289–$4601)	.008
Average cost of hospitalization	US $896	US $1795	NA
Clinical Outcome			
Cure	250 (99.6%)	108 (99.1%)	.542
Complications	1 (0.4%)	1 (0.9%)	.542
Overall mortality	0 (0.0%)	0 (0.0%)	NA

Abbreviations: CPG, clinical practice guideline; IV, intravenous; NA, not applicable.

[a] $P < .05$ indicates statistical significance.

The duration of hospitalization between patients in the CPG-compliant group and those in the CPG-noncompliant group was not significantly different. The treatment outcomes of patients were favorable and not significantly different between groups. The cost of antibiotic treatment was significantly lower in the CPG-compliant group than in the CPG-noncompliant group. The cost of hospitalization was significantly lower in the CPG-compliant group than in the CPG-noncompliant group.

The rate of appropriate antibiotic regimens according to the CPG in 360 patients in this study was significantly more than that in 970 patients reported in the previous study (70% vs 40%, $P < .001$) [7], which could be due to differences in characteristics of the patients between both groups. Therefore, the comparison of major characteristics of the patients in both groups was made as shown in Table 4. There were no significant differences in most of the characteristics of the patients in both groups.

DISCUSSION

Cellulitis is a frequently encountered infectious disease in clinical practice. Broad-spectrum antibiotics or antibiotic combinations are commonly prescribed to treat patients with cellulitis even though many guidelines recommend a narrow-spectrum, anti-Gram-positive antibiotic [2–6, 8, 9]. Our previous study at Siriraj Hospital revealed that approximately 90% of patients with cellulitis were community-acquired infection, but that 77% of them still received a broad-spectrum antibiotic or antibiotic combination [7]. This rate of antibiotic prescription is considered high because most of the isolated bacteria were MSSA or β-hemolytic streptococci, and the rate of appropriate antibiotic use for treatment of community-acquired cellulitis in our previous study was only 40%.

This study revealed the following important findings: (1) most adult patients with community-acquired cellulitis had mild-to-moderate severity and they could be managed as ambulatory patients with oral antibiotics; (2) there was no fatality observed in this study and the prevalence of subsequent complications from cellulitis was low; (3) the overall prescription rate of broad-spectrum antibiotics or antibiotic combinations in this present study was 54% compared with 77% reported from our previous study; (4) the implementation of a CPG for antibiotic treatment of community-acquired cellulitis at our hospital was effective, and the rate of appropriate antibiotic prescription according to the CPG recommendations was approximately 70% compared with the appropriate antibiotic prescription rate of 40% in our previous study; and (5) patients in the CPG-compliant group had a significantly lower rate of receiving parenteral antibiotics, a significantly lower prescription rate of broad-spectrum antibiotics or antibiotic combinations, a significantly shorter duration of antibiotic treatment, and a significantly lower cost of both antibiotic treatment and hospitalization than patients in the CPG-noncompliant group. Furthermore, the rates of patients with comorbidity were relatively low and not significantly different between groups. The mortality rate was none in both groups. These findings indicate that this CPG for antibiotic treatment of community-acquired cellulitis in adults is effective and safe, and that it facilitates more appropriate use of antibiotics, which might reduce antibiotic selection pressure for inducing antimicrobial resistance than the use of broad-spectrum antibiotics or antibiotic combinations [12]. Moreover, many published reports showed that patients who received narrow-spectrum antibiotics had lower incidence of antibiotic-associated adverse events than those who received broad-spectrum antibiotics or antibiotic combinations [5, 6].

As previously described above, there were 500 patients with cellulitis (360 patients with community-acquired cellulitis) during a period of 5 months. Therefore, there would be 1200 patients with cellulitis in the year of the study in which 864 patients were community-acquired cellulitis. Thus, estimation of the cost saving per year is based on the information from 864 patients with community-acquired cellulitis. If all of these patients received antibiotic regimens according to the CPG recommendations, the estimated annual cost of antibiotic treatment would be US $30 240. However, if the CPG is not used in all patients, then the annual cost of antibiotic treatment in those patients would be US $51 840. The difference in the annual cost of antibiotic treatment between patients in the CPG-compliant group and those in the CPG-noncompliant group was estimated to be US $21 600. The cost of hospitalization was also significantly reduced in the CPG-compliant group compared with the CPG-noncompliant group.

At least 130 patients with community-acquired cellulitis are admitted to Siriraj Hospital each year. If all hospitalized patients received the treatment recommended in the CPG, the estimated annual cost of hospitalization would be US $116 480. However, if the CPG is not used among all hospitalized patients with community-acquired cellulitis, then the estimated annual cost of hospitalization would be US $233 350. The difference in the annual cost of hospitalization between the CPG-compliant group and the CPG-noncompliant group was estimated to be US $116 870. Therefore, antibiotic treatment for cellulitis according to the CPG could also reduce the cost of treatment.

A CPG is a tool that is designed to provide physicians with treatment and decision-making guidance that is specific to a defined clinical setting or condition to standardize treatment. The success of a CPG is dependent on the quality of the CPG and the methods used to disseminate the CPG [14]. The reasons for the good CPG adherence observed in the present study include the following: (1) this CPG was developed based on local data; (2) it was designed to be a concise 1-page document that is printed in Thai language, which is the native language of the physicians at our center; (3) this CPG was disseminated via a wide range of communication methods, which is more effective than a single method of dissemination relative to effectuating changes in

Table 4. Comparison of Major Characteristics of the Patients in the Present Study and the Previous Study at Siriraj Hospital

Characteristics	Present Study (n = 360)	Previous Study (n = 970)	*P* Value[a]
Female gender	214 (59.4%)	535 (55.2%)	.161
Median age (range) (years)	62 (18–93)	62 (18–98)	.731
Clinical Presentations			
Fever	91 (25.3%)	157 (16.2%)	<.001
Hypotension	5 (1.4%)	20 (2.1%)	.422
Locations of Cellulitis			
Leg	168 (46.7%)	514 (53.0%)	.040
Foot	75 (20.8%)	199 (20.5%)	.899
Hand	35 (9.7%)	155 (11.9%)	.274
Others	82 (22.8%)	142 (14.6%)	<.001
Comorbidities			
Overall comorbidities	256 (71.1%)	731 (75.4%)	.115
Severity of Cellulitis			
Class 1	250 (69.4%)	640 (66.0%)	.233
Class 2	86 (23.9%)	243 (25.1%)	.662
Class 3	21 (5.8%)	67 (6.9%)	.484
Class 4	3 (0.8%)	20 (2.1%)	.127
Settings			
Ambulatory patients	304 (84.4%)	770 (79.4%)	.037
Hospitalized patients	56 (15.6%)	200 (20.6%)	.037
Responsible Physicians			
Medicine	137 (38.1%)	365 (37.6%)	.887
Emergency medicine	92 (25.6%)	230 (23.7%)	.485
Surgery	84 (23.3%)	242 (24.9%)	.542
Others	47 (13.1%)	133 (13.7%)	.756

[a] $P < .05$ indicates statistical significance.

physician behavior [6, 14–18]; and (4) the regular reminding of the CPG to the responsible physicians by using social media.

The common reasons that the CPG was not followed by some physicians in our study were as follows: (1) they did not determine the severity of cellulitis and routinely used intravenous antibiotics for treatment of cellulitis even if only 5% of patients in the CPG-noncompliant group had severe infection, whereas 30% of patients in the CPG-noncompliant group received intravenous antibiotics; (2) amoxicillin-clavulanate was used more often than dicloxacillin or cephalexin because it was a broad-spectrum antibiotic and it was used twice a day instead of 4 times a day for dicloxacillin or cephalexin; and (3) some physicians might not be aware of the CPG.

The strengths of this study include the fact that a multifaceted approach to communicating the implementation of the CPG was used, and that the implementation of this CPG was effectively executed without any reliance on any high-cost technologies. The limitations of this study include the fact that (1) the medical record reviewer was not blinded, which could have introduced some unintended bias, (2) the CPG addresses the antibiotic treatment of only patients with community-acquired cellulitis, so further study in patients with hospital-acquired cellulitis should be considered, (3) the multifaceted approach to communicating this guideline to physicians has to be reconducted at least once a year to inform physicians who will receive postgraduate training at Siriraj Hospital, and (4) this study was conducted at a single institution, so our results may not be generalizable to other hospitals.

CONCLUSIONS

Adherence to the CPG seems to reduce inappropriate prescription of broad-spectrum antibiotics or antibiotic combinations, and it could lower treatment costs in adults with community-acquired cellulitis without differences in favorable outcomes or adverse events between groups.

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