Effectiveness of Multifaceted Interventions on Rational Use of Antibiotics for Patients with Upper Respiratory Tract Infections and Acute Diarrhea

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Objective: *To implement multifaceted interventions to promote rational use of antibiotics for out-patients with upper respiratory tract infection (URI) and acute diarrhea.*
Material and Method: *The present study was conducted at ambulatory care facility for patients under Social Security Healthcare Benefit Scheme and Universal Health Coverage Scheme of Siriraj Hospital from January to April 2012. Multifaceted interventions were: Training responsible healthcare personnel on rational use of antibiotics, Clinical practice guidelines, Pre-printed medical record forms for patients, Throat swab or stool culture to be taken from the patients (if responsible physicians needed these); and provision of brochures containing causes, necessity and harm of antibiotics for URI and acute diarrhea to patients as well as their relatives while waiting for receiving care. Pre-printed medical records were collected every day. Each patient was called on day 3 after receiving care by an investigator to determine clinical responses.*
Results: *There were 1,241 episodes of URI and 210 episodes of acute diarrhea during the study period. Rates of antibiotic prescriptions were 13.0% for URI and 19.1% for acute diarrhea. Throat swab cultures recovered group A beta-hemolytic streptococci in 3.8% of URI patients and non-typhoidal Salmonella spp. in 14.6% of acute diarrhea patients. Clinical responses of the patients on day 3 after receiving care revealed that more than 97% of the patients who received antibiotics and who did not receive antibiotics were cured or improved.*
Conclusion: *Multifaceted interventions are very effective for promoting rational use of antibiotics for out-patients with URI and acute diarrhea at Siriraj Hospital.*

Keywords: *Antibiotics, Out-patient, Upper respiratory tract infection, Acute diarrhea*

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The ability of microorganisms to become resistant to antibiotics used against them has long been recognized and is becoming increasingly apparent[1,2]. Increasing antimicrobial resistance (AMR) presents a major threat to public health because it reduces the effectiveness of antimicrobial treatment, leading to increased morbidity, mortality, and health care expenditure[3]. The rate of development of AMR is accelerated by overuse and misuse of antimicrobials[4]. The major contributing factor responsible for development of AMR is inappropriate use of antibiotics. Antibiotics are commonly used in ambulatory care facility as well as in communities where antibiotics can be purchased without prescriptions[5]. A systematic review and meta-analysis on the effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients revealed that individuals prescribed an antibiotic in primary care for a respiratory or urinary infection can develop bacterial resistance to that antibiotic[6]. This effect not only increases the population carriage of organisms resistant to first line antibiotics, but also creates the conditions for increased use of second line antibiotics in the community. Upper respiratory tract infection (URI) and acute diarrhea are common self-limiting ailments for patients seeking care at hospital Out-Patient Departments (OPD). The causative agents of URI include viruses, bacteria and atypical pathogens. Antibiotic treatment benefits only those patients with group A β-hemolytic streptococci (GAS) infection who might subsequently suffer from

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acute rheumatic fever. The prevalence of GAS in adults with sore throat attending Siriraj Hospital was 7.9% to 11.4%[7,8]. No compelling data on antibiotic treatment of patients with URI other than GAS are beneficial. Nevertheless, most of the patients with URI receive antibiotics at ambulatory healthcare facilities. In healthy individuals with acute diarrhea, empiric antibiotic therapy is usually not indicated since acute diarrhea is almost always self-limited. Antibiotics can lead to adverse reactions and many antibiotics can disturb the normal physiology of intestinal micro environment due to their effects on the normal flora. Antibiotic therapy is contra indicated in acute diarrhea caused by non-typhoidal *Salmonella spp.* and shiga-toxin-producing *Escherichia coli*. According to the standard guidelines of several organizations, empiric antibiotic therapy is recommended only for invasive or inflammatory diarrhea, especially in special hosts with immuno compromised conditions, and for non-inflammatory diarrhea with moderate or severe dehydration such as cholera[9-12].

In Thailand, the Antibiotics Smart Use (ASU) program was initiated in 2007. The program is a collaboration among Health Systems Research Institute (Thailand), International Health Policy Program (Thailand) and Food and Drug Administration (Thailand), and it has been supported by World Health Organization, Health Systems Research Institute (Thailand), International Health Policy Program (Thailand) and Food and Drug Administration (Thailand) and Thai Health Promotion Fund. The foundation of ASU program is that no antibiotics should be used for non-bacterial infections. The ASU program aims to improve prescribing of antibiotics in Thailand by targeting both prescribers and patients with URI, acute diarrhea and simple fresh traumatic wound in community and ambulatory care facilities. The program has been successfully implemented in many community hospitals[13]. The objective of the present study was to implement multifaceted interventions to promote rational use of antibiotics for out-patients with URI and acute diarrhea at Siriraj Hospital.

Material and Method

The present study was approved by the Siriraj Institutional Review Board.

Patients

They were patients aged over 2 years with acute episodes of URI and acute diarrhea who attended ambulatory care services of the Social Security Healthcare and Universal Health Coverage Schemes at Siriraj Hospital in Bangkok from January to April 2012.

Definitions of URI and acute diarrhea

URI is defined as the presence of any symptoms of sore throat, rhinorrhea or cough, with or without fever. Acute diarrhea is defined as having three or more loose or liquid stools per day, or as having mucous or bloody defecation at least one time, with the duration of less than two weeks.

Study procedures

Pre-intervention phase

The data on diagnoses and prescribed antibiotics of the patients with URI and acute diarrhea attended ambulatory services of Siriraj Hospital from June to October 2011 were retrieved, collected and analyzed. The diagnoses of URI and acute diarrhea included the following codes according to International Classification of Diseases-10 (ICD-10) version 2010 : J00, J010, J011, J012, J013, J014, J018, J019, J020, J028, J029, J030, J038, J039, J040, J041, J042, J050, J051, J060, J068, J069, J20, H650, H651, H659, H660, H664, H669, H671, H678, A000, A00, A009, A010, A011, A012, A013, A014, A020, A022, A028, A029, A030, A031, A032, A033, A038, A039, A040, A041, A042, A043, A044, A045,A046, A047, A048, A049, A050, A051, A052, A053, A054, A058, A059, A060, A061, A062, A063, A064, A065, A066, A06, A068, A069, A070, A071, A072, A073, A078, A079, A080, A081, A082, A083, A084, A085, A09, K520, K521, K522, K5220, K5228, K5229, K523, K528, K529.

Intervention phase

The multifaceted interventions were implemented from December 2011 to April 2012. Interactive educational meetings were held in December 2012 for all responsible healthcare personnel of ambulatory care services of the Social Security Healthcare and Universal Health Coverage Schemes, Siriraj Hospital. The investigators presented the current situation on antibiotic use for patients with URI and acute diarrhea at the ambulatory care services of the Social Security Healthcare and Universal Health Coverage Schemes as well as the necessity for change. The rationale for appropriate diagnosis of each clinical syndrome of URI and acute diarrhea and the principles for prescribing antibiotics for each clinical syndrome using the Clinical Practice Guidelines (CPG) of ASU program were then distributed and explained. Evidence for each recommendation in the CPG was clarified. The pre-printed medical record forms for URI and acute

diarrhea were used to remind the healthcare personnel about the rational use of antibiotics. The responsible physicians agreed to adhere to the CPG and the pre-printed medical record forms from January 2012. Throat swab culture for URI patient and stool culture for acute diarrhea patients were offered to any patient with URI and acute diarrhea if needed and it was free of charge. The brochures containing causes, natural history, management, and necessity and harm of antibiotics for URI and acute diarrhea were provided to URI and acute diarrhea patients as well as their relatives while they waited to receive care. Each patient was called on day 3 after receiving care for URI and acute diarrhea by an investigator to determine clinical responses of URI and acute diarrhea. Pre-printed medical records filled in by responsible nurses and physicians were collected at the end of each day. The data on antibiotic prescription rates and the outcomes of URI and acute diarrhea patients, who received and those who did not receive antibiotics over the past month between January 2012 and April 2012, were provided to all responsible healthcare personnel every month.

Statistical analysis

The present study was designed to determine the antibiotic prescription rates at the pre-intervention phase of 70%$\pm$5% in patients with URI and acute diarrhea attended each ambulatory care service of Siriraj Hospital with 5% type I error. Therefore, the total number of the patients from all ambulatory care services of Siriraj Hospital during the pre-intervention phase should be at least 969 patients. It was estimated that the antibiotic prescription rate at the intervention phase was 15%$\pm$5% in patients with URI and acute diarrhea attended Social Security Healthcare and Universal Health Coverage Schemes of Siriraj Hospital with 5% type I error. Therefore, the total number of the patients from Social Security Healthcare and Universal Health Coverage Schemes of Siriraj Hospital during the intervention phase should be at least 392 patients. Descriptive statistics were used to summarize the data. Chi-square or Fisher's exact test was used to compare categorical variables. A p-value of less than 0.05 was considered significant. The SPSS software version 18 was used for the analyses.

Results

Characteristics of patients and antibiotic prescriptions during pre-intervention phase

There were 23,637 patients with URI and 4,876 patients with acute diarrhea during June to October 2011. The average number of the patients for each month, average prescription rate of antibiotics and types of prescribed antibiotics in URI and acute diarrhea patients who attended general OPD, private OPD, ambulatory services of the Social Security Healthcare and Universal Health Coverage Schemes of Siriraj Hospital are shown in Table 1 and 2. Antibiotic prescription rates of URI patients were not significantly different among locations of healthcare services. Amoxicillin and co-amoxiclav were most frequently prescribed. Only 13.6% of URI patients were prescribed antibiotics for 10 days. Antibiotic prescription rates of acute diarrhea patients were somewhat different among the different locations of healthcare services. However, norfloxacin was the most common antibiotic given the patients in all locations.

Antibiotic prescriptions during intervention phase

The data from 1,241 episodes of URI and 210 episodes of acute diarrhea during January to April 2012 showed that the rates of antibiotic prescriptions decreased to 13.0% for URI and 19.1% for acute diarrhea as shown in Fig. 1. The types of prescribed antibiotics are shown in Table 2. Amoxicillin and norfloxacin were still the most common antibiotics given to URI and acute diarrhea patients, respectively.

Throat swab and stool cultures

Throat swab cultures were done in 183 patients (14.8%) and stool cultures were performed in 41 patients (19.5%) as shown in Table 3. Seventeen patients (9.3%) of URI and 5 patients (12.2%) of acute diarrhea received antibiotics prior to each specimen collection. The most commonly isolated bacteria were normal throat flora (140 patients, 76.6%) whereas group A beta-hemolytic streptococci were recovered in 7 patients (3.8%). Only 6 specimens (14.7%) of stool cultures grew non-typhoidal *Salmonella spp*.

Clinical outcomes

Telephone interviews were available for 1,343 patients (92.6%) on day 3 after receiving care for URI and acute diarrhea from January and April 2012. Clinical responses of the patients who received antibiotics and those who did not receive antibiotics were not significantly different as shown in Table 4.

Discussion

Overall rates of antibiotics for patients with URI and acute diarrhea at Siriraj Hospital during the pre-intervention phase were 74% and 78%, respectively.

Table 1. Characteristics and types of prescribed antibiotics of URI patients during June to October 2011 and January to April 2012

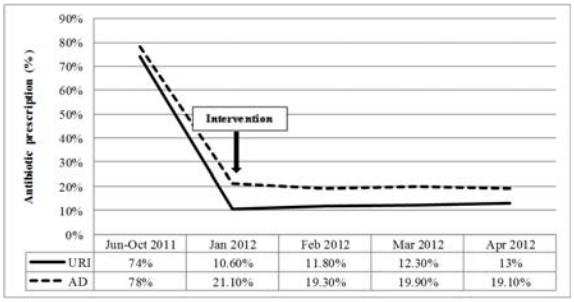
	Jun-Oct 2011				Jan-Apr 2012	
	General OPD	Private OPD	SSH	UHC	SSH	UHC
Number of patients per month	1,561	754	853	308	227	83
Antibiotic prescription per month (%)	69.1	73.2	71.9	73.9	10.1	17.5
Prescribed antibiotics (%)						
Amoxicillin	32.5	10.4	39.2	48.3	40.2	58.7
Co-amoxiclav	28.8	31.5	13.1	4.3	16.3	12.0
Roxithromycin	11.4	8.0	33.3	41.3	21.7	28.0
Clarithromycin	8.2	14.5	2.1	1.8	1.4	1.3
Azithromycin	5.9	11.3	4.4	-	2.2	-
Penicillin V	-	-	-	-	17.4	-

SSH = social security healthcare scheme; UHC = universal health coverage scheme

Table 2. Characteristics and types of prescribed antibiotics of acute diarrhea patients during June to October 2011 and January to April 2012

	Jun-Oct 2011				Jan-Apr 2012	
	General OPD	Private OPD	SSH	UHC	SSH	UHC
Number of patients per month	158	67	132	36	35	18
Antibiotic prescription per month (%)	51.3	71.6	71.2	85.1	12.3	35.7
Prescribed antibiotics (%)						
Norfloxacin	68.0	33.6	66.2	73.5	79.0	70.4
Ciprofloxacin	22.4	45.6	20.6	14.9	15.8	22.2
Ceftriaxone	7.4	-	4.7	8.2	5.2	7.4
Cefdinir	-	11.1	-	-	-	-

SSH = social security healthcare scheme; UHC = universal health coverage scheme



URI: Upper respiratory tract infection
AD: Acute diarrhea

Fig. 1 Antibiotic prescription for URI and acute diarrhea patients during June 2011 to April 2012.

The observed antibiotic prescription rate of URI patients during the pre-intervention phase was comparable to the observation made in 2001 at Siriraj Hospital[14] and similar to the rate observed in another tertiary care university in Bangkok[15]. Such antibiotic prescription rates in URI patients were considered high given the fact that only 7.9% to 11.4% of Thai patients with URI had positive throat culture for group A β-hemolytic streptococci[7,8]. The observed antibiotic prescription rate of 78% in acute diarrhea patients during the pre-intervention phase was comparable to 76.4% reported from community and general hospitals in central Thailand[16] but it was higher than 45% reported from another tertiary care university in Bangkok[17]. Such antibiotic prescription rates in acute diarrhea patients were considered high given the fact that most of the patients with acute diarrhea would recover without antibiotics[9,11,12]. The appropriate rates of antibiotic

prescriptions of less than 20% were reported from several studies[18].

The authors used multifaceted interventions to promote rational use of antibiotics in our implementation since a Cochrane review on interventions to improve antibiotic prescribing practice in ambulatory care revealed that the most effective interventions are likely to be those that address local prescribing behaviors and barriers to change. It also includes patients and the public in the educational program; local barriers should be addressed before major educational efforts are implemented[19].

The authors found that our multifaceted interventions were very effective in decreasing antibiotic prescription rates from 74% to 13% in URI and 78% to 19.1% in acute diarrhea without observing any harmful effects to the patients who did not receive antibiotics when compared with those who received antibiotics. The factors contributing to this successful implementation included: 1) The responsible healthcare personnel received information of their previous performance on antibiotic prescriptions that need to be changed and clarification of evidence-based guidelines, 2) Microbiological testing was offered free of charge when the physician wanted to confirm if the patient had bacterial infection, 3) Demand of antibiotic from the patient was less since the patient and patient's relatives received educational materials prior to having a physician encounter and 4) The information about antibiotic prescription rates, causative agents recovered from the patients as well as clinical responses of the patients, who did not receive antibiotics, were provided to the responsible healthcare personnel every month. Our findings of low prevalence of group A β-hemolytic streptococci confirmed that most of URI patients did not need antibiotics. Although only 15% of URI patients received throat swab cultures, these patients should be more likely to have bacterial cause since the responsible physicians usually performed throat swab cultures when it was suspected that the patient could have bacterial infection. The same logic was applicable to stool cultures in which only 20% of acute diarrhea patients received stool cultures. The patients who had stool cultures done should be those whom the physicians suspected might have bacterial infection. Non-typhoidal *Salmonella spp.* as the major pathogen observed from stool cultures of acute diarrhea also confirmed that most of the patients with acute diarrhea, including those with positive stool culture for Non-typhoidal *Salmonella spp.*, did not need antibiotics[20,21].

The present study results were presented to Siriraj Hospital administrators and they agreed to expand the promotion concerning rational use of antibiotics for URI and acute diarrhea patients to the entire ambulatory healthcare facilities of Siriraj hospital. The study results were also presented to the National Health Security Office (NHSO) that is responsible for healthcare of 47 million people under Universal Health Coverage Scheme. NHSO decided to use antibiotic

Table 3. Throat swab and stool cultures with isolated organisms in URI and acute diarrhea patients during January and April 2012

	Number (%)
Throat swab culture	
No	1,058 (85.2)
Yes	183 (14.8)
Group A streptococci	7 (3.8)
Non-group A streptococci	7 (3.8)
Normal throat flora	140 (76.6)
No growth	5 (2.7)
Rejected specimen	24 (13.1)
Stool culture	
No	169 (80.5)
Yes	41 (19.5)
Salmonella group B	4 (9.8)
Salmonella group E	2 (4.9)
No pathologic agents	35 (85.3)

Table 4. Clinical responses of URI and acute diarrhea patients on day 3 after therapy during January and April 2012

	Antibiotics	% Response			p-value
		Cure	Improved	Not improved	
URI (n = 1,241)	Yes (13%)	39.1	60.2	0.6	0.87
	No (87%)	36.9	62.5	0.6	
Acute diarrhea (n = 210)	Yes (19.1%)	67.5	30.0	2.5	0.26
	No (80.9%)	69.4	30.6	0	

prescription rates for URI and acute diarrhea patients as the criteria of pay-for-performance since fiscal year 2013. NHSO has allocated US$ 1.6 million for additional pay-for-performance to all healthcare centers under Universal Health Coverage Scheme. The healthcare center will receive additional full payment if its antibiotic prescription rates of URI and acute diarrhea were 20% or less, partial payment if its antibiotic prescription rates of URI and acute diarrhea were 21% to 40%, and no payment will be provided if its antibiotic prescription rates of URI and acute diarrhea were more than 40%.

In conclusion, the presented study has broadened the support for the efficacy for promoting rational use of antibiotics for outpatients with URI and acute diarrhea at Siriraj Hospital. Therefore, it is hoped that inappropriate use of antibiotics for URI and acute diarrhea in Thailand would be diminished leading to fewer incidents of adverse effects due to antibiotics, decreasing antibiotic costs and delaying antibiotic resistance in the near future.

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Potential conflicts of interest

None.

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ประสิทธิผลของชุดกิจกรรมการส่งเสริมการใช้ยาต้านจุลชีพอย่างสมเหตุผลในผู้ป่วยติดเชื้อระบบการหายใจส่วนบนและโรคอุจจาระร่วงเฉียบพลัน

อธิรัฐ บุญญาศิริ, วิษณุ ธรรมลิขิตกุล

วัตถุประสงค์: เพื่อทราบผลของชุดกิจกรรมในการส่งเสริมการใช้ยาต้านจุลชีพอย่างสมเหตุผลในผู้ป่วยนอกที่เป็นโรคหวัดและโรคอุจจาระร่วงเฉียบพลัน

วัสดุและวิธีการ: ดำเนินการที่แผนกผู้ป่วยนอกของหน่วยตรวจประกันสังคมและหน่วยบริการปฐมภูมิของโรงพยาบาลศิริราช ตั้งแต่ เดือนมกราคม ถึง เมษายน พ.ศ. 2555 ชุดกิจกรรมประกอบด้วย การอบรมบุคลากรในการใช้ยาต้านจุลชีพอย่างเหมาะสม เตรียมคู่มือแนวทางการรักษาและแบบบันทึกข้อมูลผู้ป่วย สนับสนุนค่าใช้จ่ายในการตรวจเพาะเชื้อจากคอหอยและอุจจาระในรายที่แพทย์ต้องการส่งตรวจและเตรียมแผ่นพับที่มีข้อมูลสาเหตุความจำเป็นและอันตรายของยาต้านจุลชีพให้ผู้ป่วยกับญาติระหว่างรอตรวจ แบบบันทึกข้อมูลผู้ป่วยจะถูกเก็บทุกวัน ผู้ป่วยแต่ละรายได้รับการติดตามอาการทางโทรศัพท์จากผู้นิพนธ์ในวันที่ 3 หลังการตรวจรักษา

ผลการศึกษา: *มีการรักษาโรคหวัดจำนวน 1,241 ครั้งและการรักษาโรคอุจจาระร่วงเฉียบพลันจำนวน 210 ครั้ง อัตราการได้รับยาปฏิชีวนะลดลงเหลือร้อยละ 13.0 และ 19.1 ในโรคหวัดและโรคอุจจาระร่วงเฉียบพลันตามลำดับ พบเชื้อ group A streptococci ร้อยละ 3.8 ของผู้ป่วยที่ได้รับการตรวจหาเชื้อจากคอหอยและพบเชื้อ non-typhoidal Salmonella spp. ร้อยละ 14.7 ของผู้ป่วยที่มีการตรวจหาเชื้อจากอุจจาระ ผลการรักษาในวันที่ 3 หลังการตรวจรักษา พบว่ามากกว่าร้อยละ 97 ทั้งในผู้ป่วยที่ได้รับและไม่ได้รับยาต้านจุลชีพหายหรืออาการดีขึ้น*

สรุป: ชุดกิจกรรมการส่งเสริมการใช้ยาต้านจุลชีพอย่างสมเหตุผลมีประสิทธิผลดีมากในการส่งเสริมการใช้ยาต้านจุลชีพอย่างสมเหตุผล ในผู้ป่วยนอกที่เป็นโรคหวัดและโรคอุจจาระร่วงเฉียบพลันที่โรงพยาบาลศิริราช