Antibiotic Prescription for Adults with Acute Diarrhea at King Chulalongkorn Memorial Hospital, Thailand

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Background: *In Thailand, acute diarrhea is one of the most common problems among ambulatory patients at the outpatient department (OPD). Overuse of antibiotics is associated with increased rates of antibiotic-resistant bacteria, unnecessary increased cost of treatment, and significant incidence of adverse effects. In Thailand, how frequently antibiotic is prescribed in adult patients with acute diarrhea is not known.*
Material and Method: *The authors performed a retrospective study in all adult patients with acute diarrhea attending at the OPD of King Chulalongkorn Memorial Hospital, Bangkok, Thailand between August 2009 and January 2010 as ambulatory basis. All data regarding epidemiology, clinical features, and treatment were evaluated.*
Results: *There were 390 [255 females (65.4%) and 135 males (34.6%)] patients during the study period. There were 91 (23.3%) with inflammatory diarrhea and 209 (76.7%) patients with non-inflammatory diarrhea. Only 36 (9.2%) patients had stool examination and culture results. Of 13 (36.1%) patients with positive stool cultures, four (11.1%) patients had Vibrio parahaemolyticus, two (5.7%) patients each had non-O1 Vibrio cholerae, Cryptosporidium parvum, or Plesiomonas shigelloides and V. parahaemolyticus, and one (2.9%) patient each had P. shigelloides, P. shigelloides and Salmonella, or group D Salmonella. Three hundred fifty three (90.5%) and 37 (9.5%) patients were treated by residents and faculty staffs, respectively. One hundred and seventy-six (45.1%) patients received antibiotics, which included norfloxacin (128 patients, 72.7%), ciprofloxacin (34, 19.3%), ceftriaxone and ciprofloxacin (6, 3.4%), ceftriaxone (5, 2.8%), ceftriaxone and norfloxacin (2, 1.1%), amoxicillin (1, 0.6%), and ofloxacin (1, 0.6%). One hundred and forty-eight of 353 (41.9%) residents and 28 of 37 (75.7%) faculty staffs prescribed antibiotics. According to the recommendations by WHO, the rate of overuse of antibiotics was 48.9% (86 of 176 patients).*
Conclusion: *There is a very high rate of overuse of antibiotics in Chulalongkorn Hospital. Both attributing physician- and patient-related factors should be evaluated before implementing an effective strategy to change prescribing behavior.*

Keywords: *Acute diarrhea, Antibiotic, Antibiotic prescription, Adults, Thailand*

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Acute diarrhea is a major public health problem worldwide especially in developing countries. In Thailand, it has been estimated to affect approximately 1 million individuals annually[1]. In healthy adults, empiric antibiotic therapy for acute diarrhea is generally not recommended since most are self limited and overuse of antibiotics may lead to the emergence of antibiotic-resistant bacteria. Apart from their adverse reactions, most antibiotics can disturb the normal physiology of intestinal microenvironment due to their effect on the normal flora. In addition, antibiotic therapy is contraindicated in acute diarrhea caused by non-typhoidal *Salmonella* 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 (mucous bloody stool, tenesmus, dysentery, high fever, or chills) and non-inflammatory diarrhea with moderate or severe dehydration (suspected cholera)[1-4]. In addition, all the guidelines recommend that stool culture be performed before prescribing antibiotics.

Excessive and inappropriate use of antibiotics for patients with acute diarrhea has been documented in the outpatient department (OPD) setting[5-12]. To the best of the authors' knowledge, there has been no study

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in Thailand to determine the antibiotic prescription rate in adult patients with acute diarrhea. Therefore, the present study aimed to determine physicians' practices in prescribing antibiotics to adult patients with acute diarrhea attending at the OPD.

Material and Method

Study design

A descriptive study was carried out in all adult patients with acute diarrhea attending at the OPD of King Chulalongkorn Memorial Hospital (KCMH), Bangkok, Thailand, between August 2009 and January 2010. The study was approved by the institutional review board.

Patients

The inclusion criteria included all adult patients older than 15 years of age who presented with acute diarrhea. All patients must be treated as ambulatory basis. The medical record of these patients were identified by searching the disease codes based on International Classification of Diseases-10 (ICD-10) which include A00 (cholera), A01 (typhoid and paratyphoid fever), A02 (other *Salmonella* infection), A03 (shigellosis), A04 (other bacterial intestinal infection), A05 (other bacterial food-borne intoxication), A08 (viral and other specified intestinal infection), A09 (diarrhea and gastroenteritis of presumed infection origin), and K529 (noninfectious gastroenteritis and colitis, unspecified). All data including epidemiology, clinical manifestations, microbiology and treatment were then analyzed.

Definitions

1. Acute diarrhea was 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.

2. The appropriate use of antibiotics for treatment of acute diarrhea was defined as prescribing antibiotics to the patient with acute diarrhea under the indications recommended by the treatment guidelines endorsed by KCMH which include invasive or inflammatory diarrhea (mucous bloody stool, tenesmus, dysentery, high fever, or chills) and non-inflammatory diarrhea with moderate or severe dehydration (suspected cholera).

Statistic analysis

The present study was designed to determine the antibiotic prescription rate in adult patients with acute diarrhea in KCMH. Assuming the prescription rate was 47.3% in KCMH (unpublished data from a pilot study, a few months before performing the present study), a sample size of 390 patients was required. This calculation was based on the assumption that alpha and beta errors were 0.05 and 0.20, respectively. The descriptive statistics were used to summarize the data in terms of frequency and percentage distribution. The SPSS software version 12 was used for the analyses.

Results

Patient demography

During the study period, there were 390 patients [135 males (34.6%) and 255 females (65.4%)] with the age over 15 years (Table 1). Ninety-three patients (23.8%) had underlying illnesses including cardiovascular disorders (57 patients, 14.6%), endocrinologic disorders (52, 13.3%), central nervous system diseases (14, 3.6%) and chronic kidney disease (10, 2.6%). Among these 390 patients, there were 235 (60.3%) and 155 (39.7%) patients with self-payment or supported by the Social Security Office, the Nation Health Security Office, or the Comptroller General's Department, respectively.

Clinical characteristics

Three hundred eighty patients (97.4%) presented with acute watery diarrhea. Apart from diarrhea, the most common symptom was abdominal pain (303 patients, 77.7%), followed by nausea (290, 74.4%), vomiting (235, 60.3%), fever (46, 11.8%), tenesmus (19, 4.9%) and chills (4, 1.03%). Three hundred thirty seven patients (86.4%) came to the hospital within 24 hours after the onset of diarrhea. Upon physical examination, severe, moderate, and mild dehydration were noted in one (0.3%), 18 (4.6%) and 371 (94.2%), respectively. There were 91 (23.3%) and 209 (76.7%) patients with inflammatory and non-inflammatory diarrhea, respectively.

Table 1. Baseline characteristics of 390 patients with acute diarrhea (n = 390)

	Number	Percent
Sex		
Male	135	34.6
Female	255	65.4
Age group (years)		
15-60	334	85.6
> 60	56	14.4

Microbiology

Stool examination was performed in 29 patients (7.4%), and there were white blood cells of > 10 cells/high-power field in only two patients. Stool cultures were performed in 36 patients (9.2%), and only 13 specimens grew pathogenic organism (Table 2). The most commonly isolated bacteria was *Vibrio parahaemolyticus* (6 patients, 16.8%), followed by *Plesiomonas shigelloides* (4, 11.1%), non-O1 *Vibrio cholerae* (2, 5.6%), *Cryptosporidium parvum* (2, 5.6%), and *Salmonella* (2, 5.6%) (3 patients had co-infection caused by 2 pathogens).

Antibiotic prescription rate

One hundred seventy six (45.1%) patients received antibiotics. Of these 176 patients, the most antibiotic prescribed was norfloxacin (128 patients, 72.7%), ciprofloxacin (34, 19.3%), ceftriaxone and ciprofloxacin (6, 3.4%), ceftriaxone (4, 2.8%), ceftriaxone and norfloxacin (2, 1.1%), amoxicillin (1, 0.6%) and ofloxacin (1, 0.6%) (Table 3).

Three hundred and fifty-three patients (90.5%) were treated by residents, and 37 patients were treated by faculty staffs (Table 4). One hundred forty eight of 353 (41.9%) residents and 28 of 37 (75.7%) staffs prescribed antibiotics. An overall inappropriate use of antibiotics was 48.9% (86 of 176 patients). There was only overuse of antibiotics. The highest rate of inappropriate antibiotic prescription was noted in the group of non-Medicine staff (20 of 22 patients, 90.9%), followed by the groups of Medicine residents (60 of 72 patients, 45.5%) (60 of 132 patients, 45.5%) and non-Medicine residents (6 of 16 patients, 37.5%).

Table 2. Stool cultures and isolated pathogenic organism (n = 390)

Stool culture	Number	Percent
No	354	90.9
Yes	36	9.2
No growth	23	63.9
Vibrio parahaemolyticus	4	11.1
Non-O1 *Vibrio cholerae*	2	5.6
Cryptosporidium parvum	2	5.6
Plesiomonas shigelloides and *V. parahaemolyticus*	2	5.6
P. shigelloides	1	2.8
P. shigelloides and *Salmonella*	1	2.8
Group D *Salmonella*	1	2.8

Table 3. Rate and type of antibiotics prescription (n = 390)

	Number	Percent
Antibiotic prescription		
No	214	54.9
Yes	176	45.1
Class and type of antibiotics		
Fluoroquinolones	163	92.6
Norfloxacin	128	72.7
Ciprofloxacin	34	19.3
Ofloxacin	1	0.6
Cephalosporins and fluoroquinolones	8	4.6
Ceftriaxone and ciprofloxacin	6	3.4
Ceftriaxone and norfloxacin	2	1.1
Cephalosporins	4	2.8
Ceftriaxone	4	2.8
Penicillins	1	0.6
Amoxicillin	1	0.6

Table 4. Type of caring physician and rates of appropriate and inappropriate use of antibiotics

	Number	Percent
Residents	353	90.5
Medicine residents	324	83.1
Antibiotic prescription	132	40.7
- Appropriateness	72	54.6
- Inappropriateness	60	45.5
No antibiotic prescription	192	59.3
- Appropriateness	192	100.0
Non-Medicine residents	29	7.4
Antibiotic prescription	16	55.2
- Appropriateness	10	62.5
- Inappropriateness	6	37.5
No antibiotic prescription	13	44.8
- Appropriateness	13	100.0
Staffs	37	9.5
Non-Medicine staffs	24	6.2
Antibiotic prescription	22	91.7
- Appropriateness	2	9.1
- Inappropriateness	20	90.9
No antibiotic prescription	2	9.3
- Appropriateness	2	100.0
Medicine staffs	13	3.3
Antibiotic prescription	6	46.2
- Appropriateness	6	100.0
No antibiotic prescription	7	53.9
- Appropriateness	7	100.0
Appropriate antibiotic prescription	90	51.1
Inappropriate antibiotic prescription	86	48.9

All six Medicine staffs had appropriate antibiotic prescription.

Three contributing factors significantly associated with an antibiotic prescription included the patients with self-payment, those presented with tenesmus, and those treated by non-medicine staffs.

Discussion

In the present study, an overall antibiotic use for adult patients with acute diarrhea was 45.1%, which was very high, even though all patients were treated as ambulatory basis. In addition, an overall inappropriate (overuse) use of antibiotics was 48.9% in KCMH. A recent study in both primary and secondary healthcare settings in two districts of India demonstrated that an overall antibiotic prescription rate in both adult and pediatric patients with acute diarrhea was 81.3%[6]. Unfortunately, there were no data regarding inappropriate use of antibiotics in their study. In contrast, Carpenter et al have conducted a retrospective study in both pediatric and adult patients with diarrhea in Tennessee, the United States and found that the antibiotic prescription rates in adults and children aged less than three months were only 15.6% and 10.4%, respectively[9]. However, their study did not include the data of inappropriate prescription of antibiotics. A similar study carried out in both adults and children with acute diarrhea presenting at the emergency department of hospitals in the United States showed the rate of antibiotic use was only 25%[7]. To the best of the authors' knowledge, there have been no studies to determine the antibiotic prescription rate in adult patients with acute diarrhea in Thailand. A study by Howteerakul et al at ten community and general hospitals in central Thailand described the antibiotic prescription rate in children aged less than five years with diarrhea was 76.4%[10]. Among these prescriptions, an appropriate antibiotic use was only 27.4%. Osatakul et al recently reported that 61.4% of pediatric patients with acute diarrhea attending at the OPD of ten hospitals in southern Thailand have received antibiotics[8]. However, the appropriate antibiotic prescription rate was only 44.1%. In conclusion, from these data, there is usually a very high rate of antibiotic prescription in patients with acute diarrhea at hospitals in developing countries, compared to those in the United States, despite the presence of guidelines of both the institute and the nation[1,6-8].

Of note, norfloxacin was the most commonly prescribed antibiotic in the present study, followed by ciprofloxacin and ceftriaxone. A study by Karras et al found that fluoroquinolone was the most frequently prescribed antibiotic, followed by cotrimoxazole, amoxicillin or ampicillin and metronidazole[7]. In contrast, Howteerakul et al reported that cotrimoxazole was the most commonly prescribed drug, followed by colistin, norfloxacin and nalidixic acid[10]. In a recent study by Osatakul et al in pediatric patients, the most frequently prescribed antibiotic was cotrimoxazole, followed by norfloxacin and colistin[8]. The difference between the studies in children and adults is probably due to the concern of chondrotoxicity of fluoroquinolones, compared to the safety of cotrimoxazole in pediatric patients.

All international and national guidelines recommend that stool culture must be performed before prescribing antibiotics[1-4]. Prescribing the antibiotics without ordering the stool culture generally indicates an inappropriate antibiotic use[1-4]. In the present study, stool cultures were performed in only 9.2%, despite a high rate of antibiotic prescription. This very low rate is probably due to an ambulatory basis of treatment in all patients in the present study. However, a recent study in the United States also showed that stool culture was ordered in only 5.0% of 315,828 episodes of acute diarrhea[9]. A study in Thailand by Howteerakul et al showed that the stool culture was performed in only 15.6% of all 424 patients with diarrhea[10]. In conclusion, there is a very low rate of stool culture before prescribing antibiotics in these studies. A lack of information of bacterial pathogens of acute diarrhea in Thailand or each institute leads to an imprudent use of antibiotics in clinical practice.

Surprisingly, in the present study, non-Medicine staffs were more likely to inappropriately prescribe antibiotics in approximately 91% of patients. Similar to our results, a recent study carried out in children attending at both community and general hospitals southern Thailand demonstrated that medical staffs were more likely to appropriately prescribe antibiotics than non-medical staffs[8]. Another study in central Thailand also described the higher rate of appropriate antibiotic prescription was observed in pediatricians than general practitioners[10]. A similar observation was made in two previous studies in pediatric patients carried out in the United States and Indonesia showing that well-trained specialists prescribed antibiotics less frequently than general practitioners[11,12]. Several factors may influence the difference in antibiotics prescribing practice between specialists and general practitioners. These include a time constraint to take care, no motivation to educate,

a need to satisfy, and a lack of medical knowledge to manage diarrheal patients. However, a well-designed study is needed to determine these physician- and patient-related factors influencing antibiotic prescribing behavior.

In the present study, an estimate of antibiotic cost associated with an inappropriate prescription was approximately 17.4 Baht per case, accounting for 31.4% of a total cost of treatment. Assuming a total number of patients with acute diarrhea per month are constant, an estimate of cost savings associated with reducing the inappropriate antibiotic prescription would be 3,591 Baht annually at OPD of KCMH.

The present study has some limitations. Some important data including the attitude and knowledge of caring physicians regarding management of diarrheal patients as well as the request of antibiotics by patients were not available. In addition, there were too small a number of patients who were treated by non-Medicine residents and staffs. Hence, the present results should be interpreted with caution especially for the physician-related factors influencing the rate of antibiotic prescription.

To the best of the authors' knowledge, this is the first study in Thailand to determine the antibiotic prescription rate in adults with acute diarrhea. There is a very high rate of inappropriate use (overuse) of antibiotics in KCMH. Attributing factors, either physician- or patient-related should be determined before implementation of effective strategies to change prescribing behavior.

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Potential conflicts of interest

None.

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การสั่งจ่ายยาปฏิชีวนะในผู้ใหญ่ที่มีภาวะท้องเสียเฉียบพลันที่โรงพยาบาลจุฬาลงกรณ์

สุระชัย ทรัพย์จรัสแสง, ชุษณา สวนกระต่าย

***ภูมิหลัง**: ในประเทศไทยภาวะท้องเสียเฉียบพลันเป็นหนึ่งในหลายปัญหาที่พบบ่อยที่สุดในผู้ป่วยที่มารักษาแผนกผู้ป่วยนอก การใช้ยาปฏิชีวนะที่มากเกินไปทำให้เพิ่มอัตราของแบคทีเรียที่ดื้อยาปฏิชีวนะ การสิ้นเปลืองค่าใช้จ่ายที่ไม่จำเป็น และเพิ่มผลข้างเคียงในประเทศไทยการสั่งจ่ายยาปฏิชีวนะในผู้ป่วยผู้ใหญ่ที่มีภาวะท้องเสียเฉียบพลันไม่เป็นที่ทราบกัน*

***วัสดุและวิธีการ**: การศึกษาแบบพรรณนาในผู้ป่วยผู้ใหญ่ที่มีภาวะท้องเสียเฉียบพลันที่มารักษา ที่แผนกผู้ป่วยนอกของโรงพยาบาลจุฬาลงกรณ์ กรุงเทพมหานคร ระหว่างเดือนสิงหาคม พ.ศ. 2552 ถึง เดือนมกราคม พ.ศ. 2553 ผู้ป่วยทั้งหมดต้องได้รับการรักษาแผนกผู้ป่วยนอก วิเคราะห์ข้อมูลทั้งหมดในแง่ระบาดวิทยาลักษณะทางคลินิกและการรักษา*

***ผลการศึกษา**: มีผู้ป่วยทั้งหมด 390 ราย [ผู้หญิง 255 ราย (ร้อยละ 65.4) และผู้ชาย 135 ราย (ร้อยละ 34.6)] ในระหว่างการศึกษา ผู้ป่วย 353 ราย (ร้อยละ 90.5) และ 37 ราย (ร้อยละ 9.5) ได้รับการรักษา โดยแพทย์ประจำบ้านและอาจารย์แพทย์ ตามลำดับ มีผู้ป่วย 91 ราย (ร้อยละ 23.3) และ 209 ราย (ร้อยละ 76.7) ที่มีภาวะท้องเสียแบบอักเสบและไม่อักเสบตามลำดับ มีผู้ป่วยเพียง 36 ราย (ร้อยละ 9.2) ที่ส่งตรวจ และเพาะเชื้อแบคทีเรียจากอุจจาระ ในบรรดาผู้ป่วย 13 ราย (ร้อยละ 36.1) ที่ขึ้นเชื้อแบคทีเรียจากอุจจาระ มี Vibrio parahaemolyticus 6 ราย (ร้อยละ 46.2) Plesiomonas shigelloides 4 ราย (ร้อยละ 30.8) และ non-O1 Vibrio cholerae 2 ราย (ร้อยละ 15.4) Cryptosporidium parvum 2 ราย (ร้อยละ 15.4) และ Salmonella 2 ราย (ร้อยละ 15.4) ผู้ป่วย 176 ราย (ร้อยละ 45.1) ได้รับยาปฏิชีวนะซึ่งมี norfloxacin (128 ราย ร้อยละ 72.7) ciprofloxacin (34 ราย ร้อยละ 19.3) ceftriaxone และ ciprofloxacin (6 ราย ร้อยละ 3.4) ceftriaxone (5 ราย ร้อยละ 2.8) ceftriaxone และ norfloxacin (2 ราย ร้อยละ 1.1) amoxicillin (1 ราย ร้อยละ 0.6) และ ofloxacin (1 ราย ร้อยละ 0.6) แพทย์ประจำบ้าน 148 ใน 353 คน (ร้อยละ 41.9) และอาจารย์โรงเรียนแพทย์ 28 ใน 37 คน (ร้อยละ 75.7) จ่ายยาปฏิชีวนะ จากการแนะนำขององค์การอนามัยโลก อัตราการสั่งจ่ายยาปฏิชีวนะที่ไม่เหมาะสมเท่ากับร้อยละ 48.9 (86 ใน 176 ราย)*

***สรุป**: การสั่งจ่ายยาปฏิชีวนะในผู้ใหญ่ที่มีภาวะท้องเสียเฉียบพลัน มีอัตราการสั่งจ่ายยาปฏิชีวนะที่สูงเกินไปในสถาบันของผู้นิพนธ์ ปัจจัยทั้งจากด้านแพทย์และผู้ป่วยควรได้รับการวิเคราะห์ก่อนที่จะมีมาตรการที่จะเปลี่ยนแปลงพฤติกรรมการสั่งจ่ายยาปฏิชีวนะให้เหมาะสม*