Translational and Clinical Pharmacology

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Medication selection for the treatment of acute infective diarrhea in Thai pharmacies: a qualitative study

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ABSTRACT

World Health Organization (WHO) released the treatment manual of diarrhea in 2005. We aimed to investigate the rationale for selecting medications for acute infective diarrhea in Thai community pharmacies and to see if the selection complied with the WHO manual. A theoretical 18-year-old patient with acute infective diarrhea was used for interviews. The protocol and materials for the research were approved by Institutional Review Board. A total of 30 drugstore personnel were selected by convenience sampling and included. The first author manually coded, extracted for themes, and translated the transcript. Participants did not dispense oral rehydration salt because of the feeling that diarrhea was not severe. Absorbents were dispensed because they were perceived as the first-line medication for noninfective or mild diarrhea. Antibiotics were dispensed because of the concerns for the prognosis and the expected patient pressure. None provided zinc to the patient because of the lack of knowledge of the indication of zinc. We found that dispensing for acute infective diarrhea in Thai drugstores deviated from the WHO treatment guideline. The reasons were that the pharmacy personnel were not practicing evidence-based medicine, the lack of knowledge, the patient pressure, the unavailability of products, and the perceived availability of information in local guidelines.

Keywords: WHO; Diarrhea; Community Pharmacies; Drug Utilization Review; Qualitative Research

INTRODUCTION

The inappropriate treatment of diarrhea involves the use of antibiotics when they are not indicated [1]. The use of adsorbents, antimotility agents, and antiemetics are also considered inappropriate because of the controversial information on the efficacy and safety of these medications [2]. The major challenge is the appropriate use of antibiotics for diarrhea treatment. Antibiotics are indicated for diarrhea with bloody stools (dysentery), suspected cholera infection with severe dehydration, and laboratory-proven *Giardia duodenalis* infection with symptoms [2]. However, the treatment of these diarrheas can be troublesome. In many

Author Contributions
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SP; Data curation: Leelakanok N,
Pornwattanakavee SP; Formal analysis:
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countries, antibiotics are available without a prescription [3-8]. The situation is complicated by the fact that in these countries, non-pharmacist personnel can dispense antibiotics [5]. In addition, a microbiological laboratory is not available in the drugstore. These factors impede the rational use of antibacterial medications in community pharmacies.

World Health Organization (WHO) released the manual for the treatment of diarrhea in 2005, to guide the use of medications for the treatment of diarrhea, especially for the use of antibiotics. The ultimate goal is to reduce the mortality from diarrhea in developing countries [2]. The treatment consists of 3 main goals which are to prevent dehydration by oral rehydration salt (ORS), to continue nourishing, and to reduce the duration and severity of diarrhea by using zinc supplements [2]. Even though WHO has released the manual for the treatment of diarrhea for decades, inappropriate drug treatment and inadequate patient counseling on food and fluid intake still exist [9]. A few quantitative studies have investigated the prevalence and characteristics of non-compliance to the diarrhea treatment guidelines issued by WHO [10,11]. However, qualitative research that investigates the causes of non-compliance to the guidelines is scarce.

To improve the care of patients with diarrhea and increase the rational use of medication, which in turn relieves the symptoms in patients, reduces the antibacterial selection pressure, and decreases the cost of treatment, the guideline for the treatment of diarrheal patients should be followed. This study aimed to identify the rationale behind the dispensing behavior, i.e., the reason for which drugstore personnel used to select each medication for the patient. We also analyzed the dispensed medications to see whether they complied with the WHO guideline.

METHODS

Study design

A qualitative study using face-to-face semi-structured interviews was conducted in drugstores in Chonburi, Thailand in 2018. The protocol and materials for the research were approved by the Faculty of Pharmaceutical Science, Burapha University Institutional Review Board (protocol number 14/2561). The first author has some exposure to qualitative research from taking a course from The University of Iowa, Tippie College of Business in 2016. The research assistances (RAs), which were pharmacy students, were trained by the first author. A case of a dummy 18-year-old patient with signs and symptoms of acute infective diarrhea was designed by the authors and RAs and consulted with community pharmacists for further recommendations. The semi-structured interview questions were initially created by the first author and then reviewed by 2 experts (**Table 1**). In brief, the participants were asked for a list of medications that would be dispensed to the dummy patient, the rationale for each drug, and health recommendations for this patient. Deviations from the WHO manual for the treatment of diarrhea were asked for the rationale.

Data collection and analysis

The drugstores were selected by convenience sampling. The number of participants was not calculated since the design is qualitative, but we estimated the target number of enrollments to be 25 [12]. No relationship between the interviewers and interviewees was established before commencing the study. For the inclusion criteria, any personnel in the selected drugstore that was willing to participate, regardless of the pharmacy license status, were

Table 1. Seme-structured interview questions

Information on the theoretical patient	
Age	18-year-old
Sex	Male
Signs and symptoms	Watery stools without oil, froth, mucus, or blood
	Defecation frequency of 2–3 times/day
	No nausea and vomiting
	Stomachache
	No fever
Duration	3 days
Associated food	Raw papaya salad
Underlying diseases	None
Drug allergy	None
Concurrent use of health products	No concurrent use of drugs, herbs, food supplements
Budget restriction	None
Initial interview questions	
Please dispense medications for this patient and explain why each medication was selected.	
Why were antibiotics dispensed to this patient? (if applicable)	
Why were absorbents dispensed to this patient? (if applicable)	
Why was ORS not dispensed to this patient? (if applicable)	
Why was zinc not dispensed to this patient? (if applicable)	
What health recommendations would you provide to the patient?	
How about food recommendations for this patient?	

interviewed before which the consent was distributed to the participants. Participants read and signed an informed consent form. No compensation was provided to the participants. The interview occurred at the participant's working place which is the pharmacy. Customers and colleagues were presented when the interview was conducted. An audio recording and field notes after the interview was used to collect the data.

The RAs constructed a transcript from the audio recording and field notes. Deidentification was also performed. The first author read through the transcript and sorted comments into a set of categories in Microsoft Word (Microsoft 365; Microsoft Corporation, Redmond, WA, USA). The comments were coded, and the codes were improved each time a new interview was added to the analysis. During the coding process, themes, especially those related to the pattern of medications that would be dispensed and the rationale behind the medication selection, and health information that would be counseled in patients with diarrhea, emerged and were collected. Interview questions were further improved by the data derived from themes and additional interviews were conducted by the first author on the phone. The process was completed when no new themes emerged from the data. The participants did not check the transcripts or provide feedback on the finding. The data were reported according to the Consolidated Criteria for Reporting Qualitative Research [13]. The first author translated the themes and illustrative quotes from Thai to English once when the manuscript was prepared.

RESULTS

We selected drugstores in Thailand based on the proximity to the RA residential area. Drugstores were included until the theme was considered saturated which was when no new explanation for the guideline deviation emerged. As a result, a total of 30 drugstore personnel, one person per store, were included in this study. Most of the non-pharmacist personnel that we encountered refused to participate because they were concerned about the

possible legal consequences. The repeated interview was carried out by the first author once to collect more detail on themes related to zinc prescription. The coding tree is demonstrated in **Figure 1**. The majority of the participants were female pharmacists with a working experience of more than 5 years as community pharmacists. The average interviewing time not including the time that the dummy patient was introduced to the participants was approximately 5 minutes (**Table 2**). This was because of the heavy in-store traffic.

The 86.7% of the participants dispensed ORS (**Table 3**). The reason for not using ORS was that the pharmacist felt that the diarrhea was not severe, so ORS was not needed (**Table 4**). The dispensing of unnecessary drugs occurred at a very high frequency. Absorbents were dispensed by more than 70% of the drugstore personnel because absorbents were perceived as the first-line medication for noninfective or mild diarrhea (**Table 4**). Besides, although diarrhea presented in this dummy patient was ostensibly nonbacterial of origin, 20.0% of the participants chose to give the patient antibiotics. Antibiotics were dispensed to this patient because of the concerns for the prognosis, i.e., diarrhea would not be improved without antibiotics, and the pressure from patients. The history of food taken by the patient also affected the use of antibiotics in this patient (**Table 3**). None provided zinc to the patient.

Table 2. Demographic data of the participants

Demographic data	No. (%) or mean (range)
Sex	
Male	9 (30)
Female	21 (70)
Age (yr)	35 (24–60)
Professions	
Pharmacist	22 (73.3)
Non-pharmacist	8 (26.7)
Interviewing duration (not including case introduction; min)	4.8 (2.8–10)
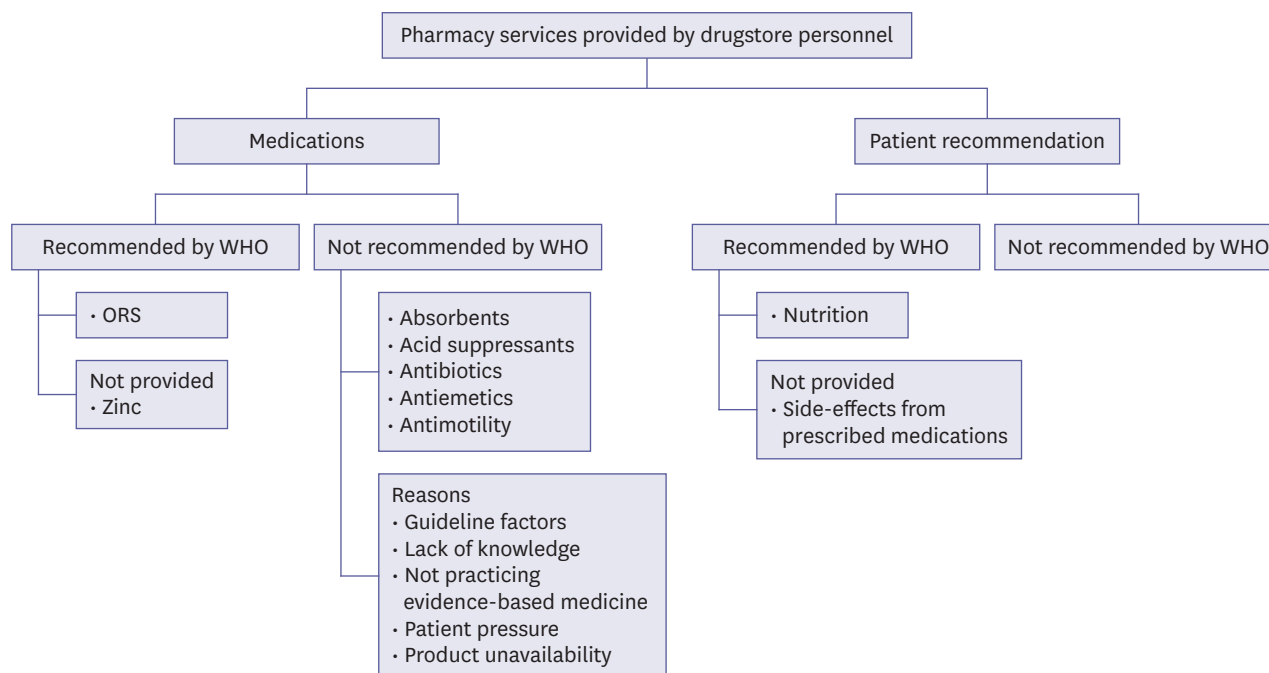
Figure 1. The coding tree from the interviews.
WHO, World Health Organization; ORS, oral rehydration salt.

https://doi.org/10.12793/tcp.2021.29.e22

The main reason was the lack of awareness, unavailability of the product, and the lack of recommendations from the local guideline (**Table 4**).

All drugstore personnel provided food recommendations, although the food recommendations were not focused on the nutrition that the patient should have. The recommendations were to have soft and easy-to-digest food ["He/she should have food easily to digest." (NP2)] and to have food that would not aggravate diarrhea, e.g., milk, raw food, seafood, spicy food, and uncooked food ["I would tell the patient to not have spicy food and fermented food. It would make diarrhea worse." (P7); "Papaya salad had to be discontinued." (P8)]. Dosage regimen was the information that most of the drugstore personnel provided to the patient while the side effects of the medications were the information that most of the drugstore personnel neglected. Interestingly, when antibiotics were dispensed, the patient sometimes was not told to finish the medication (**Table 3**).

DISCUSSION

WHO has issued guidelines for the treatment of diarrhea in 2005 to encourage the use of ORS and zinc as the first-line treatment and to encourage the nutritional recommendation during and after diarrhea. However, non-compliance to the guidelines is common, both in hospitals [10,11], and pharmacies [14]. This study was one of a few studies that investigated the rationale for the non-compliance to the guideline. In this study, several themes demonstrated that drugstore

Table 3. List of drugs and information that would have been offered to the patient

Pharmaceutical care	No. (%) form total [30]	No. (%) from pharmacists [22]	WHO recommendation
Medications			
ORS	26 (86.7)	18 (81.8)	Recommended
Absorbents			
Activated charcoal	16 (53.3)	9 (40.9)	Not recommended
Dioctahedral smectite	6 (20.0)	4 (18.2)	Not recommended
Antacids and acid suppressants			
Bismuth subsalicylate	1 (3.3)	1 (4.4)	Not recommended
Omeprazole	1 (3.3)	1 (4.4)	No recommendation
Antibiotics			
Ciprofloxacin	1 (3.3)	1 (4.4)	Not recommended
Norfloxacin	4 (13.3)	1 (4.4)	Not recommended
Antiemetics			
Domperidone	1 (3.3)	0 (0.0)	Not recommended
Antimotility			
Loperamide	1 (3.3)	1 (4.4)	Not recommended
Antispasmodics			
Drotaverine	1 (3.3)	1 (4.4)	No recommendation
Hyoscine	19 (63.3)	15 (68.2)	No recommendation
Miscellaneous			
Paracetamol	1 (3.3)	1 (4.4)	No recommendation
Rebamipide	1 (3.3)	1 (4.4)	No recommendation
Salol et menthol	1 (3.3)	1 (4.4)	No recommendation
Information for prescribed medications			
Indication	25 (83.3)	18 (81.8)	N/A
Dosage regimen	29 (96.7)	21 (95.4)	N/A
Lifestyle modification	24 (80)	18 (81.8)	N/A
Side effects from medications	3 (10)	3 (13.6)	N/A
Drug interactions	5 (16.7)	5 (22.7)	N/A
Finished the antibiotics	3 (60.0)*	2 (50.0)†	N/A

WHO, World Health Organization; ORS, oral rehydration salt, N/A, not available.
*From the total number of 5 pharmacies that would have dispensed antibiotics; †From the total number of 4 pharmacists that would have dispensed antibiotics.

Table 4. Reasons behinds the selection of medications that emerged from the data

Category	Theme	Illustrative quote
Guideline	1. Treatment guidelines for diarrhea were international and might not be applicable in the area.	"The use of a drug, rationally or not, was based on the foreign guidelines. The bacteria here and there were not the same." (P1)
	2. Local guidelines affected whether drugstore personnel dispensed which medicine.	"Thai Rational Drug Use did not list zinc for the list of important medicine for diarrhea." (P2)
	3. Over-the-counter medication, which was not covered in the guideline, may have been considered for relieving patient symptoms.	"If the patient had a fever, I would give him/her paracetamol." (NP8)
Lack of knowledge	4. Zinc was not dispensed because the drugstore personnel did not realize that zinc helped treat diarrhea.	"I have heard that there was a guideline that recommended zinc, but I did not know that zinc was recommended as the first-line, that I should have dispensed." (P2)
		"Oh, I just did not know (about zinc)." (P16)
Not practicing evidence-based medicine	5. ORS might be omitted when the drugstore personnel perceived diarrhea as not severe.	"Diarrhea in this patient was just only 2 to 3 days. It was not that severe. The patient may not need ORS. Giving activated carbon alone was sufficient since the patient has no fever and no vomiting." (P15)
	6. Activated charcoal was perceived as an effective treatment for noninfective diarrhea.	"I would give the patient activated charcoal since this was not infective diarrhea." (P5)
		"I would give the patient activated charcoal since the fever was not from diarrhea." (P21)
	7. Activated charcoal was dispensed when the drugstore personnel perceived diarrhea as not severe.	"He/she did not have a stomachache, so it was not that bad. I would just give him/her the charcoal." (NP8)
	8. Antibiotics were dispensed when the drugstore personnel perceived that the patient had suffered from diarrhea long enough.	"Having diarrhea for a day was already bad. This patient had it for 3 days! I would dispense norfloxacin for sure." (P1)
	9. Antibiotics were dispensed when the drugstore personnel perceived that the diarrhea was not getting better.	"This diarrhea, if it was watery without any mass, for 2-to-3 day long, and was not improving, I would dispense ciprofloxacin as the first-line." (P3)
	10. Antibiotics were dispensed when uncooked food was involved in the patient's history.	"I had worked in this area for many years. The papaya salad must have given the bacteria to the patient, even if he/she did not have bloody stools. Activated charcoal would not work. Antibiotics would be more effective." (P1)
Patient pressure	11. Activated charcoal was dispensed per patient requests.	"Patients requested activated charcoal, so I normally give it to them." (P2)
	12. Antibiotics were dispensed when patients expressed concern for not getting the antibiotics, even when the expression was not verbal.	"Some patients seemed to be worried if they did not get antibiotics. In this case, I would just give norfloxacin to the patients." (P19)
	13. Antimotility was dispensed when the patients had the necessary event to attend.	"If a patient had to go to work, I would give them some drugs to stop diarrhea." (P7)
		"The worse was when patients requested for antimotility. I always asked them if they needed the drug because they had very important or urgent business." (P12)
Product availability	14. Drug availability, price, and packaging affected whether drugstore personnel dispensed the medicine.	"I have never dispensed zinc since I did not have it in my pharmacy. I meant I had Blackmore zinc but who would buy 90 tablets of zinc at a very high price for 3-day diarrhea. If small blister packs of zinc that contained 10 tablets of zinc were widely available, I would give zinc to my patients." (P2)

ORS, oral rehydration salt.

personnel made their clinical judgment not based on clinical evidence. For example, failure to provide ORS was found in this study and the others [11,15,16], even though ORS is the absolute main goal for the treatment of diarrhea [17], We found that the perception about the severity of diarrhea was used as a criterion for giving the ORS. Next, in this study, zero drugstore personnel have dispensed zinc because it was not known as a treatment option. We even found a claim that zinc was not recommended in the Thai guideline. However, Thai guidelines for the treatment of acute diarrhea list zinc as one of the treatments [18,19], Our finding was agreed with the finding that zinc was not generally given to patients [15,20] and inadequate knowledge and clinical training were the reason for inappropriate drug prescription [21].

Inappropriate use of antibiotics is the commonly found deviation from diarrhea treatment guidelines [10]. In this study, drugstore personnel dispensed antibiotics without using evidence-based practice. For example, the dummy patient had diarrhea for 2 to 3 days which was defined as acute [17]. Drugstore personnel believed that the patient was suffering from

diarrhea for a long enough time that prompted the antibiotic treatment, even though the use of empiric antimicrobial therapy is not recommended in most immunocompetent patients with acute watery diarrhea [17]. The claim that patients have a longer duration of symptoms so antibiotics should be prescribed was found in another study too [22]. We also found that patient pressure drove the decision to dispense antibiotics. This was supported by several studies that demonstrated patient pressure as the cause for the prescription of unnecessary antibiotics [8,22,23]. One study found that diagnostic uncertainty [24] and limited time [25] were reasons that promote nonrational antibiotic prescription. Although these 2 factors did not emerge during the study, we can speculate that it did occur since drugstores did not have laboratories and personnel that support the microbiological diagnosis and the time that drugstore personnel used in counseling our dummy patient was short.

The history of food consumption was one of the reasons for inappropriate antibiotic dispensing. In this study, the history of consuming papaya salad encouraged the dispensing of antibiotics. However, diarrhea from food can cause by bacteria, viruses [26], and the laxative activity of the food, which in this case contains chili and tamarind juice. Drugstore personnel recommended the patient should stop having papaya salad, along with other food recommendations. We found that drugstore personnel in this study provided adequate food recommendations to the patient. However, information on side effects was not generally provided to the patients, agreeing with other studies that side effects from medications were usually omitted during patient counseling [8,15].

This study revealed the reasons why drugstore personnel did not comply with the guideline for the treatment of diarrhea. The findings are clinically relevant and can be used in helping draw relevant policies. We suggested that the information on the guideline should be disseminated in local guidelines in a format that is easy to understand. Flow charts on how the decision-making process in the diagnosis is should be provided with an emphasis on the duration and prognosis of diarrhea. Tools to alleviate the effect of patient expectation should be also provided. An easy-to-access, and affordable ORS and zinc formulation should be commercially available. Education provided to healthcare practitioners aimed to promote the rational use of antibiotics is also an evidence-based approach. Several studies support that education and training increase the rate of rational antibiotic use [27-29].

Some limitations of this study should be noted. First, this study was conducted in only one province in Thailand which may limit the generalizability of the results. Second, the limited interviewing duration might confound the process of drug dispensing since drugstore personnel might not have sufficient time for history taking and counseling. Next, this study is qualitative so the incidence reported in this study should not be used as a representative for the population. Last, the generalizability of this study is also affected by the status of antibiotics in each country. In Thailand, prescribing and dispensing can be practiced by the same healthcare practitioner. Separation of prescribing and dispensing is practiced strictly and widely in hospitals. However, at the community level, this separation can become very vague. Nonseparation is common in Asia; therefore, antibiotic dispensing without medical prescriptions, found in this study, maybe more generalizable in Asia [30-33]. To further improve the quality of this study, further in-depth studies or surveys should be performed. The effects of other factors that affect the dispensing practice of drugstore personnel, e.g. accountability mechanisms, law enforcement, pressure for profits [8], and access to antibiotics without prescription [21] should also be investigated.

In conclusion, practices that deviated from the WHO diarrhea guideline were found. Not dispensing zinc and ORS, and inappropriate use of antibiotics were common. The main reason for the deviation was that the pharmacy personnel was not practicing evidence-based medicine, the lack of knowledge, the patient pressure, the unavailability of products, and the perceived availability of information in local guidelines.

ACKNOWLEDGMENTS

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