การมีส่วนร่วมของเภสัชกรต่อปัญหาที่เกี่ยวกับการใช้ยาปฏิชีวนะในหอผู้ป่วยอายุรกรรม
Pharmacist Interventions on Problems Related with Antibiotics Use in General Medicine Wards

นิพนธ์ต้นฉบับ

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Original Article

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาผลของการมีเภสัชกรในทีมสหสาขาวิชาชีพในการใช้ยาปฏิชีวนะต่อผลลัพธ์ของผู้ป่วย **วิธีการศึกษา:** การศึกษาเชิงพรรณนาแบบไปข้างหน้าในเดือนสิงหาคม พ.ศ. 2563 ที่โรงพยาบาลขนาด 820 เตียงแห่งหนึ่งในประเทศไทย เกณฑ์การคัดผู้ป่วยเข้าการศึกษาได้แก่ ผู้ป่วยที่พักรักษาในหอผู้ป่วยอายุรกรรม มีอายุ 18 ปี ขึ้นไป และได้รับยาปฏิชีวนะอย่างน้อย 1 ชนิด ส่วนผู้ป่วยที่จำเป็นต้องใช้ยาปฏิชีวนะที่ไม่มีในโรงพยาบาล หรือปฏิเสธการรักษาจะถูกคัดออก เภสัชกรทบทวนเวชระเบียนเพื่อค้นหาปัญหาและแก้ไขปัญหาโดยใช้แบบฟอร์มแนะนำการเลือกใช้ยาปฏิชีวนะช่วยในการปรึกษาแพทย์ระหว่างการตรวจเยี่ยมผู้ป่วยประจำวัน การวิเคราะห์ข้อมูลใช้สถิติเชิงพรรณนา ได้แก่ ความถี่ ร้อยละ ค่าเฉลี่ย ส่วนเบี่ยงเบนมาตรฐาน ค่ากลาง และพิสัยควอร์ไทล์ **ผลการศึกษา:** ผู้ป่วยจำนวน 47 คน เป็นเพศหญิงร้อยละ 53.2 ค่ามัธยฐานของอายุคือ 68 ปี ผู้ป่วยทุกคนมีโรคร่วมอย่างน้อย 1 โรค โรคติดเชื้อที่พบมากที่สุดคือโรคติดเชื้อในทางเดินปัสสาวะ (ร้อยละ 26.4) รองลงมาคือปอดอักเสบ (ร้อยละ 17.0) ผู้ป่วยร้อยละ 36.2 มีภาวะพิษเหตุติดเชื้อ พบปัญหาที่เกี่ยวกับการใช้ยาปฏิชีวนะจำนวน 24 ปัญหา ในผู้ป่วย 19 คน (ร้อยละ 40.4) ปัญหาหลักคือการเลือกใช้ยาปฏิชีวนะที่มีการออกฤทธิ์ครอบคลุมเชื้อไม่เหมาะสม โดยเฉพาะเมื่อเปลี่ยนจากยาชนิดฉีดเป็นชนิดรับประทาน โดยพบ 8 ปัญหา (ร้อยละ 33.3) รองลงมาคือการใช้ยาขนาดสูงเกินไปโดยไม่ปรับตามการทำงานของไต (ร้อยละ 20.8) เมื่อสิ้นสุดการรักษามีผู้ป่วยหายดีร้อยละ 74.5 ค่ากลางของวันนอนโรงพยาบาลคือ 7 วัน **สรุป:** เภสัชกรสามารถช่วยค้นหาและแก้ไขปัญหาที่เกี่ยวกับการใช้ยาปฏิชีวนะร่วมกับสหสาขาวิชาชีพ ซึ่งอาจช่วยเพิ่มการใช้ยาอย่างสมเหตุผลและเพิ่มผลลัพธ์การรักษาของผู้ป่วย

คำสำคัญ: เภสัชกร; สหสาขาวิชาชีพ; การมีส่วนร่วมในการรักษา; ยาปฏิชีวนะ

Abstract

Objective: To determine effects of the integrated pharmacist interventions to multidisciplinary team regarding antibiotics use on patients' outcomes. **Methods:** A prospective descriptive study was performed in August 2020 in an 820-bed hospital in Thailand. Participants were patients aged 18 years or older admitted to a general medicine ward and received at least one dose of an antibiotic. Patients who need unavailable antibiotics or denied treatment were excluded. A pharmacist reviewed medical records for antibiotics related problems and modified antibiotic regimens together with physicians. The pharmacist used the self-developed antibiotics-guided form in her verbal consultations during a routine morning round. Descriptive statistics including frequency, percentage, mean, standard deviation, median and interquartile range were used for data analysis. **Results:** Of the 47 patients enrolled, the majority were women (53.2%). The median age was 68 years. All patients had at least one comorbidity. Urinary tract infections were the main infectious disease problems (26.4%), followed by pneumonia (17%). 36.2% of the patients had sepsis. Twenty-four antibiotics related problems were found in 19 patients (40.4%). Most frequent problems were improper antibiotics selection regarding spectrum based on empirical therapy particularly switching from intravenous to oral forms (8 problems, 33.3%), followed by overdose of antibiotics in kidney impairment patients (20.8%). After courses of treatment, most patients were cured (74.5%). The median length of hospital stay was 7 days. **Conclusion:** The integrated pharmacist interventions to multidisciplinary team helped identify and resolve antibiotics related problems and might improve rational use of antibiotics and improve patients' outcomes.

Key words: pharmacist; multidisciplinary; intervention; antibiotics

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Introduction

Antibiotics use causes many problems including adverse drug reactions and antibiotics resistance. In 2022, The National Antimicrobial Resistance Surveillance Center of Thailand: NARST has reported 78.3% sensitivity of *Pseudomonas aeruginosa* to ceftazidime, 77.5% to piperacillin/tazobactam and 78.5% to meropenem in all specimens which showed increasing resistance rate when compere to the last two years.[1]

The study in 2023 showed the prevalence of antibiotics use in 41 selected hospitals in Thailand and antibiotic resistance among clinical isolates were found to be 46.9%. The rate of broad-spectrum antibiotics resistance was high.

Acinetobacter baumannii and *Pseudomonas aeruginosa* were resistant to carbapenems by 80.6% and 31.4% of total isolates respectively.[2]

Multidisciplinary team consisting of pharmacists and physicians have roles in rational drug use including antibiotics. With the impacts of physician and pharmacist on antibiotics use, WHO had promoted hospitals to appoint physicians and pharmacists as a leader and co-leaders for antibiotic stewardship program, responsible for program management and outcomes.[3] There were reported effects of pharmacists incorporating with physicians on reduction of antimicrobial therapy duration and cost, but there has been a lack of evidences indicating the effects on patients' outcomes including cure rate and mortality rate.[4-6]

This study aimed to evaluate the effects of integrating a pharmacist to multidisciplinary team to identify and resolve the problems related to antibiotics use, and to assess the effectiveness of pharmacist interventions on patients' outcomes in a provincial hospital in northeastern Thailand. Ot was hypothesized that the pharmacist's activities would improve rational use of antibiotics and improve clinical outcomes of patients. This 820-bed hospital found emergence of resistant *A. baumanii, K. pneumoniae, P. aeruginosa* and *E. coli* which led to 57 million Thai bath budget loss in 2013[7], but the pharmacists to the routine patient round for improving antibiotics use was not available. In this study, the primary endpoint was the rate of antibiotics related problems detected and resolved by the pharmacist. The secondary endpoints were frequency and type of antibiotics related problems, antibiotics response rate, cure rate, and length of hospital stay.

Methods

The prospective descriptive study was performed in August 2020. Patients with bacterial infections who were admitted to male or female general medicine wards were included in the study. Patients aged 18 years and above who received at least one dose of an antibiotic met the eligibility criteria. Patients who need unavailable antibiotics which required treatment elsewhere or denied to receive treatment were excluded.

Eligible patients had received medical care from one internal medicine attending physician and one internal medicine resident physician. The pharmacist who joined the team reviewed patient medical records for antibiotics related problems and discussed with physicians, other health care providers, and the patient to modify treatment plan. The antibiotics-guided form and verbal consultations had been used to communicate with physicians during a routine morning round. The antibiotic-guided form consisted of lists of pathogens with antibiotics spectra, and antibiotics doses (normal doses and kidney impairment adjusted doses). This form was developed by the pharmacist based on up to date evidences of antibiotics suitable for pathogens coverage both as empirical and documented therapy, and dose adjustment for patients with kidney impairment. Problems related to other medications used for comorbidities were also identified and resolved. The study protocol was approved by ethical committees (No.139/63 and RE037/2563).

Data were collected from patient medical records. Descriptive statistics were used to summarize the data. Mean with standard deviation or median with interquartile range were used to summarize age, number of antibiotics use, and length of hospital stay as appropriate. Frequency with percentage was used to summarize gender, underlying diseases, infectious diseases and severity, type of drug related problems, acceptance of interventions, and results of treatment. Antibiotics related problems defined as eight categories of untreated indications, improper antibiotics selection, sub-therapeutic dosage, over-therapeutic dosage, adverse reactions, drug interactions, antibiotics use without valid indication and failure to receive antibiotics.[8] Statistical analysis were performed using SPSS software.

Results

Of the 47 patients enrolled in the study during one-month study period, 53.2% were female. The median age was 68 years. Most patients had at least one comorbidity. Urinary tract infections were the main infectious problems (26.4%), followed by pneumonia (17%). There were 36.2% of patients who had sepsis with the rate of septic shock about 21.3% (Table 1).

Median antibiotics use was 3 items per patient. The pharmacist detected 24 antibiotics related problems in 19 patients. There were 13 problems accepted for resolution by the physicians (54.17%) (Table 2). Most antibiotics related problems were improper antibiotics selection regarding spectrum based on empirical therapy particularly switching from intravenous to oral forms (33.3%), followed by overdose in kidney impairment patients (20.8%) (Table 3).

After taking courses of treatment, most patients were cured (74.5%). The median length of hospital stay was 7 days. The data shown in table 4 were all results of treatment and interventions.

Table 1 Patients' characteristics (N = 47).

Characteristics	N (%)
Gender	
Male	22 (46.8)
Female	25 (53.2)
Age (median and interquartile range)	68 (54 – 75)
History of drug allergy	3 (6.4)
Kidney impairment	23 (48.9)
Type of comorbidities	
Hypertension	17 (23.0)
Kidney diseases	15 (20.3)
Cardiovascular diseases/stroke	8 (10.8)
Asthma/chronic obstructive pulmonary disease	5 (6.8)
Gouty arthritis/rheumatoid arthritis	5 (6.8)
Cirrhosis/hepatitis	4 (5.4)
Gastrointestinal bleeding/dyspepsia	4 (5.4)
Others (anemia, cancer, dyslipidemia, tuberculosis, depression, benign prostatic hyperplasia, hyperthyroidism, Alzheimer's disease, obesity)	16 (21.6)
Infectious diseases at admission	
Urinary tract infection	14 (26.4)
Pneumonia	13 (24.5)
Acute febrile illness with unknown origin	9 (17.0)
Cellulitis	6 (11.3)
Infectious diarrhea	5 (9.4)
Intra-abdominal infection	4 (7.6)
Meningitis	2 (3.8)
Severity of infectious diseases	
Sepsis	17 (36.2)
Septic shock	10 (21.3)
Required vasopressor	9 (19.1)
Required ventilator	9 (19.1)
Reported resistant organisms	8 (17.0)
Resistant organisms (total isolations = 11)	
Multidrug-resistant *Acinetobacter baumannii*	4 (36.4)
Carbapenem-resistant *Escherichia coli*	2 (18.2)
Carbapenem-resistant *Klebsiella pneumoniae*	2 (18.2)
Carbapenem-resistant *Enterobacter cloacae*	1 (9.1)
Carbapenem-resistant *Pseudomonas aeruginosa*	1 (9.1)
Methicillin-resistant *Staphylococcus epidermidis*	1 (9.1)

Table 2 Antibiotics use and related problems (N = 47).

Antibiotics use and related problems	N (%)
Items of antibiotics use per patient (median and interquartile range)	3 (2 – 4)
Number of patients with antibiotics related problems (%)	19 (40.4)
Type of problems (total number of problems = 24)	n = 24 (%)
Improper antibiotics selection regarding spectrum	8 (33.3)
Overdose of antibiotics	5 (20.8)
Failure to receive antibiotics	3 (12.5)
Adverse drug reactions	3 (12.5)
Sub-therapeutic dose of antibiotics	2 (8.3)
Drug interactions	2 (8.3)
Antibiotics use without valid indication	1 (4.2)
Number of consultation problems	16 (66.67)
Number of accepted problems	13 (54.17)

Table 3 Antibiotics related problems and pharmacist interventions (N = 47).

Problems	Pharmacist interventions	Results
Used only meropenem in carbapenem resistant *Enterobacterales* outside urinary tract infections as documented therapy. (no ceftazidime/avibactam available)	Added amikacin	Accepted
Used only ceftriaxone in patient with meningitis who had risk for *L. monocytogenase*.	Added ampicillin	Accepted
Concurrent used of ciprofloxacin and ceftriaxone in urinary tract infection.	Used only one antibiotic	Accepted
Overdose of ceftazidime, vancomycin, ampicillin, piperacillin/tazobactam, cefixime.	Reduced doses	Accepted
Sub-therapeutic dose of cefixime, ceftazidime	Increased doses	Accepted
Patient experienced nausea from doxycycline.	Informed to take after meals immediately	Accepted
Drug interactions: Piperacillin/tazobactam + warfarin (potential for increased bleeding risk).	Switched from piperacillin/tazobactam to levofloxacin	Accepted
Used ceftriaxone without sign of infection.	Recommended to stop antibiotic	Accepted
Colistin (as documented therapy) induced acute kidney injury.	Change to high dose sulbactam	Denied
Overdose of levofloxacin, ciprofloxacin.	Reduced doses	Denied
Switching problems (no *P. aeruginosa* coverage as previous antibiotics): Ceftazidime to cefixime Piparacillin/tazobactam to cefixime.	No recommendation according to out of the service	None
Drug interactions: Levofloxacin + amitriptyline (potential for QT prolongation).	No recommendation according to the stopped use of antibiotics	None

Table 4 Outcomes of treatments and interventions (N = 47).

Outcomes	N (%)
Clinical outcomes	
Cure	35 (74.5)
Death	3 (6.4)
Discharged as palliative care.	7 (14.9)
Referred back to community hospitals after clinical outcomes had improved.	2 (4.3)
Length of hospital stay (days)	
Minimum	1
Maximum	32
Median (interquartile range)	7 (5 – 13)

Discussions and Conclusion

Most infectious diseases in this study were urinary tract infections (26.4%) that were usually defined as less severe bacterial infections and might be related to a high cure rate (74.5%). In contrast, most patients were the elderly, which

were classified as immunocompromised hosts and the rate of exposure to resistant organisms was high (17%).

As pharmacy expertise has been demonstrated as a core element of hospital antibiotic stewardship program provided by the Center for Disease Control and Prevention (CDC)[3], pharmacists should help lead implementation efforts to improve antibiotic use. The practicing pharmacist in this study had taken action according to antibiotic stewardship program with prospective audit and feedback manner by reviewing prescribed antibiotics and providing interventions. There were a total of 24 antibiotics related problems identified by the pharmacist. Most frequent problems were related with antibiotics selection regarding spectrum (8 problems, or 33.3%). *P. aeruginosa* was the most common pathogen that the physicians needed to cover regarding step-up protocol during empirical therapy. Nevertheless, switching therapy from intravenous to oral regimens was likely a step-down manner in which *P. aeruginosa* was not covered by appropriate antibiotics. The example was step-up from ceftriaxone to ceftazidime in one patient, then switching from ceftazidime to oral cefixime when the patient responded to a step-up regimen, as the fact that cefixime was unable to cover the pathogen. Other problems of antibiotics selection were needed need combination antibiotics (for carbapenem resistant pathogens and *L. monocytogenase*). These problems indicated the need of updated pharmacotherapy for the care team to improve antibiotics use.

There were 13 from 16 pharmacist's interventions of the total 24 problems accepted by the physicians. Other unaccepted problems were discussed regarding confirmation of prescriptions during the rounds. The possible causes were that some patients were responding to antibiotics which were known unable to cover the pathogen reported from isolations. So, the physician confirmed to continue current antibiotics by clinical observations. The suspected causes would be contamination or colonization of bacteria. These discussions between the pharmacist and physicians during the patient rounds were necessary to make appropriate decisions for rational antibiotics use.

The cure rate was 74.5%, superior to a previous retrospective cohort study held in 2018 in the same hospital of this study, which reported about 60.7% resolved diseases rate after pharmacist's interventions in using carbapenems and tigecycline.[7] However, the data of cure rate before integrated pharmacists to the routine patient round was unavailable. The median length of hospital stay in this study was 7 days which was less than other study that pharmacist's intervention led to the result of median of hospital stay about nine days in phase one and ten days in phase two.[5] These supported the hypothesis that integrating a pharmacist to multidisciplinary team would improve rational use of antibiotics and patients' outcomes. It is also consistent with a study in Thailand which showed trend of improving cure rate when compare with control group (63.6% vs 56.1%; P-value = 0.127).[9] A study in United Arab Emirates indicated that multidisciplinary team including infectious disease physician and infectious disease pharmacist promoted the significant reduction in length of hospital stay (P-value < 0.01), readmission (P-value < 0.01), and mortality rates (P-value < 0.01) when compared with the usual care.[10]

The additive useful tool for problems detection and intervention in this study was antibiotics-guided form. This form was not officially attached to the patient's medical record and doctor's order sheet. Therefore, the pharmacist only used it as a reminder document for himself for antibiotics selection and dosage adjustment while consulting with the physicians. Further development of the form and integration to patient care documents might help the team for appropriate antibiotics use.

Limitations of this study are the small sample size, relatively short duration of study, and no evaluation on cost of treatment. Future studies could be longer with more subjects and include cost evaluation. However, these results could also demonstrate the important roles of pharmacists to improve antibiotics use in acute care settings.

In conclusion, integrating pharmacist to multidisciplinary team improved rational use of antibiotics and improved patients' outcomes. Further study should also focus on pharmacoeconomic perspectives.

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