PHARMACIST'S ROLE IN MANAGEMENT OF HIGH-ALERT MEDICATIONS IN PEDIATRIC INTENSIVE CARE UNIT, RAMATHIBODI HOSPITAL

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ABSTRACT

The purpose of this study was to develop the role of the pharmacist in the management of high-alert medications in the pediatric intensive care unit (PICU), Ramathibodi Hospital. All patients who were admitted into PICU during March and May 2007, were prospectively detected by the pharmacist with drug therapy problems (DTPs) and medication errors (MEs) using the daily medical chart review and during ward rounds with the health care team. All identified DTPs and MEs were categorized into the types of DTPs, medication use processes, and severity. Pharmacist's interventions were provided and those acceptances were recorded. The specific high-alert medications management protocol was developed according to the nature of the DTPs, MEs, and pharmacist's interventions.

An average patient age was 61.8 $\pm$ 54.6 months in 43 patients. Twenty four (55.8%) patients were female. The patients received 182 medication items by order of 674 medication orders. A total of 216 DTPs were identified in 37 patients (86%). An average DTP per patient was 5.1. Common DTP types consisted of 192 drug interactions (88.9%), 13 with a dosage too high (6.0%) and 6 adverse drug reactions (2.8%). The severities of the DTPs were classified into category E (harm), D and C with 3, 183 and 24 events, respectively. Of those 216 DTPs were justified as 19 MEs. The MEs were categorized by medication use process errors being 16 prescribing errors, 2 administration errors and 1 transcribing error. A total of 216 pharmacist's interventions were provided based on 216 DTPs. A total of 210 of them were accepted by the health care team. A high alert medication management protocol for phenobarbital injections was chosen and developed according to the failure mode and effects analysis, because phenobarbital injections frequently resulted in MEs and patient's harm, although most DTPs were drug interactions.

Although most DTPs did not cause harm to the patient, the pharmacist had a role to play in the management of DTPs and MEs. In addition, the success of implementation of the protocol was not completely investigated however the protocol seemed to improve the quality of patient's care.

KEY WORDS: CLINICAL PHARMACY/ PEDIATRIC INTENSIVE CARE/ HIGH ALERT MEDICATION

109 pages

บทบาทเภสัชกรในการจัดการยาที่ต้องระวังเป็นพิเศษ ในหออภิบาลผู้ป่วยวิกฤติเด็ก โรงพยาบาลรามาธิบดี
PHARMACIST'S ROLE IN MANAGEMENT OF HIGH-ALERT MEDICATIONS IN PEDIATRIC INTENSIVE CARE UNIT, RAMATHIBODI HOSPITAL

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บทคัดย่อ

การศึกษานี้มีวัตถุประสงค์ในการพัฒนาบทบาทของเภสัชกรในการจัดการยาที่มีความเสี่ยงสูงในหออภิบาลผู้ป่วยวิกฤติเด็ก โรงพยาบาลรามาธิบดี ที่เข้ารับการรักษาระหว่างเดือนมีนาคม ถึง พฤษภาคม พ.ศ. 2550 โดยเภสัชกรค้นหาปัญหาทางยา และ ความคลาดเคลื่อนทางยา จากการทบทวนคำสั่งใช้ยาและร่วมทีมดูแลผู้ป่วย ปัญหาทางยาและความคลาดเคลื่อนทางยาที่ค้นพบ ถูกบันทึกแยกตามชนิดของปัญหาทางยา ความคลาดเคลื่อนในกระบวนการใช้ยา และความรุนแรง พร้อมทั้งบันทึกการแนะนำจากเภสัชกรและการยอมรับโดยทีม แล้วนำมาพัฒนาเป็นแนวทางการจัดการยาที่มีความเสี่ยงสูง โดยอาศัยข้อมูลปัญหาทางยา ความคลาดเคลื่อนทางยา และการแนะนำจากเภสัชกร

อายุเฉลี่ยของผู้ป่วยทั้ง 43 ราย คือ 61.8 $\pm$ 54.6 เดือน ผู้ป่วย 24 ราย (ร้อยละ 55.8) เป็นเพศหญิง ผู้ป่วยทั้งหมดได้รับยาทั้งสิ้น 182 รายการ จากคำสั่งแพทย์ 674 ครั้ง โดยพบปัญหาทางยา 216 ปัญหา ในผู้ป่วย 37 ราย (ร้อยละ86) ค่าเฉลี่ยของปัญหาทางยาต่อผู้ป่วย คือ 5.1 ลักษณะของปัญหาทางยาได้แก่อันตรกิริยาระหว่างยา 192 ปัญหา (ร้อยละ 88.9) ขนาดยาสูงเกินไป 13 ปัญหา (ร้อยละ 6) และอาการไม่พึงประสงค์จากการใช้ยา 6 ปัญหา (ร้อยละ 2.8) ความรุนแรงของปัญหาทางยาจัดอยู่ในกลุ่ม E (เกิดอันตรายแก่ผู้ป่วย), D และ C ได้แก่ 3, 183 และ 24 ปัญหา ตามลำดับ ซึ่งจาก 216 ปัญหาทางยานี้ถูกจัดเป็นความคลาดเคลื่อนทางยา 19 ปัญหา โดยแบ่งกลุ่มได้ตามความคลาดเคลื่อนในกระบวนการใช้ยา ได้แก่ ความคลาดเคลื่อนในการสั่งยา 16 ปัญหา ความ คลาดเคลื่อนในการบริหารยา 2 ปัญหา และความคลาดเคลื่อนในการคัดลอกคำสั่ง 1 ปัญหา เภสัชกรมีการให้คำแนะนำทั้งสิ้น 216 ครั้งตามลักษณะปัญหาทางยาที่พบ และได้รับการยอมรับจากทีม 210 ครั้ง ยา phenobarbital ชนิดฉีด ได้ถูกเลือกมาพัฒนาเป็นยาที่มีความเสี่ยงสูงเพื่อแนวทางในการสั่งใช้โดยวิธีการวิเคราะห์สาเหตุของลักษณะข้อบกพร่องและผลกระทบ เนื่องจากเป็นยาที่มีพบความคลาดเคลื่อนทางยาสูง และทำให้ผู้ป่วยเกิดอันตราย แม้ว่าปัญหาทางยาส่วนใหญ่คืออันตรกิริยาจากยา

ถึงแม้ว่าปัญหาทางยาส่วนใหญ่จะไม่ทำให้ผู้ป่วยเกิดอันตราย แต่เภสัชกรมีบทบาทในการจัดการปัญหาทางยาและความคลาดเคลื่อนทางยา และมีแนวโน้มว่าสามารถเพิ่มคุณภาพของการดูแลผู้ป่วยได้

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LIST OF ABBREVIATIONS

&	and
ADR	adverse drug reaction
cap.	Capsule
^{O}C	degree Celsius
Cl_{cr}	creatinine crearance
CT	computed axial tomography
DIS	drug information service
DTP	drug therapy problems
D5W	5% dextrose in water
e.g.	exempli gratia, for example
ER	emergency room
FMEA	failure mode and effects analysis
gr.	grain
HA	the Institute of Hospital Quality Improvement and Accreditation
HIV	human immunodeficiency virus
hr	hour
HT	hypertension
inj.	injection
IOM	Institute of Medicine
ISMP	Institute for Safe Medication Practices
IM	intramuscular
IV	intravenous
JCAHO	Joint Commission on Accreditation of Healthcare Organizations
kg	kilogram
ME	medication error
mcg	microgram
mg	milligram
min	minute
ml	milliliter

LIST OF ABBREVIATIONS (cont.)

no.	number
NCC MERP	the National Coordinating Council for Medication Error Reporting and Prevention
NICU	neonatal intensive care unit
NS	normal saline
OD	once daily
PCA	patient controlled anagelsia
PICU	pediatric intensive care unit
PCP	pneumocystis carinii pneumonia
PO	per oral, orally
R/O	rule out
RCA	root cause analysis
SLE	systemic lupus erythematosus
sol.	solution
susp.	suspension
syr.	syrup
tab.	tablet
TF	tube feeding
TPN	total parenteral nutrition
US	United States
USP	United States Pharmacopeia

CHAPTER I
INTRODUCTION

Medication errors (MEs) are preventable events which are the most common type of medical errors and costly (1-4). MEs result in increasing hospital stays and risk of mortality and thus patients and families suffer from their occurring (4-6). For this reason, the incidence and outcomes of MEs have being growing concern for preventing them (7). Health care professionals are calling for prevention strategies, especially high-alert medications which commonly caused MEs (6, 8-10). In the United States, Institute for Safe Medication Practices (ISMP) proposed a list of general high-alert medications based on error reports which were submitted to the United States Pharmacopeia (USP)-ISMP MEs reporting program (10-11). There are 19 classes of medications and 14 specific medications in the list (11).

A high-alert medications management protocol in pediatric care settings should not similar to protocol in general setting because a medication usage are distinctly different from those in settings for adult. Pediatric patients have greater risk for error because dosage adjustment needs to calculate by patient weight (12-18). Age-specific changes in pharmacokinetics and pharmacodynamics further complicate drug therapy in children. In addition, off-label using of medications, lacking of suitable formulations and appropriate strengths, and extemporaneously preparing of medications increase the likelihood of medication errors and may lead to a reduction in drug effect (19).

Schneider and colleagues found that the preparation and administration by nurse in a pediatric intensive care unit (PICU) revealed a frequency of error as high as 27% (20). Earlier Vincer and colleagues reported that there are 3.26 MEs per 100 patient-days. It equaled to a rate of almost 15% out of all neonatal intensive care unit (NICU) admissions (21). As many as 15% of these errors are judged to cause harm, and these continue to be subject to higher error rates than other wards within the hospital (22-23).

Interestingly, the previous studies found that a pharmacist has a role to prevent MEs in children. Munzenberger and colleagues reported that pharmacists in pediatric medical care team have roles in monitoring patient charts, providing admission drug histories, discharge consultations, and drug information to medical and nursing staff which led to improve pediatric medical care services (24). In addition, two following studies also reported that pharmacists have a role to detect MEs in children. Folli and colleagues found that 27 out of 479 errors at the two pediatric hospitals were potentially lethal but no harm to patients because their errors were able to intercept (25). Blurn and colleagues suggested the importance of a clinical pediatric pharmacist in detecting and preventing MEs based on their study (26).

In Thailand, although healthcare systems between two countries are different, patient safety concerning is not different from the United States. The Institute of Hospital Quality Improvement and Accreditation (HA) has set the standard for quality assurance of Thai hospitals since 1999 (27). A MEs prevention policy and high-alert medications management protocol are required for quality assurance (28). Each hospital had to create their individualized protocol by pharmacy department which posed as the leader of multidisciplinary team. The team should initiate individualized protocol which includes practical medication use process policies about prescribing, distribution, administration and safety monitoring based on their characteristics of medication errors' reports (28-31). Unfortunately, a specific protocol for pediatric intensive care unit (PICU) has not been studied. However, Kraitep reported pharmacist's role to play in identifying, resolving and preventing drug therapy problems (DTPs) and MEs and providing drug information in the PICU at Queen Sirikit National Institute of Child Health (QSNICH). This preliminary study in Thailand found that an average frequency of MEs and DRPs were equally 1.8 per 100 drug-days. Dosage errors were most problems and a pharmacist's intervention related dose reduction was performed in the first rank as high as 27.9% (32).

In Ramathibodi Hospital, one of a university hospital of Mahidol University. There are 8 beds in the PICU where were serviced by an attending physician, resident physicians and respiratory nurses but without a clinical pharmacist. Patient harm which was resulted by MEs is just reported irregularly and the high-alert medications management protocol has been also non-systematic created by nursing

staff. In addition, physicians and pharmacists have not involved in this protocol and thus the protocol has only focused on administration and safety monitoring policies.

As a result, the purpose of the present study is to develop role of the research pharmacist on management of high-alert medications in the PICU, Ramathibodi Hospital by surveying frequencies of medication errors. Not only the real time MEs reports but also the characteristics of DTPs and drug information providing by the research pharmacist will be substantial data to develop a specific high-alert medications management protocol.

Objectives of the study

To develop role of the pharmacist on management of high-alert medication in the PICU, Ramathibodi Hospital. Therefore, the objectives are:

1. To survey frequencies of medication errors and drug related problems in PICU, Ramathibodi Hospital.

2. To propose high-alert medication management protocol in the PICU, Ramathibodi Hospital.

CHAPTER II
LITERATURE REVIEW

Medication errors (MEs)

The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) defines a medication error as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use (1)." Categorized severity of MEs algorithm shown in Figure 1.

Since the extensive report in 1988, “To Err Is Human: Building a Safer Health System,” from the Institute of Medicine (IOM), states that up to 98,000 people die each year as a result of medical errors in U.S. hospitals. This is equivalent to 268 fatalities a day, or the loss of a fully loaded 767 airliner. Numerous others suffer from injuries while hospitalized, ranging from minor falls to permanent disability. The IOM report reveals that over half of these deaths and injuries are preventable (2).

Medical errors need to be significantly decreased. The “error factor” occurring in health care systems is complex, multifactorial, and challenging to solve. Faulty systems that lead to patient injury and death should be identified and new, safer systems designed. However, changes in these intricate systems will happen more effectively and rapidly only with the involvement of health care consumers. There is a need for a professional-public partnership to be forged in order to work together for solutions. If patients can learn about health care system vulnerabilities, and, most importantly, if they can learn to be more involved in their care, then perhaps some medical errors may be avoided. As with other circumstances, knowledge is power;

moreover, knowledge of vulnerable health care systems and the medical errors that take place within them may be the means to help save lives.

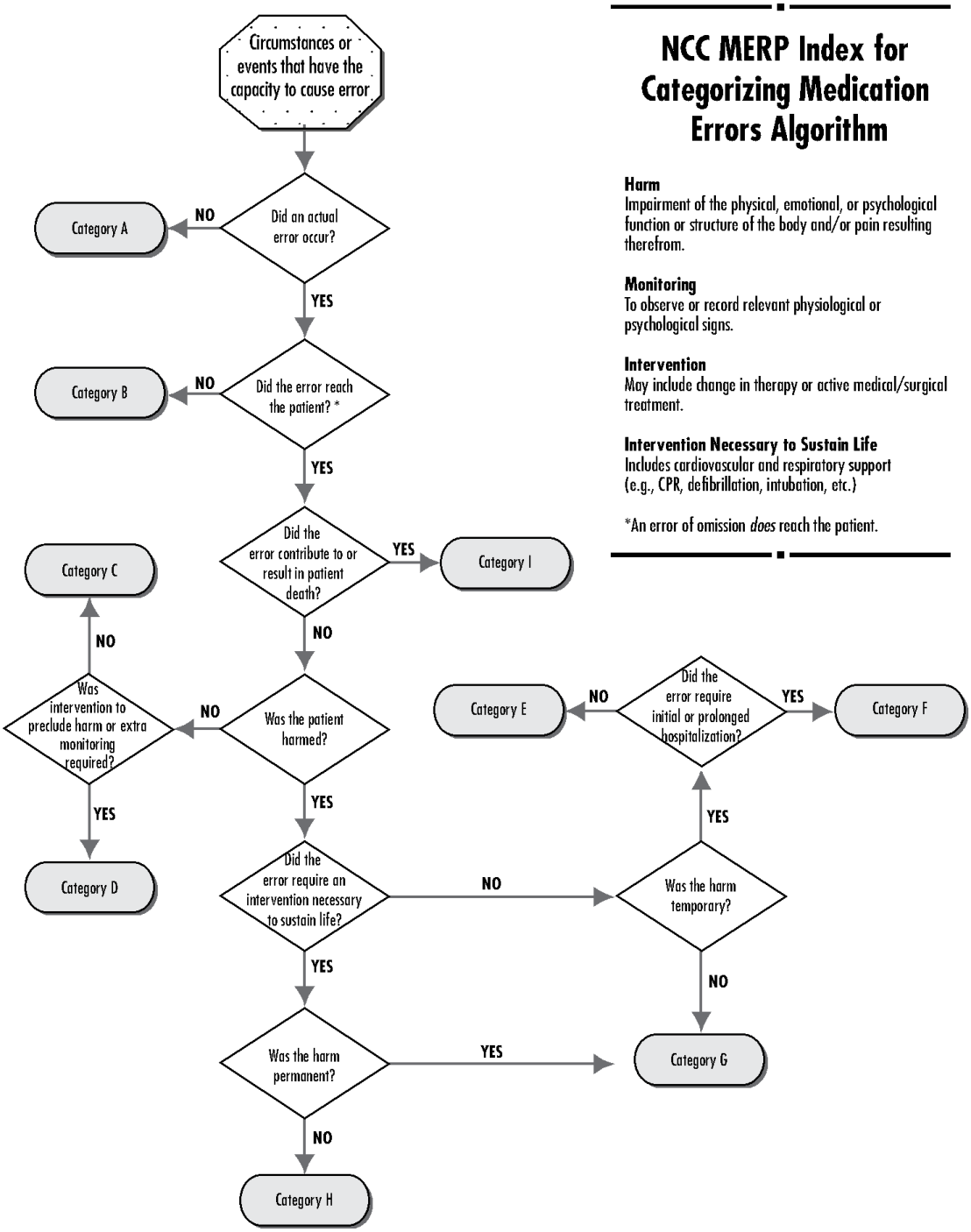

Figure 1 NCC MERP index for categorizing medication error algorithm (33)

Medication systems in hospitals are complex and multi-layered, involving many steps and many individuals. According to experts, this complexity increases the probability of failure. While many errors are caught before they can cause harm, it can be tragic whenever a patient's safety is compromised. Error can occur at any stage - prescribing, ordering, dispensing, administering, or monitoring the effects of a medication. According to the Institute for Safe Medication Practices, some common sources of medication error in health systems include (34, 35):

a) Unavailable Patient Information: Critical patient information (diagnoses, lab values, allergies, drug contradictions, etc.) is often unavailable to pharmacy, nursing, and medical staff prior to dispensing or administering drugs.

b) Unavailable Drug Information: Pharmacists often are not readily available on patient care units and written resources may not be up-to-date, which can lead to dose miscalculations or ignorance of drug interactions. Because errors occur most often during the prescribing and administration stages, accessible drug information must be readily available and close at hand for all staff who prescribe and administer drugs.

c) Miscommunication of Drug Orders: Failed communication is at the heart of many errors. This includes poor handwriting, confusion of drugs with similar names, careless use of zeroes and decimal points, confusion of metric and apothecary systems, use of inappropriate abbreviations, ambiguous or incomplete orders, and, sometimes, conflicts between practitioners.

d) Problems with Labeling, Packaging and Drug Nomenclature: Most drugs are dispensed through unit dose systems that parse medications into smaller-sized doses. These systems, however, do not always provide for thorough preparation, packaging, and labeling of medications, with screening and checking by both nursing and pharmacy personnel, and they may not be available throughout every unit in the hospital (e.g., ERs and ICUs). Drug administration procedures often do not ensure that medications remain labeled until they reach the patient's bedside, a frequent source of error.

e) Drug Standardization, Storage, and Stocking: Stocking multiple concentrations of the same drug, or storing drugs in look-alike containers or in ways that obscure drug labels, may contribute to error. Lack of safety procedures for use of

automated dispensing technology or inadequate check systems may also contribute to errors.

f) Drug Device Acquisition, Use and Monitoring: Lack of standardization in drug delivery devices, improper default settings, unsafe equipment (e.g., free-flow infusion pumps), and the lack of independent check systems for verifying dose and rate settings can all contribute to device-related errors.

g) Environmental Stress: Environmental factors like lighting, heat, noise, and excessive interruptions, can affect individual performance. The process of transcribing orders is particularly vulnerable to distractions in the environment, as staff transcribing orders are exposed to noise, interruptions, non-stop unit activity, and too-long or double shifts.

h) Limited Staff Education: Many practitioners are not as aware as they should be of situations within their own organizations that have been reported as error-prone, or of similar information published in professional literature.

i) Limited Patient Education: Medication use is a multi-step, multidisciplinary process that begins and ends with the patient. Patient education about medications - what they are taking, why they are taking it, and how they should take it - is essential to successful medication administration. Patients can be partners in the prevention of error while hospitalized and need to be educated to safely self-administer medications when they go home.

j) Quality Improvement Processes and Risk Management: Health facilities need systems for identifying, reporting, analyzing, and correcting errors and identifying trends, and measurement systems for tracking the effect of system changes. Also, organizations need to take into consideration information from outside sources about errors that have occurred elsewhere. But above all, health organizations need to cultivate a non-punitive approach to error that will encourage frank identification and analysis of errors when they occur.

The IOM report quickly moved hospital leaders into action—participating in national conferences, creating patient safety plans, collecting data, and implementing patient safety projects. All of these initiatives are steps in the right direction. Clearly, health care leaders have developed the passion needed to change the equation of harm (36-39).

Medication error rates found in observational studies are reported to vary between 1.7 and 59%, but generally accepted rates are 15%for floor stock distribution systems and 2 to 5% for unit-dose distribution systems (40). These rates do not include prescribing errors. The rates for prescribing errors are reported to be between 0.3 to 2.6% (41).

Medication errors divide into 4 main categories, namely prescribing errors, transcription/interpretation errors, dispensing errors and administration errors (42). Hartwig et al (43) describe the results of a voluntary reporting system for medication errors: 45% of all reported errors were administration errors, 32% were transcription errors, 13% were dispensing errors and 4% were prescribing errors. In another study by Leape et al (44), 39% of medication errors were found to be prescribing errors, 38% were administration errors, 12% transcription errors and 11% dispensing errors.

Prescribing errors involved prescription of a wrong drug (indication error), right drug to wrong patient (contraindication, known allergy, drug-drug interaction), wrong dose (dosing error) or wrong dosage form (e.g. tablets prescribed for a patient unable to swallow) (45). In a study by Tully and Tallis (46), 34% of patients admitted to an elderly care unit experienced one or more adverse drug reactions and drugs considered unnecessary were prescribed in 20% of the patients. These drugs accounted for a third of all adverse drug reactions. Tully and Tallis were also involved in a larger study among 416 elderly patients admitted to a teaching hospital. Almost half of all adverse drug reactions were associated with drugs that were absolutely contraindicated and/or deemed unnecessary (47). Vargas et al (48) found a relationship between the number of adverse drug reactions and the number of potential drug-drug interactions.

Preventable adverse drug reactions in hospitalized patients were associated with dosing and previous allergy to the drug, as Seeger et al (49) showed. Lesar et al (50) found an error rate of 4 errors per 1000 medication orders. Of the errors with potential for adverse patient effects, 13.9% were due to decline in renal or hepatic function requiring alteration of drug therapy, 12.1% to known drug allergy, 11.4%to using the wrong drug name, dosage form or abbreviation, 11.1% to incorrect dosage calculations and 10.8% to incorrect dosage frequency.

Causes for errors in prescribing were lack of knowledge about the prescribed drug (51), unfamiliarity with the patient (51, 52) and mental slips due to

distraction (53) or calculation errors (54). In the study by Lesar et al (50), 30% of errors were due to lack of knowledge of the drug, 29% to lack of knowledge regarding patient factors and 17.5% to dose calculations.

Different approaches were described in the literature to prevent prescribing errors. These approaches included improving education with respect to drugs and patient characteristics important for drug therapy (51), using a pharmacy computer for medication order entry (52-54) and by using computerized physician order entry (55-57).

Many drug distribution systems rely on transcription of physician orders by nursing staff, which offers substantial opportunity for error. Handwritten orders (either directly written by physician or after transcription by nurses) need to be interpreted by pharmacy personnel and translated into the dispensing of the right drug at the right dosage (42). West et al (61) have found verbal medication orders to be associated with a lower rate of errors, mainly due to a smaller rate of transcription 328 errors. These results are not in line with other studies, as verbal orders are generally perceived to be associated with a high rate of errors (62, 63). Illegible handwriting and the use of abbreviations and decimal points are especially associated with erroneous interpretation (63). Prevention of this category of errors can best be achieved by computerized physician order entry, which eliminates the need for both transcription and interpretation (42).

Errors can occur even after a correct interpretation of the medication order in the pharmacy. These errors can be subdivided into 4 categories: calculation errors, preparation errors, dispensing errors and distribution errors (64). Possibilities for prevention of dispensing errors are the use of bar-coding, the use of strict preparation procedures and the use of double-checks. The unit-dose system provides the possibility for double-checking (64, 65). By using an automated dispensing system, Klein et al (66) showed that the error rate could be reduced from 0.84 to 0.65%.

Administration errors occur in the last part of the distribution process, when the drug is administered to the patient. The errors that can occur in this stage involve the 5 ‘rights’: giving the right drug to the right patient at the right dose by the right route at the right time. A common classification includes wrong patient, wrong

dose, wrong time, omissions, wrong drug, extra dose, improper route or method, wrong rate of flow, un-ordered drug and duplication of a drug (67).

Look-alike packages, lack of education on drugs, lack of double-checking, unclear medication orders (e.g. illegible handwriting, verbal orders) and under-staffing are common causes for these errors (67).

Preventive measures should include computerized physician order entry, the use of computer lists for administration (including printed drug names, dosages and routes and times of administration), the education of nurses and the introduction of double-checks (67). Furthermore, automated cart filling (66) and bar-coding may also be of use in this stage (67).

Drug therapy problems

A drug therapy problem is an event or circumstance involving medication therapy that actually or potentially interferes with an optimum outcome for a specific patient. There are at least the following categories of medication-related problems (40, 68):

a) Untreated indications. The patient has a medical problem that requires medication therapy (an indication for medication use) but is not receiving a medication for that indication.

b) Improper drug selection. The patient has a medication indication but is taking the wrong medication.

c) Subtherapeutic dosage. The patient has a medical problem that is being treated with too little of the correct medication.

d) Failure to receive medication. The patient has a medical problem that is the result of not receiving a medication (e.g., for pharmaceutical, psychological, sociological, or economic reasons).

e) Overdosage. The patient has a medical problem that is being treated with too much of the correct medication (toxicity).

f) Adverse drug reactions. The patient has a medical problem that is the result of an adverse drug reaction or adverse effect.

g) Drug interactions. The patient has a medical problem that is the result of a drug-drug, drug-food, or drug-laboratory test interaction.

h) Medication use without indication. The patient is taking a medication for no medically valid indication.

Drug therapy problems can be divided into 2 categories: problems that involve an error (extrinsic drug therapy problems) and problems that involve no errors (intrinsic drug therapy problems) (68).

In the first category a mistake is made somewhere in the drug distribution and/or production process (from the prescribing of the drug to the administration of the drug). These drug problems can be called medication errors. Medication errors may or may not result in patient morbidity. The second category consists of problems that occur even when no errors have been made in the entire process of drug distribution. These problems are called adverse drug reactions. Adverse drug reactions always result in discomfort or harm to the patient. Relationships between the definitions of medication errors and drug therapy problems are shown in Figure 2.

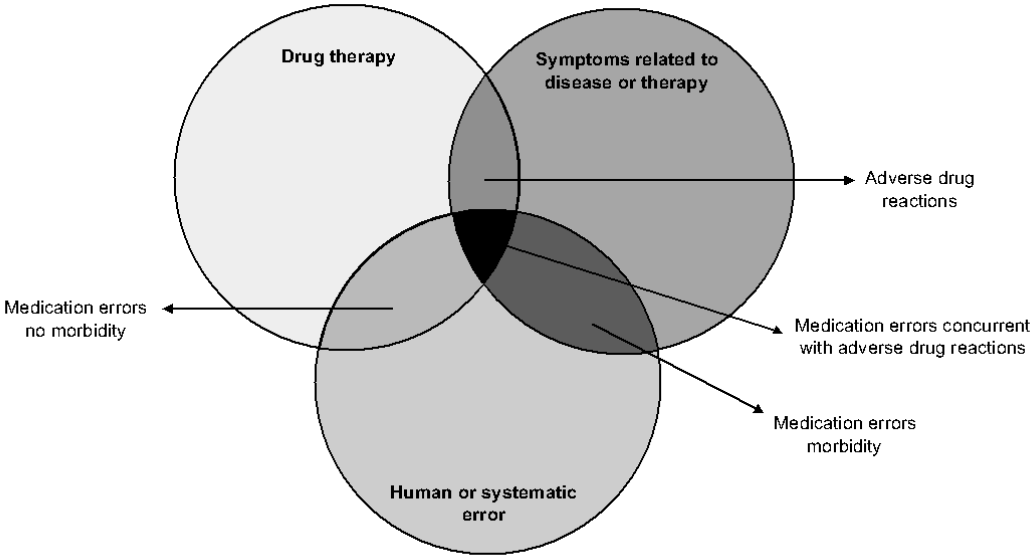

Figure 2 Relationships between the definitions of medication errors and drug therapy problems (68)

For the type of medication error, a distinction was made between distribution errors (i.e. deviations from the prescription) and prescribing errors. Bates et al (18) found that almost 1% of medication errors resulted in an adverse drug event.

Adverse drug reactions are regularly encountered in hospitalized patients. Incidences reported in studies published since 1991 vary between 1.9 and 37.3% (42). The wide range of incidences depends largely on the methods used to gather information on adverse drug reactions (e.g. intensive monitoring, spontaneous reporting) (70, 71). A meta-analysis reports an incidence of 10.9% for both serious and non-serious adverse drug reactions; fatal reactions occurred in 0.32% of hospitalized patients (72).

Pharmaceutical care

Pharmaceutical care is the responsible provision of drug therapy for the purpose of achieving definite outcomes. The process of pharmaceutical care involves drug therapy (the actual provision of medication) but also decisions about medication use for individual patients. As appropriate, this includes decisions not to use medication therapy as well as judgments about medication selection, dosages, routes and methods of administration, medication therapy monitoring, and the provision of medication-related information and counseling to individual patients (68, 73).

Specifically, this involves:

a) Identifying potential or actual drug therapy problems;

b) Resolving actual drug therapy problems; and,

c) Preventing potential drug therapy problems.

Patients may possess characteristics that interfere with the achievement of desired therapeutic outcomes. Patients may be noncompliant with prescribed medication use regimens, or there may be unpredictable variations in patients' biological responses. Thus, in an imperfect world, intended outcomes from medication-related therapy are not always achievable (73).

Patients bear a responsibility to help achieve the desired outcomes by engaging in behaviors that will contribute to-and not interfere with-the achievement of desired outcomes. Pharmacists and other health professionals have an obligation to educate patients about behaviors that will contribute to achieving desired outcomes:

a) Quality of Life. Some tools exist now for assessing a patient's quality of life. These tools are still evolving, and pharmacists should maintain familiarity with the literature on this subject (74, 75). A complete assessment of a patient's quality of

life should include both objective and subjective (e.g., the patient's own) assessments. Patients should be involved, in an informed way, in establishing quality-of-life goals for their therapies.

b) Responsibility. The fundamental relationship in any type of patient care is a mutually beneficial exchange in which the patient grants authority to the provider and the provider gives competence and commitment to the patient (accepts responsibility) (68). Responsibility involves both moral trustworthiness and accountability.

In pharmaceutical care, the direct relationship between an individual pharmacist and an individual patient is that of a professional covenant in which the patient's safety and wellbeing are entrusted to the pharmacist, who commits to honoring that trust through competent professional actions that are in the patient's best interest. As an accountable member of the health-care team, the pharmacist must document the care provided (76-79). The pharmacist is personally accountable for patient outcomes (the quality of care) that ensue from the pharmacist's actions and decisions (80).

The primary goal of pharmacists should be to improve the quality of life of individual patients through activities which ensure individual patients are receiving drug therapy to achieve the desired outcomes. These outcomes are defined as (68):

a) cure of a disease;
b) elimination or reduction of a patient's symptomatology;
c) arresting or slowing of a disease process; and,
d) preventing a disease or symptomatology.

The activities of the pharmacist may be described by the following steps (73):

1. Establish the patient-pharmacist relationship;
2. Collect, synthesize, and interpret the relevant information;
3. List and rank the patient's drug therapy issues;
4. Establish a desired pharmacotherapeutic outcome for each drug therapy issue;
5. Determine feasible pharmacotherapeutic alternatives;

6. Choose the “best” pharmacotherapeutic solution and individualize the therapeutic regimen;

7. Design a therapeutic drug monitoring plan;

8. Implement the individualized regimen and monitoring plan; and

9. Follow up to measure success in individual cases and in long-term implementation.

Pharmacists also have professional and societal responsibilities. Professional responsibility includes participating in policy and procedure development for the provision of pharmacy services, the education of pharmacists and other health care professionals, and research related to patient care or therapeutic problems in general. Societal responsibilities include participation in health promotion, public education, appropriate resource utilization, research, and development of standards of care. However, the pharmacist’s primary responsibility is to assist individual patients to achieve their desired outcome(s) (81).

Leape at al (82) have shown that the presence of a pharmacist on rounds in a medical intensive care unit was associated with a lower rate of prescribing errors (3.5 prescribing errors per 1000 patient-days with a pharmacist, compared with 10.4 prescribing errors per 1000 patient-days without a pharmacist). In a study by Bond et al (83), it was shown that increased staffing for clinical pharmacists was associated with lower drug costs. Better patient care is mentioned by the authors as one of the reasons for this cost reduction.

Clinical pharmacy services in pediatrics care

Medicines’ management or pharmaceutical care in pediatric patients is particularly demanding, mainly because the majority of available drugs have been developed for use in adults. As a result, in children, drugs are often unlicensed or used off-label, suitable formulations or appropriate strengths are lacking, and drugs have to be extemporaneously prepared, liquids and injections diluted, and tablets split. These factors increase the likelihood of medication errors and may lead to a reduction in drug effect. Age-specific changes in pharmacokinetics and pharmacodynamics further complicate drug therapy in children. All these challenges provide unique opportunities for pharmacists to improve the quality of care for pediatric patients (19).

Conroy et al (85) reported that over two-thirds of 624 children admitted to wards in five European hospitals were prescribed drugs that were unlicensed in children or the use of which was off-label in children.

Nurses and parents may be required to subdivide prevent tablets, open capsules or dilute injections in order to administer the correct dosage. Such practices can potentially lead to a reduction in drug effect and/or toxicity (86). Moreover, this increases the likelihood of 10-fold medication error in children; for drugs with a narrow therapeutic index, a 10-fold dosage increase may lead to serious morbidity or mortality (87). Fortescue et al (88) conducted a prospective cohort study in 1,020 patients who were admitted to two academic medical centers in the US during a 6-week period in April and May 1999. They modeled the data and concluded that ward-based clinical pharmacists might have prevented 81% of potentially harmful errors.

The earliest study looking at pharmacists' interventions was conducted in 1971 in the US by Munzenberger et al (24). This study identified the pharmacist's role as monitoring patient charts, providing admission drug histories, providing discharge consultations, and providing drug information to medical and nursing staff. Pharmacists' involvement in the above areas led to improved pediatric medical care and provided a valuable service to doctors and nurses working in the unit during the study. However, the authors stressed that in order for pharmacists to provide these services fully they need to be readily available on the ward at all times, an aspiration that has still not been met 30 years on.

A study by Folli et al (25) involving two pediatric hospitals in the US identified a total of 281 and 198 errant orders at the two institutions, respectively, over 6 months. No harm to patients because of errors occurred during the study and the frequency of errant orders declined as physician training status increased. Within both hospitals, 27 errors were potentially lethal, which the authors feel justifies the additional cost of a clinical pharmacist. However, the authors point out that the true specificity of error detection cannot be determined from the data as the number of potentially errant orders identified by the pharmacist but not changed by the physician were not recorded.

Again in the US, Blum et al (26) repeated the study by Folli et al (25) over 3 months with similar results. This study again shows the importance of a clinical pediatric pharmacist in detecting and preventing medication errors.

A study by Koren et al (88) in Canada recorded a number of dose administration errors, particularly 10-fold errors, many of which could have led to serious morbidity or mortality. As with Folli et al (25), these findings present a strong case for the role of a clinical pediatric pharmacist, as "prevention of man-made morbidity and mortality should always be a goal of patient care" (25).

Another study in Canada, by Strong and Tsang (89), found 361 interventions over 2 weeks; however, interventions resulting from drug information questions were not included. The physician acceptance rate (percentage of pharmacists' interventions accepted by physicians) was found to be 95.8%. 190 out of 361 interventions had an impact on patient care; of these, 93% of interventions were found to have a positive effect. Eighty-two randomly selected interventions were assessed and 8.5% were classified as life-saving. The authors also calculated a cost avoidance of $679 (1991 value) over 2 weeks, which represents $17,654 annually. However, this is likely to be an underestimate as no control group was included in the study, so it was not possible to accurately estimate how an intervention influenced cost in terms of duration of treatments, length of hospital stay, costs avoided as a result of allergy notification, and ADR identification. Nevertheless, the study demonstrated that "pharmacists' interventions which represent only a proportion of a pharmacist's responsibilities, improve the quality of patient care and result in cost avoidance" (89).

In the US, Lal et al (90) documented 504 clinical interventions and services accepted over a 6-month period. Pharmacists' interventions were found to have decreased hospital stay from 4.38 to 4.26 days (a decrease of 2.7%) and led to a cost saving of $7,227.83 during the study period. This study also demonstrated improved pharmacy relationships with nurses and doctors, with a 50% reduction in the number of complaints filed with the pharmacy by ward staff. As with the Strong and Tsang study (89), a possible limitation is an underestimation of the cost saving.

A total of 610 interventions were identified over 4 months in a US study by Falck et al (91), Over this time the pharmacist spent 227 hours devoted to pharmacy activities in the pediatric intensive care unit (PICU), which represents

2.7 interventions per hour. Limitations included inability to evaluate correlations between pharmacist time spent in the PICU and patient length of stay, doses dispensed and interventions completed. These measurements could justify the need for consistent as opposed to sporadic pharmacist involvement with the care team (91), the same conclusion reached by Munzenberger et al (24).

An interesting US study by Chan and Kotzin (92) compared pharmacists' clinical intervention trends between pediatric and adult inpatients. Over 4 years the study documented 706 interventions in pediatric compared with 379 in adult patients. The mean time spent by a pharmacist per intervention was 35.4 minutes for pediatric and 31.1 minutes for adult patients. The incidence of interventions was 75.3 per 10,000 orders written for children compared with 4.8 per 10,000 orders written for adults. The incidence of drug therapy problems for children was 165.0 per 10,000 orders written compared with only 8.7 per 10,000 orders written for adults. Overall, a higher incidence of interventions was reported in children than adults. Limitations of the study included the fact that it was performed retrospectively, and that it lacked sufficient data to perform cost and explicit quality of care analysis. Another limitation was that there was a change in the clinical pharmacy staffing during the study period, which may have affected the number of interventions recorded because of variation in experience. Overall the study highlights the value of a pediatric clinical pharmacist.

A 24-week (79-day) study in the US by Krupicka et al (93) documented 172 interventions for 77 patients, equivalent to 35 recommendations per 100 patient-days. The average time spent by the pharmacist in the PICU was 0.73 hours/day. Patients with recommended interventions on admission had a longer intensive care unit and hospital stay, and the pharmacist spent more time on these patients. There was a $1,977 (1997 value) cost saving during the study, which is equivalent to $9,135 annually. A limitation of the study was that there was no control group, so benefits had to be assumed rather than proven causal. In addition, a patient's clinical course was not factored into potential savings as a result of interventions, and there was no direct evidence of a positive or lasting impact of medical staff education.

The study conducted in the UK was by Guy et al (94). During the 4 weeks of the study, 363 interventions were recorded: 190 interventions were detected by

pharmacists, 80% of which were accepted by medical staff. 60% of interventions resulted in prescriptions being amended; advice was acknowledged in 6% of cases, while 0.5% of detected errors were regarded as life threatening. The majority of interventions were resolved within 5 minutes. Limitations of the study include the fact that only one pharmacist and nurse were available in the active phase of the study to promote and manage the project. Staff shortages in pharmacy may have resulted in incomplete data capture and, in addition, not all returns were fully completed. Thus, the chosen time period may have affected the results.

Virani and Crown (95) recorded 48 interventions over 4 weeks in a Canadian study, of which the physicians accepted 98%. Forty-four interventions were analyzed, of which 86% were judged to have a positive effect. Total drug cost per patient-day decreased by 14% in the 12 months after having a clinical pharmacist on the ward. The total drug cost was decreased by 21%, which represents a cost saving of $5,485.80 during the study period. The small number of patients and interventions during the study may have limited the results. The small number of patients was further compounded by a reduced number of admissions during the study period. The cost analysis was retrospective, which meant it was not possible to determine the extent to which a single factor was responsible for the observed changes. However, the high percentage of accepted interventions in this study demonstrates how a clinical pharmacist positively influences patient outcomes in the pediatric population.

A recent study by Condren et al (96) in the US documented a total of 4,605 interventions for 3,978 patients over 12 months. Ninety-one percent of recommendations were accepted by the physician. A total of 223 adverse drug events or medication errors were prevented or detected during the study period, which resulted in an estimated cost saving of $458,516 (2,002 value). However, data used to derive cost savings of interventions were based on adult patients, so may be misleading as no validated data were available to guide the economic analysis of interventions in the pediatric population. There is also uncertainty about the outcome of interventions: for example, it is unknown whether the interventions resulted in shorter hospital stays or an overall decrease in healthcare costs. Nevertheless, this study justifies the role of pharmacists within the pediatric medical team through a reduction in medication errors.

In Thailand, Kraitep (32) studied role of pharmacists in clinical pharmacy services in the pediatric intensive care unit at Queen Sirikit National Institute of Child Health (QSNICH). The study reported pharmacist's role to play in identifying, resolving and preventing drug therapy problems (DTPs) and MEs and providing drug information in the PICU This preliminary study in Thailand found that an average frequency of MEs and DRPs were equally 1.8 per 100 drug-days. Dosage errors were most problems and a pharmacist's intervention related dose reduction was performed in the first rank as high as 27.9%**.** Overall percentage of health care team satisfaction score was 85.6% and every member agreed that a clinical pharmacist should participate with the team.

High alert medications

High-alert medications are drugs that bear a heightened risk of causing significant patient harm when they are used in error. Although mistakes may or may not be more common with these drugs, the consequences of an error with these medications are clearly more devastating to patients (11).

Since the Joint Commission began tracking sentinel events in 1995, the Accreditation Committee of the Joint Commission's Board of Commissioners has reviewed 89 cases related to medication errors. Medication errors are one of the most common causes of avoidable harm to patients in health care organizations.

A study was conducted by the Institute for Safe Medication Practices (ISMP) during 1995 and 1996 to determine the drugs and situations most likely to cause harm to patients. Approximately 161 health care organizations submitted data on serious errors that had taken place during this period. The results of the study showed that a majority of medication errors resulting in death or serious injury were caused by a specific list of medications.

Medications that have the highest risk of causing injury when misused are known as high-alert medications. The top five high-alert medications identified by the ISMP study are insulin; opiates and narcotics; injectable potassium chloride (or phosphate) concentrate; intravenous anticoagulants (heparin); and sodium chloride solutions above 0.9 percent (8).

From 157,364 errors reported in USP's 2002 MedMarx database, these high-alert medications are among the top six medications involved in errors that result in harm, according to the U.S. There are 82,585 errors that reach the patient. Five of the top seven medications involved in errors that reached a patient are high-alert. Of errors that reached the patient, the majority did not result in harm. The data shows that 2,994 errors resulting in harm and insulin causes more harm to patients (97).

The Institute for Safe Medication Practices Canada (ISMP Canada) has received error reports related to insulin and narcotics that have caused patient harm. In the case of both types of drugs, incidents involving the use of "u" as abbreviation for units as well as misinterpretation of the decimal place have resulted in errors of 10-fold dosage increase. Opiate narcotics events often involve either a mix-up between an epidural infusion and a regular intravenous infusion, or the wrong concentrations input into patient controlled analgesia (PCA) pumps. Other well-known medication errors that have caused patient harm include the misuse of concentrate of potassium chloride (KCl) and the intrathecal injection of vincristine (a chemotherapy drug) (98). The high alert medication list was different from US (8, 97).

During August and September, 2003, more than 350 practitioners responded to an ISMP survey designed to identify which of these medications were most frequently considered high alert by individuals and organizations (10).

ISMP's list of high alert medications finally were based on error reports submitted to the USP-ISMP Medication Errors Reporting Program and reports of harmful errors in the literature, ISMP created a list of potential high-alert medications. Further, to assure relevance and completeness, the clinical staffs at ISMP, members of ISMP's advisory board, and safety experts throughout the US were review the potential list. This list of drugs and drug categories reflects the collective thinking of all who provided input.

There are 19 classes/categories of medications and 14 specific medications that present in ISMP's high alert medication lists as follow (11):

<u>Classes/categories of medications</u>

- adrenergic agonists, IV (e.g., epinephrine)
- adrenergic antagonists, IV (e.g., propranolol)
- anesthetic agents, general, inhaled and IV (e.g., propofol)

- cardioplegic solutions
- chemotherapeutic agents, parenteral and oral
- dextrose, hypertonic, 20% or greater
- dialysis solutions, peritoneal and hemodialysis
- epidural or intrathecal medications
- glycoprotein IIb/IIIa inhibitors (e.g., eptifibatide)
- hypoglycemics, oral
- inotropic medications, IV (e.g., digoxin, milrinone)
- liposomal forms of drugs (e.g., liposomal amphotericin B)
- moderate sedation agents, IV (e.g., midazolam)
- moderate sedation agents, oral, for children (e.g., chloral hydrate)
- narcotics/opiates, IV and oral (including liquid concentrates, immediate- and sustained-release formulations)
- neuromuscular blocking agents (e.g., succinylcholine)
- radiocontrast agents, IV
- thrombolytics/fibrinolytics, IV (e.g., tenecteplase)
- total parenteral nutrition solutions

Specific medications

- amiodarone, IV
- colchicine injection
- heparin, low molecular weight, injection
- heparin, unfractionated, IV
- insulin, subcutaneous and IV
- lidocaine, IV
- magnesium sulfate injection
- methotrexate, oral, non-oncologic use
- nesiritide
- nitroprusside sodium for injection
- potassium chloride for injection concentrate
- potassium phosphates injection
- sodium chloride injection, hype

On July 18, the Joint Commission's Board of Commissioners approved the 2004 National Patient Safety Goals (NPSGs), Joint Commission on Accreditation of Healthcare Organizations (JCAHO) establishes these goals to help accredited organizations address specific areas of concern in regards to patient safely. Improve the safety of using high alert medications was one of the goal (37-39).

The Institute of Hospital Quality Improvement and Accreditation (HA), Thailand, has set the standard for quality assurance of Thai hospitals since 1999 (27). A MEs prevention policy and high-alert medications management protocol are required for quality assurance (28).

Three principles may be used to safeguard the use of high-alert medications (99):

1. Reduce or eliminate the possibility of error (for example, reducing the number of high-alert medications stocked by the hospital; reducing the available concentrations and volumes; and removing high-alert drugs from clinical areas).

2. Make errors visible (for example, having two individuals independently check infusion pump settings for high-alert drugs is one way to make errors visible and thus caught before reaching the patient).

3. Minimize the consequences of errors (for example, fatal errors have occurred when the contents of 50 mL vials of 2% lidocaine were injected instead of mannitol, which has a similar appearance-had lidocaine 2% been only available in the clinical area in a 10 mL vial, if administered erroneously in place of another drug in a 10 ml vial, the amount of lidocaine injected would likely not have been fatal).

Steps in the Ideal Medication Use Process (99):

1. Physician enters a drug order into the computer system.

2. The computer checks for drug interations, allergy interactions and dosing.

3. A pharmacist verifies the order, reviewing system generated alerts and screens for issues not caught by the computer system.

4. The system-generated label moves to the filling area, where a technician fills the order in the pharmacy.

5. A pharmacist checks the technician's work.

6. A nurse receives the drug and checks the nursing record against the medication sent.

7. The nurse administers the drug to the patient after checking the patient's nameband against the order, telling the patient the name of the drug, the dose, and its purpose, thereby allowing the patient to also serve as a double-check (where possible).

8. Unused drugs are returned to the pharmacy, where a pharmacist/technician reviews them for mistakenly unadministered drugs.

9. Extra (missing doses) doses requested are reviewed by a pharmacist/technician to understand why the doses are not where the nurses expect.

Key Change Concepts for Safeguarding High-Alert Medications (99):

1. Build in system redundancies (e.g. unit dose drug distribution).

2. Use fail-safes (e.g. pumps with electronic fail-safe clamping mechanisms to prevent free flows).

3. Reduce options (e.g. instead of having the option of ordering heparin in various concentrations, like 20,000 units/250mL and 20,000 units/500mL and 25,000 units/500mL - only one option should be available).

4. Use forcing functions, which are techniques that reduce the possibility that a medication can be administered in a potentially lethal manner (e.g. using oral syringes, for oral liquid doses, that will not fit with IV tubing and to which needles cannot be attached; and computer order entry which can be used to 'force' the physician to order standardized products).

5. Externalize or centralize error-prone processes (e.g. centralizing all IV solution preparations).

6. Use differentiation (e.g. identify and isolate look-alike and sound-alike products; use generic names which do not tend to sound alike as often as brand names).

7. Store medications appropriately (e.g. separate potentially dangerous drugs with similar names or similar packaging).

8. Screen new products (e.g. pharmacy and therapeutics should inspect all new drugs and drug delivery devices for poor labeling and packaging).

9. Standardize and simplify order communication (e.g. minimize verbal orders and the use of abbreviations).

10. Limit Access (e.g. high-alert medications should only be stored in the pharmacy where only a pharmacist can access them).

11. Use Constraints (e.g. pharmacy screening of all orders for high-alert medications prior to preparation and administration; automatic stop orders and dose or duration limits).

12. Use Reminders (e.g. use auxiliary labels on high-alert medications; computer screens with warning information about high-alert drugs).

13. Standardize Dosing Procedures (use standard dosing tables or charts, rather than calculate doses based upon weight or renal function which is error-prone).

Root cause analysis (RCA)

RCA aims to identify preventable causes of a recent, serious, untoward event (100). RCA is a disciplined inquiry that is pursued dispassionately by a team of current participants or seasoned experts in various components of a complex system that has failed. The team begins by recreating a detailed chronology of the steps that gave rise to, and subsequently may have exacerbated or amplified, an adverse event. The full sequence of events that surround an incident are dissected and analyzed for random and systematic errors. Team discussions may identify some of these errors and their interactions. Others may be discovered by review of previous RCAs of related or analogous adverse events or of data on similar, previously reported errors.

By design, RCAs are focused inquiries that are aimed at characterizing and preventing specific errors. The circle of inquiry around the sentinel event may identify other components of a process that also are prone to error; however, the purpose is not to identify all potential vulnerabilities in a complex system. Steps in a process that are peripheral to the event of primary interest may be scrutinized superficially, if at all. Thus, hazards in a process of comparable or even greater consequence than the sentinel event may be overlooked in an RCA. One approach to minimizing this limitation of RCA has become known as aggregate RCA. Aggregate RCAs combine focused RCAs of errors and near misses that have been recorded over a defined period of time (101). The root causes of error that are identified by the individual RCAs are

examined for trends and interactions to identify steps in a process that give rise to adverse events. When successful, this process reveals vulnerabilities that may not be apparent or considered important in focused RCAs; however, aggregate RCA still is biased toward finding steps and safeguards in a system that has failed in the recent past.

Other potentially catastrophic vulnerabilities that fail infrequently may not be identified or corrected by this approach. A model system for error prevention that identifies potential problem areas before an adverse incident occurs would be of greater use in the medical community. Such a model would not replace RCA because this system is needed to address failures after they occur; however, it might limit the need for RCAs by proactively decreasing the number of medical errors that otherwise would generate RCAs. Many proactive models for error prevention exist and have been used in other industries. For example, Hazard Analysis and Critical Control Points is a proactive model for error prevention that has long been used by the US Food and Drug Administration (102). This model gained momentum within the food industry after public concern arose over botulinum poisoning from canned foods; however, it has not been adopted widely within other industries. A related approach to error avoidance, FMEA, may be particularly suitable for application in complex, multi-process systems in health care.

Failure mode and effects analysis (FMEA)

FMEA is a proactive error prevention system that is designed to identify problems in infrastructure and systems before adverse events occur (103). A primary tenet of FMEA is an acknowledgment that medical errors are inevitable. By this approach, the primary burden of error prevention is placed-not on individuals-but on the designers of the systems in which they work (51).

In an FMEA, an error-prone process is identified and a multi-disciplinary team is formed to analyze the process from multiple perspectives. The team systematically assesses failure modes and the urgency with which each failure mode should be addressed. Where RCA can be thought of as an expanding circle of inquiry that is focused on a sentinel event, FMEA is a linear process that examines a selected process from start to finish. The FMEA analysis helps to prioritize changes that need

to be made. One or more failure modes may warrant immediate corrective action, whereas the risk of others may be deemed acceptable. Examples of acceptable risk include failure modes that are associated with tolerable consequences or those with a rate of occurrence that is estimated to be remote, even if associated with catastrophic consequences. Involving a multidisciplinary team in FMEA creates an environment of shared responsibility for error avoidance that extends beyond the analysis; however, FMEA also is highly time consuming. For that reason, this form of prevention is best geared toward processes that are vulnerable to serious medical errors.

The history of FMEA dates back more than 30 years. The first FMEAs were conducted within the aerospace industry in the 1960s. In contrast to other competing failure prevention methods, FMEA was described in universally understandable terms that largely are free of industry-specific jargon. This promoted applications that bridged across companies and industries (104). Also, individuals who had limited technical or systems training could participate productively in multi-disciplinary FMEA teams. As these attributes of FMEA became known, leaders in the chemical and mechanical engineering industries also began to adopt this approach.

The automotive industry brought FMEA into the mainstream. A task force was developed jointly by Chrysler, Ford, and General Motors to establish requirements for the manufacture of automobile and truck components. The resulting quality system standard, called QS-9000, requires application of FMEA to identify and address failure modes (105). FMEA is used across the automobile manufacturing industry as the primary system for error and risk reduction. FMEA has been used in the health care industry since the early 1990s. Early applications included critical systems in drug product development and the manufacture and prevention of medication errors in hospitals (102, 106). In the mid-1990s, the Institute for Safe Medication Practices recommended the use of FMEA to prevent errors in dispensing medications. More recently, the Veterans Affairs' National Center for Patient Safety has implemented a prospective prevention system that incorporates many features of FMEA (107). This system, Health Care Failure Mode Effects and Analysis (HFMEA), modifies and expands FMEA for application to health care. The Department of Veterans Affairs (VA) now uses HFMEA as the primary method for evaluating and preventing major errors within their hospitals.

Successful implementation of an FMEA-based error prevention process by the VA caught the attention of the JCAHO. In July 2001, JCAHO introduced a new leadership standard, L.D.5.2. This standard requires department heads in healthcare organizations to perform an FMEA on at least one clinical process a year (103). Through this standard, the JCAHO now mandates an organized, prospective approach as a routing component of institutionalized patient care in the United States.

ICUs may be particularly suited to FMEA for several reasons. First, critically ill patients are exceptionally vulnerable to major, preventable adverse events. Because of impaired consciousness, endotracheal intubation, and physical restraints, many patients in ICUs cannot protect themselves or call for help when they are threatened. Also, they have limited or no functional reserve to withstand physical or chemical insults or therapy-induced deviations from homeostasis. Secondly, the care that is provided in ICUs is particularly prone to error (108-110). Critically-ill patients are subject to a broad range of common and unusual life-threatening events that can occur suddenly. These threatening events occur with similar likelihood on all days of the year and at all times of day or night, including times when the staff may not be prepared fully to respond (e.g., during changes of shift). Also, the risk of communication errors is exceptionally high in ICUs because critical illnesses often require the urgent coordination of many people, on-site and off, who assemble into loose teams that reconstitute frequently. The potential for adverse interactions between multiple therapies likewise is particularly high. Critically-ill patients receive twice as many medications on average as do patients in general in-patient care units, often in conjunction with other therapeutic interventions (e.g., mechanical ventilation, hemodialysis). Thirdly, although every patient is unique, complex, sequential care processes often are repeated in ICUs, with minor variation from one patient to the next. Many of these processes are amenable to FMEA. For all of these reasons, hospitals that are seeking to gain experience with FMEA are well-advised to introduce this technique early in the ICUs. Performing a failure mode and effects analysis in an intensive care unit: the process

Apkon et al (111) developed a set of standard processes for delivering continuous drug infusions in PICU in the children’s hospital of an academic medical center in order to improve patient safety, efficiency in staff workflow, hemodynamic

stability during infusion changes, and efficient use of resources by using FMEA to examine the impact of process changes on the reliability of delivering drug infusions. They found that standardization of infusion delivery reduced the frequency for completing the most unreliable elements of the process and reduced the riskiness of the individual elements. Both contribute to a safer system.

CHAPTER III
MATERIALS AND METHODS

Materials

1. Data collection form for patient's profile (Appendix A).
2. Data collection form for MEs and DTPs (Appendix B).
3. Data collection form for drug information service (Appendix C).
4. Patient's charts and patient's medical profiles.

Methods

1. Definition of terms

The terms used throughout the study were defined as follows:

1.1 Medication error

A medication error was defined by National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use".

In addition to classifying by category, the events were also categorized according to the medication error index developed by the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP). The events were considered whether the errors occurred. If the errors occurred, how severe of harm the errors caused. Harm was defined as impairment of the physical. emotional. or psychological function or structure of the body and/or pain resulting therefrom. The categories of severity were listed as follows (1):

1.1.1 No error

- Category A: Circumstances or events that have the capacity to cause error.

1.1.2 Error, No Harm

- Category B: An error occurred but the error did not reach the patient (An error of omission does reach the patient).

- Category C: An error occurred that reached the patient but did not cause patient harm.

- Category D: An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm.

1.1.3 Error, Harm

- Category E: An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention.

- Category F: An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization.

- Category G: An error occurred that may have contributed to or resulted in permanent patient harm.

- Category H: An error occurred that required intervention necessary to sustain life.

1.1.4 Error, Death

- Category I: An error occurred that may have contributed to or resulted in the patient's death.

1.2 Drug related problem

Drug related problem (DRP) was defined as undesirabIe event experienced by patient that involves or is suspected to involve in drug therapy and that actually or potentially interferes with a desired patient outcome'. In the present study, DRPs will be categorized by severity of harm as same as MEs (i.e., category A-I) and by characteristics of problems as follows (113):

1.2.1 Appropriate indication

1.2.1.1 Needs additional drug therapy

- The patient has a new medical condition requiring initiation of new drug therapy and has a chronic disorder requiring continuation of drug therapy.

- The patient has a medical condition that requires combination pharmacotherapy to attain synergism/potentiation of effects.

- The patient is at risk to develop a new medical condition preventable by the use of prophylactic drug therapy and/or premedication.

1.2.1.2 Unnecessary drug therapy

- The patient is taking a medication for which there is no valid medical condition at this time.

- The patient's medical problem(s) are associated with drug abuse, alcohol use, or smoking.

- The patient's medical condition is better treated with non-drug therapy.

- The patient is taking multiple drugs for a condition for which only single-drug therapy is indicated.

- The patient is taking drug therapy to treat an avoidable adverse reaction associated with another medication.

1.2.2 Efficacy

1.2.2.1 Wrong drug

- The patient has a medical problem for which this drug is not effective.

- Patient is allergic to this medication.

- Patient is receiving a drug that is not the most effective for the indication being treated.

- The patient has risk factors that contraindicate the use of this drug.

- The patient is receiving a drug that is effective but not the least costly.

- The patient is receiving a drug that is effective but not the safest.

- The patient has an infection involving organisms that are resistant to this drug.

- The patient has become refractory to the present drug therapy.

- The patient is receiving an unnecessary combination product when a single drug would be appropriate.

1.2.2.2 Dosage too low

- The dosage used is too low to produce the desired response for this patient or drug, dose, route, or formulation conversions were inadequate for this patient.

- Dose and interval flexibility (insulin sliding scales, “as need” analgesics) were inadequate for this patient.

- Timing of prophylaxis (presurgical antibiotic given too early) or treatment was inadequate for this patient.

- The drug was incorrectly administered for this patient.

- The bioavailability of the drug is altered due to an interaction with another drug or food the patient is taking or the effect of the drug has been altered due to enzyme inhibition/induction from another drug the patient is taking.

1.2.3 Safety

1.2.3.1 Adverse drug reaction

- The patient has identified risk factors that make this drug too dangerous to be used or the patient has experienced an idiosyncratic reaction to this drug.

- The patient is having an allergic reaction to this medication.

- The drug was administered too rapidly for this patient

- The bioavailability of the drug is altered due to an interaction with another drug or food the patient is taking or the effect of the drug has been altered due to enzyme inhibition/induction from another drug the patient is taking.

- The effect of the drug has been altered due to a substance in the food the patient has been eating.

- The effect of the drug has been altered due to displacement from binding sites by another drug the patient is taking.

- The patient's laboratory test result has been altered sired due to interference from a drug the patient is taking.

1.2.3.2 Dosage too high

- Dosage is too high for this patient or drug, dose, tales, route, formulation conversions were inappropriate for this patient.

- The patients' drug dose was escalated too rapidly.

- The patient has accumulated drug from chronic administration.

- The bioavailability of the drug is altered due to an interaction with another drug or food the patient is taking or the effect of the drug has to an been altered due to enzyme inhibition/induction from another drug the patient is taking.

1.2.4 Appropriate compliance

- The patient did not receive the appropriate drug regimen because a medication error (prescribing, dispensing, administration, monitoring) was made.

- The patient did not comply (adherence) with the recommended directions for using the medication.

- The patient did not take the drug as directed owing to the high cost of the product.

- The patient did not take the drug(s) as directed because of lack of understanding of the directions.

- The patient did not take the drug(s) as directed because it would not be consistent with the patient's health beliefs.

1.3 Drug information service

Drug information service (DIS) was defined as "the services which provided answers to drug information requests. These were expected to improve patient outcomes and decreased health care cost through the provision of unbiased information that supported rational, cost effective, patient and disease specific drug therapy" (113). In this study, requested questions were divided into 14 categories which modified from drug information service record form by Ministry of Public Health as follows (114):

a) Availability of dosage forms.

b) Identification of product.

c) General product information such as medication contents, medication group, mechanism of action.

d) Cost.

e) Compatibility/stability/route of administration.

f) Drug interaction (drug. laboratory, disease, food).

g) Pharmaceutics (compounding, formulation).

h) Pharmacokinetics (absorption. distribution, metabolism and excretion/levels/hemodialysis, peritoneal dialysis).

i) Therapy evaluation/drug of choice.

j) Dosage/regimen recommendations.

k) Adverse effects.

l) Poisoning/toxicology.

m) Teratogenicity/lactation/infant risks.

n) Others.

1.4 High alert medications

High-alert medications were defined by ISMP as "drugs that bear a heightened risk of causing significant patient harm when they are used in error. Although mistakes may or may not be more common with these drugs, the consequences of an error with these medications are clearly more devastating to patients" (11).

1.5 Pharmacist's intervention classification

Pharmacist's intervention classification was adapted from Kraitep (32) and Leape and colleagues (82). It was categorized as follows:

a) Clarification or correction of order.
b) Provision of drug information.
c) Dosage/interval adjustment.
d) Recommendation of alternative therapy.
e) Identification of drug interaction.
f) Identification of drug allergy.
g) Identification of adverse drug events.
h) Identification of systems error.
i) Therapeutic drug monitoring.
j) Miscellaneous or Unspecified.

1.6 Result of pharmacist's intervention

Result of pharmacist's intervention was adapted from Kraitep (32) and categorized as follows:

1.6.1 Accepted intervention

It was defined as drug therapy was adjusted according to pharmacist's suggestion.

1.6.2 Partially accepted intervention

It was defined as drug therapy was partially adjusted according to pharmacist's suggestion or the suggestion was accepted but actions were not changed at the time of study.

1.6.3 Not-accepted intervention

This was defined as drug therapy was not adjusted according to pharmacist's intervention.

1.7 PICU-day.

PICU-day is defined as the total number of days of each PICU patient, whom research pharmacist participated with the pediatric intensive care team for identifying, resolving and preventing drug therapy problem and medication error, admits in pediatric intensive care unit in their episode of hospital admission.

If a patient admits in the PICU several times during the same episode of hospital admission, the PICU-day is counts only by total number of days that this patient admit in PICU during study period.

1.8 Drug-day

Drug-day is defined as the total number of day which drugs were taken for each PICU patient during admission in the PICU.

1.9 Medication

A medication in the present study was defined as “drug” by World Health Organization (WHO) as “any substance with the potential to prevent or cure disease or enhance physical or mental welfare, and in pharmacology to any chemical agent that alters the biochemical physiological processes of tissues or organisms (115). Therefore, intravenous fluids, intravenous nutritional products, gases, and blood products are excluded.

1.10 Medication item

A medication item was defined as a medication which specific dosage form and strength.

1.11 Medication order

1.11.1 Order for continue

An order for continue was defined as a medication that physician prescribe for patient continually until discontinue ordering.

1.11.2 Order for one-time

An order for one time was defined as a medication that physician prescribe for patient single time.

1.11.3 Order as patient need

A order as patient need was defined as a medication that physician prescribe for patient, both order for continue and order for one time, but will be given to patients when patient required the medication.

2. Study design

Applied research is performed by the research pharmacist to determine role of pharmacist in development the high-alert medications protocol. The

frequencies of MEs and DRPs by prospective detecting used to propose a high alert medication protocol and apply to at least one patient.

3. Ethical Approval

This study was reviewed and approved by Committee on Human Rights Related to Researches Involving Human Subjects, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, based on the Declaration of Helsinki, protocol number 12-49-44.

4. Study population

4.1 The sample sized

The sample sized was estimated using the following formula (116).

$$n = \frac{Z^2_{\alpha}\, p\,(1-p)}{d^2}$$

where n = number of patients

Z_{α} = Z score at probability of $\alpha/2 \leq 0.05$ (90% confidence interval) = 1.645

p = proportion of patients whose drug therapy problem were identified from Kraitep (32)

d = allowable error of proportion of patients whose medication errors were identified from Kraitep (32)

The result from Kraitep showed that the incidences of medication errors in PICU at QSNICH was 46% (p = 0.46) of admitted patients, by 47 out of 100 patients. Allowable error in this study was determined at 30% of proportion of patients whose medication errors were identified (d = 0.138). Therefore, the sample size used in this study according to above formula was:

$$n = \frac{(1.285)^2\,(0.46)\,(1-0.46)}{(0.092)^2}$$

$$= 35.3 \text{ patients}$$

Therefore the number of recruited patients in the study period should be at least 36 patients.

4.2 Inclusion criteria

a) All patients who admitted at PICU of Ramathibodi Hospital, a university hospital of Mahidol University.

b) Patient who admitted on this ward and received at least one continue-order medication.

4.3 Exclusion criteria:

Patients who will be discharged or referred to another care unit within 24 hours after admitting in PICU.

5. Period of study

The study period start from June 2006 to August 2007. Data collection period start from March 1, 2007 to May 31, 2007.

6. Process

6.1 The frequencies and characteristics of DTPs and MEs before implementation the high-alert medication management protocol.

6.1.1 Preparation of documents for data collection. i.e., patient's profile (Appendix A), medication errors and drug related problems (Appendix B) and drug information service (Appendix C).

6.1.2 The research pharmacist reviewed both patient chart and medication profile of patients who will be admitted in PICU following to inclusion criteria and then record patients' information in the data collecting form (Appendix A).

6.1.3 Activities of the research pharmacist participation on patient care team.

6.1.3.1 Both patient charts and medication profiles were reviewed and recorded in patients' information in the data collecting form (Appendix A). The research pharmacist identified DTPs and MEs and resolve patients' problems base on literature review on drug information sources and then record in the data collecting form (Appendix B).

6.1.3.2 Daily rounds with patient care team, which compose of an attending physician, resident physicians and respiratory nurses,

between 10-12 a.m. on every working day was performed. During the round, research pharmacist intervened and discussed for identifying DTPs and MEs and appropriating management for all PICU patients. Result of pharmacist's interventions were recorded in the data collecting form (Appendix B). Providing drug information for patient-related questions during round will be also recorded in the data collecting form (Appendix C).

6.1.3.3 The research pharmacist provided 24-hour on-call service in off-working hours for emergency patient-related question. Providing drug information was recorded in the data collecting form (Appendix C).

6.1.4 Daily (including weekend and holidays) patient monitoring by the research pharmacist was performed as 6.1.3.1-6.1.3.2 until the patients discharge or move to another care unit.

6.1.5 The research pharmacist summarized patients profile summary, total number of DTPs and MEs when the patient discharge or refer to another care unit in the data collection form (Appendix A and Appendix B).

6.1.6 Data collecting.

6.1.6.1 Patient information data (Appendix A).

- Demographic data: patient's name, gender, age, weight, hospital number, date of admission and PICU diagnosis.

- Pharmacotherapeutic data: past medical history, history of drug allergy, adverse reaction, current medication, dosage regimen, laboratory test, history of non-prescription drug used, drug-day.

6.1.6.2 DTPs and MEs data (Appendix B).

- The number and category of DTPs, MEs.

- The number and category of research pharmacist's intervention.

- The number of accepted intervention, partially accepted intervention and not accepted intervention.

6.1.6.3 DIS data (Appendix C).

- The number and category of requested question, and requestor.

- The number of emergency question.

6.1.7 The research pharmacist reported all type E to I of MEs and DRPs and the pharmacist's intervention to an attending physician weekly.

6.1.8 Data presentation and analysis.

6.1.8.1 Patients' demographic data

- The number and percentage of categorized subgroup of gender and patients' admission diagnosis.

- The mean of age and body weight of PICU patients.

- The number and percentage of categorized subgroup of medication orders and medication items.

6.1.8.2 Drug therapy problems (DTPs) data

- The number and percentage of each category of DTPs, DTPs per patient, DTPs per PICU-day, DTPs per 100 medication orders, DTPs per 100 drug-days, category of pharmacist intervention for DTPs and number of acceptance.

6.1.8.3 Medication error (MEs) data

- The number and percentage of each category of MEs, MEs per patient, MEs per PICU-day, MEs per 100 medication orders, MEs per 100 drug-days, details of MEs and pharmacist intervention for MEs.

6.1.8.4 Drug information service (DIS) data

- The number and percentage of each category of requested question, categorized subgroup of requestor, number of emergency question.

6.2 High-alert medication management protocol development.

6.2.1 The research pharmacist will proposed at least one medication item that should be develop as high alert medication management protocol following criteria:

- The medication items which were in top 10 medications caused all types DTPs.

- The medication items caused DTPs types A to D and result in potentially lethal to patient.

- The medication items caused DTPs types E to I.
- The medication items which were in top 10 medications caused all types MEs.
- The medication items caused MEs types A to D and result in potentially lethal to patient.
- The medication caused MEs types E to I.

6.2.2 The research pharmacist proposed high alert medication management protocol that includes:

- Prescribing policy.
- Medication preparation and administration policy.
- Medication safety monitoring and management policy.

6.2.3 The proposed protocol was used in at least one patient as case study.

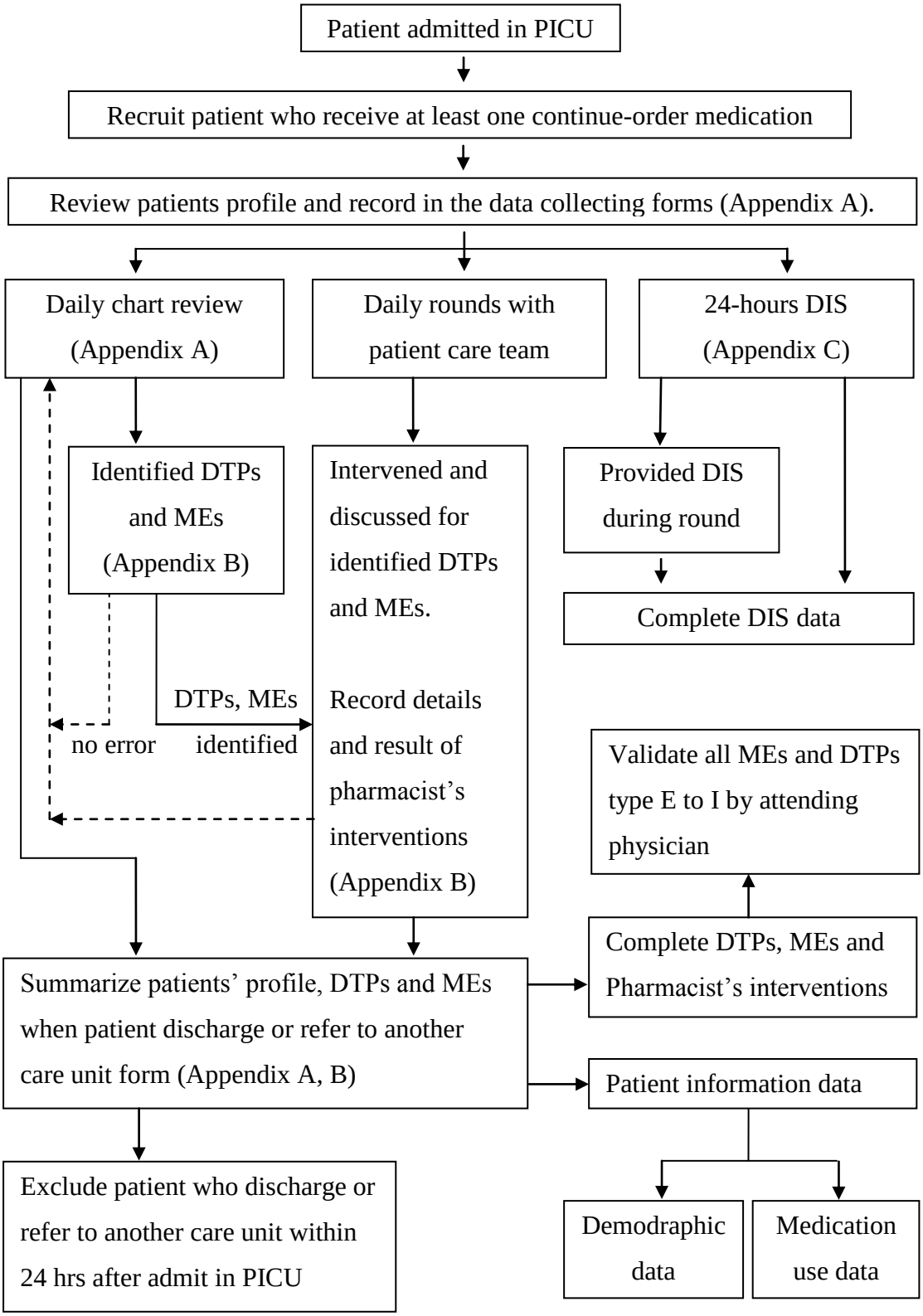

Figure 3 Flow chart of patient monitoring by research pharmacist

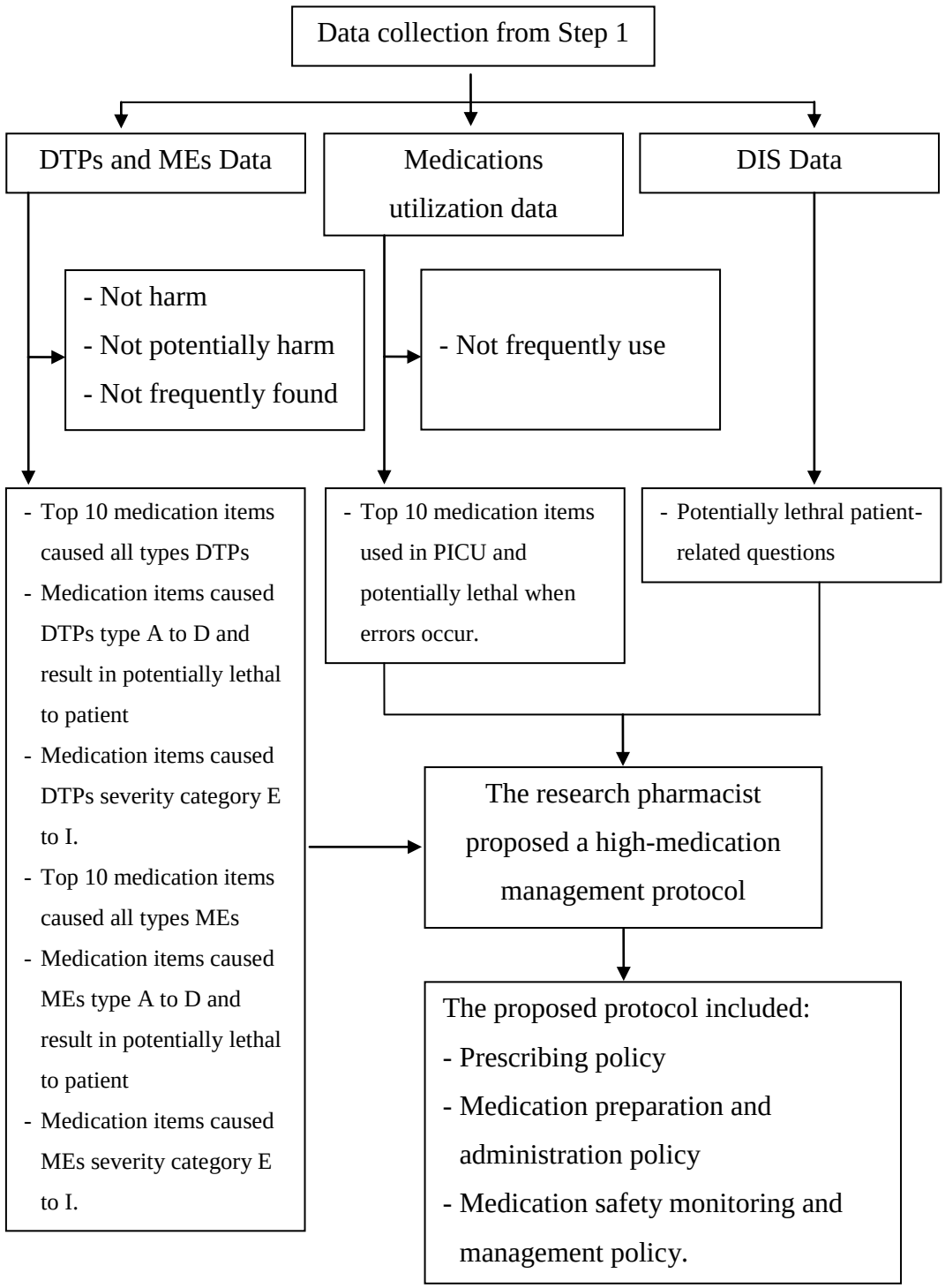

Figure 4 Study work flow

CHAPTER IV
RESULTS

During the study period, 43 patients were recruited during March 1, 2007 to May 31, 2007 following the conclusion criteria. The results of this study were presented as following.

I Patient's demographic data.

II Medication utilization.

III Drug therapy problems.

IV Medication errors.

V Pharmacist's interventions and drug information services.

VI Management of high alert medication.

I Patient's demographic data

Characteristics of all patients are presented in Table 1. An average patient's age was 61.8 months. The age ranged from 1 month to 192 months (Standard deviation = 54.6 months). Range of patients' body weight was 2.0 kg to 79.0 kg, with the average 18.8 kg. Twenty four (55.8%) patients were female. Range of patients' body weight was 2.0 to 79.0 kg. Patients' admission diagnosis was categorized and described in Table 1.

Table 1 Admission diagnosis of patients

Admission diagnosis category	**Number of patients (%)**
Respiratory systems	9 (20.9)
Congenital disorders	7 (16.3)
Circulatory systems	5 (11.6)
Nervous systems	3 (7.0)
Musculoskeletal systems	3 (7.0)
Critical laboratory finding	3 (7.0)
Health status and health services	3 (7.0)
Neoplasm	2 (4.7)
Digestive systems	2 (4.7)
External causes of morbidity and mortality	2 (4.7)
Conditions in the perinatal period	2 (4.7)
Total	**43 (100)**

The others underlying factor that associated with drug therapy were presented in Table 2. Two out of 43 patients (4.7%) have allergic history.

Table 2 Underlying factor of patients

Characteristics	**Number of patients (%)**
Hepatic impairments	4 (9.3)
Renal impairments	7 (16.3)

Total number of PICU-day in this study period was 391 days. An average PICU-day was 9.1 $\pm$ 12.6 days, range from 2 to 77 days. Most of the patients (70%) needed intensive care less than the average PICU-day of this study. There are 674 medication orders from physicians. Each patient was received at least 4 medication orders to maximum 38 medication orders. An average medication orders per patient was 15.7 $\pm$ 9.5 orders. PICU-day and number of medication orders of each patient shown in Table 3.

Table 3 PICU-days and number of medication order for each patient

Patient number	PICU-day (days)	Number of medication orders (orders)
1	3	10
2	4	12
3	77	38
4	3	15
5	4	6
6	35	28
7	13	24
8	3	13
9	13	20
10	5	14
11	26	38
12	4	6
13	8	17
14	9	24
15	5	4
16	2	8
17	2	8
18	2	13
19	4	14
20	5	5
21	5	21
22	3	16
23	3	9
24	2	6
25	2	6
26	8	15
27	12	11
28	4	9
29	4	8
30	4	22
31	3	5
32	7	8
33	4	6
34	2	8
35	19	30
36	5	15
37	20	19
38	5	11
39	11	29
40	7	11
41	12	28
42	11	34
43	11	30
Total	**391**	**674**

II Medication utilization

Six hundred and seventy-four medications orders can be categorized into 3 types of medication orders as presented in Table 4.

Table 4 Types of medication orders

Type of medication orders	**Number of orders (%)**
Order for continue	367 (54.5)
Order for one-time	265 (39.3)
Order as patient need	42 (6.2)
Total	**674 (100)**

One hundred and eighty-two medication items were used by 674 medication orders. Medication items can be categorized into 59 medications group by AHFS pharmacologic categorization (117) as described in Table 5. The common medication groups, which are ranked by number of medication items, were antibacterials (24 items), replacement electrolytes (14 items), anticonvulsants (8 items) and analgesic and antipyretics (8 items).

Most medications items, which were prescribed by physician, were fentanyl inj., midazolam inj. and furosemide inj. by 37, 28 and 25 orders respectively. Details of all are described in Appendix D.

Quantity of medication items usage presented by number of total drug-days. Total drug-days of all 43 patients were 4,543 days. The common medication groups used in PICU, were ranked by number of total drug-days, were replacement electrolytes (603 drug-days), antibacterial (450 drug-days) and anxiolytics sedatives and hypnotics (420 drug-days). Table 6 shows number of total drug days of each medication groups.

Most medications items, which caused the highest total drug-days, were fentanyl inj., and midazolam inj., by 259 and 216 drug-days, respectively. Total drug-days of each medication items are also described in Appendix D.

Table 5 Medication groups, AHFS pharmacologic categorization and number of medication items

Medication group	AHFS pharmacologic categorization	Number of Medications items (items)
Antibacterials	8.12	24
Replacement electrolytes	40.12	14
Anticonvulsants	28.12	8
Analgesics and antipyretics	28.8	8
Antiulcer agents and acid suppressants	56.28	7
Adrenals	68.4	7
Anxiolytics, sedatives, and hypnotics	28.4	6
Adrenergic agents	12.8	6
Vasodilating agents	24.12	6
Antifungals	8.14	5
Diuretics	40.28	5
Immunosuppressive agents	92.44	5
Topical anti-infectives	84.4	5
Antineoplastic agents	10	4
Calcium-channel blocking agents	24.28	4
EENT anti-inflammatory agents	52.8	4
Antidiabetic Agents	68.2	3
Antihistamine Drugs	4	3
EENT Anti-infectives	52.4	3
Miscellaneous		52
Total		**182**

Table 6 Medication groups, AHFS pharmacologic categorization and total drug-days

Medication group	**AHFS pharmacologic categorization**	**Total drug-days (days)**
Replacement Electrolytes	40.12	603
Antibacterials	8.12	450
Anxiolytics, Sedatives, and Hypnotics	28.4	420
Analgesics and Antipyretics	28.8	407
Diuretics	40.28	314
Adrenergic Agents	12.8	242
Antiulcer Agents and Acid Suppressants	56.28	230
Multivitamin Preparations	88.28	183
Adrenals	68.4	178
Renin-Angiotensin-Aldosterone System Inhibitors	24.32	154
Vasodilating Agents	24.12	151
Anticonvulsants	28.12	148
Calcium-Channel Blocking Agents	24.28	104
EENT Anti-inflammatory Agents	52.8	80
Antiglaucoma Agents	52.40	79
Skeletal Muscle Relaxants	12.20	64
Topical Anti-infectives	84.4	58
Immunosuppressive Agents	92.44	50
Miscellaneous		628
Total		**4,543**

Replacement electrolytes were the most used during study period by 603 drug-days. None replacement electrolyte was order as patient's need. There is NSS neb. That categorized in this group but did not used as replacement electrolytes. It used as intranasal spray to restores moisture to pulmonary system.

The most common antibacterial usage were meropenem inj. (13 orders, 74 drug-days), ceftriaxone inj. (13 orders, 65 drug-days), and amikacin inj. (9 orders, 51 drug-days). Most common antibacterials usage were intravenous form, therefore 8 oral out of 24 antibacterials were ordered. Most of medication orders' type was order for continues, by 83 out of 84 orders (98.8%). Only one time order was neomycin tab.

Anxiolytics, sedatives, and hypnotics, which common used, were midazolam inj. and chloral hydrate sol. by 216 drug-days (28 orders) and 182 drug-days (21 orders), respectively. Most medication orders were one-time order (77.8%) and as patients' need (18.5%).

Fentanyl inj. was analgesics and antipyretics, which used for continuous sedation (118). Most of analgesics and antipyretics orders were orders for one-time and as patient's need, by 35 orders (51.5%) and 29 orders (42.6%) out of 68 orders.

Furosemide and HCTZ, which were common diuretics, used in both injection and oral form. Eleven HCTZ orders (9 HCTZ syr. and 2 HCTZ tab.) were used in 181 drug days (142 and 39 drug-days, respectively), whereas furosemide orders' amount is greater than HCTZ but have lower drug-days of HCTZ. Thirty furosemide orders (25 furosemide inj. orders, 5 furosemide syr. orders) were used in 132 drug days (116 and 16 drug-days respectively). There was one mannitol for one-time. Although mannitol is one of diuretics, it can be used for decreasing intracranial pressure/cerebral edema (118) as well.

Both injection and inhalation form of adrenergic agents were used. The common injection form of adrenergic agents usage were dopamine inj. (8 orders, 40 drug-days) and dobutamine inj. (4 orders, 38 drug-days), while the most common inhalation adrenergic agents was salbutamol NB. Inhalation adrenergic agents, which combined with ipratropium (anticholonergic agents) also categorized in this group. Most medication order type was order for one-time (81.1%).

Antiulcer agents and acid suppressants also commonly used in PICU. Lansoprazole tab. (5 orders, 66 drug-days), ranitidine inj. (16 orders, 64 drug-days), omeprazole inj. (10 orders, 52 drug-days) and esomeprazole inj. (6 orders, 32 drug-days) were common medication orders. Most orders were prescribing for continue, by 39 out of 40 orders (97.5%).

Intravenous multivitamin preparations, which added in total parenteral nutrition, were not counted as medication items. Only oral multivitamin preparation used was MTV syr. (15 orders, 180 drug-days).

Adrenals medications consist of many formulations for several indication: tablet, injection and inhalation. The most common were prednisolone tab. (7 orders, 81 drug-days) and methyl prednisolone inj. (11 orders, 42 drug days).

Common anticonvulsants usage during study period was phenobarbital. Phenobarbital was used by 9 orders, phenobarbital tab. (2 orders, 78 drug-days) and phenobarbital inj. (7 orders, 25 drug days)**.** The most medication order type was order for continue by 15 orders (60%).

Although each medications were ordered once or twice, they also used for a long time. Alprostadil inj. (prostaglandins E1), was ordered once, had 76 drug-days that was the longest drug-day in this study.

Details of medication orders and drug-days of each medication items described in Appendix D.

III Drug therapy problems (DTPs) data

Two hundred and sixteen DTPs were identified in 37 patients (86%) and average DTPs per patient was 5.1 or 70.8 DTPs per 100 PICU-day. In other words, 4.8 DTPs per 100 drug-days or 32 DTPs per 100 medication orders were identified.

In those 37 patients, DTPs identified, DTPs were founded in total 360 PICU-days or 60 DTPs per 100 PICU-days.

The number of DTPs classifying by type and severity are presented in Table 7. Safety was the most common type of DTPs (94%) was detected. Drug interaction, which is one type of drug safety type, was the most common DTPs by 192 events (89%).

Actual DTPs which were reached patient were categorized in severity category C-E. Therefore, total actual DTPs were 210 (97.2%), the remaining were categorized in severity category A-B, which does not reach patient. DTPs. DTPs caused patient harm (reached patient and need interventions) only 3 events (1.4%), which were in severity category E.

Table 7 Number of DTPs classifying by type and severity

Type of DTPs	Number of DTPs classified by severity category					Total (%)
	A	**B**	**C**	**D**	**E**	
Appropriate indication						
Need additional drug Therapy	0	0	1	0	0	1 (0.5)
Efficacy						
Dosage too low	0	1	2	1	0	4 (1.8)
Dosage too high	1	4	3	5	0	13 (6.0)
Safety						
Adverse drug reaction	0	0	3	0	3	6 (2.8)
Drug interaction	0	0	15	177	0	192 (88.9)
Total	**1**	**5**	**24**	**183**	**3**	**216 (100)**

The common medication item that causing DTPs were midazolam inj., furosemide inj., and chloral hydrate sol. by 23, 20 and 18, respectively.

Digoxin elixir was the most medication item that caused the highest number of DTPs per 100 medication orders (by 400 DTPs per 100 medication orders) and caused the highest DTPs per 100 drug days (by 400 DTPs per 100 drug-days).

Detail of the number of DTPs, DTPs per 100 medication order, DTPs per 100 drug-days classifying by medication items are shown in Table 8.

Table 8 The number of DTPs, DTPs per 100 medication order, DTPs per 100 drug-days classifying by medication items

Medication itemss	Number of DTPs	Number of DTPs per 100 medication orders	Number of DTPs per 100 drug-days
Midazolam inj.	20	80.0	17.2
Furosemide inj.	18	112.5	28.1
Chloral hydrate sol.	15	53.6	6.9
Ranitidine inj.	11	157.1	57.9
Vecuronium inj.	10	166.7	90.9
Amikacin inj.	8	38.1	4.4
Spironolactone inj.	8	72.7	12.5
HCTZ syr	8	114.3	32.0
Omeprazole inj.	7	140.0	43.8
Phenytoin inj.	6	75.0	21.4
Phenobarbital inj.	6	66.7	11.8
Furosemide susp.	5	50.0	9.6
Dexamethasone inj.	5	45.5	11.9
Methylprednisolone inj.	5	38.5	10.0
KCl elixir	4	36.4	9.3
KCl inj.	3	37.5	13.6
Digoxin elixir	4	400.0	400.0
Ceftazidime inj.	4	40.0	3.6
Captopril syr	4	30.8	6.2
Paracetamol drop	4	133.3	40.0
Prednisolone tab.	4	200.0	57.1
50% MgSO4 inj.	3	150.0	42.9
Ceftriaxine inj.	3	33.3	2.1
Fentanyl inj.	3	60.0	7.5
Lansoprazole tab.	2	200.0	100.0
Tacrolimus cap.	2	200.0	100.0
Nifedipine tab.	2	25.0	5.7
Voriconazole inj.	2	40.0	4.5
Cefotaxime inj.	2	40.0	4.5
Phenytoin Infratab.	2	100.0	22.2
Hydrocortisone inj.	2	5.4	0.8
Ferous Sulfate drop	2	100.0	40.0
Cotrimoxazole inj.	2	28.6	2.5

Table 8 The number of DTPs, DTPs per 100 medication order, DTPs per 100 drug-days classifying by medication items (cont.)

Medication itemss	Number of DTPs	Number of DTPs per 100 medication orders	Number of DTPs per 100 drug-days
Aspirin gr.I tab.	2	100.0	16.7
CaCO3 tab.	2	200.0	66.7
HCTZ tab.	2	100.0	33.3
Phenobarbital tab.	2	33.3	5.1
Haloperidol inj.	1	33.3	4.2
Heparin inj.	1	100.0	25.0
Ketoconazole tab.	1	100.0	25.0
Diazepam inj.	1	100.0	20.0
Tacrolimus inj.	1	100.0	20.0
Bosentan tab.	1	100.0	16.7
Nifedipine syr.	1	25.0	3.6
Vancomycin inj.	1	100.0	12.5
Mycophenolate moferil	1	50.0	2.6
Chlorpheniramine inj.	1	50.0	2.6
Omeprazole cap.	1	50.0	4.8
Sildenafil tab.	1	100.0	9.1
Gentamicin inj.	1	100.0	9.1
Hydrocortisone tab.	1	100.0	9.1
Isoniazid tab.	1	100.0	8.3
Erythromycin susp.	1	100.0	7.7
Phosphate sol.	1	16.7	1.3
Acetazolamide susp.	1	100.0	7.1
Erythromycin tab.	1	100.0	5.3
Montelukast tab.	1	100.0	5.3
Doxofylline sol.	1	50.0	1.3
Azathioprine tab.	1	100.0	3.8
Total	**216**		

IV Medication errors (MEs) data

From total identifying 216 DTPs, 197 DTPs might not be justified as medication used process errors due to 192 were either unavoidable drug interaction or non-contraindicated drug interaction, 4 were unpreventable adverse drug reaction and one was patients need additional drug therapy.

The remaining 19 DTPs resulted by medication use process errors, or MEs, shown in Table 9.

Table 9 Number of DTPs categorized by medication used process error

Medication used process error	**Number of DTPs (%)**
No error	**197 (91.2)**
Error	**19 (8.8)**
Prescribing error	16 (7.4)
Transcribing error	1 (0.5)
Administration error	2 (0.9)
Total	**216 (100)**

MEs were identified in 12 patients (27.9%) and average MEs per patient was 0.4 or 4.9 MEs per 100 PICU-day. In other words, 4.1 MEs per 1,000 drug-days or 2.81 MEs per 100 medication orders were identified. Characteristic of MEs which can be categorized by DTPs as shown in Table 10.

Table 10 Number, characteristic and severity of MEs.

Characteristic of MEs	**Number of DTPs classified by severity category**					**Total (%)**
	A	**B**	**C**	**D**	**E**	
Dosage too low		1	2	1		4 (20.0)
Dosage too high	1	4	3	5		13 (68.5)
Adverse drug reaction					2	2 (10.5)
Total	**1**	**5**	**5**	**6**	**2**	**19 (100)**

In those 12 patients who were identified MEs, MEs were founded in 199 PICU-days or 9.5 MEs per 100 PICU-days. The research pharmacist made 19 interventions to prevent MEs and resolve DTPs. The details of management of MEs and pharmacist's intervention were described in Table 11-22.

Table 11 Detail of identified MEs in patient no. 1 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 1 (case no. 3) A 2 months old, Thai male infant admitted after post PA banding operation. During admission, patients required peritoneal dialysis.	
4 MEs were detected.	**4 interventions performed.**
- Vancomycin inj. dosage needed to reduce according to patients Cl_{cr}. MEs: prescribing error DRPs: dose too high Severity category: D	- Intervention to: physician Pharmacist suggested physician to adjust vancomycin inj. dosage by therapeutic drug monitoring and pharmacist's calculation. Monitoring renal function for safety was required. Acceptance: accepted
- Phenobarbital inj. dosage needed to reduce according to patients Cl_{cr}. MEs: prescribing error DRPs: dose too high Severity category: D	- Intervention to: physician Pharmacist suggested physician to adjust phenobarbital inj. dosage by therapeutic drug monitoring and pharmacist's calculation. Monitoring sign of seizure and toxicity were required. Acceptance: accepted

Table 11 Detail of identified MEs in patient no. 1 and pharmacist's intervention (cont.)

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 1 (case no. 3) (cont.)	
- Patients had seizure during night time then physician order phenobarbital inj. 40 mg IV push stat and nurse were administration as orders. After injection, patient developed bradycardia and required intervention. MEs: prescribing error, administration error DRPs: adverse reaction Severity category: E	- Intervention to: physician, nurse Pharmacists were identified that patient's bradycardia probable come from rapid phenobarbital inj. administration more than 30 mg/min. Moreover, Patient has underlying heart disease that may increase risk for ADR. Acceptance: accepted

Table 12 Detail of identified MEs in patient no. 2 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 2 (case no. 4) A 6 months old, Thai male infant admitted with pneumonitis with right upper lung atelectasis.	
1 ME was detected.	**1 intervention performed.**
- Digoxin elixir dosage needed to reduce according to patients Cl_{cr} = 45 ml/min. MEs: prescribing error DRPs: dose too high Severity category: D	- Intervention to: physician Pharmacist suggested physician to reduce digoxin elixir to 25-75% of normal dose and increase interval to 36 hrs. Monitoring QT-wave and drug level when achieve steady state were required. Acceptance: accepted

Table 13 Detail of identified MEs in patient no. 3 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 3 (case no. 6) A 5 years old, Thai boy admitted with pneumothorax.	
2 MEs were detected. - Montelukast tab. was ordered ½ tab. PO OD which did not specific time of administration. Nurse administrated in the morning instead of nighttime. MEs: prescribing error, administration error DRPs: dosage too low Severity category: C	**2 interventions performed.** - Intervention to: physician, nurse Pharmacist intervened physician to specific time of administration in physician order and intervened nurse to change schedule of administration. Acceptance: accepted

Table 14 Detail of identified MEs in patient no. 4 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 4 (case no. 7) A 3 years old, Thai boy. Admitted with leiomyosarcoma.	
2 MEs were detected. - Nurse at PICU cannot transcribe when to discontinue ceftazidime inj. according to physician's order 21 days ago from previous ward. MEs: prescribing error, transcribing error DRPs: dose too high Severity category: C	**2 interventions performed.** - Intervention to: physician, nurse Pharmacist notify nurse and asked physician in PICU to confirm discontinuation of ceftazidime inj. according to the treatment plan. Physician ordered to discontinue ceftazidime inj. again. Acceptance: accepted

Table 15 Detail of identified MEs in patient no. 5 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 5 (case no. 10) An 8 months old, Thai male infant admitted with Pneumonia R/O PCP with HIV precaution.	
2 MEs were detected. - Cotrimoxazole inj. IV drip rate too high. MEs: prescribing error, administration error DRPs: dose too high Severity category: D	**2 interventions performed.** - Intervention to: physician, nurse Pharmacist notified nurse and intervened physician to increase infusion rate of cotrimoxazole inj. from 30 mins. to 60 mins. to prevent ADR, thrombocytopenia. Blood chemistry was needed to be monitor. Acceptance: accepted

Table 16 Detail of identified MEs in patient no. 6 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 6 (case no. 11) A 6 months old, Thai male infant admitted with interstitial lung disease.	
1 ME was detected. - Cotrimoxazole inj. concentration was too high. Physician ordered cotrimoxazole inj. 30 mg to be diluted in 20 ml of D5W. MEs: prescribing error DRPs: dose too high Severity category: B	**1 intervention performed.** - Intervention to: physician Pharmacists suggested physician to increase volume of D5W to 40 ml for preventing crystallization of drug that may cause phlebitis. Monitoring phlebitis at injection site was required. Acceptance: accepted.

Table 17 Detail of identified MEs in patient no. 7 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 7 (case no. 13) A 3 years old, Thai girl admitted with complete AV canal with portal HT.	
1 ME was detected. - Physician switched order of phenobarbital inj. 30 mg IV q 12 hrs to phenobarbital tab. 30 mg PO without increasing dose. MEs: prescribing error DRPs: dose too low Severity category: D	**1 intervention performed.** - Intervention to: physician Pharmacist suggested that appropriate dose should be phenobarbital tab. (30 mg) 1½ tab. PO in the morning and 1 tab. PO before bedtime. Therapeutic drug monitoring of phenobarbital was required in next 7 days. Acceptance: accepted.

Table 18 Detail of identified MEs in patient no. 8 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 8 (case no. 14) A 3 years old, Thai boy admitted after liver transplant. Patient's weight was 14 kg.	
1 ME was detected. - Tacrolimus dosage too high. Physician want to order tacrolimus 0.01 mg/kg/ day but order tacrolimus inj. 3.4 mg dilute to 24 ml IV infusion. MEs: prescribing error DRPs: dose too high Severity category: B	**1 intervention performed.** - Intervention to: physician Pharmacist suggested corrected dose must be tacrolimus 0.14 mg dilute to 24 ml IV infusion. Acceptance: accepted.

Table 19 Detail of identified MEs in patient no. 9 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 9 (case no. 29) An 8 years old, Thai female infant admitted with AVM rupture.	
1 ME was detected. - Physician ordered maintenance dose of phetytoin inj. 5 mg/kg/day. MEs: prescribing error DRPs: dose too low Severity category: C	**1 intervention performed.** - Intervention to: physician Pharmacist suggested recommended maintenance dose of phenytoin inj. in pediatric patient age between 7-9 years old is 7-8 mg/kg/day. Acceptance: accepted.

Table 20 Detail of identified MEs in patient no. 10 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 10 (case no. 33) An 1 year old, Thai boy admitted with cyanide poisoning.	
1 ME was detected. - Patients developed seizure so physician order phenobarbital inj. 200 mg IV push stat. MEs: prescribing error DRPs: dose too high Severity category: B	**1 intervention performed.** - Intervention to: physician Pharmacists intervened physician to change administration order from IV push stat to IV drip in 10 mins., because administration phenobarbital inj. rate more than 30 mg/min may result to cardiovascular adverse reaction. Acceptance: accepted.

Table 21 Detail of identified MEs in patient no. 11 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 11 (case no. 35) A 5 months old, Thai male infant admitted with complex heart disease for Glenn's operation.	
2 MEs were detected.	**2 interventions performed.**
- Physician ordered fentanyl 0.3 mg/kg/ dose instead of 3 mcg/kg/dose. MEs: prescribing error DRPs: dose too high Severity category: B	- Intervention to: physician Pharmacists intervened physician to correct order. Recommeded dose of fentanyl for adjunct to anesthesia given 2-3 mcg/kg/dose. Acceptance: accepted.
- Unclearified medication order. Physician ordered 7.5% $NaHCO_3$ inj. 3 ml dilute IV but did not specific solution, concentration and rate of administration. MEs: prescribing error DRPs: dose too high Severity category: A	- Intervention to: physician Pharmacists intervened physician to clearified order and suggested that 7.5% $NaHCO_3$ can be diluted by NS, D5W, or TPN and must be infuse over 4-8 hours. Acceptance: accepted.

Table 22 Detail of identified MEs in patient no. 12 and pharmacist's intervention

Patients information and details of MEs and severity	**Pharmacist's intervention and acceptance**
Patient no. 12 (case no. 36) A 8 years old, Thai girl admitted with severe headache from SLE.	
1 ME was detected. - Phenobarbital prescribing error. Patients developed seizure so physician order phenobarbital 400 mg IV push stat. MEs: prescribing error DRPs: dose too high Severity category: B	**1 intervention performed.** - Intervention to: physician Pharmacists intervened physician to change administration order from IV push stat to IV drip in 15 mins. Rapid administration phenobarbital rate more than 30 mg/min may result cardiovascular adverse reaction. Acceptance: accepted.

Medication mostly caused MEs was phenobarbital inj. by 5 MEs (100 MEs per 100 medication orders or 12.5 MEs per 100 drug-days) as shown in Table 23. By the way, phenobarbital tab. also caused MEs by 1 MEs (50 MEs per 100 medication orders or 1.3 MEs per 100 drug-days). Total MEs from phenobarbital was 6 events by 5 prescribing errors and 1 administration error. DRPs category of these MEs were "dose too high" and "adverse reaction". MEs from phenobarbital inj. cause one patient harm and need to treat that symptom.

Pharmacist can identified 6 MEs (31.5%) before its reach patients. All prevented MEs were prescription errors. Two of these prevented MEs (33.3%) were phenobarbital dosing error.

Table 23 Medication items caused MEs, number of MEs per 100 medication orders and number of MEs per 100 drug-days.

Medications items	Number of MEs	Number of MEs per 100 medication orders (medication orders)	Number of MEs per 100 drug-days (drug-days)
Phenobarbital inj.	5	100.0 (5)	12.5 (40)
Cotrimoxazole inj.	3	100.0 (3)	12.5 (24)
Ceftazidime inj.	2	28.6 (7)	80 (25)
Montelukast tab.	2	200.0 (1)	10.5 (19)
Digoxin elixir	1	25.0 (4)	7.7 (13)
Fentanyl inj.	1	2.7 (37)	0.4 (259)
7.5% $NaHCO_3$ inj.	1	33.3 (3)	20.0 (5)
Phenobarnital tab.	1	50.0 (2)	1.3 (78)
Phenytoin inj.	1	14.3 (7)	5.3 (19)
Tacrolimus inj	1	100 (1)	25.0 (4)
Vancomycin inj.	1	12.5 (8)	2.5 (40)
Total	**19**		

V Pharmacist's interventions and drug information service

Two hundred and sixteen interventions were performed by pharmacist which were equal to 216 DTPs. Identifying of drug interactions were recommended by 192 (88.9%). Pharmacist's intervention categorized as shown in Table 24.

Table 24 Pharmacists interventions

Pharmacists intervention	Number of interventions (%)
Identifying of drug interactions	192 (88.9)
Compatibility/stability/route of administration recommendations	8 (3.8)
Dosage/regimen recommendation	6 (2.7)
Identified adverse drug reaction	6 (2.7)
Therapeutic drug monitoring	2 (0.9)
Clarification or correction of order	1 (0.5)
Drug of choice recommendations	1 (0.5)
Total	216 (100)

Most pharmacist's interventions were intervention to physician by 210 (97.2%). Ninety-eight percent of pharmacist interventions were accepted and implemented by health care team. Acceptances of pharmacist's interventions show in Table 25.

Table 25 Acceptances of pharmacist's interventions

Acceptance of pharmacist's intervention	Number of interventions to health care team		
	Physician	Nurse	Total (%)
Accepted	206	6	212 (98.2)
Partially accept	2		2 (0.9)
Not accept	2		2 (0.9)
Total	**210**	**6**	**216 (100)**

Pharmacist providing drug information services are categorized as shown in Table 26. There was none emergency DIS request when pharmacist was not available in PICU. Most requested DIS were came from physician by 72 (64.9%). Most requested DIS from physician were "general product information" by 19 respectively. In the meanwhile, the most requested DIS from nurses were "compatibility/stability/ route of administration" by 21.

Table 26 Pharmacist providing drug information services

Acceptance of pharmacist's intervention	Number of DIS requested by health care team		
	Physician	Nurse	Total (%)
Availability of dosage forms	8	3	11 (9.9)
Identification of product	1		1 (0.9)
General product information	19	12	31 (28.0)
Compatibility/stability/route of administration	6	21	27 (24.3)
Drug interaction	14		14 (12.6)
Pharmacokinetics	6		6 (5.4)
Drug of choice	2		2 (1.8)
Dosage/regimen recommendations	5		5 (4.5)
Adverse effects	9	3	12 (10.8)
Poisoning/toxicology	2		2 (1.8)
Total	**72**	**39**	**111 (100)**

VI Management of high alert medication

FMEA of phenobarbital inj.: phenobarbital inj. was selected to be high alert medication from following characteristic.

- Phenobarbital inj. was most anticonvulsants that have been used by 7 medication orders in 25 drug days. Frequently usage of phenobarbital inj. resulted in more DTPs and MEs than other anticonvulsants.
- Phenobarbital inj. caused DTPs by 6 events, which were 66.7 DTPs per 100 medication orders or 11.8 DTPs per 100 drug-days. Phenobarbital inj. also the most drug which caused 5 MEs (100 MEs per 100 medication orders or 12.5 MEs per 100 drug-days). More than 80% of DTPs from phenobarbital inj. were MEs by 5 out of 6. Only one patient harmed from MEs.
- Major cause of MEs was lack of product information in: dosage and regimen, dosage adjustment in renal insufficiency, administration and adverse reaction. Available and easily to accessed phenobarbital inj. prescribing and administration may prevent MEs

High alert medication management of phenobarbital inj.: research pharmacists proposed phenobarbital usage protocol (117-122) as present in Table 27. The proposed protocol was provided to physicians and nurses in PICU.

Table 27 Proposed phenobarbital usage protocol

Phenobarbital usage protocol
Phenobarbital tab. 30 mg. (gr. ½) **Gardenal® inj.** 200 mg/4 ml (lyophilized powder & solution) After reconstituted keep below 25 ^{O}C, protected from light, discard after 15 hrs. may be diluted with 0.45 or 0.9% sodium chloride and 5% dextrose solution
Usual pediatric dose: ▪ Epilepsy: loading dose: 10-20 mg/kg/dose maintenance dose: 3 to 6 mg/kg/day divided into 2-3 doses ▪ Sedation: 6 mg/kg/day divided into 3 doses
Dose adjustment: ▪ Renal impairment (CL_{cr} < 10 ml/min): dose reduction recommended, adjust dosing interval every 12 to 24 hrs. ▪ Hepatic impairment: dose reductions recommended. ▪ Supplement dose after hemodialysis: 100% ▪ Supplement dose after peritoneal dialysis: 50%
Contraindications: ▪ acute intermittent porphyria, personal or familial history ▪ hypersensitivity to barbiturates ▪ respiratory disease with evidence of dyspnea or obstruction ▪ history or sedative or hypnotic addiction
Precaution: ▪ The usefulness of parenteral phenobarbital sodium in terminating acute seizure episodes is limited by the slow onset of action of the drug. ▪ Parenterally administered phenobarbital sodium may be useful to prevent seizure recurrence after seizures are initially terminated with other anticonvulsants (e.g., diazepam, phenytoin sodium) or for termination of status epilepticus that does not respond to initial therapy with other anticonvulsants.
Administration information: ▪ Phenobarbital inj. is administered by IM or slow IV injection. ▪ IV administration of the drug should be reserved for emergency treatment of acute seizure states. ▪ The drug must be administered IV slowly at a rate not greater than 30 mg/mins.
Monitoring parameters: ▪ When phenobarbital inj. is administered IV, the onset of action usually occurs within 5 minutes and maximum effects are achieved within 30 minutes. ▪ Therapeutic plasma concentrations are usually attained after 2–3 weeks of a usual dosage. Plasma phenobarbital concentrations of greater than 50 mcg/ml may produce coma, and those in excess of 80 mcg/mL are potentially lethal. ▪ Patients should be closely monitored for notable changes in behavior that could indicate the emergence or worsening of suicidal thoughts or behavior or depression.

Table 27 Proposed phenobarbital usage protocol (cont.)

Phenobarbital usage protocol
Pharmacokinetics: ▪ Phenobarbital is a potent inducer of the enzymes involved in the metabolism of other drugs. ▪ Alkalinization of the urine and/or increasing the urinary flow rate substantially increases the rate of excretion of unchanged phenobarbital. Unmetabolized drug may accumulate in patients with oliguria or uremia.
Usual pediatric dose: ▪ Epilepsy: 3 to 6 mg/kg/day divided into 2-3 doses ▪ Sedation: 6 mg/kg/day divided into 3 doses
Drug interactions (contraindicate): ▪ Praziquantel (theoretical) ▪ Voriconazole (theoretical)

The proposed phenobarbital usage protocol was used in one patient as case study. Patient admitted in PICU during night shift that research pharmacist's service not available. Physician prescribed phenobarbital inj. according to phenobarbital usage protocol and nurses accepted physician orders and administrated phenobarbital inj. to patient correctly as describes in following case study.

Case study.

A 2 months old, Thai male infant was referred from another hospital. Patient's weight was 4.2 kg.

5 hrs PTA: Patient's mother was held patient on her shoulder. During she stepped down the stairs from 2nd floor, she was syncope. Patient fell down from his mother shoulder to the concrete floor. He was lay on the floor, eyes were wide-opened, no crying, no breathing.

His mother took him to the nearest hospital. CT brain found subarachnoid and intraventricular hemorrhage. He was referred to Ramathibodi hospital. At ER, patient developed seizure.

Impression: Severe head injury with intracerebral hemorrhage with subarachnoid hemorrhage with seizure.

After having surgery, patient admitted in PICU.

Medications:

1. Ranitidine 5 mg IV q 8 hrs.
2. Ceftriaxone inj. 375 mg IV OD
3. Phenobarbital inj. (15 mg/kg/dose)
   60 mg IV stat slow push in 5 mins.
   then Phenobarbital 30 mg tab. (6 mg/kd/day)
   ½ tab TF q 12 hrs.

Physician calculated the desired phenobarbital inj. dose according to proposed protocol as following. The physician order was correct and specific administration method. Physician chose phenobarbital tab. as maintenance dose because it was easier to administration and patient's gastrointestinal track did not have absorption problem. There was neither DTPs nor MEs in prescribing process.

Nurse transcribed physician's order correctly. Nurse reconstituted phenobarbital inj. with the solution, which came together, in a syringe and administration via infusion pump in 5 minutes according to the order. There was neither DTPs nor MEs in both transcribing and administration process.

During 9 days of patient's admission, he continued received phenobarbital tabs. There were no DTPs and MEs identified.

Proposed protocol can be used as a reference for prescribing, transcribing, administration and monitoring by physician and nurse when pharmacist not available in other medical wards.

CHAPTER V
DISCUSSION

The role of clinical pharmacy which was exclusively studied in PICU has been limited (19). This is because most clinical pharmacist's activities are initiated in adult patients. Moreover, the differences in pediatric pathophysiology often lead to more complicated pharmacotherapeutic management plan in adult patients. Accordingly, only a few studies had been performed in pediatric patients (24-26, 88-94). The past studies shown differences in settings, design, duration, size, methodology and definition. In addition, the objectives of the present study are not similar to those studies. As a result, the DTPs and ME of the present study seems to be different to explored.

All DTPs identified in the present study were in only 3 categories: appropriate indication, efficacy and safety, while patients' compliance was not identified since all medication orders, both in intravenous form and oral form, were completely administered to all PICU patients by PICU nurses. The majority of the present study found that MEs and DTPs might compare with the study in QSNICH which conducted by Kraitep (32).

Incidence of DTPs identified in the present study was 4.8 DTPs per 100 drug-days or 70.8 DTPs per 100 PICU-day. It was found that 89% of PICU patients were exposed to DTPs (both potential and actual problems). Most problems were involved in safety category, particularly drug interactions. However, all identified drug interactions were not contraindicated. Monitoring patient's laboratory parameters after administration of interaction medication items were required for safety.

In previous study, the incidence of DTPs identified in PICU patients (46%) including PICU patients were 1.8 DTPs per 100 drug-days or 19.6 DTPs per 100 PICU-days reported by Kraitep (32). Kraitep reported that nutritional support agents, such as multivitamin, trace elements and zinc sulfate, were the most caused

DTPs by patients needed supplement in both partial parenteral nutrition (PPN) and enteral nutrition to prevent or correct patient's nutritional status (32), whereas medication items that common that causing DTPs in the present study were sedative drugs.

Intravenous and enteral nutritional products were excluded in the present study due to they were prescribed by expert nutritionists instead of resident physicians in PICU. Differences in definition of terms and categorization of medication item between the present study and Kraitep's also reflected in differences of results. Total 102 DTPs were identified in Kraitep's study (32). Thirty four of them were DTPs of nutritional support agents. The remaining 68 DTPs term in 36 patients were identified according to the present study's definition of term. Unfortunately, patient days cannot be counted. Antimicrobial agents were common caused those DTPs.

The Kraitep's incidence was lower than the result of the present study by differentiation of patient's demographic data in age, body weight, length of stay and number of medication item used. The present study has 4 times greater medication items used and almost twice average length of stay. There were 1,514 drug-days per month in the present study, while Kraitep's were 957 drug-days per month. There were 182 medication items used while Kraitep's were used only 40 medication items (32). Most DTPs in the present study were drug interactions that resulted from variety medication items usage. Pharmacist's interventions for DTPs were also difference, according to different types or DTPs.

Twenty eight percent of PICU patients were exposed to MEs (4.1 MEs per 1,000 drug-days). Dosage too high was the most identified errors as same as wrong dose from Kraitep's study (32). Underlying factors of patients also associate with MEs. Insufficiency of renal function caused dosage too high that require adjusting. Most MEs were mostly categorized into severity category D (31.6%), only 10.5% were in severity category E and caused patient's harm. Phenobarbital inj. was mostly caused MEs (12.5 MEs per 100 drug-days). In contrast, with many intervention studies, patient's harm cannot identify and did not report most medication items that caused MEs (24-26, 32, 90-96).

In this study, it was found that one patient was harm from prescribing error and administration error according to the prescribing error. This patient received

loading dose of phenobarbital inj. rapid push and developed bradycardia. Although, the patient had underlying heart disease but cannot be rule out drug caused.

Some DTPs and MEs may require more than one intervention but research pharmacist counted as one according to each DTP. For example, One patients with renal failure were identified vancomycin inj. dosage too high and required TDM. Research pharmacists counted only one dosage/regimen recommendation. Actually, research pharmacist had to suggest physician to order for collection trough level of serum vancomycin in exactly time. And have to confirm with PICU nurse to collect sample in that time too. Identification of drug interactions by research pharmacist were mostly performed intervention for DTPs. Dosage/regimen suggestion was also mostly performed for MEs by research pharmacist. Total 216 interventions by research pharmacist were performed and were accepted by the health care team 210 interventions (97.2%). The acceptance was similar to the other study about pharmacist's intervention. Leape et all (82) made 366 recommendations related to drug ordering within 6 months, of which 362 (99%) were accepted by physicians. Strong and Tsang (89), found 361 interventions over 2 weeks; however, interventions resulting from drug information questions were not included. The physician acceptance rate (percentage of pharmacists' interventions accepted by physicians) was found to be 95.8%. Kraiteps made 103 interventions for identified MEs and DTPs during 6 months of study and were accept by 97.1%

The provided DIS of the present study mostly general product information to physicians and compatibility/stability/route of administration were provided to nurse, which were similar to Kraitep's study (32). Lack of medications' information might be one of the important causes of DTPs and MEs.

Pharmacists' services on medical settings can identified medical related errors (MEs and DTPs). Preventing and resolving of these errors can be made through clinical pharmacy activities (24-26, 32, 90-96). However, clinical pharmacists are not available to all medical settings. The real caused of problems has to be analyzed and further planning about prevention.

The present study also developed the medication usage protocol from all identified DTPs, MEs and number of medication used. FMEA were used as a tool to select the high alert medications. All top 10 medications caused DTPs, MEs and the

most used were selected in FMEA process. It found that phenobarbital inj. was the most anticonvulsants that have been used by (7 medication orders in 25 drug days). Phenobarbital also caused DTPs by 6 events, which were 66.7 DTPs per 100 medication orders or 11.8 DTPs per 100 drug-days. Phenobarbital inj. also the most medication items which caused 5 MEs (100 MEs per 100 medication orders or 12.5 MEs per 100 drug-days). More than 80% of DTPs from phenobarbital inj. were MEs by 5 out of 6. Only one patient harmed from MEs.

In the present study, FMEA were used to develop phenobarbital inj. usage guideline and apply successfully in one patient because phenobarbital inj. was the most anticonvulsants that have been used, usually caused DTPs and actual harmed the patient.

On the other hand, the methodology of high alert medication management with ISMP (11), it was different. ISMP methodology was developed by surveying healthcare professional opinions throughout the US and reviewing the potential list. The medications in that list come from sentinel events of different medical settings that it might be not caused problem in the user's setting.

Phenobarbital inj. that was selected to be high alert medication for PICU and was not presented in current ISMP's high alert medication list (11) because it might not cause any DTPs or MEs in the situation of healthcare settings in the US. Comparing medication items in this lists with top 10 medications caused DTPs, MEs and the most used of the present study. Several medications still familiar, such as (11):

- inotropic medications, IV (e.g., digoxin, milrinone)
- liposomal forms of drugs (e.g., liposomal amphotericin B)
- moderate sedation agents, IV (e.g., midazolam)
- moderate sedation agents, oral, for children (e.g., chloral hydrate)
- narcotics/opiates, IV and oral (including liquid concentrates)
- magnesium sulfate injection
- potassium chloride for injection concentrate
- potassium phosphates injection

The methodology of development high-alert medication usage protocol by FMEA in this study should be useful because it based on sentinel reports of each medical setting, will be more specific and more beneficial.

During 3 months of the study, there were 43 patients included follow the inclusion criteria. The sample size of the present study was calculated from the incidences of DTPs from the result of Kraitep's study (32), which were conducted a study in QSNICH which were the largest children hospital in Thailand. The settings of QSNICH is an academic hospital as same as Ramathibodi Hospital. There are 8 beds in PICU equal to Ramathibodi's. The number of patient was minimal and duration of the present study was lower according to limitations. However, the study period of earlier studies varied from 2 weeks to 12 months (24-26, 88-94). Although, the shortest study, conducted by Strong and Tsang (89) in Canada, had 2 weeks of duration also demonstrated that "pharmacists' interventions can improve the quality of patient care and result in cost avoidance from the short period of the study.

Most patients admitted to PICU in the present study were children age over 1 year old. Only 27.9 percent of patients were infants, which contrast to 43 percent from Kraitep's study. The older age of patients also showed higher average numbers of patients' weight. The other patients' demographic data were also difference. The mean PICU day of the present study was 9.1 days, whereas 5.2 days in Kraitep's. The differences of patient's age and length of stay may result differences in identification of DTPs and MEs. Younger patients were likelihood to have higher rate of DTPs and MEs, while longer length of stay may result in higher rate of DTPs and MEs too.

In addition, medication utilization and patients' demographic data are important to understanding the result of the present study. The PICU admission diagnosis of the present study were similar to Kraitep's (32), which were pneumonia with respiratory failure (35%) and post cardiac surgery (27%). However, medication usage was different. There are 182 medication items prescribed by 674 medication orders, which were higher than Kraitep's. The study in QSNICH had 40 medication items prescribed. The differences of medication items resulted from availability of medication items in the hospital formulary. QSNICH's hospital formulary had about 800 medication items, whereas Ramathibodi hospital's had more than 2,000 medication items. The higher number of medication items my resulted in higher rates of DTPs and MEs from drug interactions and look alike/sound alike drugs. There were 2,947 medication orders in Kraitep's study. However, he did not define the

definition of types of medication orders and cannot be compared with the present study.

Most of physician orders in the present study were order for continue by 54.5%. However, the number of orders for one time was 39.3%. The high number of order for one time showed that PICU patients were unstable. There are changes in patients' treatment that resulted from progression of disease. Physicians have to changes medications order every day to treat each patient and that can be cause higher risk of prescribing errors. Nurses have to take physicians' order as well. This may result in higher risk of transcribing and administration errors.

Since infectious disease commonly caused life-threatening conditions, broad spectrum antibacterials were frequently prescribe. Ceftriaxone inj. and meropenem inj. were common prescribed. Ceftriaxone used as empiric/specific therapy for community acquired infections, whereas meropenem inj. used as empiric/specific therapy for hospital acquired infections (117-120). Imipenem was not commonly prescribed due to potential seizures, especially in patients with neurological disorders (117, 119). Amikacin was the most used aminoglycosides since it can cover most problematic hospital-acquired organisms and use as combination therapy with betalactam antibiotics (117-120). Vancomycin was usually prescribed for patients who were infected with methicillin-resistant *Staphylococcus aureus* (MRSA) (117-120) which commonly occurred after prolonged PICU admission. Most of antibacterial orders' were order for continues. The antibacterial usage was similar to Kraitep's study (32), according to similar PICU admission diagnosis as well.

Most PICU patients need mechanical ventilation, since respiratory system disorders was the most patients' admission diagnosis. Fentanyl inj. and midazolam inj. were prescribed for maintain sedation during patients on mechanical ventilation (117-120), that resulted in highest total drug-days.

Patient's severity may affect patient's medication therapy and medication-used problems, both DTPs and MEs. The severity of those patients could be described by number of PICU-days, drug-days and medication used in term of items and orders. The higher parameter of these parameters may reflect more severe patient's condition. For the present study, these parameter were used as indicators of detected problems. Therefore, the parameter which could well present the actual number of medication

usage, particularly drug-day, may be well described the actual incidence rate. Most studies still reported their identified problems per patient-days (32, 82). When considering number of problem per medication item, the difference in the duration of each medication item may also not represent the actual incidence. For number of problem per medication order, orders for continuation may not represent the actual incidence rate due to the difference in duration of medication used from each order, longer duration of usage of medication item may commonly result in higher number of identified problems.

Although, the turning of residents in PICU may affect the result of this study because of the difference in professional skills, expertise and experience in critical care practice, clinical pharmacist's activities were firstly established in this PICU. Improve education and training of all medical professionals in the use of medication is also likely to have positive impact (13-15). Routine training course for physicians and nurses about how to use medication safely by expert physicians and pharmacists should be performed.

Limitation of the study

1. Clinical pharmacist's only performed serviced only in morning shift. Therefore, DTPs and MEs from medication used in other shifts cannot be detected before they exposed to patients.

2. The study was only performed in one medical ward at PICU at Ramathibodi Hospital, the results thus only represented medication related problems (DTPs and MEs) which may be different from other PICU. High alert medication management protocol should be based on each setting.

3. Number of patients in the present study was limited because of long hospital stay.

CHAPTER VI
CONCLUSION

Identifying potential or actual medication problems, DTPs and MEs, resolving actual medication problems and preventing potential drug therapy problems as clinical pharmacist activities in PICU in the present study. Most patients involves were children, age more than 1 year old. Disease of respiratory system and congenital disorders were the most frequent cause of admission. Each patient were mostly receive medications approximately 16 items per admission, which was usually approximate 9 PICU-days. Antibacterials were frequently prescribed as well as sedative agents.

It was found that 89% of PICU patients were exposed to DTPs (both potential and actual problems) (4.8 DTPs per 100 drug-days). Most problems were involved in safety category, particularly drug interactions.

For MEs, 27.9% of PICU patients were exposed to these problems (4.1 MEs per 1,000 drug-days). Dosage too high was the most identified errors. According to patients' status, medication usage in renal impairment patients required dosage adjustment. Those MEs were mostly caused by phenobarbital inj. Those problems were mostly categorized into severity category D (31.6%), only 10.5% were in severity category E and caused patient's harm. Dosage suggestion by research pharmacist was also mostly performed and was accepted by the health care team.

Total 216 interventions were performed by research pharmacists. The most interventions were identifying of drug interactions. Health care team acceptance rate was 97.2%. Total 111 DIS by research pharmacists were provide.

FMEA by clinical pharmacist found that major cause of MEs was lack of product information of phenobarbital inj. in: dosage and regimen, dosage adjustment in renal insufficiency, administration and adverse reaction. High alert medication management protocol, phenobarbital inj. usage guideline, was proposed by research pharmacist and provided to health care team. A successful used of the proposed guideline was applied in one patient.

Pharmacist activities in medical ward can identify, prevent and resolve DTPs and MEs. However, pharmacist cannot be available all time and errors can be reach patients. High alert medication management protocol is the tool that aids health care team to provide safe medication used and prevent DTPs and MEs. FMEA can be used to generate high alert medication lists; according to each setting has differences of prevalence of DTPs and MEs.

Recommendations

Some DTPs and MEs which potentially harm to patient may use to develop more medication usage protocol to prevent error and improve patient safety. In order to develop and implement high alert medication management protocol for entire hospital, the following recommendation may be beneficial:

1. Generation list of high alert medication items by using FMEA from occurrence report or sentinel events from each medical ward. Scoring FMEA should be used for ranking top high alert medication (110, 111).
2. Summarized high alert medication items from each medical ward to generate high alert medication list for each department.
3. Summarized high alert medication items from each department to generate high alert medication list for entire hospital.
4. Every member in healthcare team, physicians, nurse, and pharmacist, should participate for generation high alert medication management protocol.
5. The protocol should be available to access easily for healthcare team, such as implemented as clinical supporting data in computerize physician order electronic system.

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APPENDICES

APPENDIX A

Data collection form for patient's profile

PICU Ramathibodi hospital:	**Patient's profile number**	**1]** _____
Paste Sticker Here Name / HN / Age	**HN**	**2]** _____
	Gender ❑ 1 male ❑ 2 female	**3]** ❑ 1 ❑ 2
	Date of Birth **Age** month(s)	**4]** _____
CC:	**Weight** kg	**5]** _____
	Height cm	**6]** _____
HPI:	**Admission date**	
	Discharge date	
PMH:		
Allergic history:	**Allergy** ❑ 1 known ❑ 2 not known	**7]** ❑ 1 ❑ 2
Diagnosis:	**Diagnosis ICD-10**	**8]** _____
Problem lists:	**Admission day**	**9]** _____
	PICU day	**10]** _____
	Number of medication received	**11]** _____
	Number of DTP found	**12]** _____
	Number of ME found	**13]** _____

Date	**A Day**	**PICU Day**	**Hospital course**	**T** (^{O}C)	**P** (/min)	**BP** (mmHg)	**RR** (/min)

DTP = Drug therapy problem, ME = medication error, A Day = Admission day, PICU Day = Admission to PICU day

Data collection form for patient’s profile (cont.)

Medication Summary

Medications	Start date	Stop date	Drug-day	No. ME	No. DTP	No. DIS

Date	**A Day**	**PICU Day**	**Hospital course (continue)**	**T** (^{o}C)	**P** (/min)	**BP** (mmHg)	**RR** (/min)

DTP = Drug therapy problem, ME = medication error, A Day = Admission day, PICU Day = Admission to PICU day

Data collection form for patient's profile (cont.)

Laboratory

Hemetology		Date										
		A Day / PICU Day										
Hb	(g/dL)	12-18										
Hct	(%)	37-52										
RBC	$x10^6$ /mm	4.2-5.4										
MCV	(fL)	88-99										
MCH	(pg)	27-31										
MCHC	(%)	31-35										
WBC	(/mcL)	4,000-11,000										
Platelet	$x10^3$ /mm	150-440										
ANC	$x10^3$ /mm	1.8-7.7										
% N		40-74										
% L		19-48										
% M		3.4-9										
% E		0-7										
% B		0-1.5										

Blood chemistry		Date										
		A Day / PICU Day										
FBS	mg/dL	76-110										
BUN	mg/dL	7-20										
SCr	mg/dL	0.5-1.5										
CrCl	ml/min	100-120										
Na	mEq/L	135-145										
K	mEq/L	3.5-5.0										
Cl	mEq/L	98-107										
CO_2	mEq/L	21-34										
Ca	mg/dL	8.1-10.4										
P	mg/dL	2.2-5										
Mg	mg/dL	1.9-2.6										
Uric acid	mg/dL	2.4-7.0										
Chol	mg/dL	100-200										
TG	mg/dL	50-200										
HDL	mg/dL	35-100										
LDL	mg/dL	70-160										
AST	U/L	0-37										
ALT	U/L	0-40										
AP	U/L	39-117										
GGT	U/L	7-50										
TB	mg/dL	0.3-1.2										
DB	mg/dL	0-0.5										
TP	gdL	6.6-8.7										
Albumin	g/dL	3.3-5.5										
Globulin	g/dL	1.5-3.5										
LDH	U/L	50-240										

Data collection form for patient's profile (cont.)

Laboratory

Urinalysis	Date										
	A Day / PICU Day										
Color	Yellow-Amber										
Appearance	Clear										
pH	4.6-8.0										
Specific gravity	1.003-1.030										
Albumin	Neg										
Sugar	Neg										
Blood	Neg										
Ketone	Neg										
WBC /HPF	0-5										
RBC /HPF	0-2										
Cast /LPF	0-1										
Epi. cell /HPF	5-10										
Bacterial	Neg										

Other	Date										
	A Day / PICU Day										

Data collection form for patient's profile (cont.)

Medication Profile

Items	Drug-Dose-Regimen / Monitoring parameter

APPENDIX B

Data collection form for MEs and DTPs.

DTP / ME [Patient profile number _____ HN _____]

No.	Date /Time	Drug-Dose-Regimen / Remarks	DTP category	Steo of ME	Severity		Interventions			
					Category	❑ 1 require intervention ❑ 2 not require intervention	❑ 1 before use ❑ 2 after use	❑1 to physician ❑ 2 to nurse ❑ to pharmacist	Intervention category	❑ 1 accepeted ❑ 2 not accepted

DTP category: **1** need additional drug therapy / **2** unnecessary drug therapy / **3** wrong drug / **4** dosage too low / **5** dosage too high / **6** adverse drug reaction / **7** drug interaction / **8** appropriate compliance
Step of ME: **1** prescribing error / **2** transcribing error / **3** dispensing error / **4** administration error / **5** monitoring error
Severity: **0** no rooro occurred / **0.5-A** capacity to cause error, but no error occurred / **0.5-B** potential error / **1-C** without harm to the patient / **2-D** requiring increased patient monitoring, but no harm to patient or vital sign / **3** requiring increase patient monitoring and laboratory test, with a change in vital sign but ultimately no harm / **3.5-E** resulting in the need of treatment or intervention and caused temporary harm / **4-F** resulted in need for treatment of another drug, increased LOS, patient transfer to the higher level of care, or required intervention to prevent permanent impairment or damage / **5-G** resulted in permanent patient harm / **5.5-H** resulted in near death event / **6-I** resulted in patient death
Intervention category: **1** clarification or correction of order / **2** provision of drug information / **3** dosage/interval adjustment / **4** recommendation of alternative therapy / **5** identification of drug interaction / **6** identification of drug allergy / **7** identification of adverse drug events / **8** identification of system error / **9** therapeutic drug monitoring / **10** miscellaneous or unspecified

APPENDIX C

Data collection form for drug information service.

Drug information for Patient-Specific Question Request/Response Form

Number _____ **Date** _____ **Time** _____ 1 _____

Emergency ❑ 1 Yes ❑ 2 No 2 _____

Requestor _____

Profession ❑ 1 Attending physician ❑ 2 Resident ❑ 3 Nurses ❑ 4 Other _____ 3 _____

Patient name _____ **HN** _____

Question _____

_____

_____

_____

Potentially lethal question ❑ 1 Yes ❑ 2 No 4 _____

Category of question 5 _____

❑ 1 Availability of dosage forms ❑ 2 Identification of product

❑ 3 General product information ❑ 4 Cost

❑ 5 Compatibility/stability/route of admin ❑ 6 Drug interaction

❑ 7 Pharmaceutics ❑ 8 Pharmacokinetics

❑ 9 Therapy evaluation/drug of choice ❑ 10 Dosage/regimen recommendations

❑ 11 Adverse effects ❑ 12 Poisoning/toxicology

❑ 13 Teratogenicity/lactation/infant risks ❑ 14 Others

Answer _____

_____

_____

References _____

_____

_____

Date _____ **Time** _____ of answer

Time for searching and generating answer 6 _____

❑ 1 Not more than 15 minutes ❑ 2 Not more than 1 hours

❑ 3 Not more than 3 hours ❑ 4 Not more than 1 day

❑ 5 More than 1 day _____ ❑ 6 More than 3 days _____

❑ 7 More than 7 days _____

APPENDIX D

Medication groups, medication items, type of medication orders and drug-days.

Medication Items	Type of medication order (orders)				Drug day (days)
	Continue	One-time	As patient's need	Total	
Antibacterials					
Ceftriaxine inj.	13	0	0	13	65
Meropenem inj.	13	0	0	13	74
Amikacin inj.	9	0	0	9	51
Vancomycin inj.	8	0	0	8	40
Cefotaxime inj.	8	0	0	8	35
Ceftazidime inj.	5	0	0	5	40
Cloxacillin inj.	5	0	0	5	16
Cotrimoxazole inj.	3	0	0	3	24
Cefazolin inj.	2	0	0	2	5
Ampicillin/Sulbactam inj.	2	0	0	2	13
Cotrimoxazole susp.	2	0	0	2	13
Neomycin tab.	1	1	0	2	5
Erythromycin susp.	1	0	0	1	12
Erythromycin tab.	1	0	0	1	14
Gentamicin inj.	1	0	0	1	11
Amoxicillin cap.	1	0	0	1	1
Amoxicillin/Clavulanic acid susp.	1	0	0	1	6
Ampicillin inj.	1	0	0	1	2
Azithromycin inj.	1	0	0	1	5
Cefepime inj.	1	0	0	1	4
Cotrimoxazole tab.	1	0	0	1	3
Penicillin G sodium inj.	1	0	0	1	6
Roxithromycin tab.	1	0	0	1	3
Teicoplanin inj.	1	0	0	1	2
Replacement electrolytes					
KCl elixir	1	12	0	13	50
ZnSO4 sol.	13	0	0	13	171
Trace Element sol.	10	0	0	10	150
50% MgSO4 inj.	0	8	0	8	22
KCl inj.	0	6	0	6	11

Medication groups, medication items,

type of medication orders and drug-days (cont.)

Medication Items	Type of medication order (orders)				Drug day (days)
	Continue	One-time	As patient's need	Total	
Replacement electrolytes (continue)					
NaCl tab.	5	0	0	5	57
CaCO3 tab.	2	0	0	2	39
10% MgCl2 sol.	1	1	0	2	16
10% MgSO4 sol.	1	1	0	2	5
Chelated Mg tab.	1	1	0	2	5
Phosphate sol.	1	0	0	1	13
K2PO4 inj.	0	1	0	1	2
NSS neb.	1	0	0	1	4
Shohl's sol.	1	0	0	1	58
Anticonvulsants					
Phenobarbital inj.	3	4	0	7	25
Phenytoin inj.	4	3	0	7	19
Phenobarbital tab.	1	1	0	2	78
Phenytoin Infratab.	2	0	0	2	9
Levitiracetam tab.	2	0	0	2	4
Sodium Valproate inj.	1	1	0	2	3
Sodium Valproate syr.	2	0	0	2	6
Clonazepam tab.	0	1	0	1	4
Analgesics and Antipyretics					
Fentanyl inj.	0	29	8	37	259
Paracetamol syr.	1	1	9	11	43
Paracetamol drop	0	0	5	5	44
Paracetamol tab.	0	0	5	5	23
Morphine inj.	0	2	2	4	9
Pethidine inj.	1	2	0	3	6
Aspirin gr. I tab.	2	0	0	2	22
Paracetamol inj.	0	1	0	1	1

Medication groups, medication items,

type of medication orders and drug-days (cont.)

Medication Items	Type of medication order (orders)				Drug day (days)
	Continue	One-time	As patient's need	Total	
Adrenals					
Methylprednisolone inj.	6	5	0	11	42
Dexamethasone inj.	1	7	0	8	28
Prednisolone tab.	6	1	0	7	81
Hydrocortisone inj.	0	2	0	2	12
Hydrocortisone tab.	1	0	0	1	11
Fluticasone inh	1	0	0	1	2
Mometasone inh	1	0	0	1	2
Antiulcer Agents and Acid Suppressants					
Ranitidine inj.	16	0	0	16	64
Omeprazole inj.	10	0	0	10	52
Esomeprazole inj.	5	1	0	6	34
Lansoprazole tab.	5	0	0	5	66
Omeprazole cap.	1	0	0	1	8
Ranitidine tab.	1	0	0	1	2
Sucralfate susp.	1	0	0	1	4
Anxiolytics, Sedatives, and Hypnotics					
Midazolam inj.	0	23	5	28	216
Chloral Hydrate sol.	0	16	5	21	182
Diazepam inj.	0	2	0	2	6
Hydroxyzine syr.	0	1	0	1	1
Hydroxyzine tab.	1	0	0	1	2
Lorazepam tab.	1	0	0	1	13
Vasodilating Agents					
Sildenafil tab.	2	0	0	2	21
Beraprost tab.	2	0	0	2	39
Bosentan tab.	1	0	0	1	5
Alprostadil inj.	0	1	0	1	76

Medication groups, medication items,

type of medication orders and drug-days (cont.)

Medication Items	Type of medication order (orders)				Drug day (days)
	Continue	One-time	As patient's need	Total	
Vasodilating Agents (continue)					
Iloprost inj.	1	0	0	1	1
Nitroglycerine inj.	0	1	0	1	9
Adrenergic Agents					
Salbutamol neb.	3	16	0	19	134
Dopamine inj.	2	6	0	8	40
Dobutamine inj.	0	4	0	4	38
Ipratopium/Albuterol neb.	1	1	1	3	11
Ipratopium/Fenoterol neb.	0	2	0	2	18
Atropine inj.	0	1	0	1	1
Antifungals					
Voriconazole inj.	2	0	0	2	7
Ketoconazole tab.	1	0	0	1	2
Conventional amphotericin B inj.	1	0	0	1	18
Liposomal amphotericin B inj.	1	0	0	1	5
Nystatin sol.	1	0	0	1	7
Diuretics					
Furosemide inj.	1	23	1	25	116
HCTZ syr.	9	0	0	9	142
Furosemide susp.	3	2	0	5	16
HCTZ tab.	2	0	0	2	39
Manitol inj.	0	1	0	1	1
Immunosuppressive Agents					
Tacrolimus cap.	2	1	0	3	10
Tacrolimus inj.	1	0	0	1	4
Azathioprine tab.	1	0	0	1	26
Mycophenolate mofetil cap.	1	0	0	1	6

Medication groups, medication items,

type of medication orders and drug-days (cont.)

Medication Items	Type of medication order (orders)				Drug day (days)
	Continue	One-time	As patient's need	Total	
Immunosuppressive Agents (continue)					
Antithymoglobulin inj.	0	1	0	1	4
Topical Anti-infectives					
Cotrimazole Cream	2	0	0	2	10
Nystatin Cream	2	0	0	2	14
Fusidic acid Cream	1	0	0	1	5
Mupirocin oint.	1	0	0	1	26
Sodium Benzoate sol.	1	0	0	1	3
Antineoplastic Agents					
Carboplatin inj.	1	1	0	2	3
Etoposide inj.	1	1	0	2	6
Ifosfamide inj.	1	0	0	1	5
Imatinib tab.	1	0	0	1	13
Calcium-Channel Blocking Agents					
Amlodipine tab.	4	1	0	5	88
Nifedipine tab.	0	2	0	2	7
Nifedipine syr.	0	1	0	1	5
Nicardipine inj.	0	1	0	1	4
EENT Anti-inflammatory Agents					
Fluticasone neb.	1	2	0	3	17
Budesonide NB	1	1	0	2	22
Fluticasone/Salmeterol inh	2	0	0	2	39
Antazoline/Tetryzoline ED	1	0	0	1	2
Antidiabetic Agents					
Insulin human	0	2	0	2	5

Medication groups, medication items,

type of medication orders and drug-days (cont.)

Medication Items	Type of medication order (orders)				Drug day (days)
	Continue	One-time	As patient's need	Total	
Antidiabetic Agents (continue)					
Insulin aspart inj.	0	1	0	1	4
Insulin detemir inj.	0	1	0	1	1
Antihistamine Drugs					
Chlorpheniramine inj.	3	1	0	4	28
Cetirizine tab.	1	0	0	1	2
Chlorpheniramine tab.	1	0	0	1	1
EENT Anti-infectives					
Chloramphenical Eye oint.ment	3	0	0	3	13
Glycerine of borax sol.	1	0	0	1	5
Neomycin/Polymyxin B/Gramicidin ED	1	0	0	1	3
Mucolytic Agents					
Bromhexine syr.	4	0	0	4	13
N-Acetylcysteine neb.	0	2	1	3	27
Carboxymethylcysteine syr.	1	0	0	1	3
Topical Anti-inflammatory Agents					
Aescin gel	1	0	0	1	3
Hydrocortisone cream	1	0	0	1	16
Triamcinolone acetonide Oral paste	1	0	0	1	5
Alkalinizing Agents					
7.5% NaHCO3 inj.	0	3	0	3	5
Sodamint tab.	1	0	0	1	1
Antiprotozoals					
Hydroxychloroquine tab.	1	0	0	1	26
Metronidazole inj.	0	1	0	1	1

Medication groups, medication items,

type of medication orders and drug-days (cont.)

Medication Items	Type of medication order (orders)				Drug day (days)
	Continue	One-time	As patient's need	Total	
Antivirals					
Acyclovir inj.	1	0	0	1	3
Ganciclovir inj.	1	0	0	1	7
Blood Derivatives					
20% Albumin inj.	0	7	0	7	13
5% Albumin inj.	0	3	0	3	7
Cardiac Drugs					
Digoxin elixir	4	0	0	4	13
Milrinone inj.	1	2	0	3	24
Iron-removing Agents					
Calcium polystyrene sulfonate Powder	0	1	0	1	1
Sodium polystyrene sulfonate Powder	0	1	0	1	6
Multivitamin Preparations					
MTV syr.	15	0	0	15	180
MTV tab.	1	0	0	1	3
Prokinetic Agents					
Domperidone susp.	7	0	0	7	29
Metoclopramide inj.	0	1	0	1	1
Renin-Angiotensin-Aldosterone System inhibitors					
Spironolactone inj.	9	1	0	10	110
Captopril syr.	5	0	0	5	44
Sympathomimetic Agents					
Adrenaline inj.	0	6	0	6	12
Pseudoephredine tab.	1	0	0	1	2

Medication groups, medication items,
type of medication orders and drug-days (cont.)

Medication Items	Type of medication order (orders)				Drug day (days)
	Continue	One-time	As patient's need	Total	
Vitamin K Activity					
Vitamin K inj.	7	2	0	9	26
Viatmin K tab.	1	0	0	1	3
Ammonia Detoxicants					
Lactulose sol.	0	2	0	2	2
Antianemia Drugs					
Ferous sulfate drop	6	0	0	6	39
Antidiarrhea Agents					
Infloran® cap.	1	0	0	1	26
Antiemetics					
Ondansetron inj.	3	0	0	3	22
Antiflatulents					
Simethicone drop	1	0	0	1	4
Antiglaucoma Agents					
Acetazolamide susp.	6	0	0	6	79
Antigout Agents					
Allopurinol tab.	1	0	0	1	8
Antihemorrhagic Agents					
Recombinant activated factor VII inj.	0	1	0	1	1
Anti-inflammatory Agents					
Montelukast tab.	1	0	0	1	19
Antilipemic Agents					
Cholestyramine sachet	2	1	0	3	11

Medication groups, medication items,
type of medication orders and drug-days (cont.)

Medication Items	Type of medication order (orders)				Drug day (days)
	Continue	One-time	As patient's need	Total	
Antimycobacterials					
Isoniazid tab.	1	0	0	1	11
Antithrombotic Agents					
Heparin inj.	0	1	0	1	2
beta-Adrenergic Blocking Agents					
Atenelol tab.	2	0	0	2	19
Cathartics and Laxatives					
Saline enema	0	2	0	2	2
Choletitholytic Agents					
Ursodeoxycholic acid cap.	4	0	0	4	23
EENT Local Anesthetics					
Kamistad® gel	1	0	0	1	3
General Anesthetics					
Ketamine inj.	0	4	0	4	4
Hematopoietic Agents					
GCSF inj.	3	0	0	3	15
Parasympathomimetic Agents					
Pyridostigmine tab.	1	0	0	1	3
Pituitary					
Desmopressin inj.	0	1	0	1	1
Protective Agents					
Mesna inj.	1	0	0	1	5

Medication groups, medication items,

type of medication orders and drug-days (cont.)

Medication Items	Type of medication order (orders)				Drug day (days)
	Continue	One-time	As patient's need	Total	
Psychotherapeutic Agents					
Haloperidol inj.	0	1	0	1	1
Respiratory Smooth Muscle Relaxants					
Doxofylline sol.	1	0	0	1	19
Serums					
IVIG inj.	0	1	0	1	3
Skeletal Muscle Relaxants					
Vecuronium inj.	0	11	0	11	64
Topical Emollients, Demulcents, and Protectants					
Zinc Paste	5	0	0	5	5
Other Miscellaneous Therapeutic Agents					
Octreotide inj.	0	1	0	1	5
Total	**367**	**265**	**42**	**674**	**4543**

APPENDIX E

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ABSTRACTS

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Poster Presentations

P.048 Drug Therapy Problem Management by Pharmacist in Paediatric Intensive Care Unit at a Large Teaching Hospital, Thailand

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Background: Drug therapy problem (DTP) is an undesirable event experienced by patient in drug therapy and that actually or potentially affected to a desired patient outcome.[1] Most DTP resulted by medication errors and adverse drug events. Paediatric population predisposed to DTP because of age-specific changes in pharmacokinetics and pharmacodynamics, off-label using of medications, lacking of suitable formulations and appropriate strengths, and extemporaneously preparing of medications. Although patient harm in children can be reduced by pharmacists,[2] few DTP studies has been investigated in Thailand.

Objective: To determine frequency and characteristics of DTPs and pharmacist's intervention resolving DTPs in paediatric intensive care unit (PICU) at Ramathibodi Hospital.

Method: All patients who were admitted in PICU during March and May 2007 were prospectively detected DTP by pharmacist's daily medical chart review and ward round with health care team. All identified DTPs were categorised into type of DTP, medication used process and severity. Pharmacist's interventions were provided and recorded. The SPSS version 15.0 was performed by descriptive analysis.

Result: An average patient's age was 61.8 ± 54.6 months in 43 patients. Twenty four (55.8%) patients were female. The common admission diagnosis were diseases of the respiratory system and congenital disorders by 9 (20.9%) and 7 (16.3%), respectively. The patients received 15.7 ± 9.5 medications during their admission. Total 216 DTPs (70.8 DTPs per 100 patient-days) in 37 patients (86.0%) were identified. Actual DTPs were 210 (97.2%) events but they caused patients' harm only 3 (1.4%) events. One hundred and ninety seven DTPs might not be justified as medication used process errors due to 192 potential adverse drug-drug interaction and 5 other DTPs were not contraindication for prescribing. The remaining 16 out of 19 (84.2%) DTPs resulted by prescribing errors. The most common medication causing DTPs was phenytoin tablet (6.0 DTPs per one time of phenytoin tablet used) and phenytoin injection (5.7 DTPs one time of phenytoin injection used). The most interventions were identification of drug interactions by 192 (96.8%). Ninety-eight percents of 216 interventions were accepted and implemented by health care team.

Discussion: Although most DTPs did not cause harm to patients, the pharmacists had role to play in providing drug information and resolving DTPs and might resulted to prevent and reduce patients' harm.

Conclusion: DTPs were common problems among PICU patients and drug interactions were majority types of DTPs. Pharmacist's management of DTPs in PICU improved patient's care quality.

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