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ผลของการให้คำปรึกษาของเภสัชกรในผู้ป่วยปลูกถ่ายอวัยวะตับ

Evaluation of Counseling from Pharmacist to Liver Transplant Patients

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บทคัดย่อ

ความเป็นมา: *ผู้ป่วยปลูกถ่ายอวัยวะมีการปรับ–เปลี่ยนยากดภูมิคุ้มกันตามระดับยาในเลือด รวมถึงปรับ–เปลี่ยนยาอื่น ๆ ผู้ป่วยกลุ่มนี้ได้รับยาร่วมกันหลายรายการ และมีโอกาสเพิ่มความเสี่ยงปัญหาจากการใช้ยา*

วัตถุประสงค์: *เพื่อศึกษาปัญหาการใช้ยาในผู้ป่วยปลูกถ่ายอวัยวะที่เภสัชกรให้คำปรึกษาแก่ผู้ป่วยก่อนพบแพทย์ เปรียบเทียบกับการให้คำปรึกษาแก่ผู้ป่วยก่อนและหลังพบแพทย์*

วิธีการศึกษา: *การศึกษาเชิงสังเกต เก็บข้อมูลผู้–ป่วยย้อนหลัง ณ คลินิกปลูกถ่ายอวัยวะตับ ระหว่างวันที่ 1 มกราคม พ.ศ. 2564 ถึง 31 ธันวาคม พ.ศ. 2565 โดยแบ่งเป็นเภสัชกรให้คำปรึกษาแก่ผู้ป่วยก่อนพบแพทย์ในช่วงปี พ.ศ. 2564 ส่วนช่วงปี พ.ศ. 2565 เภสัชกรให้คำ–ปรึกษาแก่ผู้ป่วยทั้งก่อนและหลังพบแพทย์ เครื่องมือที่ใช้ประเมินปัญหาการใช้ยาคือ PCNE classification version 9.1 ข้อมูลถูกจัดกลุ่มเป็น ปัญหาที่สามารถป้องกันได้ และ ไม่สามารถป้องกันได้*

ผลการศึกษา: *ในช่วงปี พ.ศ. 2564 พบปัญหาจากการใช้ยาทั้งหมด 15 ปัญหา จากการให้คำปรึกษาก่อนพบแพทย์ 240 ครั้ง แบ่งปัญหาได้เป็น 4 กลุ่ม คือ กระบวนการ*

Abstract

Background: *The prescribed immunosuppressants for organ transplant patients were adjusted according to blood level. Other drugs were also adjusted. These patients frequently have polypharmacy, which leads to increased risk for drug-related problems (DRPs).*

Objectives: *This study aimed to determine DRPs detected during counseling to organ transplant patients by pharmacist at pre-doctor visit comparing to counseling at pre- and post-doctor visit.*

Method: *A retrospective, observational study was performed in the liver transplant clinic from January 1, 2021 to December 31, 2022. In 2021, pharmacists counseled patients at pre-doctor visit (pre-counseling) but in 2022, pharmacists counseled twice at pre- and post-doctor visit (pre- and post-counseling). Pharmacists identified DRPs using the PCNE classification version 9.1 and DRPs were grouped into*

รับบทความ: *27 ตุลาคม 2566* ***แก้ไข:*** *7 ธันวาคม 2566* ***ตอบรับ:*** *13 เมษายน 2567*

ที่เกี่ยวข้องกับผู้ป่วย 11 ครั้ง (ร้อยละ 73.3) อาการไม่พึง–ประสงค์ 2 ครั้ง (ร้อยละ 13.3) กระบวนการเกี่ยวกับยา 1 ครั้ง (ร้อยละ 6.7) และ การเลือกใช้ยา 1 ครั้ง (ร้อยละ 6.7) โดยจัดเป็นปัญหาจากการใช้ยาที่สามารถป้องกันได้ 13 ปัญหา (ร้อยละ 86.7) ในช่วงปี พ.ศ. 2565 พบปัญหาจากการใช้ยาทั้งหมด 19 ปัญหา จากการให้คำปรึกษาก่อนและหลังพบแพทย์ 314 ครั้ง แบ่งปัญหาได้เป็น 4 กลุ่ม คือ กระบวนการเกี่ยวกับยา 6 ครั้ง (ร้อยละ 31.6) อาการไม่–พึงประสงค์ 6 ครั้ง (ร้อยละ 31.6) กระบวนการที่เกี่ยว–ข้องกับผู้ป่วย 5 ครั้ง (ร้อยละ 26.3) และ การเลือกใช้ยา 2 ครั้ง (ร้อยละ 10.5) โดยจัดเป็นปัญหาจากการใช้ยาที่สามารถป้องกันได้ 13 ปัญหา (ร้อยละ 68.4)

***สรุปผล**: การให้คำปรึกษาทั้งก่อนและหลังพบแพทย์ ลดปัญหาปัจจัยจากผู้ป่วยอย่างมีนัยสำคัญทางสถิติ และมีแนวโน้มลดความไม่ร่วมมือการใช้ยา เทียบกับให้คำปรึกษาก่อนพบแพทย์เพียงอย่างเดียว*

preventable DRPs and non-preventable DRPs.

***Results**: In 2021, 15 DRPs were found from 240 pre-counseling. Four categories of DRPs were identified: patient-related problems (11, 73.3%), adverse drug effects (2, 13.3%), drug-use process problems (1, 6.7%), and drug selection problems (1, 6.7%). Thirteen (86.7%) of those were classified as preventable DRPs. In 2022, 19 DRPs were found from 314 pre- and post-counseling. Four categories of DRPs were identified: drug-use process problems (6, 31.6%), adverse drug effects (6, 31.6%), patient-related problems (5, 26.3%), and drug selection problems (2, 10.5%). Thirteen (68.4%) of those were classified as preventable DRPs.*

***Conclusion**: The results of the study indicate that pre- and post-counseling from pharmacists can significantly reduce patient-related problems, and tend to decrease non-adherence when compared with pre-counseling alone.*

คำสำคัญ: ปัญหาการใช้ยา; ปลูกถ่ายอวัยวะตับ; การให้คำปรึกษาจากเภสัชกร; การประสานรายการยา; ความปลอดภัยผู้ป่วย

Keyword: drug-related problems; liver transplantation; pharmacist counseling; medication reconciliation; patient safety

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Introduction

The Organ Donation Center in Thailand re–ported numbers of liver transplant recipients in 2021 and 2022 as 54 and 100, respectively.[1] This is a sharp increase in the number of recipients as liver transplantation became a lifesaving treatment option for more patients with end-stage liver disease, hepatocellular carcinoma, and acute liver failure.[2] Long-term care after transplantation is important to maintain graft function. The most important factor is adherence to immunosuppressive drugs, as non-adherence can

lead to graft rejection.[3] Therefore, the identification and management of drug-related problems (DRPs) opens opportunities to improve medication safety. Other research indicates pharmacists to be beneficial in the management of many diseases and special patient populations and contribute to patient safety, with reductions in drug-associated mortality and hospitalizations.[4]

Initially, pharmacists who joined the liver transplantation clinic performed counseling to patients only pre-doctor visit. DRPs were noted in the follow-up consultation form. Such notes included non-adherence and/or incorrectly calculated medication quantities. Pharmacist concerns such problems that leads to a post-doctor visit counseling session being established for each patient. There is currently no research comparing the prevalence of DRPs in liver transplant recipients receiving solely counseling at pre-doctor visit (pre-counseling) with recipients receiving both counseling at pre- and post-doctor visit (pre- and post-counseling).

Objectives

This study aims to investigate the prevalence and types of DRPs in transplant recipients in the outpatient surgery liver transplant clinic, specifically by comparing pre-counseling alone against pre- and post-counseling.

Methods

Ethics approval

This study was a retrospective, observational study conducted between January 1, 2021 – December 31, 2022 at Maharaj Nakorn Chiang Mai Hospital and was approved by Research Ethics Committee Faculty of Medicine Chiang Mai University (EXEMPTION 0381/2023).

Study design and setting

Liver or pancreas transplantation patients were eligible if they were scheduled for a check-up in outpatient surgery liver transplant clinic, every Thursday. During this medical check-up, patients were seen by a specialized nurse practitioner, hepatologists, and pharmacists. Patients were asked to bring their medications to the clinic. Pharmacists perform medication reconciliation, check laboratory (blood chemistry and drug level), and have conversations about how patients take each medicine, adherence, adverse drug reactions, herb or dietary supplement use, and confirms patients to have blood withdrawal before taking medicine. This process is called pre-counseling and takes approximately 15 minutes per patient. After patients meet hepatologists, pharmacists check medicines that doctors prescribe and explain to patients how to take each medicine, what medicine is stopped or started or increased dose or decreased dose or the same dose. This process is called post-counseling and takes approximately 15 minutes per patient. A retrospective, observational study was performed in the liver transplant clinic at Maharaj Nakorn Chiang Mai Hospital from January 1, 2021 to December 31, 2022. In 2021, pharmacists performed only pre-counseling but in 2022, pharmacists performed pre- and post-counseling. All findings during the check-up were written in the patient's medical records for further follow-up.

Patients

Liver or pancreas transplantation patients scheduled for medical check-ups at the outpa-

tient surgery liver transplant clinic every Thursday between January 1, 2021 and December 31, 2022 were included in this analysis.

Data collection

For the analysis of the primary objective, the following baseline characteristics were obtained from the medical record: age, gender, indications for liver transplantation, time after transplantation, information about re-transplantation, comorbidities, and number of drugs on the medication list during consultation.

Assessment of drug-related problems

The recorded information were categorized into predefined categories of DRPs. These categories were based on the classification of the Pharmaceutical Care Network Europe (PCNE) classification V9.1.[5] Each identified DRP was categorized as one DRP. All DRPs were independently categorized by two pharmacists. Next, they compared their classifications and when dissensus existed, the panel members reviewed their classifications and discussed these until consensus was reached. Pharmacists grouped DRPs into preventable DRPs and non-preventable DRPs. Non-preventable DRPs were side effects.

Statistical analysis

No formal sample size calculation was performed. All patients in the study during this period were included. Variables were described with descriptive statistics: n (%) for nominal and ordinal variables and median (inter-quartile range; IQR) for continuous variables. Statistical software, STATA for Windows, version 14.0 was used for the analysis. For all statistical tests, a two-sided *p*-value of < 0.05 was considered to indicate statistical significance.

Results

Pharmacist counseled 61 patients with a median age of 56 years (IQR: 44-62.5) and a median of 7 medications (IQR: 5-9.5). The most frequent indication for transplantation was hepatocellular carcinoma (n=36, 59.0%), and comorbidities in recipients were diabetes mellitus (n=23, 37.7%). Table 1 presents the clinical and demographic characteristics of the study.

Drug Related Problems

In 2021 from 240 visits or counseling, pharmacists found 15 DRPs. The most frequent DRPs in 2021 were: patient-related problems (73.3%), side effects (13.3%), drug selection (6.7%), and drug use process (6.7%). In 2022 from 314 visits or counseling, 19 DRPs were found. The most frequent DRPs in 2022 were: drug use process (31.6%), side effects (31.6%), patient-related problems (26.3%), and drug selection (10.5%). Tables 2 and 3 present drug-related problems of the study.

Table 4 shows the prevalence and examples of drug-related problems in 2021 and 2022. In 2022, DRPs of taking tacrolimus before tacrolimus blood level collection was lower than in 2021 (0.0% versus 20.0%) with a statistical significance (*p*-value = 0.041). Less non-adherence (26.3% versus 53.3%) was detected in 2022 compared to 2021 but not statistically significant (*p*-value = 0.108). Higher DRPs as dosage too low (21.1% versus 0.0%) were detected in 2022 compared to 2021 but not statistically significant (*p*-value = 0.058).

The number of DRPs for non-adherence and inappropriate timing of taking tacrolimus before blood level collection in patients who

Table 1 Clinical and demographic characteristics

	No. of patients (%) [n=61]
Age (year) (median, IQR)	56 (44-62.5)
Gender	
Male (n, %)	44 (72.1%)
Indication for liver transplantation	
Hepatocellular carcinoma	36 (59.0%)
Cirrhosis	25 (41.0%)
Hepatitis B virus	17 (27.9%)
Other[a]	10 (16.4%)
Hepatitis C virus	9 (14.8%)
Acute liver failure	1 (1.6%)
Time after transplantation (months) (median, IQR)	27 (1.5-52.5)
Re-transplantation	0
Comorbidities[b]	
Other[c]	39 (63.9%)
Diabetes mellitus	23 (37.7%)
None	19 (31.1%)
Chronic kidney disease	9 (14.8%)
Cardiovascular disease	1 (1.6%)
Gastrointestinal fistula	1 (1.6%)
Number of drugs on medication list during consultation (median, IQR)	7 (5-9.5)

[a] Other includes Wilson disease (n=2), biliary atresia (n=2), intraductal papillary neoplasm of the bile duct (n=1), chronic hepatitis from autoimmune hemolytic anemia (n=1), ruptured hepatic hemangiomas (n=1), recurrent hepatoblastoma (n=1), gastrointestinal stromal tumor with liver metastases (n=1) and diabetes mellitus type 1 (n=1)

[b] Comorbidity : every comorbidity is counted separately

[c] Other : dyslipidemia (n=19), hypertension (n=16), hepatitis B virus (n=10), hepatitis C virus (n=3), beta-thalassemia trait (n=3), hypothyroid (n=2), adrenal insufficiency (n=2), gout (n=1), benign prostatic hyperplasia (n=1), acute myeloid leukemia (n=1), transient ischemic attack (n=1), asthma (n=1), vitiligo (n=1), severe depression (n=1), biliary atresia (n=1), pulmonary hypertension (n=1), late latent syphilis (n=1), seizure (n=1), anemia (n=1) and avascular necrosis of the femoral head (n=1)

received pre- and post-counseling from pharmacists was reduced from pre-counseling alone. The number of DRPs for dosage too low in patients who received pre- and post-counseling from pharmacists was increased from pre-counseling alone. The number of preventable DRPs in

Table 2 Prevalence of drug related problems in 2021

DRPs	Definition	Number of events	% of DRPs [n = 15]
Drug selection	Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements	1	6.7
Drug use process	Drug over-administered by a health professional	1	6.7
Patient related	• Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason	1	73.3
	• Patient uses/takes more drug than prescribed	6	
	• Inappropriate timing or dosing intervals	3	
	• Patient unable to understand instructions properly	1	
Other	Other cause; specify	2	13.3

Table 3 Prevalence of drug related problems in 2022

DRPs	Definition	Number of events	% of DRPs [n = 19]
Drug selection	Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements	2	10.5
Drug use process	• Drug under-administered by a health professional	5	31.6
	• Drug not administered at all by a health professional	1	
Patient related	• Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason	1	26.3
	• Patient uses/takes more drug than prescribed	2	
	• Inappropriate timing or dosing intervals	2	
Other	Other cause; specify	6	31.6

patients who received pre- and post-counseling from pharmacists was reduced from pre-counseling alone (68.4 % versus 86.7%).

Discussion

In this study, non-adherence was the most frequent reported DRP in 2021. Our result along

Table 4 Prevalence and examples of drug related problems (DRPs) in 2021 and 2022

DRPs	Incidences of DRPs (%)		*p*-value	Example of DRPs
	Pre-counseling in 2021 [n=15]	Pre- and post-counseling in 2022 [n=19]		
Non-adherence	8 (53.3%)	5 (26.3%)	0.108	Prescribed tacrolimus 3 mg (Advagraf®) 2x1 ac total 6 mg/day but patient took tacrolimus 3 mg (Advagraf®) 1x1 ac total 3 mg/day
Side effect	2 (13.3%)	6 (31.6%)	0.212	Side effect tacrolimus induced tremor
Drug interaction				
• Drug-herb	1 (6.7%)	2 (10.5%)	0.698	Use herb (not know the name) with tacrolimus. Cause decreasing tacrolimus blood level
Indication				
• Wrong drug	0 (0.0%)	0 (0.0%)	-	-
• Unnecessary drug	1 (6.7%)	0 (0.0%)	0.252	Prescribed mycophenolate sodium (Myfortic®) that was stopped already
• Untreated indication	0 (0.0%)	2 (10.5%)	0.196	In admission, adjusted mycophenolate sodium (Myfortic®) from 180 mg 1x2 pc to 360 mg 1x2 pc but home medication not prescribed
Not optimal dose				
• Dosage too high	0 (0.0%)	0 (0.0%)	-	-
• Dosage too low	0 (0.0%)	4 (21.1%)	0.058	- Prescribed tacrolimus (Advagraf®) less amount than follow up date - In admission, medication reconciliation is tacrolimus 3 mg (Advagraf®) 3x1 ac total 9 mg/day. Prescribed tacrolimus 3 mg (Advagraf®) 1x1 ac total 3 mg/day
Others	3 (20.0%)	0 (0.0%)	0.041*	Took tacrolimus before tacrolimus blood level collection

*indicates a statistically significant difference of *p*-value < 0.05

with Mulder et al., non-adherence was the most frequent reported medication-related problem.[6] This study showed pre- and post-counseling can significantly reduce patient-related problems, especially inappropriate timing of taking tacrolimus before blood level collection, and tend to decrease non-adherence when compared with pre-counseling alone.

Pre- and post-counseling showed that increased DRPs and dosages were too low for the amount of medicine of less than the follow-up date. So post-counseling by pharmacists that explained instructions for use change or same dose and reminded patients to take blood level before taking tacrolimus at next visit can improve adherence, patient safety, and effectiveness of treatment. Overall preventable DRPs in pre- and post-counseling were decreased compared to pre-counseling alone.

Our study found DRP of dosage too low in pre- and post-counseling was increased. For example on admission, medication reconciliation is tacrolimus 3 mg (Advagraf®) 3 x 1 ac total 9 mg/day. But home medication prescribed tacrolimus 3 mg (Advagraf®) 1 x 1 ac total 3 mg/day. We found these DRPs at the outpatient surgery liver transplant clinic and the patient's tacrolimus blood level was correspondingly low. We found more DRPs from the discharge setting. In the study of Flamme-Obry et al., showed that counseling patient by the clinical pharmacist at discharge can help to reduce DRPs in kidney recipients.[7] So, in the future we plan to extend the job description to discharge counseling.

The strengths of our study are the real-life clinical setting and all DRPs were independently categorized by two pharmacists. A limitation of our study was that we did not perform medication errors classification that can affect harm and clinical outcomes for patients. Further research is needed to study the medication error classification.

Conclusion

Results of the study indicate that pre- and post-counseling from pharmacists can significantly reduce patient-related problems, especially inappropriate timing of taking tacrolimus before blood level collection (p-value = 0.041), and tend to decrease non-adherence when compared with pre-counseling alone. So pre- and post-counseling from pharmacists is one of the important process to improve safety of organ transplant patients.

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