

Evaluation of a Clinical Pharmacist Intervention on Clinical and Drug-Related Problems Among Coronary Heart Disease Inpatients

A pre-experimental prospective study at a general hospital in Indonesia

*Vina A. Sagita,¹ Anton Bahtiar,² Retnosari Andrajati²

تقويم فعالية تدخل الصيدلاني السريري لحل المشاكل السريرية والدوائية عند المرضى الداخليين المصابين بمرض القلب التاجي
دراسة استباقية قبل-تجريبية في مستشفى عام بإندونيسيا

فيينا أناستازيا ساجتا، أنتون بهتيار، ريتنوساري اندراجاتي

ABSTRACT: Objectives: This study aimed to evaluate the role of a clinical pharmacist intervention in decreasing subsequent clinical and drug-related problems (DRPs) among coronary heart disease (CHD) inpatients with at least one previous DRP. **Methods:** This pre-experimental study with a pre-post design was carried out from January to April 2017 among inpatients with at least one previous DRP at a general hospital in Tangerang District, Banten, Indonesia. Clinical and DRPs were documented prospectively by a clinical pharmacist, with DRPs classified using Version 6.2 of the DRP classification scheme of the Pharmaceutical Care Network Europe Foundation. The intervention consisted of a discussion of identified DRPs with physicians, patients, pharmaceutical logistics clerks, nurses and nutritionists. Following this, any subsequent clinical and DRPs were re-identified and further interventions were conducted as necessary. **Results:** A total of 75 inpatients were included in the study. Pre-intervention, there were 443 DRPs and 202 clinical problems. The most frequent DRPs were adverse drug reactions (52.6%), followed by drug effects (41.8%). Most DRPs were of moderate severity and would have resulted in moderate consequences had the pharmacist not intervened. The interventions resulted in a significant reduction in the number of DRPs, type of DRPs and number of clinical problems ($P < 0.05$ each). Patients with complications were 26.047 times more likely to have no reduction or an increased number of clinical problems compared to patients without complications ($P < 0.05$). **Conclusion:** Clinical pharmacist interventions were found to reduce subsequent DRPs and clinical problems among CHD patients with at least one previous DRP.

Keywords: Coronary Heart Disease; Drug Interactions; Adverse Drug Reactions; Pharmacists; Indonesia.

المخلص: الهدف: تهدف هذه الدراسة لتقويم دور الصيدلاني السريري في التدخل لتقليل المشاكل السريرية والدوائية اللاحقة عند المرضى الداخليين المصابين بمرض القلب التاجي الذين تعرضوا من قبل لنوبة واحدة من ذلك المرض، على الأقل. الطريقة: أجريت هذه الدراسة الاستباقية قبل-التجريبية في الفترة من يناير إلى أبريل من عام 2017م على مرضى أصيبوا من قبل بنوبة واحدة على الأقل بهذا المرض، وذلك في مستشفى عام في منطقة تانجانغرانق ببانتينج في إندونيسيا. وقد سجلت وصنفت كل مشاكل المرضى السريرية والدوائية بواسطة صيدلاني سريري باستخدام النسخة رقم 6.2 من نظام تصنيف المشاكل الدوائية الذي أصدرته شبكة الرعاية الصيدلانية الأوروبية. وشمل التدخل مناقشة للمشاكل المتعرف عليها مع الأطباء والمرضى وكتابة الخدمات اللوجستية الصيدلانية والمرمضات واختصاصي التغذية. وعقب ذلك تم التعرف على أي مشاكل سريرية أو دوائية لاحقة، وتم التدخل فيها عند الضرورة. النتائج: ضمت هذه الدراسة 75 مريضاً. وكان هنالك قبل التدخل 443 مشكلة دوائية و 202 مشكلة سريرية. وكانت أكثر المشاكل الدوائية حدوثاً هي الآثار الجانبية (52.6%) وتلتها آثار الدواء (41.8%). وكانت معظم المشاكل الدوائية متوسطة الشدة، وكان من الممكن أن تحدث نتائج ذات آثار متوسطة الشدة لولا تدخل الصيدلي السريري، إذ أفضى ذلك التدخل لخفض معنوي في أعداد وأنواع المشاكل السريرية والدوائية عند المرضى ($P < 0.05$ ، في الحالات). وكان احتمال زيادة المشاكل السريرية أو عدم نقصان عددها أكبر بمقدار 26.047 مرة عند المرضى الذين تعرضوا لمضاعفات من الذين لم يتعرضوا لمضاعفات ($P < 0.05$). الخلاصة: وجدنا أن تدخل الصيدلي السريري يقلل من المشاكل السريرية والدوائية اللاحقة عند المرضى الداخليين المصابين بمرض القلب التاجي الذين تعرضوا من قبل لنوبة واحدة من المرض على الأقل.

الكلمات المفتاحية: مرض القلب التاجي؛ تفاعل الأدوية؛ الآثار الضارة للأدوية؛ الصيادلة؛ أندونيسيا.

ADVANCES IN KNOWLEDGE

- A clinical pharmacist intervention was found to significantly reduce clinical and drug-related problems (DRPs) among coronary heart disease (CHD) inpatients with at least one previous DRP at a general hospital in Indonesia.
- The most frequent type of potential DRPs observed in the study were adverse drug reactions. Most DRPs were of moderate severity and, without intervention, were forecast to result in moderate consequences with regards to the health of the patients.

²Department of Pharmaceuticals, ¹Faculty of Pharmacy, University of Indonesia, Depok, West Java, Indonesia

*Corresponding Author's e-mails: vina.anastasia@ui.ac.id and vinanastasia@gmail.com

APPLICATION TO PATIENT CARE

- The findings of this study may be used by physicians, pharmacists and other healthcare workers in order to reduce DRPs and clinical problems among CHD inpatients.

NEARLY ONE-THIRD OF ALL DEATHS WORLD-wide are due to cardiovascular diseases (CVDs), with coronary heart disease (CHD) the leading cause of CVD-related deaths.^{1,2} In 2015, the World Health Organization estimated that approximately 17.7 million people died globally as a result of CHD.³ In Europe, CVD was responsible for four million deaths in 2015, with CHD the cause of 19% and 20% of deaths among men and women, respectively.⁴ A total of 15.5 million people in the USA were found to be living with CHD in 2016.⁵ In Indonesia, the overall prevalence of CHD in 2013 for individuals aged 15 years and over was 0.5% based on an official diagnosis and 1.5% based on a diagnosis or related symptoms; this increased to 1.7% and 3.2%, respectively, in those over 75 years old.⁶ For those in the 15–24-year-old age group, the prevalence was 0.1% based on a diagnosis and 0.7% based on a diagnosis or symptoms.⁶

In CHD, the coronary arteries that supply oxygen to the heart become narrower due to a build-up of plaque. The disease may clinically manifest as stable *angina* (i.e. chest pain) or acute coronary syndrome (ACS).⁷ The goal of CHD treatment is to control these symptoms and prevent progression of the disease by reducing relevant risk factors such as hypertension and dyslipidaemia.⁸ It is common for patients to take five or more drugs simultaneously as part of lifelong therapy. Unfortunately, polypharmacy increases the risk of a drug-related problem (DRP), defined as an event or circumstance involving drug therapy that can interfere with a desired health outcome.⁹

The occurrence of DRPs can reduce the benefits of drugs and cause increased morbidity and mortality.¹⁰ According to the classification scheme of the Pharmaceutical Care Network Europe Foundation (PCNEF), four types of DRPs exist, including drug effects, adverse drug reactions (ADRs), treatment cost-related problems and other problems.¹¹ Cases involving inappropriate drug dosages, regimens or drug interactions and poor adherence to a drug regimen may result in drug treatments having non-optimal effects or no effect. Other DRPs include non-allergic ADRs, unnecessary drug treatment and patient dissatisfaction with therapy.¹² The detection and prevention of DRPs can enhance the quality of life of patients and optimise healthcare costs.¹⁰ In 2004, a study from Norway found that 81% of hospitalised patients had DRPs.¹³ Other research has indicated that between 69–78% of CVD patients have DRPs.^{14,15} In 2011, a study reported that cardiovascular

drugs were one of the major causes of all DRPs.¹⁶ Identified risk factors for ADRs include age, gender, polypharmacy, drug administration with a narrow therapeutic index, decreased renal elimination and the use of oral anti-coagulants and diuretics.¹⁷

Pharmacists can help to identify and resolve DRPs through appropriate interventions.¹⁰ Examples of pharmacist interventions include advising patients of drug information and instructions for use or changing the drug prescription, dosage, formulation or regimen. In addition, if needed, pharmacists can also provide medication counselling and education for patients regarding ADR presentations and drug interactions.¹² Research has shown that involving pharmacists in multi-disciplinary teams decreases morbidity and mortality.¹⁸ A study performed in Indonesia evaluated the role of pharmacist interventions in decreasing DRPs among CVD and stroke inpatients.¹⁹ This study aimed to evaluate the number and type of DRPs and clinical problems following a clinical pharmacist intervention among CHD inpatients with at least one previous DRP at a general hospital in Tangerang District, Banten, Indonesia. It was hypothesised that the intervention would result in a reduction in DRPs and an improvement in the inpatients' clinical condition.

Methods

This pre-experimental prospective study with a pre-post design was carried out from January to April 2017 at a general hospital in Tangerang District. Only inpatients aged ≥ 35 -years-old with national health insurance, who had been diagnosed with CHD, were receiving CHD medications and had experienced at least one DRP previously were included in the study. Patients with infectious diseases and pregnant or lactating women were excluded, as well as patients with incomplete medical records or those who were unwilling to participate or lost to follow-up during the study period. Out of 111 inpatients, 21 patients were unwilling to participate, three did not have a DRP and 12 patients were diagnosed with infections, resulting in a total sample of 75 inpatients.

The drug therapy details, laboratory parameters and demographic details of all inpatients were prospectively reviewed by a clinical pharmacist. During ward rounds, drug and dose selection, drug regimens and patients' drug use patterns were evaluated in

Table 1: Demographic and clinical characteristics of coronary heart disease inpatients in Indonesia (N = 75)

Characteristic	n (%)
Age in years	
35–59	48 (64)
≥60	27 (36)
Gender	
Male	53 (70.7)
Female	22 (29.3)
Clinical manifestation	
Non-ACS symptoms	50 (66.7)
ACS	25 (33.3)
Number of comorbidities	
1–2	50 (66.7)
>2	25 (33.3)
Presence of complications	
Yes	15 (20)
No	60 (80)
LOS in days	
1–5	69 (92)
>5	6 (8)
Number of drugs prescribed	
1–5	19 (25.3)
>5	56 (74.7)

ACS = acute coronary syndrome; LOS = length of stay.

order to identify DRPs as per Version 6.2 of the PCNEF classification scheme.¹¹ Interventions consisted of reporting and discussing identified DRPs during interviews with various recipients, including physicians, patients, pharmaceutical logistics clerks, nurses and nutritionists. The type of intervention was classified as either independent (i.e. specifically tailored to an individual recipient) or concurrent (i.e. provided to several or all recipients at the same time). It is important to note that each DRP could be targeted with more than one intervention. After the interventions, the pharmacist continued monitoring the patient until discharge, conducting further interventions as necessary for any subsequent DRPs.

The overall number of clinical problems and the overall number and subtypes of DRPs before and after the intervention were calculated for every patient. A specific subtype of DRP could occur as a result of different drugs. The severity of identified DRPs was classified as major, moderate or minor.²⁰ Major DRPs were defined as those requiring intervention to prevent

Table 2: Acceptance of a clinical pharmacist intervention for clinical and drug-related problems among coronary heart disease inpatients in Indonesia (N = 459)

Acceptance of intervention	n (%)
No intervention	2 (0.4)
Not accepted	14 (3.1)
Accepted	443 (96.5)

major or irreversible detrimental effects or due to lack of appropriate therapy in circumstances where evidence-based options were available. Moderate DRPs included DRPs whereby interventions would result in moderate benefit for the patient, while minor DRPs were defined as those requiring only minor adjustments, such as modifications to dosage timings.²⁰ Harmful, unpleasant and unintended responses to drugs at normal doses were considered to constitute ADRs.¹⁷

The probable consequences of a lack of intervention were categorised as insignificant, minor, moderate, major or catastrophic.²⁰ For example, insignificant consequences referred to circumstances where no harm or injury to the patient and a low financial loss would result as a lack of intervention. Minor consequences included minor injuries, minor treatment, no prolonged length of stay (LOS) or re-admission to the hospital and the potential for minor financial loss, while moderate consequences included major temporary injuries, prolonged LOS or re-admission to the hospital, a cancellation or delay in planned treatments/procedures and the potential for financial loss. Major consequences included major permanent injuries, prolonged LOS or re-admission to the hospital, morbidity upon discharge and the potential for significant financial loss. Finally, catastrophic consequences of a lack of intervention included the death of the patient, the potential for large financial losses and/or threat to the patient's goodwill or reputation.²⁰

Data were analysed using the Statistical Package for the Social Sciences (SPSS), Version 23.0 (IBM Corp., Armonk, New York, USA). A Wilcoxon signed-rank test was used to assess the differences between pre- and post-intervention DRPs and clinical problems. A Chi-squared test was used to assess the relationship between DRPs and risk factors such as age, gender, clinical manifestations, LOS, comorbidities, complications from other CVDs and the number of drugs administered. Logistic regression was used for the multivariate analysis of risk factors (advance test). A *P* value of <0.05 was considered statistically significant.

Ethical approval for this study was obtained from the Ethics Committee of the Faculty of Medicine at the University of Indonesia (#956/UN2.F1/ETIK/2016). Informed consent was provided by all patients and/or

Table 3: Drug-related and clinical problems before and after a clinical pharmacist intervention among coronary heart disease inpatients in Indonesia (N = 75)

	Pre-intervention			Post-intervention			P value*
	n	Mean ± SD	Median (IQR)	n	Mean ± SD	Median (IQR)	
Clinical problems	202	2.69 ± 0.97	2 (2–4)	26	0.35 ± 0.73	0 (0)	<0.01
Number of DRPs	443	5.91 ± 3.22	5 (4–8)	53	0.71 ± 1.30	0 (0–1)	<0.01
Types of DRPs	199	2.65 ± 0.78	3 (2–3)	37	0.49 ± 0.66	0 (0–1)	<0.01

SD = standard deviation; IQR = interquartile range; DRP = drug-related problem.

*Using a Wilcoxon signed-rank test.

their relatives. Data confidentiality and security were ensured throughout the study period.

Results

The mean age of the patients was 56.4 ± 8.4 years, with the majority being 35–59 years old (64%). Most of the patients were male (70.7%). The most frequent clinical manifestations of CHD among the patients were non-ACS symptoms (66.7%) [Table 1]. The median LOS was two days (interquartile range [IQR]: 2–4 days), with 92% staying 1–5 days. The median number of comorbidities was two (IQR: 1–3). Hypertension (96%), cholesterol (38.7%) and type 2 diabetes mellitus (30.7%) were the most common comorbidities. The majority of the patients had no complications (80%). Overall, a total of 561 different kinds of drugs were prescribed, falling into 44 drug classes. The most common class was antihypertensives (33.6%), followed by antiplatelets (21.6%) and anticholesterol medications (12.8%). Patients received a median of seven different types of drugs (IQR: 5–9 types).

The pharmacist interventions were not fully accepted (96.5%) [Table 2]. Initially, a total of 443 DRPs and 202 clinical problems were identified and received interventions. Patients had a median of five DRPs (IQR: 4–8 DRPs). There were 199 different subtypes of DRPs, with patients experiencing a median of three subtypes (IQR: 2–3 subtypes) [Table 3]. Nonoptimal drug effects (37.5%), non-allergic ADRs (39.1%) and unnecessary drug treatments (1.8%) were the dominant subtypes of DRPs [Table 4]. Post-percutaneous coronary intervention hand pain (27.2%), chest pain (21.8%) and shortness of breath (11.4%) were the dominant pre-intervention clinical problems [Table 5].

Pre-intervention DRPs varied in terms of severity, with 35 minor (7.9%), 336 moderate (75.8%) and 72 major (16.3%) DRPs. Interventions were performed for 138 actual (31.2%) and 305 potential (68.8%) DRPs. Of the actual DRPs, 107 (77.5%) were attributable to drug effects, 22 (15.9%) were attributable to ADRs and nine (6.5%) were due to treatment cost-related problems. For the potential DRPs, 77 (25.2%) and 228 (74.8%)

were due to drug effects and ADRs, respectively [Table 6]. The most predominant type of intervention for DRPs was concurrent (n = 310; 70%). The consequences of a lack of intervention for DRPs were projected to be insignificant in two cases (0.5%), minor in 33 cases (7.4%), moderate in 336 cases (75.8%), major in 71 cases (16%) and catastrophic in one case (0.2%).

Following the intervention, there were 53 DRPs, 37 subtypes of DRPs and 26 clinical problems [Table 3].

Table 4: Number and subtype of drug-related problems before and after a clinical pharmacist intervention among coronary heart disease inpatients in Indonesia (N = 443)

DRP	n (%)	
	Pre-intervention (n = 443)	Post-intervention* (n = 53)
Drug effects	184 (41.5)	28 (6.3)
None	0 (0)	0 (0)
Nonoptimal	166 (37.5)	22 (4.5)
Wrong effect	0 (0)	0 (0)
Indication untreated	18 (4.1)	8 (1.8)
ADRs	250 (55.8)	25 (5.6)
Non-allergic	173 (39.1)	22 (5)
Allergic	0 (0)	0 (0)
Toxic	77 (17.4)	3 (0.7)
Treatment cost-related	9 (2)	0 (0)
More costly than necessary	1 (0.2)	0 (0)
Unnecessary treatment	8 (1.8)	0 (0)
Other	0 (0)	0 (0)
Patient dissatisfaction [†]	0 (0)	0 (0)
Unclear [‡]	0 (0)	0 (0)

DRP = drug-related problem; ADR = adverse drug reaction.

*Post-intervention percentages are calculated out of the total number of pre-intervention DRPs. There was an 88% reduction in the overall number of DRPs following the intervention. [†]Despite optimal clinical and economic treatment outcomes. [‡]More clarification necessary.

Table 5: Number of clinical problems before and after a clinical pharmacist intervention among coronary heart disease inpatients in Indonesia (N = 202)

Clinical problem	n (%)	
	Pre-intervention (n = 202)	Post-intervention* (n = 26)
Chest and hand pain	6 (3)	0 (0)
Chest pain and a burning sensation	3 (1.5)	0 (0)
Chest pain and a sensation of heaviness	4 (2)	0 (0)
Chest, back and shoulder pain	21 (10.4)	0 (0)
Chest pain	44 (21.8)	1 (0.5)
Palpitations	4 (2)	1 (0.5)
Epigastric pain	5 (2.5)	0 (0)
Nausea	10 (5)	1 (0.5)
Vomiting	2 (1)	0 (0)
Cold sweat	7 (3.5)	0 (0)
Coughing	4 (2)	3 (1.5)
Shortness of breath	23 (11.4)	6 (3)
Headache/vertigo	4 (2)	1 (0.5)
Post-PCI/CA hand pain	55 (27.2)	1 (0.5)
Swallowing pain	1 (0.5)	0 (0)
Joint pain	-	2 (1)
Diarrhoea	1 (0.5)	-
Constipation	1 (0.5)	0 (0)
Melaena	1 (0.5)	0 (0)
Easily fatigued	4 (2)	5 (2.5)
Haematuria	1 (0.5)	0 (0)
Back and shoulder pain	-	2 (1)
Restless sleep	1 (0.5)	1 (0.5)
Oedema	-	2 (1)

PCI = percutaneous coronary intervention; CA = coronary angiography.

*Post-intervention percentages are calculated out of the total number of pre-intervention clinical problems. There was an 87.1% reduction in the overall number of DRPs following the intervention.

Table 6: Pre-intervention drug-related problems among coronary heart disease inpatients in Indonesia (N = 443)

DRPs	n (%)			
	Drug effects	ADRs	Treatment cost-related problems	Total
Actual	107 (77.5)	22 (15.9)	9 (6.5)	138 (31.2)
Potential	77 (25.2)	228 (74.8)	0 (0)	305 (68.8)
Total	184 (41.8)	250 (56.2)	9 (2)	443 (100)

DRP = drug-related problem; ADR = adverse drug reaction.

Overall, the number and subtypes of DRPs significantly decreased by 88% and 81.4%, respectively, while clinical problems significantly decreased by 87.1% ($P < 0.01$ each). Clinical manifestations of CHD were associated with a reduction in clinical problems, although this difference was not statistically significant ($P = 0.21$). In addition, the effect of age and comorbidity on the number of DRPs was also not significant ($P = 0.18$ and 0.16 , respectively). While clinical problems were significantly affected by age ($P = 0.02$), the effect of comorbidities was not significant ($P = 0.21$). Conversely, there was a significant reduction in the number of DRPs, subtypes of DRPs and clinical problems among patients with complications ($P = 0.04$ each). In the advance test, patients with complications were 26.047 times more likely to have an increase or no reduction in the number of clinical problems compared to patients without complications ($P < 0.05$).

Discussion

Advanced age is a major risk factor of myocardial infarction, a cause of ACS-related CHD.^{21,22} According to previous research, the majority of CHD patients in Indonesia are elderly (>75 years old).⁶ However, most of the patients in the current study were middle-aged; this is likely due to the high proportion of non-ACS-related CHD cases. According to the American Heart Association, nearly half of all males and one-third of all females between 40–60 years old in the USA will develop some manifestation of CHD.⁵ This finding is in agreement with the results of the current study. Moreover, the majority of the patients in the current study did not have complications; once again, this may be because most were not elderly and therefore still had well-functioning organs. The LOS varied from 1–5 days for the majority of patients. This is in accordance with the unpublished clinical protocols of the studied hospital, which recommends a treatment plan of five days.

In the current study, patients received a median of seven drugs. A previous study reported a range of 6–16 cardiovascular drugs prescribed to patients in India.¹⁰ Antihypertensives, antiplatelets and anti-cholesterol medications are the primary treatments for CHD.²³ Accordingly, these drugs were the most frequently prescribed classes of drugs in the present study. However, while the majority of patients in the current study did not have ACS-related symptoms or complications, it was noted upon review that more ACS drugs were prescribed than non-ACS drugs.²³ In terms of severity, most of the DRPs in the present study were moderate; similarly, Shareef *et al.* noted that 58.5% of DRPs among CHD patients in a hospital in

India were moderately severe.²⁴ The most common type of DRPs in the present study were potential ADRs. These likely occurred because the recommended drug therapies for CHD patients are anti-anginal, fibrinolytic and anticoagulant medications, which can have many drug interactions and therefore result in a higher risk of ADRs.^{23,25} In contrast, drug effects caused the greatest number of actual DRPs; such problems may be due to the inappropriate timing and/or dosing intervals of drugs or failure on the part of the patient to take the drugs as prescribed.

Most interventions for DRPs in the present study were given concurrently to multiple recipients in order to increase awareness of potential drug interactions. In order to properly manage potential DRPs caused by drug interactions, separate and specifically timed doses of different drugs are recommended.^{23,25} Although clinicians in the current study seemed aware of these recommendations, the task of administering medications fell primarily to nurses who may not have been as equally well-informed. In addition, there was often not enough time to re-check correct drug dosages and certain dietary instructions regarding potential food-drug interactions were not properly communicated to nutritionists. Such logistical shortcomings should be addressed. The consequences of a lack of pharmacist intervention for most DRPs in the present study were deemed to be moderate as it was assumed that no intervention would have risked the health of the inpatients.

Gattis *et al.* found that the inclusion of a pharmacist on multidisciplinary teams significantly reduced mortality and heart failure events among patients with CVDs.¹⁸ The results of the current study similarly underline the importance of pharmacists, in that the intervention significantly decreased the number and type of DRPs and the number of clinical problems among CHD inpatients. This was in line with a comparable study of CVD patients in India, which demonstrated that a clinical pharmacist intervention positively influenced cardiovascular health-care management by preventing and resolving DRPs.²⁴ Another study in Indonesia also observed that a pharmacist intervention significantly decreased DRPs among stroke and CVD patients in an intensive care unit.¹⁹

In the current study, only age significantly affected the number of clinical problems post-intervention, while complications affected the number and subtypes of DRP and number of clinical problems. Since the type of CHD can influence the drug treatment required, it may also have affected the number of DRPs.²³ Age-related physiological changes can also affect the pharmacokinetic and pharmacodynamic properties of medication.²⁶ In the current study, the presence of

complications was found to significantly increase the chance of an increase or no reduction in clinical problems by 26.047 compared to patients without complications. Cardiovascular complications causing heart remodelling or aortic *stenosis* could result in a deterioration of the patient's clinical condition.²⁵

This study was subject to certain limitations. The identification and evaluation of DRPs and the content of the interventions were based solely on information from the available literature and the authors' experience as pharmacists. In addition, the study took place under conditions in which many of the clinicians involved did not fully support the research. Furthermore, no control group was included to compare DRP prevalence between cases with and those without pharmacist intervention. As a result, it was difficult to ascertain whether the intervention was the sole cause of the observed reduction in DRPs and clinical problems. Additionally, treatment cost-related DRPs could not be accurately evaluated in the study, as all treatments were covered by the patients' national health insurance.

Conclusion

This prospective study found that DRPs and clinical problems among CHD inpatients with at least one previous DRP were significantly reduced following a clinical pharmacist intervention. In most cases, DRPs were moderately severe; furthermore, the consequences of not intervening in the majority of DRPs was projected to be moderate, potentially risking the health of the inpatients. These findings indicate that a pharmacist intervention can optimise therapy and improve the clinical conditions of CHD inpatients.

ACKNOWLEDGEMENTS

The authors wish to acknowledge the aid of the Director and the Head of Pharmaceutical Installation for granting permission for the study to be performed at the hospital. In addition, the authors would like to thank all of the cardiologists who cooperated in this study, especially Siti E. Nauli, cardiologist supervisor, and Yulian Rahmadini and Dewi Fatmawati, pharmacist supervisors. All other parties who assisted with this study are also acknowledged.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

FUNDING

No funding was received for this study.

References

- Gaziano TA, Bitton A, Anand S, Abrahams-Gessel S, Murphy A. Growing epidemic of coronary heart disease in low- and middle-income countries. *Curr Probl Cardiol* 2010; 35:72–115. doi: 10.1016/j.cpcardiol.2009.10.002.
- Wong ND. Epidemiological studies of CHD and the evolution of preventive cardiology. *Nat Rev Cardiol* 2014; 11:276–89. doi: 10.1038/nrcardio.2014.26.
- World Health Organization. Cardiovascular diseases (CVDs): Fact sheet. From: www.who.int/mediacentre/factsheets/fs317/en/ Accessed: Oct 2017.
- Townsend N, Nichols M, Scarborough P, Rayner M. Cardiovascular disease in Europe: Epidemiological update 2015. *Eur Heart J* 2015; 36:2696–705. doi: 10.1093/eurheartj/ehv428.
- Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics: 2016 update - A report from the American Heart Association. *Circulation* 2016; 133:e38–360. doi: 10.1161/CIR.0000000000000350.
- National Institute of Health Research and Development, Indonesia Ministry of Health. [Indonesia basic health research 2013]. From: <http://labmandat.litbang.depkes.go.id/riset-badan-litbangkes/menu-risikesnas/menu-risikesdas/374-rkd-2013> Accessed: Oct 2017.
- Sayols-Baixeras S, Lluís-Ganella C, Lucas G, Elosua R. Pathogenesis of coronary artery disease: Focus on genetic risk factors and identification of genetic variants. *Appl Clin Genet* 2014; 7:15–32. doi: 10.2147/TACG.S35301.
- Aaronson PI, Ward JP. *The Cardiovascular System at a Glance*, 3rd ed. Hoboken, New Jersey, USA: Wiley-Blackwell, 2007. Pp. 74–117.
- Urbina O, Ferrández O, Luque S, Grau S, Mojal S, Pellicer R, et al. Patient risk factors for developing a drug-related problem in a cardiology ward. *Ther Clin Risk Manag* 2014; 11:9–15. doi: 10.2147/TCRM.S71749.
- Abraham RR. Drug related problems and reactive pharmacist interventions for inpatients receiving cardiovascular drugs. *Int J Basic Med Sci Pharm* 2013; 3:42–8.
- Pharmaceutical Care Network Europe Foundation. Classification for drug-related problems, Version 6.2. From: www.pcne.org/upload/files/11_PCNE_classification_V6-2.pdf Accessed: Oct 2017.
- DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. *Pharmacotherapy: A pathophysiologic approach*, 8th ed. New York, USA: McGraw Hill Medical, 2011. Pp. 9–10.
- Blix HS, Viktil KK, Reikvam A, Moger TA, Hjemaas BJ, Pretsch P, et al. The majority of hospitalised patients have drug-related problems: Results from a prospective study in general hospitals. *Eur J Clin Pharmacol* 2004; 60:651–8. doi: 10.1007/s00228-004-0830-4.
- Niquille A, Bugnon O. Relationship between drug-related problems and health outcomes: A cross-sectional study among cardiovascular patients. *Pharm World Sci* 2010; 32:512–19. doi: 10.1007/s11096-010-9401-1.
- Gastelurrutia P, Benrimoj SI, Espejo J, Tuneu L, Mangues MA, Bayes-Genis A. Negative clinical outcomes associated with drug-related problems in heart failure (HF) outpatients: Impact of a pharmacist in a multidisciplinary HF clinic. *J Card Fail* 2011; 17:217–23. doi: 10.1016/j.cardfail.2010.10.009.
- Andreazza RS, Silveira De Castro M, Sippel Köche P, Heineck I. Causes of drug-related problems in the emergency room of a hospital in southern Brazil. *Gaceta Sanit* 2011; 25:501–6. doi: 10.1016/j.gaceta.2011.05.016.
- Kaufmann CP, Stämpfli D, Hersberger KE, Lampert ML. Determination of risk factors for drug-related problems: A multidisciplinary triangulation process. *BMJ Open* 2015; 5:e006376. doi: 10.1136/bmjopen-2014-006376.
- Gattis WA, Hasselblad V, Whellan DJ, O'Connor CM. Reduction in heart failure events by the addition of a clinical pharmacist to the heart failure management team: Results of the Pharmacist in Heart Failure Assessment Recommendation and Monitoring (PHARM) Study. *Arch Intern Med* 1999; 159:1939–45. doi: 10.1001/archinte.159.16.1939.
- Simarmata M. [Pharmacist intervention on drug-related problems in patients with stroke and cardiovascular disorders the intensive care unit, Dr.Mintoahardjo Navy Hospital, Jakarta]. MSc Thesis, 2010, University of Indonesia, Depok, Jakarta, Indonesia.
- SHPA Committee of Specialty Practice in Clinical Pharmacy. SHPA standards of practice for clinical pharmacy. *J Pharm Pract Res* 2005; 35:122–48. doi: 10.1002/j.2055-2335.2005.tb00322.x.
- Wilson PW, Douglas PS. Epidemiology of coronary heart disease. From: www.uptodate.com/contents/epidemiology-of-coronary-heart-disease Accessed: Nov 2017.
- Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2016; 37:267–315. doi: 10.1093/eurheartj/ehv320.
- Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, et al. 2013 ESC guidelines on the management of stable coronary artery disease: The Task Force on the Management of Stable Coronary Artery Disease of the European Society of Cardiology. *Eur Heart J* 2013; 34:2949–3003. doi: 10.1093/eurheartj/ehv296.
- Shareef J, Sandeep B, Shastry CS. Assessment of drug related problems in patients with cardiovascular diseases in a tertiary care teaching hospital. *J Pharm Care* 2014; 2:70–6.
- O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013; 127:e362–425. doi: 10.1161/CIR.0b013e3182742cf6.
- Chan DC, Chen JH, Kuo HK, We CJ, Lu IS, Chiu LS, et al. Drug-related problems (DRPs) identified from geriatric medication safety review clinics. *Arch Gerontol Geriatr* 2012; 54:168–74. doi: 10.1016/j.archger.2011.02.005.