

Original Research

DRUG USE PATTERN AND IMPACT OF CLINICAL PHARMACIST INTERVENTION IN PRESCRIBING DRUGS FOR PATIENTS WITH ACUTE KIDNEY INJURY AT THONG NHAT HOSPITAL

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ABSTRACT: (1) Introduction: Medication management in patients with acute kidney injury (AKI) poses numerous challenges due to the rapid fluctuations in renal function over a short period. This necessitates frequent reassessment of drug indications and dosages to ensure both treatment efficacy and patient safety. This study aimed to investigate the drug use characteristics and evaluate the effectiveness of clinical pharmacist interventions in prescribing medications for patients with AKI; (2) Materials and Methods: A before-and-after study was conducted on inpatients diagnosed with AKI at Thong Nhat Hospital, Vietnam, during the pre-intervention period (from February 2022 to August 2022) and the intervention period (from September 2022 to March 2023). Clinical pharmacist interventions included reviewing prescriptions and providing guidance on dose adjustments for patients with AKI. Prescriptions were considered appropriate if the indications and dosages complied with drug usage guidelines and the Vietnamese National Drug Formulary. The effectiveness of the intervention was evaluated by comparing the appropriateness of prescribing between the two study periods; (3) Results: A total of 97 patients in the pre-intervention period and 94 patients in the intervention period were included. The proportion of patients receiving at least one drug potentially impairing kidney function in both periods was 33.5%, while 90.6% of patients were prescribed at least one drug that required dose adjustment or discontinuation in cases of renal impairment. The proportion of appropriately dosed prescriptions was higher in the intervention period compared to the pre-intervention period (94.7% vs. 84.5%, $p = 0.022$). However, the overall rate of appropriate prescribing did not differ significantly between the two periods (79.8% vs. 71.1%, $p = 0.165$); (4) Conclusion: The rate of appropriate prescribing for AKI patients was relatively high. Clinical pharmacist interventions contributed to improving the appropriateness of drug dosing.

Keywords: Acute kidney injury; characteristics of medication use; appropriate prescription; clinical pharmacist

1. INTRODUCTION

Acute kidney injury (AKI) is characterized by an abrupt deterioration in renal function, encompassing both structural impairment and functional loss within the kidneys. AKI is a prevalent issue in hospitalized patients, particularly among the elderly, those with multiple comorbidities, and those undergoing polypharmacy. It can lead to an increase in the risk of developing chronic kidney disease, progression to end-stage renal disease, and elevated mortality [1]. Annually, worldwide, an estimated 13.3 million patients are diagnosed with AKI, among which 1.7 million cases result in mortality [2]. Patients with AKI should have the use of nephrotoxic drugs minimized whenever possible and need dose adjustments for drugs excreted through the kidneys, like the management of chronic kidney disease [3]. The proportion of patients with renal impairment using at least one inappropriate medication was about 36.8% [4]. As the renal function in AKI undergoes rapid changes, medication administration in AKI patients may be more complicated compared to those with chronic kidney disease. This necessitates physicians to frequently assess and adjust medication indications and dosages. Thong Nhat Hospital in Vietnam is a first-class general hospital under the Vietnam Ministry of Health, specializing in geriatric care. The use of multiple medications and the presence of multiple comorbidities in patients can be the factors contributing to an increased risk of AKI. This study aimed to investigate the drug use pattern and evaluate the effectiveness of clinical pharmacist interventions in prescribing drugs for patients with AKI.

2. MATERIALS AND METHODS

2.1. Study design and setting

A before-and-after study was conducted among inpatients diagnosed with AKI at Thong Nhat Hospital, Vietnam. The study consisted of two periods:

- The pre-intervention period (from February 1st, 2022 to August 1st, 2022): In this period, there were no interventions in the physician's prescriptions for AKI patients.
- The intervention period (from

September 1st, 2022 to March 1st, 2023): In this period, clinical pharmacist interventions including: (1) Reviewed the prescriptions at the Nephrology department for a minimum of 12 hours per week; proposed appropriate dosages to physicians based on each patient's current renal function; monitored and adjusted doses if renal function deteriorated or improved. (2) Developed and updated comprehensive appendices detailing antibiotic dose adjustments based on renal function in the Hospital Guideline.

Data was collected during both periods, including patient and medication use characteristics obtained from medical records. The patient characteristics included age, sex, serum creatinine (SCr), estimated glomerular filtration rate (eGFR), department, classification of AKI and length of hospitalization. The medication usage characteristics were recorded from the time of AKI diagnosis until patient discharge, including the active ingredient, dosage, and route of administration.

2.2. Study population

All patients aged 18 or older who were diagnosed with AKI, acute kidney failure, or episodes of acute-on-chronic kidney disease at Thong Nhat Hospital were included in the study. Patients were excluded from the study if they were hospitalized for less than 48 hours; had fewer than 2 SCr values during hospitalization; experienced a SCr increase of less than 26.5 $\mu\text{mol/l}$ compared to baseline; were diagnosed with chronic kidney disease stage 5 (eGFR < 15 ml/min/1.73m²); were undergoing chronic dialysis; or had undergone kidney transplantation.

2.3. Study outcomes and definition

We investigated characteristics of medication use, including: total number of medications, drugs potentially impairing kidney function, intravenous (IV) and oral (PO) antibiotics and non-antibiotics requiring dose adjustment or discontinuation in case of renal impairment. Drugs potentially impairing kidney function were defined according to the hospital formulary at Thong Nhat Hospital.

We analyzed the appropriate use of prescription drugs including appropriateness of drug indications and dosages. The appropriateness of drug indication or dosage was determined if the drug indication or dosage complied with the drug instructions or the Vietnamese National Drug Formulary. Overall appropriate prescription meant that patients received both right drug indications and dosages of all drugs.

The impact of pharmacist interventions was evaluated by comparing the overall appropriate prescribing between the two stages.

2.4. Statistical analysis

Data was recorded and analyzed by the Statistical Package for Social Sciences software, version 20.0. Patients and drug characteristics were described by descriptive statistics. Continuous variables were expressed as means $\pm$ standard deviation (SD) for normal distribution (including baseline eGFR), and medians (interquartile range [IQR]) for non-normal distribution (including age, baseline SCr, length of hospital stay, number of medications per patient). Categorical variables were shown in frequency and percentage (sex, department, classification of AKI, drug characteristics, appropriateness of prescribing). To compare the pre-intervention and intervention periods, we used either the Student's t-test or non-parametric tests (Mann-Whitney U test) for continuous variables and chi-square or Fisher's exact tests for categorical variables. Statistical significance was set at $p < 0.05$.

2.5. Ethics approval

The study protocol was approved by the Institutional Review Board of Thong Nhat Hospital, Ho Chi Minh City, Vietnam (63/2022/BVTN-HDDD). The patients' personal information was kept confidential. All procedures followed the ethical standards set by the institutional and national research committees. The need for informed consent was waived by the Institutional Review Board due to the retrospective nature of the study.

3. RESULTS

3.1. Characteristics of the study population

The study included 191 patients with 97 persons in the pre-intervention and 94 persons in the intervention period. Most patients in two periods were older individuals, with males being predominant, and pre-renal AKI was the most common type in both phases. Characteristics of the study population are summarized in **Table 1**.

3.2. Characteristics of drug use pattern

The median number of medications per patient in both periods was 10 (7-14). The status of medication usage was presented in **Table 2**. The most used drug potentially impairing kidney function in both periods was ACEI/ARB. The most used IV antibiotic group that required dose adjustment or discontinuation in renal impairment in both periods was β -lactam. For non-antibiotic medications, the most frequently used IV drug was metoclopramide, while the most used PO medication was the novel oral anticoagulants.

3.3. Impact of clinical pharmacist interventions

The overall proportion of appropriate medication use in both phases was 75.4%. Specifically, the appropriateness of indications was observed in 84.3% of total cases, while the appropriateness of dosages was noted in 89.5% of the cases. The pre-intervention phase had a higher percentage of appropriate indications compared to the intervention phase, however this difference was not statistically significant (**Table 3**). The intervention stage had higher proportion of appropriate dosage and overall appropriateness compared to the pre-intervention stage, with only the difference in dosage appropriateness being statistically significant (**Table 3**).

In both phases, the most frequently inappropriately indicated medication was drotaverine (4.2%), while ciprofloxacin and levofloxacin were the two least appropriate in terms of dosage (both comprised 2.1%). The statistics for medications with inappropriate indications and dosages are presented in **Tables 4 and 5**.

Table 1. Patients’ characteristics

Characteristics	Pre-intervention (n = 97)	Intervention (n = 94)	p-value
Age (years), median (IQR)	75 (64-83)	76 (63.8-85.3)	0.679
≥ 75	49 (50.5%)	49 (52.1%)	0.824
Sex, n (%)			
Male	54 (55.7%)	45 (47.9%)	0.281
Baseline SCr (μmol/l), median (IQR)	99.5 (78.1-130)	100.5 (77.3-127)	0.793
Baseline eGFR (ml/phút/1,73m2), median (IQR)	63.5 ± 29.7	61.8 ± 24.4	0.657
Department, n (%)			
Nephrology	19 (19.6%)	23 (24.5%)	0.244
Intensive Care Unit	21 (21.6%)	12 (12.8%)	
Others	57 (58.8%)	59 (62.8%)	
Classification of AKI, n (%)			
Pre-renal	77 (79.4%)	83 (88.3%)	0.095
Intra-renal	12 (12.4%)	10 (10.6%)	0.708
Post-renal	12 (12.4%)	8 (8.5%)	0.384
Length of hospital stay (days), median (IQR)	10 (7-16)	10 (7-18.3)	0.963

4. DISCUSSION

There was not significant difference in the baseline characteristics of patients between the pre-intervention and intervention periods. The median age of patients in both phases was 76 years. This may be because Thong Nhat Hospital specializes in treating geriatric patients, who are more susceptible to AKI compared to younger adults [5]. Pre-renal AKI patients in both phases accounted for 83.8%. Elderly patients often have poor nutrition, multiple comorbidities such as hypertension and heart failure, and use medications like diuretics and ACEI/ARBs, which increase the risk of pre-renal AKI [5].

The patterns of medication usage among patients varied between the pre-intervention and intervention phases. Patients in the pre-intervention phase used more drugs potentially impairing kidney function and antibiotics that required dosage adjustments or discontinuation due to renal impairment than patients in the intervention phase, with statistically significant difference. By contrast,

patients in the intervention phase used more non-antibiotic PO medications that required dosage adjustments or discontinuation due to renal impairment than patients in the pre-intervention phase, with statistically significant difference. This indicates that during the intervention phase, the physicians have been attentive to avoiding the use of drugs potentially impairing kidney function and have restricted the use of antibiotics that require dose adjustment in patients with AKI.

In our study, the drug potentially impairing kidney function most frequently used were ACEI/ARB. According to Zhu et al. [6], the use of ACEI/ARB in AKI can improve the overall survival rate, both during hospitalization and post-discharge, due to the favorable effects of ACEI/ARB on the cardiovascular system. ACEI/ARB reduces the mortality rate related to cardiac diseases, including heart failure and coronary artery disease. However, the use of ACEI/ARB is associated with a higher risk in developing acute kidney disease [6].

Table 2. Characteristics of medication use

Characteristics	Pre-intervention (n = 97)	Intervention (n = 94)	p-value
Number of medications per patient, median (IQR)	11 (7.5-15)	9 (6.8-14)	0.24
Using at least one drug potentially impairing kidney function n (%)	41 (42.3%)	23 (24.5%)	0.009
ACEIs/ARBs	20 (20.6%)	16 (17%)	-
Aminoglycosides	3 (3.1%)	1 (1.1%)	-
Colistin	17 (17.5%)	4 (4.3%)	-
Vancomycin	4 (4.1%)	1 (1.1%)	-
NSAIDs	2 (2.1%)	1 (1.1%)	-
Tenofovir disoproxil fumarate	0 (0%)	1 (1.1%)	-
Using at least one medication requiring dose adjustment or discontinuation in renal impairment, n (%)	88 (90.7%)	85 (90.4%)	0.944
Antibiotics, n (%)	71 (73.2%)	52 (55.3%)	0.01
Intravenous antibiotics, n (%)	71 (73.2%)	52 (55.3%)	0.01
Aminoglycosides	3 (3.1%)	1 (1.1%)	-
β-lactams	61 (62.9%)	48 (51.1%)	-
Colistin	17 (17.5%)	4 (4.3%)	-
Fosfomycin	13 (13.4%)	5 (5.3%)	-
Fluconazole	3 (3.1%)	2 (2.1%)	-
Oral antibiotics, n (%)	0 (0%)	0 (0%)	-
Non-antibiotic medications, n (%)	68 (70.1%)	77 (81.9%)	0.056
Intravenous non-antibiotic medications, n (%)	36 (37.1%)	33 (35.1%)	0.773
Cerebrolysin	0 (0%)	1 (1.1%)	-
Enoxaparin	8 (8.2%)	12 (12.8%)	-
Drotaverine	1 (1%)	2 (2.1%)	-
Metoclopramide	9 (9.3%)	13 (13.8%)	-
Morphine	5 (5.2%)	2 (2.1%)	-
NSAIDs	2 (2.1%)	0 (0%)	-
Pethidine	7 (7.2%)	0 (0%)	-
Tramadol	1 (1%)	0 (0%)	-
Tranexamic acid	8 (8.2%)	9 (9.6%)	-
Oral non-antibiotic medications, n (%)	51 (52.6%)	64 (68.1%)	0.029
Allopurinol	1 (1%)	6 (6.4%)	-
Colchicine	4 (4.1%)	5 (5.3%)	-
Cilostazol	1 (1%)	2 (2.1%)	-
Drotaverine	4 (4.1%)	3 (3.2%)	-
Digoxin	5 (5.2%)	2 (2.1%)	-
Fenofibrate	3 (3.1%)	1 (1.1%)	-
Gabapentin	1 (1%)	2 (2.1%)	-
Pregabalin	0 (0%)	5 (5.3%)	-
Rosuvastatin	3 (3.1%)	2 (2.1%)	-
Trimetazidine	4 (4.1%)	4 (4.3%)	-
SGLT2 inhibitors	2 (2.1%)	7 (7.4%)	-
Novel oral anticoagulants	3 (3.1%)	9 (9.6%)	-

Table 3. Appropriateness of medication use

Appropriateness, n (%)	All (N = 191)	Pre-intervention (n = 97)	Intervention (n = 94)	p-value
The appropriateness of indications	161 (84.3%)	82 (84.5%)	79 (84%)	0.925
The appropriateness of dosages	171 (89.5%)	82 (84.5%)	89 (94.7%)	0.022
Overall appropriateness	144 (75.4%)	69 (71.1%)	75 (79.8%)	0.165

Table 4. The frequency of inappropriate indications

Drug/class names	Inapropriate case	Pre-intervention (n = 97)	Intervention (n = 94)
Alfuzosin	Contraindicated of alfuzosin extended release in patients with severe renal impairment (CrCl < 30 ml/min)	1	0
Cerebrolysin	Contraindicated in patients with severe renal impairment (eGFR < 30 ml/min/1,73m2)	0	1
Cilostazol	Contraindicated in patients with CrCl < 25 ml/min	1	2
Colchicine	Contraindicated in patients with severe renal impairment (eGFR < 30 ml/min/1,73m2)	2	1
Dabigatran	Contraindicated in patients with severe renal impairment (eGFR < 30 ml/min/1,73m2)	0	2
Dexketoprofen	Contraindicated in patients with severe renal impairment (eGFR < 30 ml/min/1,73m2)	1	0
Drotaverine	Contraindicated in patients with severe renal impairment (eGFR < 30 ml/min/1,73m2)	4	4
Fenofibrate	Contraindicated in patients with severe renal impairment (eGFR < 30 ml/min/1,73m2)	1	0
Gliclazide	Contraindicated in patients with severe renal impairment (eGFR < 30 ml/min/1,73m2)	0	1
Empagliflozin	Contraindicated in patients with eGFR < 20 ml/min/1,73m2	1	0
Hydrochlorothiazide	Contraindicated in patients with severe renal impairment (eGFR < 30 ml/min/1,73m2)	0	1
Meloxicam	Contraindicated in patients with severe renal impairment (CrCl < 30 ml/min) without dialysis	0	1
Pethidine	Contraindicated in patients with severe renal impairment (eGFR < 30 ml/min/1,73m2)	3	0
Piroxicam	Contraindicated in patients with severe renal impairment (CrCl < 30 ml/min)	1	0
Rosuvastatin	Contraindicated in patients with severe renal impairment (CrCl < 30 ml/min)	1	2
Tenofovir disoproxil fumarate	Contraindicated in patients with severe renal impairment (CrCl < 30 ml/min)	0	1
Trimetazidine	Contraindicated in patients with severe renal impairment (CrCl < 30 ml/min)	2	1

Table 5. The frequency of inappropriate dosages				
Drug names	Inapropriate case		Pre-intervention (n = 97)	Intervention (n = 94)
	Recommended dosage	Actual dosage		
Amoxicillin/ clavulanate	CrCl 10-30 ml/min: 500mg/100mg twice daily	1000mg/200mg twice daily	2	0
Cefoperazon/ sulbactam	CrCl < 15 ml/min: Sulbactam 1g per day	Sulbactam 6g per day	1	0
Ciprofloxacin	CrCl < 30 ml/min: 400mg once daily	400mg twice daily	4	0
Colistin	CrCl 10-30 ml/min: 4.5-5 million units per day	9 million units per day	2	0
Fosfomycin	CrCl 10-20 ml/min: 6g per day	12g per day	2	0
Levofloxacin	CrCl 10-50 ml/min: 750mg every other day	500mg per day	2	2
Meropenem	CrCl 10-25 ml/min: 1g twice daily	1g thrice daily	1	1
Teicoplanin	CrCl < 30 ml/min: 400mg every third day	400mg per day	1	1
Bambuterol	CrCl ≤ 50 ml/min: 10mg per day	20mg per day	0	1
Dabigatran	CrCl 30-50 ml/min: 150mg once daily	150mg twice daily	1	0
Digoxin	CrCl < 30 ml/min: 0.0625mg every other day	0.25mg every other day	3	0
Trimetazidine	CrCl 30-60 ml/min: 35mg once daily	35mg twice daily	1	1
AKI patients in two periods prescribed inappropriate indications accounted for 15.7%. This percentage was higher than that of renal patients using contraindicated medications in the study by MacRae et al. (3.9%) [7]. This difference may be attributed to the method of determining medications with inappropriate indications in the studies. Our study assessed the appropriateness of medication indications based on the Vietnamese National Drug Formulary and prescribing information, while the study by MacRae et al. [7] relied on the National Formulary of England. The proportion of appropriate indications was similar between the intervention and non- intervention phases (84% vs 84.5%, p = 0.925), possibly because clinical pharmacy interventions focused more on dosage adjustments than on indications. The medication with the highest percentage of inappropriate indication in the study was drotaverine (4.2%). This could be attributed to the lack of adverse events reports associated with drotaverine in patients with renal impairment at the hospital. Therefore, information about the contraindication of drotaverine in patients with severe renal impairment did not received much attention. AKI patients in two periods prescribed inappropriate dosages consisted of 10.5%.				

This result was lower than in the study by Roux-Marson et al. (39.5%) [8]. The proportion of appropriate dosage was higher in the intervention phase than in the non-intervention phase (94.7% vs 84.5%, $p = 0.022$). Clinical pharmacist interventions in the hospital primarily involved adjusting drug dosages based on renal function, mainly antibiotics. Our study indicated that these interventions enhanced the appropriateness of dosage. There were some improvements in errors related to antibiotic dosing. The errors of inappropriate dosage among antibiotics such as amoxicillin/clavulanate, cefoperazone/sulbactam, ciprofloxacin, colistin, and fosfomycin were eliminated during the intervention phase. Studies by Joosten et al. [9] and Sukkha et al. [10] also demonstrated that antibiotics were the most frequently adjusted drug dosages by clinical pharmacists.

Our study indicated that antibiotics were the most common medications with inappropriate dosages, of which ciprofloxacin and levofloxacin were the two least appropriate in terms of dosage (both comprised 2.1%). This finding is aligned with the study by Prajapati et al. [11]. Clinicians frequently administer elevated antibiotic dosages to ensure effective bacterial eradication and mitigate the emergence of antibiotic resistance among critically ill AKI patients. Nonetheless, the potential for toxicity from excessive antibiotic dosing warrants careful consideration.

The proportion of patients using at least one inappropriate medication was 24.6%. Meanwhile, in the studies by Antoniak et al. [12] and Kimura et al. [13], the percentages of patients with renal impairment using at least one inappropriate medication were reported as 59.1% and 40%, respectively, higher than our study's proportion. The overall appropriate prescribing in the intervention phase was higher compared to the non-intervention phase, although the difference was not statistically significant (79.8% vs 71.1%, $p = 0.165$). The most common group of inappropriate medications in our study was the antibiotic. In contrast, the drug category frequently inappropriately prescribed was anticoagulants such as enoxaparin in the study by Antoniak et al. [12], or analgesics such as NSAIDs in the study by Kimura et al. [13].

Limitation

This study had some limitations. It is a retrospective study that relies on data from medical records. Information regarding weight and height necessary for calculating creatinine clearance may have been incomplete or inaccurately documented. However, information regarding renal function and prescribed medications was accurately recorded in the medical records.

5. CONCLUSIONS

The proportion of appropriate prescribing in patients with AKI is relatively high. The clinical pharmacist intervention contributes to enhancing the appropriateness of dosage.

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