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Short Report

Prevalence and patterns of polypharmacy in peritoneal dialysis patients: an experience from a general hospital in Thailand

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ABSTRACT

Patients on peritoneal dialysis have a burden from comorbidities and risk of medication prescription. Our study aimed to determine the prevalence, patterns, and factors associated with polypharmacy in peritoneal dialysis patients. A single-center cross-sectional study was conducted in a sample of 245 patients who were undergoing peritoneal dialysis. Polypharmacy is defined as five or more medications per day. The results of our study showed that the prevalence of polypharmacy was 96%. The most common drug prescription type was blood pressure-lowering agents. In the multivariate model, only hypertension was a significant independent factor associated with polypharmacy (OR 6.97; 95%CI 1.34-36.15; p =0.021, after adjusting for age, gender, diabetes mellitus and dyslipidemia). In conclusion, a high prevalence of polypharmacy was identified in peritoneal dialysis patients in our study. Further studies should focus on drug interactions, awareness of medical nonadherence, and over-the-counter medication.

Key words: renal failure, medication, CAPD, chronic kidney disease, dialysis, drug

INTRODUCTION

The prevalence of chronic renal failure has increased from 13.8% to 14.5% according to the US Renal Data System report.[1] The number of peritoneal dialysis patients in Thailand is now increasing due to the universal coverage (UC) policy. According to a study by Changsirikulchai at el., the total number of patients undergoing peritoneal dialysis (PD) in Thailand from 2008 to 2016 was 11,417 patients.[2] Importantly, end-stage renal disease (ESRD) patients have multiple comorbidities and complications from their disease such as hypertension (HT); diabetes mellitus (DM) ; heart disease; bone and mineral; and anemia, which lead to the use of multiple medications.[3,4]

Polypharmacy is defined as the intake of five or more medications per day.[5,6] Extreme use of multiple medications

has increased the risk of adverse drug reactions and interactions that cause hospitalization and mortality.[7-9] Polypharmacy in hemodialysis (HD) patients was related to increased length of stay in the hospital, morbidity- mortality, and medication- related problems.[10] In chronic kidney disease (CKD) patients who had glomerular filtration rate (GFR) greater than 30 ml/min/1.73^2, the prevalence of polypharmacy in all patients was 80%, and the median intake was eight medications per day (range, 0- 27).[11] The most commonly prescribed drugs were beta-blockers, angiotensin- converting enzyme inhibitors (ACEIs), and statins. Stage of CKD, age, body mass index (BMI), DM, cardiovascular disease (CVD), and smoking status were significantly associated with polypharmacy (11). However, DM was the only factor associated with the initiation of polypharmacy (OR 2.46, p=0.003 (95% CI 1.36-4.45).[11] Furthermore, a recent study reported an increase in drug prescription 6 months after the initiation of PD and an increasing trend.[12]

Although several reports have studied polypharmacy in noncommunicable disease (NCD) and geriatric patients,[13-15] the study of polypharmacy in PD patients is limited in Thailand. We do not know current practices or patterns and the frequency of medications, which is an important knowledge gap that should be considered. Therefore, we studied the prevalence, patterns of medication intake, and factors associated with polypharmacy in PD patients.

MATERIALS AND METHODS

Study Population and Design

A cross- sectional study was conducted in the outpatient NCD clinic, Nakhon Nayok General Hospital, central region of Thailand between May 1, 2019, and July 31, 2019. Eligibility criteria included age older than 15 years and currently undergoing PD. Patients who were admitted to the hospital at the time of data collection and had no medication data were excluded from the study. The study was approved by the ethical committee of Nakhon Nayok Hospital (REC 02/2019).

Data Collection

Baseline characteristics including sex, age, marital status, insurance, comorbidities, smoking status, a pattern of polypharmacy, body weight, height, and body mass index (BMI) were reviewed from the medical records. Smoking status was defined as never, former, and current smokers. DM was described as hemoglobin A1C >= 6.5% or the use of antidiabetic drugs. Dyslipidemia (DLP) was defined as cholesterol >= 200 mg/dL or low- density lipoprotein cholesterol >100 mg/dL and triglyceride > 150 mg/dL or the use of lipid-lowering drugs. HT was diagnosed if systolic blood pressure >= 140 or diastolic blood pressure >= 90 mmHg or treatment with antihypertensive drugs. BMI was calculated as weight (kg)/height (m^2). In our study, heart disease was defined as congestive heart failure, atherosclerosis, arrhythmia, coronary artery disease, or hypertensive heart disease.

Definitions

Medication intake was defined as a prescription by a physician that was recorded in the medical record. Polypharmacy was defined as intake of five or more medications per day excluding the over-the-counter medications (OTC).

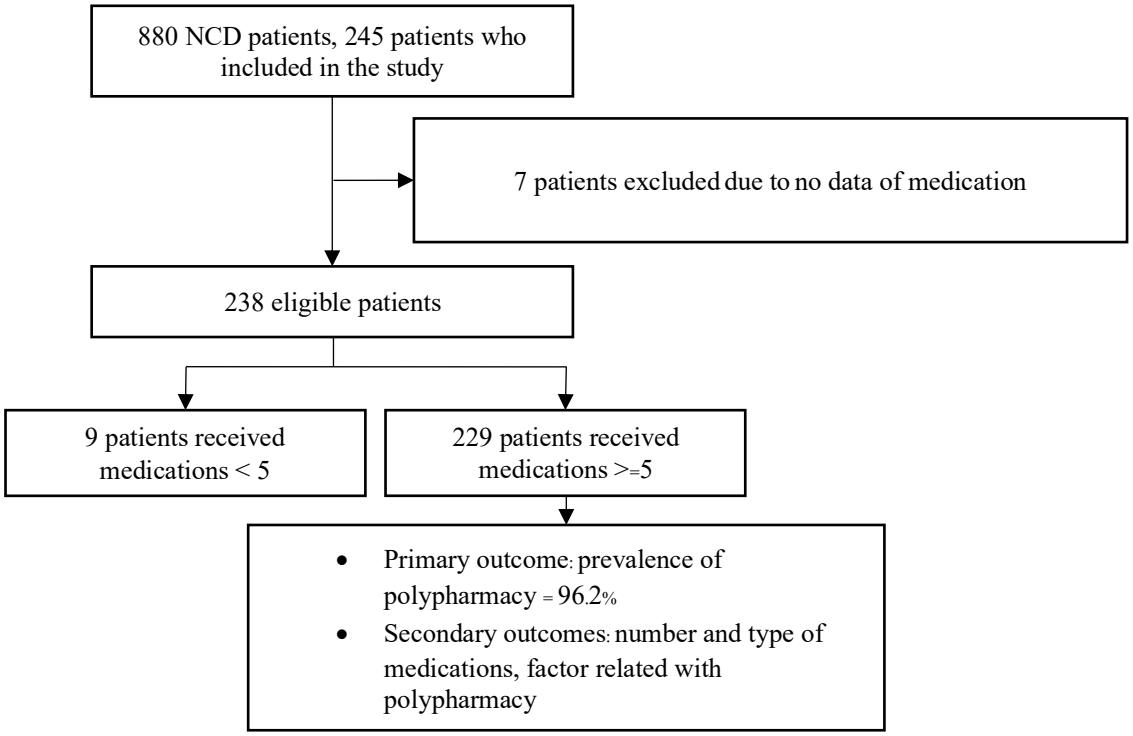

Figure 1 Flowchart of continuous ambulatory peritoneal dialysis (CAPD) who receiving medications (n = 238)

Study Outcomes

The prevalence of polypharmacy was a primary outcome in our study. Additionally, the pattern of polypharmacy and factors associated with polypharmacy were secondary outcomes.

Statistical Analysis

The prevalence of polypharmacy was reported as a percentage. All baseline characteristics were analyzed as descriptive analyses. Continuous variables were reported as the median ± interquartile range (IQL) . Categorical variables were described as a percentage. Factors associated with polypharmacy were expressed in odds ratios (ORs) with 95% confidence intervals (CIs) by using the logistic regression model. P- values < 0. 05 were considered statistically significant. All analyses were calculated using SPSS version 21.

RESULTS

Between 1 May and 31 July 2019, 880 NCD patients were enrolled in the study, of which 245 (27.8%) were PD patients. Seven patients were excluded from our study due to lack of data on medication intake as shown in Figure 1. Table 1 summarizes the baseline clinical parameters of 238 patients in our study. The median age of the patients was 56.3 years (IQR 15.4-95.8 years) and half of the patients were female. Almost all participants had UC insurance. We identified coexisting illnesses and found 94.1%, 62.2%, 49.2%, 23.5%, and 23.1% for HT, DM, DLP, gout, and heart disease, respectively. The mean of number of medications per patient in our study was 9.74 (SD 3.17, range 2-22) (total number of medications used per patient is shown in Figure 2).

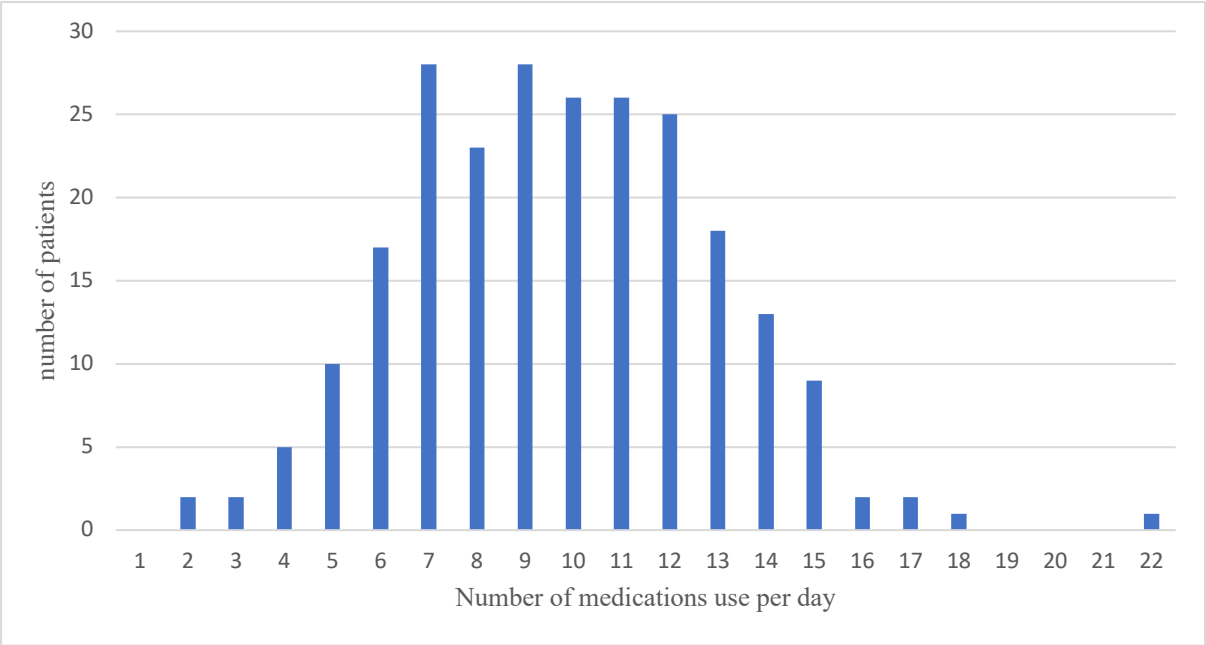

Figure 2 Total number of medications used per patient (N-238).

Of the 238 PD patients, 229 (96%) were taking at least 5 medications. Fifty-two percent of patients were prescribed 10 or more different medications per day. When we stratified by drug class, the antihypertensive drug group, which included loop diuretics, erythropoietin, platelet aggregation inhibitors and lipid-powering drugs, was the most common drug (Table 1).

Table 1. Baseline characteristics, comorbidities, and medications of peritoneal dialysis patients (N=238)

Baseline characteristics	**Number** (%)
Age, years; Median (IQR[a])	56.3 (15.4-95.8)
Gender, n (%)	
Male	115 (48.3)
Female	123 (51.7)
Marital status	
Married	157 (66)
Single	55 (23.1)
Widow	22 (9.2)
Divorce	4 (1.7)
Health insurance	
Universal coverage	231 (97.1)
Reimbursement	3 (1.3)
Social security	2 (0.8)
State enterprise	2 (0.8)

Baseline characteristics	Number (%)
BMI, kg/m^2 ; Median (IQR[a])	22.96 (14.02-43.21)
Comorbidities, n (%)	
Hypertension	224 (94.1)
Diabetic mellitus	148 (62.2)
Dyslipidemia	117 (49.2)
Gout	56 (23.5)
Heart disease	55 (23.1)
Thalassemia	3 (1.3)
Chronic obstructive pulmonary disease	1 (0.4)
Smoking status, n (%)	
Never smoking	207 (87)
Forming smoking	30 (12.6)
Current smoking	1 (0.4)
Polypharmacy [b]	229 (96.2)
Type of medication (n%), common use	
Calcium channel blockers, dihydropyridine	151 (63.4)
Loop diuretic	122 (51.3)
Erythropoietin	117 (49.2)
Platelet aggregation inhibitors	114 (47.9)
HMG-CoA-reductase inhibitors	113 (47.5)
Hydralazine	112 (47.1)
Alpha-blockers	92(38.7)
Proton pump inhibitors	67 (28.2)
Laxative agents	64 (26.9)
Angiotensin II receptor blockers	61 (25.6)
Insulin	39 (16.4)
Vitamin D analogs	37 (15.5)
Colchicine	36 (15.1)
Nitrate	25 (10.5)
Methyldopa	24 (10.1)
Angiotensin-converting enzyme inhibitor	22 (9.2)
Spironolactone	20 (8.4)
Allopurinol	19 (8.0)
Vitamins and Minerals	
Folic acid	157 (66.0)
Ferrous sulfate	143 (60.1)
Calcium	101 (42.4)
Potassium chloride	68 (28.6)
Vitamin B complex	64 (26.9)

[a] IQR, interquartile range, [b] Polypharmacy was described as intake of five or more medications per day excluding over-the-counter medications (OTC)

Analysis of antihypertensive drugs showed that calcium channel blockers, hydralazine, alpha-blockers, angiotensin II receptor blocker (ARB), methyldopa,

angiotensin-converting enzyme inhibitor (ACEI), and spironolactone were taken by 63.4%, 47.1%, 38.7%, 25.6%, 10.1%, 9.2%, and 8.4% of patients, respectively.

As shown in Figure 3, the most commonly prescribed individual drugs were furosemide (51.3%), erythropoietin (49.2%), simvastatin (47.5%), and hydralazine (47.1%), followed by aspirin (40.3%), doxazosin (37.0%), and metoprolol (33.2%).

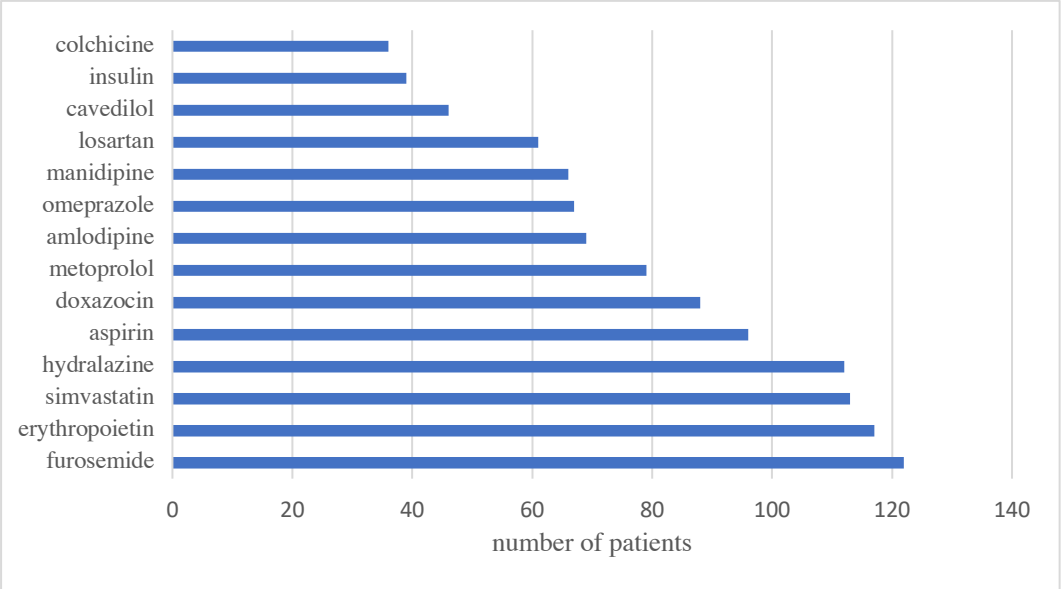

Figure 3 The most common medication intakes (N=238)

The univariate analysis by logistic regression found that age, HT, and DLP were associated with polypharmacy as shown in Table 2. However, when analyzed in the multivariate model, only HT was significantly associated with polypharmacy (OR 6.97; 95%CI 1.34-36.15; p =0.021, after adjusting for age, gender, DM and DLP).

Table 2 Factors associated with polypharmacy inpatient with peritoneal dialysis (N=238)

Parameters	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	p-value	Adjusted OR	95% CI	p-value
Age	1.05	1.00-1.10	0.045	1.05	1.00-1.11	0.066
Male	3.41	0.69-16.76	0.131	4.74	0.84-26.62	0.077
Hypertension	9.91	2.18-45.0	0.003	6.97	1.34-36.15	0.021
Diabetes mellitus	0.82	0.20-3.35	0.778	0.43	0.08-2.19	0.307
Dyslipidemia	8.21	1.01-66.73	0.049	6.57	0.74-58.38	0.091

DISCUSSION

PD is the frontline of renal replacement therapy in UC Thai patients. A previous study reported multiple comorbidies.[3-4] and medication uses in dialysis patients.[10-11] Therefore, it is important to explore medication types and identify drug interactions to improve the quality of life for patients. Nevertheless, the data on polypharmacy in PD patients are limited in the Thai population.

Based on the baseline characteristics, the median age of our population was younger than that in previous reports that studied GFR < 30 ml/min/1.73^2 with or without HD .[10-11] The differences in median age can be explained by multiple factors such as genetics, ethnicity, and etiology of renal failure. The most common comorbidity in our patients was HT. The decline in GFR was correlated with an increase in the percentage of HT.[11]The control of blood pressure is difficult in patients who have advanced stages of renal failure.[3-4] Several studies showed that almost all CKD patients with or without HD had coexisting HT.[10-11]

A high rate of polypharmacy was found in our study, which is similar to previous studies analyzing HD patients.[10.16-17] Many medications were taken due to multiple comorbidities in ESRD patients.[18-19] The frequency of polypharmacy in our study was similar to that in a previous study that analyzed stage IV-V CKD patients without dialysis.[11] A previous study showed the relationship between the number of medications and the decrease in GFR, and patients who had declined kidney function required multiple drugs.[11] Of course, almost all patients who coexist with HT receive antihypertensive drugs. Our results were similar to those of a previous study.[11]

Most of the prescriptions for antihypertensive drugs in our study were calcium channel blockers and depended on individual physicians, which differs from that previous studies.[11-12] According to the study by Schmidt IM et al, beta-blockers were the most prescribed hypertensive agent in stage IV-V CKD patients.[11] Campos LG et al showed that ACEI was the most antihypertensive drug taken after 6 months PD.[12] The recommended first-line blood pressure lowering agents is beta-blockers.[20] In cases where blood pressure cannot be controlled, dihydropyridine calcium blockers can be added as second-line therapy to control BP.[21-22] and ACEIs or ARBs can be added as a third-line therapy.

In our study, nearly half of the PD patients received erythropoietin injection because of its presence in the UC package, and our result was similar to the study of Campos LG et al from the USA that found an increase in EPO use in patients with UC insurance after 6 months of dialysis .[12]

Because of the benefits of loop-diuretics in ESRD patients who have urine, half of our patients received furosemide. A previous study showed that long-term use of furosemide can increase urine volume in CAPD patients, and help to control fluid balance. However, residual renal function was not preserved .[23]

We found high rate of lipid-lowering drugs in our patients (47.3%), which is likely due to the new guidelines for DLP in CKD patients.[24] Furthermore, folic acid (66.0%) was the most frequently administered vitamin and mineral in our study. Folic acid prescribed following the guidelines of PD. The causes of deficiency are from the decline in metabolism and uptake of folate in ESRD patients. Studies of patients undergoing dialysis including HD and PD had a decreased level of folic acid in their serum after dialysis, and the serum levels became normal after supplementation with oral folic acid.[25-27] Only 16.8% and 5.9% of our patients were prescribed anxiolytic drugs and antipsychotic drugs, respectively.

In our study, we found only patients who had comorbidities with HT associated with polypharmacy that correlated with the previous study.[11] A high prevalence of hypertension was found in approximately 29-30% of our population.[28] A previous study in CKD patients that included GFR <30 ml/min/1.73^2 found several factors, such as age,[11] DLP, [11] BMI,[11] smoking,[11] and CVD,[11] that were related to polypharmacy. However, we did not find factors related to polypharmacy in our study due to the lower median age, BMI, and percentage of smoking in our population which differs from the previous study.

Although approximately 62% of patients also had DM, we did not find an association between DM and polypharmacy due to the limitation of medication in patients who decline renal function. Almost all of our patients used insulin injection to control glucose levels. Our results were similar to those of a previous study[29] but different from those of another study performed in CKD patients without dialysis.[11] DLP was not related to polypharmacy due to the younger age, and the low BMI of our population lead to a low level of lipid serum. However, we did not collect data on the lipid profile in our study.

Our study had some limitations. We did not record OTC or nonadherence medication because our data were obtained from the medical records. We did not record the dosage of medication to evaluate the appropriate dose, serious adverse events, or drug interactions. The timeframe of our study was short, and no long-term follow-up was performed to study the effect of the drugs.

The strength of our study, is that this is the first study on polypharmacy in PD patients in the Thai population. We knew that HT was a factor associated with polypharmacy, and we identified the pattern of medication, especially in the HT group.

Future studies should evaluate OTC medications and medical nonadherence. Multiple studies have reported the benefits of medication reconciliation in dialysis patients.[30-32]

CONCLUSIONS

A high prevalence of polypharmacy in PD patients was found in our study. HT was an independent factor associated with polypharmacy. Importantly, the evaluation of medical nonadherence before adding the blood pressure-lowering agents is considered.

CONFILCT OF INTEREST

All authors declare that they have no conflict of interest.

ACKNOWLEDGEMENT

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WHAT IS ALREADY KNOWN IN THIS TOPIC?

- A heavy burden of polypharmacy was found in PD patients.
- Blood pressure-lowering agents were frequently used in PD patients.
- The most commonly prescribed antihypertensive drugs were calcium channel blockers.

WHAT IS ALREADY ADDED TO THE CURRENT KNOWLEDGE IN THIS TOPIC?

- Polypharmacy was found in ESRD either HD or PD patients.

- HT was an independent factor associated with polypharmacy.

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