

Renal Data from Asia – Africa

Medication Prescribing Patterns among Chronic Kidney Disease Patients in a Hospital in Malaysia

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ABSTRACT. To determine the medication prescribing patterns in hospitalized patients with chronic kidney disease (CKD) in a Malaysian hospital, we prospectively studied a cohort of 600 patients in two phases with 300 patients in each phase. The first phase was carried out from the beginning of February to the end of May 2007, and the second phase was from the beginning of March to the end of June 2008. Patients with CKD who had an estimated creatinine clearance ≤ 50 mL/min and were older than 18 years were included. A data collection form was used to collect data from the patients' medical records and chart review. All systemic medications prescribed during hospitalization were included. The patients were prescribed 5795 medications. During the first phase, the patients were prescribed 2814 medication orders of 176 different medications. The prescriptions were 2981 of 158 medications during the second phase. The mean number of medications in the first and second phases was 9.38 ± 3.63 and 9.94 ± 3.78 respectively (P -value = 0.066). The top five used medications were calcium carbonate, folic acid/vitamin B complex, metoprolol, lovastatin, and ferrous sulfate. The most commonly used medication classes were mineral supplements, vitamins, antianemic preparations, antibacterials, and beta-blocking agents. This study provides an overview of prescription practice in a cohort of hospitalized CKD patients and indicates possible areas of improvement in prescription practice.

Introduction

Appropriate drug selection for patients with chronic kidney disease (CKD) is important in order to avoid unwanted drug effects and to ensure optimal patient outcomes.^{1,2} Rational

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drug prescription is a difficult task in CKD patients. These patients are at higher risk of drug-related problems since they need complex therapeutic regimens that require frequent monitoring and dosage adjustments. In addition, they usually have other comorbidities including diabetes mellitus, hypertension, coronary artery disease and infection.³⁻⁵ Inappropriate use of medications can increase adverse drug effects, which can be reflected by excessive length of hospital stays, excessive health care utilization, and costs.^{1,6-8}

CKD is becoming a worldwide public health

problem with an increasing incidence and prevalence, poor outcomes, and high cost.⁹ The prevalence of CKD and particularly the ESRD is increasing in Malaysia at an alarming rate. The number of prevalent dialysis patients increased linearly from 4540 in 1998 to almost more than 16,000 by the end of 2007. The dialysis prevalence rate continued to increase linearly over the last ten years, from 205 per million population in 1998 to at least 615 in 2007.¹⁰ In Malaysia, there is no clear picture of the over-all medication profile in CKD population. These patients have many comorbidities and complications, and they are expected to require a large number of medications.

The objectives of this study were to describe prescribing patterns for hospitalized CKD patients by studying random samples from two consecutive years, and to identify areas in need of improvement in order to rationalize drug use, thereby minimizing medication errors and improving therapeutic outcomes. To our knowledge, no similar study has been performed in our country.

Patients and Methods

The study was conducted in the nephrology unit at Penang General Hospital, Penang, Malaysia. The nephrology unit is a 35-bed center that provides care to patients from all over Penang State.

We studied a cohort of CKD patients in the Penang dialysis center prospectively. A random sample of 600 patients admitted to the nephrology center was selected for the study and divided into two phases with equally numbered patients. The first phase was carried out from the beginning of February to the end of May 2007, and the second was from the beginning of March to the end of June 2008. To try to avoid bias and ensure randomization, a random number generator was used to generate 75 numbers per month to selected cases according to their admission numbers.

We recruited to the study patients with CKD, who had an estimated creatinine clearance \leq 50 mL/min at admission, were older than 18 years, and were admitted to the nephrology

center for more than 24 hours.

A data collection form was used to collect data from the patients' medical records and chart review. Data included age, gender, ethnic group, weight, medical history and comorbidities, diagnostic tests, dialysis information, drug therapy during the patients' hospitalization in the nephrology center, and drugs' strength and dosage and route of administration.

All systemic medications prescribed in the ward during hospitalization were included. The numbers and percentages of patients using every medication were presented and then medications were classified into categories based on Anatomical Therapeutic Chemical (ATC) classification recommended by the World Health Organization (WHO).¹¹

Statistical analysis

Data from the two phases were compared. Continuous variables were expressed as mean \pm SD. Discrete variables were expressed as counts and percentages. A chi-square test was used to test for differences between discrete variables. Student's "t" test was used to compare differences between the continuous variables. Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 15.

Results

Baseline characteristics of the patients are shown in Table 1. There were no significant differences between the first and the second groups in terms of age, gender, weight, dialysis, comorbidities, or number of medications prescribed during the study. In the first phase group, the mean number of comorbid conditions was 3.23 ± 1.29 ranging from zero to ten. In the second phase group, the mean was 3.08 ± 1.27 with a range from zero to six ($P = 0.226$).

The patients were prescribed 5795 medications. During the first phase, the 300 patients were prescribed 2814 medication orders of 176 different medications and 2981 of 158 medications during the second phase. In the first phase

Table 1. Comparison of demographic and clinical characteristics of the patients in this study.

Characteristic	First phase	Second phase	P-value
Gender, no. (%)			0.220*
Male	168 (56.0)	153 (51.0)	
Female	132 (44.0)	147 (49.0)	
Ethnic group, no. (%)			0.016*
Chinese	153 (51.0)	120 (40.0)	
Malay	97 (32.3)	134 (44.7)	
Indian	48 (16.0)	45 (15.0)	
Others	2 (0.7)	1 (0.3)	
Age, mean \pm SD	55.56 \pm 14.15	55.30 \pm 14.37	0.781**
Weight, mean \pm SD	59.20 \pm 10.81	58.84 \pm 11.77	0.853**
Stage of CKD, no. (%)			0.044*
Stage 5 (ESRD)	266 (88.7)	281 (93.7)	
Stage 4	23 (7.7)	16 (5.3)	
Stage 3	11 (3.7)	3 (1.0)	
Dialysis, no. (%)			0.679*
No. dialysis	56 (18.7)	55 (18.3)	
Hemodialysis	163 (54.3)	154 (51.3)	
Peritoneal dialysis	35 (11.7)	45 (15.0)	
Dialysis only during hospitalization	46 (15.3)	46 (15.3)	
Number of drugs in hospital, mean \pm SD	9.38 \pm 3.63	9.94 \pm 3.78	0.064**
Comorbidities, no. (%)			
Anemia	262 (87.3)	239 (79.7)	0.011*
Hypertension	240 (80.0)	252 (84.0)	0.202*
Diabetes mellitus	187 (62.3)	168 (56.0)	0.115*
Coronary artery disease	77 (25.7)	62 (20.7)	0.147*
Hyperlipidemia	40 (13.3)	29 (9.7)	0.159*
Cerebrovascular disease	24 (8.0)	25 (8.3)	0.881*

*Chi-square test, **Student t-test.

group, the mean number of medications used in the ward during hospitalization was 9.38 \pm 3.63 medications with a range of 1–22 medication per patient and a median of nine. Polypharmacy (use of \geq 5 medications) was a factor in 281 (93.7%) of the patients. In the second phase group, the mean number of medications used in the ward during hospitalization was 9.94 \pm 3.78 medications with a range of 1–22 medication per patient and a median of nine. Polypharmacy was a factor in 286 (95.3%) of the patients. The medications prescribed per patient in the second phase group were more, but the difference was not significant ($P = 0.066$).

The top 20 used medications were calcium carbonate (oral), folic acid/vitamin B complex (oral), metoprolol (oral), lovastatin (oral), ferrous sulfate (oral), nifedipine (oral), furosemide (oral), gliclazide (oral), aspirin (oral), po-

tassium chloride (oral), insulin (SC rapid acting), furosemide (IV), ranitidine (oral), cloxacillin (IV), perindopril (oral), ceftazidime (IV), ranitidine (IV), ampicillin/sulbactam (IV), prazocin (oral), and ferrous fumarate (oral).

Calcium carbonate was the most commonly prescribed medication, used in 197 (65.7%) and 201 (67.0%) patients during the first and second phases, respectively. The use of second most commonly used drug was the combination of folic acid and vitamin B complex; 127 (42.3%) and 163 (54.3%) patients in the two phases groups, respectively. The third commonly prescribed medication was metoprolol; 128 (42.7%) and 151 (50.3%) patients. Lovastatin and ferrous sulfate were also common medications in our cohort. In general, there was no significant difference in the use of most of the medications in the two groups, Table 2.

Table 2. The top 20 used medication classes of chronic kidney disease patients during hospitalization.

No.	Medication	First phase N (%)	Second phase N (%)	P-value*
1	Mineral supplements	239 (79.7)	236 (78.7)	0.763
2	Vitamins	213 (71.0)	234 (78.0)	0.049
3	Antianemic preparations	212 (70.7)	211 (70.3)	0.929
4	Antibacterials	164 (54.7)	173 (57.7)	0.459
5	Beta blocking agents	148 (49.3)	167 (55.7)	0.121
6	Calcium channel blockers	147 (49.0)	166 (55.3)	0.120
7	Diuretics	147 (49.0)	135 (45.0)	0.326
8	Serum lipid reducing agents	140 (46.7)	140 (46.7)	1.000
9	Drugs used in diabetes	136 (45.3)	134 (44.7)	0.870
10	Drugs for acid related disorders	98 (32.7)	116 (38.7)	0.125
11	Antithrombotic agents	87 (29.0)	106(35.3)	0.097
12	Analgesics	63 (21)	91 (30.3)	0.009
13	Agents acting on the renin–angiotensin system	88 (29.3)	65 (21.7)	0.031
14	Cardiac therapy	56 (18.7)	71 (23.7)	0.134
15	Antihypertensives	57 (19.0)	47 (15.7)	0.281
16	Drugs for functional gastrointestinal disorders	51 (17.0)	50 (16.7)	0.827
17	Other therapeutic products	28 (9.3)	32 (10.7)	0.586
18	Blood substitutes and perfusion solutions	15 (5.0)	24 (8.0)	0.185
19	Corticosteroids	25 (8.3)	14 (4.7)	0.069
20	Laxatives	21 (7)	13 (4.3)	0.158

*Chi-square test.

The use of most of the classes did not differ significantly between the first and second phase groups ($P > 0.05$). Exceptions include a significant increase in the use of vitamins and a significant decrease in the use of analgesics, and the renin–angiotensin drugs ($P < 0.05$).

Discussion

The sample of patients in our study is a reasonable representative of prescribing patterns in the nephrology unit at PGH as the patients in the study sample were around 50% of all the patients admitted to the nephrology center during the study time.

The patients in this study were on multiple medications. The mean of nine systemic medications used during hospitalization was not significantly different between the two phases of the study and in agreement with other studies where ESRD patients required a range of six to 12 medications.¹² However, this number seems to be lower than the mean mentioned in some recent studies. Manley et al reported a mean of 12.3 different medications from which

10.0 were home medications.¹³ Another study reported a mean of eight medications with a range from one to 28 medications.¹⁴

Patients with advanced stages of CKD have many health problems, including salt and water retention, phosphate retention, secondary hyperparathyroidism, diabetes, hypertension, chronic anemia, hyperlipidemia, and heart disease. To address all these medical problems, most patients require fluid restriction, multiple dietary restrictions, phosphate binders, vitamin D preparations, antihypertensive medications, hypoglycemic agents, erythropoietin, iron supplements, and a variety of other medications. The most commonly used medications in this study were expected based on the comorbidities and complications of CKD and were similar to other studies.¹³⁻¹⁶

In this study, erythropoietin was underprescribed, and compounded by a very high frequency of blood transfusion. For most patients who were not on erythropoietin, the reason was financial. Other studies from other parts of the world have also shown underprescription of erythropoietin.¹⁴ The use of iron

was higher in this study compared to others which ranged from 13% in the Bailie et al study¹⁴ to 44.7% in the Manley et al study.¹³

A very high percentage of the patients were prescribed antibiotics during their hospitalization (54.7 versus 57.7%). This can be explained by the high risk of access-related infections seen in patients on hemodialysis and the high risk of peritonitis in patients on peritoneal dialysis.¹⁷⁻¹⁹

Around half of the patients in both groups were prescribed beta blockers for treatment of hypertension, mostly metoprolol, a beta-blocker that is eliminated by hepatic metabolism, followed by calcium channel blockers (CCB) used in more than half of the patients, and ACE inhibitors used in around one quarter of the patients. The use of most classes was comparable with a report from the USA in 1998 except for the use of beta blocking agents, which is much higher in this study patients.¹⁵ Two recent studies from the USA have shown very close rates of CCB and beta blockers use, but their use of ACE inhibitors was much more than in this study (more than 40% in their studies compared to around 25% in the current study).^{13,14}

The use of diuretics was very common among patients of the study sample, where more than 45% of them were prescribed a diuretic, mostly a loop diuretic (furosemide); loop diuretic use ranges from 9.2% in the USA to 21.3% in Europe, especially in patients with residual renal function (RRF) with reported decrease in overall mortality in the users of diuretics.²⁰

Around 47% of the patients were using serum lipid reducing agents. This is higher than the other studies where the percentage ranged from 8.0% only¹⁵ to 29.2%.¹³ Most of the patients were on lovastatin.

Around 45% of the patients were treated with antidiabetic agents. The most common agent used for control of diabetes was insulin followed by gliclazide. As around 60% of the patients in the study sample had diabetes as a comorbidity, there appears to be a mismatch between the number of patients with diabetes and the number of patients treated for diabetes. This is similar to other studies.^{13,15} The current

finding requires further investigations to explain if that was suboptimal treatment or because some diabetic patients might control their disease by diet only.

Regarding antithrombotic agents, aspirin was one of the medications in around 20–27% of the patients. This is higher than that reported among the United States ESRD patients¹⁵ and lower than that reported in the Manley et al study (33.4%)¹³ and the Bailie et al study (37%).¹⁴ They all concluded that the use of aspirin among their patients was less than it should be. This can also be concluded in this study.

It is concluded that the data from this assessment of medication prescribing patterns suggest a high number of medications use in the CKD patients with increased possibility of drug interactions and adverse drug events (ADEs). This study may help to identify educational and quality improvement opportunities to prevent medication-related problems in this population.

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