

Potentially Inappropriate Medications in Hospitalized Elderly Patients with Kidney Disease

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Objective: Our purpose was to use the Beers criteria to determine potentially inappropriate medications in people 65 years of age and older who were hospitalized in the Nephrology and Endocrinology Department of The Second General Hospital in Ulaanbaatar, Mongolia from October to December in 2017. **Methods:** A total of 75 patients' medical records were selected who were aged ≥ 65 and diagnosed with kidney diseases. The patient's age, sex, serum creatinine, the number of potentially inappropriate medications prescribed were determined. Descriptive statistics, frequency analysis, and t-tests were used for normally distributed variables. The Mann-Whitney U test was used for variables with a non-normal distribution. **Results:** Most patients for whom data were creatine clearance data were available (36/41, 87%) were prescribed at least one potentially inappropriate medication, and the number prescribed of potentially inappropriate medications was moderately correlated with length of hospital stay ($r = .326$, $p < .05$). The frequency of potentially inappropriate medications prescribed in patients with CrCL < 60 ml/min was significantly higher than in patients with CrCL level 60 – 90 ml/min (29/31 vs. 7/10, $X^2(1) = 50.45$, $p < .001$). A total of 195 potentially inappropriate medications were prescribed to 75 elderly patients diagnosed with renal disease, and these included antibiotics, anticonvulsants, proton pump inhibitors, and calcium channel blockers. **Conclusion:** Potentially inappropriate medications were frequently prescribed to hospitalized geriatric patients with kidney disease. Health care professionals in Mongolia need to collaborate to optimize pharmacotherapy based on renal function to avoid the complications of potentially inappropriate medications for geriatric patients with kidney disease.

Keywords: Elderly People, Pharmacotherapy Monitoring, Potentially Inappropriate Medications, Kidney Disease, Mongolia

Introduction

Older adults often require multiple medications for treatment of chronic conditions, and age-associated organ system changes alter the pharmacokinetic and pharmacodynamic profiles of medications. Thus, the elderly are more at risk of adverse drug reactions compared to the general population¹⁻³.

The Beers criteria for potentially inappropriate medications used in older adults lists medications to avoid and provides a well-validated tool for screening prescriptions harmful for older adults⁴. The list is updated every three years by the American Geriatric Society. Potentially inappropriate medications are medications with risks that outweigh the therapeutic benefit and should be avoided in people 65 years of age and older. The prevalence of potentially inappropriate medications reported in several papers ranges from 35 to 47%⁵. Polypharmacy and potentially inappropriate medications are estimated to cause adverse drug effects in up to 35% outpatient and 40% inpatient older adults⁶. One study evaluating potentially inappropriate medications among older adults with cardiovascular diseases in Mongolia revealed that 13 to 24.2% of patients 65 years of age and older admitted to the three main state hospitals of Ulaanbaatar were prescribed potentially inappropriate medications⁷.

The health burden of non-communicable diseases such as cardiovascular illness and diabetes mellitus has increased year by year in Mongolia and is thus becoming a leading cause of kidney disease. Large cross-sectional studies conducted in six regions of the world revealed that hypertension, diabetes, obesity, and high cholesterol level were all independently associated with chronic kidney disease, and the prevalence of chronic kidney disease was 18.0% (15.5-20.8%) in Mongolia⁸⁻¹².

In adults, the normal estimated glomerular filtration rate (eGFR) is more than 99 ml/min/1.75m². eGFR declines with age, even in people without kidney disease. Since many drugs are excreted by the kidneys, older adults with kidney disease are more likely to have alterations in drug pharmacokinetics and pharmacodynamics compared to young adults with kidney disease, and selection of medications and dosing for elderly patients should be cautiously considered to prevent medication-related harm¹³⁻¹⁴.

Although there are some research studies on the prevalence of renal diseases and its risk factors in Mongolia, we are aware

of only one single study on the use of potentially inappropriate drugs in the elderly⁷⁻¹². We are unable to identify other peer-reviewed studies on the use of potentially inappropriate drugs in elderly Mongolian patients with kidney disease. Therefore, the purpose of this study was to determine the pattern of potentially inappropriate medications for elderly patients with kidney disease hospitalized in the Nephrology and Endocrinology Department of the Second General Hospital in Ulaanbaatar, Mongolia.

Materials and Methods

Study subjects and data collection

We conducted a retrospective chart review of patients hospitalized at the Nephrology and Endocrinology Department of The Second General Hospital in Ulaanbaatar, Mongolia, from October to December in 2017. A total of 75 patient's medical records were selected from all charts in the mentioned time. The inclusion criteria were patients aged ≥ 65 , diagnosed with acute and chronic kidney disease on the chart as a primary or co-morbid diagnosis, and had chronic kidney disease as a complication from another organ system disease. Patients not diagnosed with any form of renal failure, who were < 64 years of age and were hospitalized less than four days and whose medications were frequently changed, were excluded. We sought to collect the following information from the medical records: patient's age, gender, anthropometric measurements (weight and height), serum creatinine, and the potentially inappropriate medications prescribed. We collected the reported cause of kidney disease, and the co-morbid disease diagnoses and complications as written by physicians who had treated the patient during the time they were hospitalized. Since direct measurements of the creatine clearance (CrCL) were not available, we calculated the estimated creatinine clearance with Cockcroft-Gault equation¹⁵ based on the patients' age, weight, height, and serum creatinine when these parameters were available. The patients were divided in 2 groups based on their creatine clearance, those with CrCL < 60 ml/min and CrCL 60 - 90 ml/min. Potentially inappropriate medications were identified using The Beers criteria for potentially inappropriate medications to use in older adults updated every three years by the American Geriatric Society⁴.

Statistical analysis

Descriptive and frequency analyses were used for continuous and nominal variables. Measures of central tendency were the mean ± SD for normally distributed variables and median with minimum and maximum for non-normally distributed variables. The t-test was used to determine significant differences between groups of normally distributed variables, while the Mann-Whitney U test was used to compare groups of non-normally distributed variables. The Pearson and Spearman correlation tests were utilized to determine the correlation between variables. Frequencies were compared using the chi-square test. Statistical significance was set at $p < .05$. All statistical analyses were performed using SPSS 22.0 software (IBM Corp., USA).

Ethical statements

The study was conducted with permission from the Director, responsible for Research and Education of The Second General Hospital, and was approved by the Ethics Committee of Mongolian National University of Medical Sciences (Protocol No.2019/D, dated 01.23.2019).

Results

Clinical and demographic characteristics of study subjects

The clinical and demographic characteristics of study subjects are

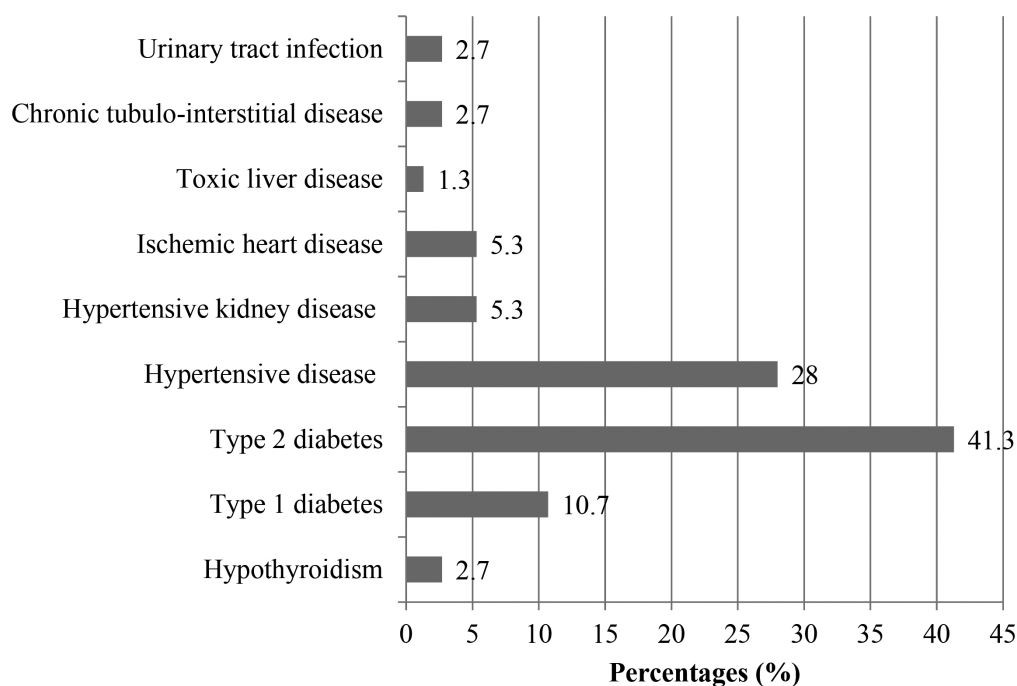


Figure 1. Percentage of co-morbid diseases in study patients (N=75).

Table 1. Patient’s demographic and clinical characteristics

Independent variables	Frequency	Percent
Total patients	75	100.0
Male	33	44.0
Female	42	56.0
Patients with acute kidney failure	3	4
Patients with chronic kidney disease	50	66.7
Patients with other kidney complication	56	74.7
Patients with other than kidney comorbidity	41	54.7

Table 2. Baseline characteristics of study patients with kidney disease.

Independent variables	Total patients (N=75)		Patient groups (N=41)		p-value
	N	Mean±SD; Median (Min, Max)	CrCL 60 - 90 ml/min (N=10)	CrCL <60 ml/min (N=31)	
Age ^a (years)	75	73.2±6.7	70.5±5.9	72.5±6.1	<.587
Weight ^a (kg)	65	68.5±12.5	71.0±9.6	70.2±13.1	<.166
Height ^a (cm)	63	160.0±10.6	160.6±11.2	162.1±7.9	<.380
BMI ^a (kg/m ²)	63	27.1±4.5	27.7±4.3	26.7±4.9	<.897
Serum Creatinine ^b (μM/L)	50	123.8 (43, 761)	64.9 (43, 110.4)	212.1 (89.7, 761)	<.001
Creatinine clearance ^b (mL/min)	41	42 (7, 99)	76.0 (61, 99)	31.13 (7, 59)	<.001
Number of PIMs ^b	63	2 (0, 10)	2.9 (1, 10)	3.1 (0, 9)	<.635
Length of hospital stay ^b (days)	75	8 (5, 16)	8.0 (7, 11)	8.3 (6, 12)	<.679

^aIndependent-test, ^bNon parametric Mann-Whitney U test. Abbreviations: BMI - Body mass index; PIMs - Potentially inappropriate medications.

Table 3. Patients stratified by CrCL and whether they were prescribed potentially inappropriate medications.

Was one or more potentially inappropriate medication used?	Number of patients		p-value
	CrCL 60 - 90 ml/min	CrCL <60 ml/min	
Yes	7	29	<.001
No	3	2	

^aChi-square test $X^2(1) = 50.45$. Abbreviation: creatine clearance - CrCL

Table 4. Correlations between variables.

	Age (yrs)	Weight (kg)	Height (cm)	BMI (kg/m ²)	PIM (N)	Length of hospital stay (days)	Creatinine (μM/L)	CrCL (mL/min)
Age (years)	1							
Weight (kg)	-.266*	1						
Height (cm)	.046	.467**	1					
BMI (kg/m ²)	-.246	.658**	-.348**	1				
PIMs	.078	.043	.171	-.080	1			
Length of hospital stay (days)	.069	-.101	-.002	-.109	.326**	1		
Creatinine (μM/L)	.042	.116	.087	.027	.228	.182	1	
CrCL (mL/min)	-.160	.160	.002	.181	-.120	-.214	-.722**	1

**Correlation is significant at the p<.01 level (2-tailed), *Correlation is significant at the p<.05 level (2-tailed). Abbreviations: BMI- Body mass index; PIM - potentially inappropriate medications; CrCL - creatinine clearance.

presented in Table 1. Most patients were diagnosed with chronic kidney disease and had one or more co-morbid diseases and other kidney complication diagnoses. The co-morbid diseases of patients with kidney failure are presented in Figure 1. Type 1 and 2 diabetes and hypertensive diseases were the most common co-morbid diseases at 10.7%, 41.3%, and 28%, respectively.

General characteristics of the patients

The baseline characteristics of our study participants with kidney disease are presented in Table 2. The most common comorbid diseases in our patients with renal disease were type 2 diabetes (41%) and hypertension (28%). Although all 75 patients were diagnosed with some form of kidney failure, serum creatinine laboratory results were missing in 25 of their medical records. Of the 50 patients with a serum creatinine level, the patient's

Table 5. The potentially inappropriate medicines prescribed to study population.

Pharmacologic classes	Drugs	Total patients (N=75) N (%)	Prescription number to CKD patients groups (N=41)	
			CrCL 60 - 90 ml/min (N=10)	CrCL <60 ml/min (N=31)
Proton pump inhibitors	Omeprazol	13 (17.3)	1	6
	Pantoprazol	4 (5.3)	-	-
Antithrombotic	Acetylsalicylic acid	10 (13.3)	2	5
ACEI	Lisinopril	6 (8.0)	2	6
ARB	Losartan	14 (18.7)	3	7
Calcium channel blockers	Nifedipine	10 (13.3)	1	6
	Amlodipine	14 (18.7)	2	5
Diuretics	Furosemide	17 (22.7)	1	12
	Spironolactone	4 (5.3)	1	3
Antihistamine	Diphenhydramine	4 (5.3)	-	4
Antidepressants	Amitriptyline	11 (14.7)	1	5
Anticonvulsants	Diazepam	7 (9.3)	1	2
	Gabapentin	22 (29.3)	3	9
Opioid analgesic	Tramadol	1 (1.3)	-	-
Steroid hormones	Dexametazone	2 (2.7)	-	2
Non steroid anti-inflammatory drugs	Ketoprofen	2 (2.7)	-	-
	Ibuprofen	2 (2.7)	-	-
	Diclofenac	1 (1.3)	-	-
Anti-infective drugs	Nitrofurantoin	17 (22.7)	1	6
	Nitroxoline	8 (10.7)	2	4
	Cefazolin	3 (4.0)	-	3
	Cefotaxime	4 (5.3)	1	3
	Ceftriaxone	2 (2.7)	-	-
	Ciprofloxacin	2 (2.7)	-	-
	Levofloxacin	3 (4.0)	-	-
	Ketoconazole	10 (13.3)	-	4
Total prescription		195	23	98

Abbreviations: CKD- chronic kidney disease, ACEIs – Angiotensin-converting enzyme inhibitors, Angiotensin II receptor blockers

weight or height was missing for nine patients. Therefore, we could estimate the CrCL in only 41 patients.

Table 3 shows that the frequency of potentially inappropriate medications prescribed in patients with CrCL <60 ml/min was significantly higher than in patients with CrCL level 60 – 90 ml/min.

We performed a bivariate correlation analysis estimating the correlation between serum creatinine and creatinine clearance, number of prescribed potentially inappropriate medications, hospitalized days, and patients' physical base characteristics (Table 4). The number prescribed of potentially inappropriate medications was moderately correlated with length of hospital

stay ($r = .326, p < .01$).

Potentially inappropriate medicines prescribed to the elderly patients

The pharmacological group of each medication and the number of potentially inappropriate medicines prescribed are presented in Table 5. A total of 195 potentially inappropriate medications was prescribed to 75 elderly patients, and the top three most frequently prescribed potentially inappropriate medications were gabapentin (29.3%), nitrofurantoin (22.7%), and amlodipine (18.7%). By the pharmacologic group, anti-infective, anticonvulsants, proton pump inhibitors, and calcium channel

blockers were the commonly prescribed medications in both patient groups.

Discussion

In our study of patients diagnosed with decreased kidney function, most patients (63/75, 84%) were prescribed potentially inappropriate medications, and the number prescribed of potentially inappropriate medications correlated with length of hospital stay ($r = .326$, $p < .05$). The frequency of potentially inappropriate medications prescribed in sicker patients with CrCL <60 ml/min was significantly higher than in patients with CrCL level 60 – 90 ml/min ($p < .001$). Considering that in the elderly, GFR declines linearly, with age and the decline is more substantial in females than males, serum creatinine level alone cannot predict kidney function in older adults with kidney disease, and GFR should be checked regularly. A decrease in GFR can have a considerable effect on drug metabolism and excretion and promote adverse drug reactions¹⁴⁻¹⁷.

Elderly patients often have multiples comorbidities, such as hypertension, cardiovascular disease, diabetes, and other organ system complications, and require many different medications making it difficult to treat disease while preventing unwanted adverse drug reactions. The potentially inappropriate medications listed in the Beers criteria commonly result in adverse drug reactions in the elderly with renal disease and can produce life-threatening complications. Therefore, prescribing potentially inappropriate medications should be avoided, and if the clinician cannot find an alternative medicine, the potentially inappropriate medication should be closely monitored in collaboration with other specialists such as clinical pharmacists and geriatricians^{14,15,17}.

We found that a total of 195 potentially inappropriate medications were prescribed to 75 elderly patients, and the top three most frequently potentially inappropriate medications prescribed were gabapentin (29.3%), nitrofurantoin (22.7%), and amlodipine (18.7%). Other studies that have examined the prevalence of potentially inappropriate medications prescriptions using Beers criteria reported that 30-34% of prescriptions were for potentially inappropriate medications and the most commonly prescribed potentially inappropriate medications were antihistamines (diphenhydramine), analgesics (NSAIDs, ibuprofen, naproxen) anti-infective, anticonvulsants and other

pharmacologic groups similar with our study^{5-7,20,21}.

Our study was limited by its small sample size and retrospective data collection, therefore, which limited our ability to estimate the prevalence, burden, and risk factors of potentially inappropriate medications prescribed for elderly patients with kidney diseases. Our study shows that the patients diagnosed any form of kidney failure, not checked serum creatinine in all patients above 60 years of age. However, 34 patients of the 75 total were missing all the measurements needed to evaluate kidney function, indicating our need for concurrent data collection. Our future efforts will likely focus on prospective studies of doctors' knowledge and attitude towards prescription selection, dose regimens for potentially inappropriate medications, and the prevalence of drug-related complications in the elderly and patients with kidney diseases.

Conclusion

We determined that potentially inappropriate medications were frequently prescribed to elderly patients with impaired renal function. Health care professionals need to collaborate to optimize pharmacotherapy based on renal function and to avoid prescribing potentially inappropriate medications for geriatric patients with kidney diseases.

Conflict of Interest

The authors declare there were no potential conflicts of interest related to the research, authorship, and publication of this article.

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