Patients Aged 80 Years or Older are Encountered More Potentially Inappropriate Medication Use

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Abstract

Background: Polypharmacy and potentially inappropriate medications (PIMs) are prominent prescribing issues in elderly patients. This study was to investigate the different prevalence of PIM use in elderly inpatients between 65–79 years of age and 80 years or older, who were discharged from Geriatric Department in West China Hospital.

Methods: A large-scale cohort of 1796 inpatients aged 65 years or over was recruited. Respectively, 618 patients were 65–79 years and 1178 patients were 80 years or older. Updated 2012 Beers Criteria by the American Geriatric Society was applied to assess the use of PIM among the investigated samples.

Results: A review of the prescribed medications identified 686 patients aged 80 years or older consumed at least one PIM giving a rate of 58.2%. Conversely, 268 (43.4%) patients aged 65–79 years consumed at least one PIM ($\chi^2 = 40.18$, $P < 0.001$). Patients aged 80 years or older had higher hospitalization expenses, length of stay, co-morbidities, medical prescription, and mortality than patients aged 65–79 years (all with $P < 0.001$). Patients aged 80 years or older were prescribed with more benzodiazepines, drugs with strong anticholinergic properties, megestrol, antipsychotics, theophylline, and aspirin. In multiple regression analysis, PIM use was significantly associated with female gender, age, number of diagnostic disease, and number of prescribed medication.

Conclusions: The finding from this study revealed that inpatients aged 80 years or older encountered more PIM use than those aged 65–79 years. Anticholinergic properties, megestrol, antipsychotics, theophylline, and aspirin are medications that often prescribed to inpatients aged 80 years or older. Doctors should carefully choose drugs for the elderly, especially the elderly aged 80 years or older.

Key words: Beers Criteria; Elderly; Polypharmacy; Potentially Inappropriate Medication

INTRODUCTION

The elderly experiences more chronic medical conditions than younger people, takes more medications, and is more likely to suffer from the adverse effects of multiple medications. Potentially inappropriate medications (PIMs), defined as those adverse risks exceeding their health benefits when compared with alternative therapies,[1] are a preventable cause of negative clinical and economic consequences in older people.[2-5]

With aging, geriatric patients, especially in very old age, are more vulnerable to drug-related problems, including PIM and potential adverse drug reactions.[6-8] The Beers criteria are one of the most popular guidelines for PIM use in elderly, which was initially released in 1991 and updated in 1997,

2003, and 2012.[9-11] Research has documented widespread PIM prevalence in elderly persons, which ranged from 9.8% to 46.5%.[5,12-15] However, to our knowledge, there are not any kind of data to show the comparison of PIM prevalence between the elderly aged 65–79 years and those aged 80 years or older.

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In this study, we investigated the different prevalence of PIM use in elderly inpatients between aged 65–79 years and aged 80 years or older, who were discharged from the Geriatric Department of West China Hospital using the 2012 Beers criteria. We found inpatients aged 80 years or older have more PIM use and encounter more potential inappropriate prescription of benzodiazepines, drugs with strong anticholinergic properties, megestrol, antipsychotics, theophylline, and aspirin than patients aged 65–79 years.

METHODS

Study design and ethical considerations

This was a retrospective cross-sectional study conducted in Geriatric Department of West China Hospital, a nonprofit tertiary care academic hospital. The study protocol was approved by the Research Ethics Committee of Sichuan University before the commencement of the study (ChiCTR-ECS-14004441).

Setting and participants

From October 2012 to April 2013, all patients aged 65 years or older who were discharged from the geriatric wards in West China Hospital were sampled for the study. Then, the subjects were divided into two groups as patients aged 65–79 years, and patients aged 80 years or older. All medications consumed on an as-needed basis; vitamin or mineral supplement, drug for topical use, and herbal medicines were not included in this study. The patients were excluded if no medication was used or the medication administration records were unavailable or incomplete.

Data collection

The electronic medical records (EMRs) of the patients were retrieved from the Information Center of West China Hospital, and the information obtained was transferred into a prepared spreadsheet. Retrieved information included age, gender, length of stay, prognosis (discharge or death), the total hospital charges, expenses for medicine, the primary medical conditions (diagnosis), and the prescribed drugs and dosages.

Study outcomes

The PIM analysis included all subjects who were eligible for this study. To investigate the difference of PIM use occurrence between patients aged 65–79 years and those aged 80 years or older, a full-length updated American Geriatric Society version (2012) of the Beers criteria was downloaded and printed out. All of the drugs included in the Beers criteria were assessed according to their availability in China. The prescribed medications were then assessed using these criteria to determine their appropriateness. To minimize interpretation bias, two raters were trained to use Beers criteria. Each rater evaluated the data set independently, and all disagreements were resolved through discussion.

Statistical analysis

Data generated from the EMRs were recorded on a spreadsheet and analyzed using SPSS version 16.0 (SPSS Inc., USA). Descriptive statistics was expressed as mean or median, frequencies or percentages. The list of PIMs found among patients was compiled and calculated as percentages. Chi-square test was used to compare categorical data, and the Student's t-test or nonparametric test was applied to compare continuous variables for mean or median, respectively. Logistic regression analysis was carried out to identify the independent factors associated with PIM use–univariate analysis was carried out, and the variables which were statistically significant at α level of 0.1 were included in multivariate stepwise regression. P value of <0.05 was considered statistically significant.

RESULTS

Demographics of participant patients

This study included a total of 1796 participants aged 65 years or older. Ten patients were excluded from the analysis because they were not prescribed any medication at the time of hospitalization. Among 1786 patients, 618 (34.4%) patients aged 65–79 years (74 ± 4 years) and 1178 (65.6%) patients were 80-year-old and above (85 ± 4 years) [Table 1].

Co-morbidity and outcome of death

Patients aged 80 years or older had more co-morbidities than those aged 65–79 years (6.5 ± 1.9 vs. 5.5 ± 2.1, $P < 0.001$) [Table 1]. Patients aged 80 years or older were greater vulnerability to hypertension, infectious disease, lower urinary tract symptoms (LUTS)/benign prostatic hyperplasia (BPH), chronic obstructive pulmonary disease (COPD), insomnia, coronary heart disease, chronic constipation, cerebrovascular disease, osteoporosis, dementia, chronic kidney disease (CKD), history of fractures, Parkinson's disease, and chronic seizures (all with $P < 0.05$) [Table 2]. In all of participants, 104 patients died finally. Seventy-eight (6.6%) of them aged 80 years or older, but 26 (4.2%) of them aged 65–79 years ($P < 0.001$) [Table 1].

Potentially inappropriate medication use

Compared with patients aged 65–79 years, patients aged 80 years or older were prescribed more medications (17.6 ± 10.4 vs. 14.2 ± 9.9). About 58.2% (686) of the patients aged 80 years or older consumed at least one PIM. However, only 43.4% (268) of the patients aged 65–79 years consumed at least one PIM ($\chi^2 = 40.18$, $P < 0.001$) [Table 1]. Table 3 lists top 10 of PIM categories using the 2012 Beers criteria prescribed in each group respectively. Notably, more patients aged 80 years or older were prescribed with benzodiazepines, drugs with strong anticholinergic properties, megestrol, antipsychotics, theophylline, and aspirin. When categorized by gender, female patients encountered more PIMs than male (54.5% vs. 52.6%, $P < 0.05$). However, except drugs with strong anticholinergic properties and non-COX-selective nonsteroidal anti-inflammatory drugs (NSAIDs), other prescriptions in top 10 PIMs were not different between female and male patients [Table 4].

Health economics outcomes

Patients aged 80 years or older had longer hospital stays (23 [14–34] vs. 16 [11–28] days, $P < 0.001$). In

Table 1: Characteristics of the study subjects

Characteristics	Age (years)		Statistical values	P
	65–79 (n=618)	≥80 (n=1178)		
Gender				
Men, n (%)	420 (68.0)	925 (78.5)	24.04*	<0.001
Women, n (%)	198 (32.0)	253 (21.5)	24.04*	<0.001
Number of diagnostic disease (mean ± SD)	5.5 ± 2.1	6.5 ± 1.9	10.34†	<0.001
Number of prescribed medication (mean ± SD)	14.2 ± 9.9	17.6 ± 10.4	6.68†	<0.001
Length of hospital stay, days, and median (IQR)	16 (11–28)	23 (14–34)	5.91*	<0.001
Hospitalization cost, $, median (IQR)	2699.8 (1583.1–5323.7)	3558.4 (2057.8–6818.8)	4.05*	<0.001
Death, n (%)	26 (4.2)	78 (6.6)	4.33*	0.037
Frequency of PIM, n (%)	268 (43.4)	686 (58.2)	40.18*	<0.001

*χ^2 values; †t values. PIM: Potentially inappropriate medication; SD: Standard deviation; IQR: Interquartile range.

Table 2: Prevalence of diagnosis in patients, n (%)

Diagnosis	Age (years)		χ^2	P
	65–79 (n = 618)	≥80 (n = 1178)		
Hypertension	335 (54.2)	807 (68.5)	35.79	<0.001
Infectious disease	230 (37.2)	507 (43.0)	5.68	0.017
LUTS/BPH	180 (29.1)	504 (42.8)	32.07	<0.001
COPD	172 (27.8)	496 (42.1)	35.35	<0.001
Insomnia	173 (28.0)	459 (39.0)	21.39	<0.001
Coronary heart disease	153 (24.8)	403 (34.2)	16.95	<0.001
Chronic constipation	132 (21.4)	406 (34.5)	33.18	<0.001
Cerebrovascular disease	156 (25.2)	362 (30.7)	5.95	0.015
Osteoporosis	55 (8.9)	164 (13.9)	9.55	0.002
Dementia	19 (3.1)	123 (10.4)	30.21	<0.001
CKD	28 (4.5)	85 (7.2)	4.96	0.026
History of fractures	18 (2.9)	89 (7.6)	15.59	<0.001
Parkinson's disease	9 (1.5)	59 (5.0)	14.04	<0.001
Chronic seizures	3 (0.5)	20 (1.7)	4.71	0.030
DM/IGT	185 (29.9)	368 (31.2)	0.32	0.570
Cancer	142 (23.0)	267 (22.7)	0.02	0.881
Heart failure	99 (16.0)	216 (18.3)	1.50	0.220
Atrial fibrillation	38 (6.1)	101 (8.6)	3.34	0.068
Anxiety/depression	41 (6.6)	86 (7.3)	0.27	0.601
Delirium	7 (1.1)	17 (1.4)	0.30	0.586

LUTS/BPH: Lower urinary tract symptoms/benign prostatic hyperplasia; COPD: Chronic obstructive pulmonary disease; CKD: Chronic kidney disease; DM/IGT: Diabetes mellitus/impaired glucose tolerance.

all the participants, median hospitalization cost was $3244.9 ($1886.3–$6174.7). Patients aged 80 years or older showed higher hospitalization cost ($3558.4 [$2057.8–$6818.8] vs. $2699.8 [$1583.1–$5323.7], $P < 0.001$), compared with patients aged 65–79 years [Table 1].

Factors associated with potentially inappropriate medication use

In univariate analysis, we included the variables such as age, gender, number of prescribed medication, length of hospital stay, hospitalization cost, and number of diagnostic diseases. Among variables, the multivariate Logistic regression detected that the characteristics such as female gender (odds ratio [OR] = 1.411, 95% confidence interval [CI] = 1.106–1.799), age (OR = 1.017, 95% CI = 1.001–1.033), number

of diagnostic disease (OR = 1.291, 95% CI = 1.215–1.370), and number of prescribed medication (OR = 1.082, 95% CI = 1.064–1.100) were significantly associated with PIM exposure [Table 5].

Discussion

Inappropriate use of medications in elderly patients has not caught attention widely in China until recently. Our data showed that patients aged 80 years or older encountered more PIM use (58.2%) than patients aged 65–79 years (43.4%) identified by 2012 Beers criteria. In the most commonly taken PIMs, patients aged 80 years or older have been uncovered to encounter more prescription of benzodiazepines, drugs with strong anticholinergic properties, megestrol, antipsychotics, theophylline, and aspirin than patients aged 65–79 years.

Comorbidity and potentially inappropriate medication

Several data from our study could explain the phenomena. First of all, patients aged 80 years or older had more co-morbidities (6.5 ± 1.9) than younger (5.5 ± 2.1). Patients aged 80 years or older suffered more from COPD, LUTS/BPH, insomnia, chronic constipation, osteoporosis, dementia, CKD, history of fractures, Parkinson's disease, and chronic seizures [Table 2]. As the result, increasing number of multimorbidity with age often makes it necessary to prescribe several drugs for one patient at a time. Gallagher et al.[16] found that the average number of drugs prescribed to 65-year-old patients is five simultaneously and prescription peaks in the 75–84 years old group. Hence, these frailty senile patients were more vulnerable to damage with PIMs. Similarly, patients aged 80 years or older in our study were more often prescribed with inhaled anticholinergic agents and theophylline to treat COPD, benzodiazepines to improve insomnia, and antipsychotics to control behavioral problems of dementia and so on. It has been shown that anticholinergic drugs could increase the risk for dementia and mortality.[17] Benzodiazepines and antipsychotics can significantly increase the risk of fall, fracture, and mortality in the elderly.[18-22] Unfortunately, these medications are often prescribed by physicians in China due to the lack of necessary vigilance of PIMs in elderly.

Table 3: Prevalence of PIMs identified using 2012 Beers criteria

Name of PIM	Number of elderly receiving drugs, n (%)		χ^2	P
	65 years ≤ Age < 80 years	Age ≥ 80 years		
Benzodiazepines	169 (27.3)	454 (38.5)	22.418	<0.001
Drugs with strong anticholinergic properties	35 (5.7)	145 (12.3)	19.851	<0.001
Megestrol	35 (5.7)	131 (11.1)	14.39	<0.001
Antipsychotics	14 (2.3)	89 (7.6)	20.981	<0.001
Theophylline	22 (3.6)	80 (6.8)	7.901	0.005
Non-COX-selective NSAIDs, oral	31 (5.0)	66 (5.6)	0.273	0.661
Spironolactone	31 (5.0)	56 (4.8)	0.061	0.806
Metoclopramide	37 (6.0)	49 (4.2)	2.969	0.085
Aspirin	0 (0.0)	41 (3.5)	19.547	<0.001
Antiarrhythmic drug (Class Ia, Ic, III)	12 (1.9)	20 (1.7)	0.138	0.710

PIM: Potentially inappropriate medication; COX: Cyclooxygenase; NSAIDs: Nonsteroidal anti-inflammatory drugs.

Table 4: Prevalence of PIMs in different gender identified using 2012 Beers criteria

Name of PIM	Number of elderly receiving drugs, n (%)		χ^2	P
	Male (n = 1345)	Female (n = 451)		
Benzodiazepines	456 (33.9)	167 (37.0)	1.456	0.228
Drugs with strong anticholinergic properties	153 (11.4)	27 (6.0)	4.819	0.028
Megestrol	136 (10.1)	30 (6.7)	2.581	0.108
Antipsychotics	84 (6.2)	19 (4.2)	1.176	0.278
Theophylline	81 (6.0)	21 (4.7)	1.101	0.294
Non-COX-selective NSAIDs, oral	77 (5.7)	20 (4.4)	10.876	0.001
Spironolactone	64 (4.8)	23 (5.1)	0.085	0.770
Metoclopramide	62 (4.6)	24 (5.3)	0.375	0.540
Aspirin	34 (2.5)	8 (1.8)	0.841	0.359
Antiarrhythmic drug (class Ia, Ic, III)	21 (1.6)	11 (2.4)	1.487	0.223

PIM: Potentially inappropriate medication; COX: Cyclooxygenase; NSAIDs: Nonsteroidal anti-inflammatory drugs.

Table 5: Multivariate analysis of variables independently associated with PIM use

Factor associated with PIM use	OR (95% CI)	P
Gender (women)	1.411 (1.106–1.799)	0.006
Age	1.017 (1.001–1.033)	0.043
Number of diagnostic disease	1.291 (1.215–1.370)	<0.001
Number of prescribed medicine	1.082 (1.064–1.100)	<0.001

PIM: Potentially inappropriate medication; 95% CI: 95% confidence interval; OR: Odds ratio.

Polypharmacy and potentially inappropriate medication

Second, as the result of co-morbidities,[23,24] patients aged 80 years or older were prescribed with more medications (17.6 ± 10.4) than younger (14.2 ± 9.9). Polypharmacy is particularly common among the elderly, making them especially susceptible to drug-drug interactions (DDIs). Polypharmacy has been shown to significantly associate with PIM and DDIs.[25-27] According to a study in 2007, DDIs caused 4.8% of hospital admissions among the elderly, increasing their risk nearly 8.5-fold relative to the general population.[28] DDIs also contribute to higher cost and prolonged duration of hospital stays.[29]

Benzodiazepines were the most common potentially inappropriate medication

Finally with aging, more elderly were troubled with insomnia and depression. To solve this problem, benzodiazepines were commonly used in hospitalized elderly by physicians. Our data suggested that the most commonly encountered PIM in this study was benzodiazepine. Older patients (age ≥80 years) were prescribed with more benzodiazepine than younger (65 years ≤ age < 80 years), which makes our result different from other studies. Keith et al.[2] and Fadare et al.[30] discovered that NSAIDs were the most common PIM use in the elderly patients in Italy and Nigeria, respectively. However, Oliveira et al.[25] showed that short-acting nifedipine was the most one in Brazilian. It might due to the difference of doctor's prescription behaviors among these countries. Other potential factors of high prevalence of benzodiazepines use in hospitalized elderly in China are often solely for the convenience for the staff, which were also found in nursing home in the USA before.[31,32] Few of doctors are willing to try nondrug therapy to help elderly patients solve problems such as insomnia or delirium before prescribing medication. On the other hand, many of the elderly with co-morbidities are unwilling to try nondrug method and are convinced that it is the best choice to take medicine.

Limitations

Several limitations should be noted in this study. First, updated 2012 Beers criteria are utilized to screen PIM in this study due to the lack of national criteria.[11] Some authors have formulated new explicit and implicit criteria that have been adapted for a specific country.[25,33-36] Beers criteria allow for a relative assessment of drug use risk in the elderly but do not address other type of potential PIMs that are not unique to aging, including dosing of primarily renal cleared medications, DDIs, therapeutic duplication, and traditional Chinese medicine. Second, this is a retrospective cross-sectional study. All of the data were gathered from EMR, and we could not rule out several interference factors such as accuracy and integrity of diagnosis. Third,

its single-center nature seems to influence adversely the generalizability of the results in the mainland of China. However, the study uncovered the prevalence of PIM use in different age China elderly. The EMR of the inpatients in West China Hospital are complete and detailed. Finally, this study does not describe the adverse drug interaction caused by PIM use because it is a retrospective cross-sectional study and analysis was based on EMR-reported data. It is difficult to review and predicate the relationship between adverse outcome and PIM use exactly.

In conclusion, the finding from this study revealed that inpatients aged 80 years or older encountered more PIM use than those aged 65–79 years. PIMs defined by the 2012 Beers criteria have been shown to be associated with female gender, age, polypharmacy, and co-morbidities. Taking into account the increasing elderly population and the importance of the health program for the care of this population, all of the physicians in China must pay more attention to the information about PIM and carefully choose drugs that are safer for the elderly, especially the elderly aged 80 years or older.

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Conflicts of interest

There are no conflicts of interest.

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