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ORIGINAL ARTICLE

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Are the kind of medications and patient's background associated with improving polypharmacy in elderly?

Shiori Tomita MD[1] | Daiki Kobayashi MD, MPH, MBA [1] | Kuniyoshi Hayashi PhD[2] | Hiroko Arioka MD[1]

[1]General Internal Medicine, St. Luke's International Hospital, Tokyo, Japan

[2]Graduate School of Public Health, St. Luke's International University, Tokyo, Japan

Correspondence
Shiori Tomita, General Internal Medicine, St. Luke's International Hospital, 9-1 Akashicho, Chuoku, Tokyo, Japan.
Email: shiori.t07@gmail.com

Abstract

Background: Polypharmacy is associated with negative outcomes in older population. Managing polypharmacy is important but there is no definite method for regulating it. Our aim was to evaluate what medications and patient's background are associated with reducing polypharmacy.

Methods: A prospective, single-center, cohort study was conducted from June to October in 2016. Participants were 65 and older hospitalized patients. We evaluated the difference between the numbers of medications used at the time of admission and discharge for individual drug class. Univariate analyses using paired *t* tests were applied to evaluate reduction in prescription medications, and logistic regression was used to evaluate factors for any reduction of prescription medications used at discharge.

Results: There were 494 subjects, and the mean of age was 79.6 ± 7.8 years. The mean number of medications used at admission was 6.9 ± 4.7 and that at discharge was 6.8 ± 4.3. The types of medications that reduced between admission and discharge were drugs for functional gastrointestinal disorders and agents acting on the renin-angiotensin system, etc. Individual components that were strongly associated with a reduction of the number of medications used were only length of hospital stay (OR 0.99, 95% CI, 0.99-1.0), while the number of medications on admission was related to increasing medication during hospitalization (OR 1.05, 95% CI, 1.01-1.06).

Conclusions: Most of the kinds and the number of medications prescribed might not be changed during hospitalization despite those were probably the causes of admission. The factor associated with improvements in polypharmacy was length of hospital stay.

KEYWORDS

acute care hospital, drug/medical use evaluation, geriatrics, physician prescribing, polypharmacy

1 | INTRODUCTION

Polypharmacy, defined as use of multiple medications, is a worldwide problem. The increase in the number of elderly who are frail and have multiple chronic comorbid conditions may be one of the leading causes of polypharmacy.[1] In an aging population, inappropriate medications are more likely to result in an adverse outcome. We do not have a absolute definition for polypharmacy, but most research has defined polypharmacy as taking five or more medications.[2]One report demonstrated that, when taking five or more medications, the mortality rate of elderly people exhibits an odds ratio (OR) of 1.09 ($P < 0.001$).[3] Polypharmacy has also become a cause of side effects in the older population; therefore, many studies are in progress. It has been reported that 2.9% of inpatients exhibit adverse drug effects,[4] and a cohort study demonstrated that 27.6% of adverse drug events are considered preventable. Moreover, of these adverse drug events, 38% are categorized as serious, life-threatening, or fatal.[5] The inappropriate use of medications has been associated with poor clinical outcomes in observational studies of older adults.[6] Especially, it is said that prescribing cascade contributes to polypharmacy,[7] for example, diuretics for edema because of NSAIDs, psycholeptics like haloperidol for delirium because of benzodiazepine, and anti-Parkinson drugs for extrapyramidal symptoms because of anti-muscarinic drugs. Polypharmacy is also a big problem in Japan. In a revision of the fee schedule in 2016, new rules for polypharmacy mandated. If the doctor is able to reduce the number of prescribed oral medications by more than two during the hospitalization of patients who prescribed more than five medications on admission, hospital could demand medical fee on discharge. The STOPP (Screening Tool of Older Person's Prescriptions) criteria and the START (Screening Tool to Alert doctors to Right Treatment) criteria are the tools for screening inappropriate prescriptions and potential appropriate prescriptions[8,9] which should become one of the help to solve polypharmacy for the elderly people, but the appropriate solutions for decreasing the number of medications are uncertain.[10] Therefore, the object of this study was to examine the relationships of reductions in medications during hospitalization with the classifications of the medication and patient factors.

2 | MATERIALS AND METHODS

2.1 | Study overview

This study was single-center, prospective cohort study. The study period was from 1 June 2016 to 31 October 2016.All 494 patients were urgently admitted to St Luke's International Hospital in Japan during this period. The patients were admitted through the ER or the outpatient clinic by the decision of ER doctor or outpatient clinic doctor. The study was approved by the Ethics Committee of St. Luke's International Hospital, and informed consent was waived.

We included patients who over 65 years old and were admitted to our internal medicine department during an emergency. The definition of emergency was that the time between the decision for admission and arrival to the inpatient hospital room was less than 24 h. We excluded the patients for whom the medications being used on admission were unknown and those who died during their hospital stay.

In this study, we classified and extracted the numbers and names of prescribed medications on admission and at discharge using the Anatomical Therapeutic Chemical (ATC) classification system.[11] Some researches related to polypharmacy used this classification system.[12] ATC classification contains all kinds of medications and we can interpret each classification as those effects in the body. Additionally,in this study, because there are no Chinese medicines in the ATC classification, we classified and extracted this information for Chinese medicines separately. The medications that were defined as prescribed medications in this study were exclusively oral medicines, that is, we did not count external use medicines, or injection, like insulin or ointment. We also counted medications that were the same type but were applied at different doses as more than one drug because of the system design. All data were derived from the hospital informatics database provided by the Information Centre of St Luke's International Hospital.

2.2 | Primary end points

(1) The numbers of medications and the ratio of the numbers of prescribed medications on admission and discharge were examined by medications class, and (2) the reduction in the number of medications on discharge compared with that on admission is set as the primary end point. We considered the number of prescribed medications on the last day of hospitalization as the medication upon discharge.

2.3 | Statistical analysis

The patients who were urgently admitted to the hospital constituted the sample. For the first end point, we used paired *t* test to determine whether some significant decreases were present when we compared the mean number of medications prescribed upon admission and at discharge. We also evaluated the ratio of medications between admission and discharge. A threshold *P* value of <0.01 was used to indicate statistical significance.

For the second primary end point, we used logistic regression to identify the variables that were independently associated with a decrease in the number of medications. Here, we defined age, sex, length of hospital stays, and body mass index (BMI) as explanatory variables. We divided age into three groups (≥75, 65-75, and <65 years) and divided BMI into three groups (underweight, <18.5; normal weight, 18.5-24.9; and overweight, ≤25 kg/m^2).[13] Additionally, we regarded the increase or decrease in the number of medications between admission and discharge as an outcome. Therefore, through logistic regression analysis, we assessed the effects of these four variables against the outcome. A threshold $P < 0.01$ was used to indicate statistical significance in this research.

TABLE 1 Baseline characteristics (n = 494)

Age			
Mean ± SD		79.6 ± 7.8	
Sex n (%)			
Male		247 (50.0)	
The number of medications		Admission	Discharge
Mean ± SD		6.9 ± 4.7	6.8 ± 4.3
Median (range)		7 (0-26)	7 (0-23)
The number of medications on admission by age			
	<75 (n = 144)	75-85 (n = 200)	≧85 (n = 150)
0-4 n (%)	68 (47.2)	54 (27.0)	41 (27.3)
5-9 n (%)	50 (34.7)	85 (42.5)	68 (45.3)
10-14 n (%)	20 (13.8)	49 (24.5)	29 (19.3)
Over 15 n (%)	6 (4.2)	12 (6.0)	12 (8.0)
Living place before admission			
Home, n (%)		429 (86.8)	
Hospital, n (%)		2 (0.4)	
Care home, n (%)		47 (9.5)	
Unknown, n (%)		16 (3.2)	

All analyses were performed with R Statistical Software, version 3.3.2. (Foundation for Statistical Computing, Vienna, Austria).

3 | RESULTS

3.1 | Descriptive statistics

The final cohort included 494 patients with a mean age of 79.6 ± 7.8 years. Table 1 shows the mean number of medications on admission and discharge, 6.9 ± 4.7 and 6.8 ± 4.3, respectively. Most of the patients (86.8%) admitted from their own home. Most of the rest patients (9.5%) came from nursing homes.

Table 1 presents the proportions of the numbers of medications by age. From the numbers of medications, we discovered that 47.2%, 34.7%, 13.8%, and 4.2% of the patients under 75 years old had 0-4 prescriptions, 5-9 prescriptions, 10-14 prescriptions, and over 15 prescriptions, respectively. Among the group of over 75, more than 70% people are in polypharmacy.

3.2 | Univariate analysis (paired *t* tests)

Table 2 presents the results of paired *t* tests of the numbers of prescribed medications upon admission and at discharge by ATC classification. We skipped analysis of some medications that were not prescribed during this period. In this statistical hypothesis test, we observed significant reduction results for some medications: A03 drugs for functional gastrointestinal disorders and C09 agents acting on the renin-angiotensin system. On the other hand, the results of N06 psychoanaleptics, R03 drugs for obstructive airway diseases, R05 cough and cold preparations, etc., showed a significant increase.

3.3 | Multivariate analysis (logistic regression analysis)

We set age, sex, length of hospital stays, and BMI as explanatory variables. Additionally, we regarded increases and decreases in the numbers of medications between admission and discharge as an outcome in this logistic regression analysis. In this regard, we investigated the important explanatory variables based on the statistical significance level of 0.05. Table 3 indicates that the length of hospital stay is related to decrease the number of medication (OR 0.99; 95%CI, 0.99-1.0, $P < 0.01$). The number of medication on admission is related to increase in the number of medication on discharge (OR 1.05; 95% CI, 0.40-0.94; $P<0.05$).On the other hand, sex, age, and BMI are not associated with a decrease in the number of medication.

4 | DISCUSSION

Our study demonstrated that more than half of 65- to 74-year-old patients and more than 70% of ≥75-year-old patients used five or more medications, which means that most of the elderly people in the hospital experience polypharmacy. A large European retrospective cross-sectional study also found that 51% of patients over the age of 65 who receive home care take more than six medications per day.[14] In this study, we use the ATC classification to divide medications. The ATC classification is helpful in determining the type of medications that might be reduced to avoid polypharmacy.

In previous research, the side effects that are most commonly considered to be the cause of admission have been found to be vasovagal neuroregulatory syncope, overdose, acute kidney failure, and dehydration.[15] Falls are also known as the main cause of admission

TABLE 2 Paired *t* tests of the numbers of prescribed medications upon admission and at discharge

ATC classification	The mean number of medications prescribed upon admission	The mean number of medications prescribed at discharge	*P*-value	Pre- and postratio
A02 drugs for acid-related disorders	0.76	0.85	0.1	1.12
A03 drugs for functional gastrointestinal disorders	0.11	0.04	<0.01	0.36
A05 bile and liver therapy	0.27	0.19	<0.05	0.70
A06 drugs for constipation	0.18	0.17	0.62	0.94
A07 antidiarrheals, intestinal, anti-inflammatory/antiinfective agents	0.02	0.01	0.25	0.50
A09 digestives, incl. enzymes	0.29	0.25	0.3	0.86
A10 drugs used in diabetes	0.19	0.17	0.47	0.89
A11 vitamins	0.03	0.12	<0.01	4.00
A12 mineral, supplements	0.02	0.02	0.56	1.00
A16 other alimentary tract and metabolism products	0.02	0.02	0.56	1.00
B01 antithrombotic agents	0.52	0.55	0.47	1.06
B02 antihemorrhagics	0.04	0.04	0.74	1.00
B03 antianemic preparations	0.16	0.14	0.46	0.88
C01 cardiac therapy	0.2	0.2	1	1.00
C02 antihypertensives	0.06	0.06	0.9	1.00
C03 diuretics	0.34	0.27	0.11	0.79
C04 peripheral vasodilators	0.03	0.01	<0.05	0.33
C07 beta-blocking agents	0.2	0.24	0.23	1.20
C08 calcium channel blockers	0.38	0.35	0.44	0.92
C09 agents acting on the renin-angiotensin system	0.41	0.28	<0.01	0.68
C10 lipid modifying agents	0.31	0.28	0.25	0.90
D01 antifungals for dermatological use	0.03	0.03	0.84	1.00
G04 urologicals	0.15	0.14	0.55	0.93
H02 corticosteroids for systemic use	0.11	0.13	0.39	1.18
H03 thyroid therapy	0.08	0.11	0.16	1.38
J01 antibacterials for systemic use	0.07	0.25	<0.01	3.57
J02 antimycotics for systemic use	0.01	0.04	<0.01	4.00
J04 antimycobacterials	0	0.02	<0.05	NA
L01 antineoplastic agents	0.03	0.01	0.09	0.33
L02 endocrine therapy	0.03	0.03	1	1.00
L04 immunosuppressants	0.04	0.03	0.33	0.75
M01 anti-inflammatory and antirheumatic products	0.06	0.05	0.49	0.83
M02 topical products for joint and muscular pain	0.03	0.03	0.84	1.00
M03 muscle relaxants	0.02	0.02	0.78	1.00
M04 antigout preparations	0.14	0.1	0.11	0.71
N02 analgesics	0.1	0.13	0.1	1.30
N03 antiepileptics	0.11	0.12	0.81	1.09
N04 anti-Parkinson drugs	0.1	0.06	0.09	0.60
N05 psycholeptics	0.47	0.5	0.6	1.06
N06 psychoanaleptics	0.16	0.26	<0.01	1.63
N07 other nervous system drugs	0.02	0.02	0.28	1.00
R03 drugs for obstructive airway diseases	0.03	0.13	<0.01	4.33
R05 cough and cold preparations	0.12	0.18	<0.01	1.50
R06 antihistamines for systemic use	0.07	0.05	0.16	0.71
Chinese medicine	0.09	0.06	0.12	0.67

ATC, anatomical therapeutic chemical.

TABLE 3 Logistic regression analyses of association between variables and reduction of medications

Variable	Odds ratio	95% CI	*P*-value
Age (y.o) <75	Reference		
75-85	1.0	0.91-1.12	0.80
≧85	1.02	0.91-1.16	0.66
BMI(kg/m^2) <18.5	0.94	0.84-1.04	0.20
18.5-25	Reference		
≧25	0.96	0.85-1.13	0.80
Sex female	1.07	0.97-1.16	0.16
Length of hospital stay categorical	0.99	0.99-1.0	<0.01
The number of medication on admission	1.05	1.04-1.06	<0.01
Living space on admission	Reference		
Home			
Hospital	0.5	0.2-1.15	0.10
Care home	0.99	0.83-1.16	0.80

BMI, body mass index; CI, confidence interval.

of elderlies, and a meta-analysis of medications that are the cause of falls among elderlies revealed that the OR for antihypertensive medicine and diuretics is 1.24 and 1.07 ($P < 0.05$), respectively.[16] For appropriate patients, agents acting on the renin-angiotensin system medicines are important medications, although these medications might sometimes be decreased during hospitalization due to the disease present upon admission or due to complications such as kidney failure, hyperkalemia,[17] or hypotension.

Beers criteria set the definition of inappropriate prescriptions as follows. Prescriptions of which risk outweigh the benefit for elderly people.[18] Some reports have stated that approximately 21%-41.2% of patients receive inappropriate prescriptions. The medications that are prescribed inappropriately are proton pump inhibitors, calcium channel blockers, antispasmodic medications for chronic constipation, and long-acting benzodiazepines.[19,20] Based on these reports, it is possible that "drugs for acid-related disorders," "calcium channel blockers," "drugs for functional gastrointestinal disorders," and "psycholeptics" could be decreased during hospitalization because these medications are excessively and inappropriately prescribed. However, these medications were not decreased in this research except "drugs for functional gastrointestinal disorders" and "agents acting on the renin-angiotensin system." We hypothesize that other possibly inappropriate medications are often used in emergency setting. We have to review the prescription list occasionally, otherwise we may continue to prescribe medications inappropriately during hospitalization. It has been reported that the risk factors for adverse drug reactions (ADRs) are the presence of heart failure, liver disease, the number of medications, previous ADR, renal failure, and ≥4 comorbid conditions.[21] Almost all the patients who admit to acute hospital have those problems; thus, we have to think more about ADRs.

The results of the logistic regression analysis revealed that length of hospital stay was associated with significant reductions in the medication statistics. Although age was not related to reduction of medications in this research, the number of inappropriate prescriptions among those over the age of 85 years decreased in one cohort study.[22] We try to decrease medications for elderly people because of side effects or prognoses,[23] but most of the people are tend to be treated with excess medications in spite of the patients are advanced age especially in acute hospital on admission. Longer hospital stay reflects the bad condition of the patients; thus, the doctors may try to reduce medications during hospitalization depending on the patient's conditions and care backgrounds.

Our study has several important limitations. First, the data were collected automatically, so the contents of the data are possibly uncertain. For example, we counted different doses (e.g, 2.5 and 5 mg of the same drug) as different medications.Second, because our study was a single-center study, the results could be influenced by many factors, for example, the prescription patterns of the doctor or hospital, patient characteristics, and their disease severity. However, the strengths of our study are that we collected the data prospectively, and we were able to identify some medications that are possibly related to polypharmacy. From this dataset, we can continue to analyze the associations of each medication with polypharmacy.

In conclusion, Japan faces an aging society to a greater extent than other countries, and thus, the phenomenon occurring in Japan will eventually be a problem for other countries. This is the first study to explore the types of medications that may be reduced based on emergence and preventable hospital admissions. Two medication classes: "drugs for functional gastrointestinal disorders" and "agents acting on the renin-angiotensin system" are more likely to be decreased during hospitalization. Our findings also suggest that only length of hospital stay is associated with improving polypharmacy.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

ORCID

Shiori Tomita http://orcid.org/0000-0002-6162-8825

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