Impact of pharmacist-led medication therapy management in ambulatory elderly patients with chronic diseases

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Abstract

Aims: This study aimed to assess the impact of pharmacist-led medication therapy management (MTM) for ambulatory elderly patients with chronic diseases. Methods: Consecutive patients were enrolled from pharmacist outpatient clinics from January 2016 to June 2018. Eligible subjects were performed with MTM services by the pharmacists and had clinical data for at least 2 clinic visits within a consecutive 12-month period after the first MTM visit. The drug-related problems (DRPs) and recommendations were evaluated using The Pharmaceutical Care Network Europe (PCNE) Classification for Drug related problems V8.03. Results: A total of 525 DRPs were identified during the study period. Treatment effectiveness P1 (53.71%) was the most common problems of DRPs. The most frequently recommended intervention was changing the drug (48.76%). These interventions were accepted by the patients in 92.38% and were completely implemented in 90.48%. The number of drugs taken was the significant associated factor for DRPs. Post-intervention group showed lower levels in systolic blood pressure (SBP) and diastolic blood pressure (DBP) compared to the pre-intervention group. There were statistically significant changes in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG) between the pre- and post-intervention group. The average cost of medications per patient for every month decreased from 387.72 Ren Min Bi (RMB) to 355.17 RMB (P=0.009). Conclusion: We confirmed that pharmacists has a valuable role to perform MTM services for ambulatory elderly patients, not only in identifying and solving the DRPs, but also in improving clinical outcomes (BP and lipid level) and cost saving.

What is already known about this subject

- MTM services has been demonstrated positive effects on drug compliance, clinical effectiveness and safety.
- Little is known about the incidence and characteristics of drug-related problems and the impact of pharmacist-led medication therapy management for ambulatory elderly patients with chronic diseases in China.

What this study adds:

- The proportion of patients with DRPs was high, with an average 2.15 per patient.
- Interventions by pharmacists significantly reduced the cost of medication and improved clinical outcomes (BP and lipids level).
- It suggests that the pharmacist-led MTM services played an important role in improving health outcomes and saving medication cost.

Main text

1 Introduction

A drug-related problem (DRP) is defined as "an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes" [1]. Strong evidence had shown that the negative outcomes associated with DRPs are a major health issue [2]. The majority of hospitalizations and emergency department visits caused by DRPs were preventable, and an effective drug review for the successful detection of DRPs remains an unmet clinical need.

Population aging is a global phenomenon [3]. Aging is accompanied with decline of functional reserves and adaptability. Elderly patients also often have concomitant medical conditions that require multiple drugs. It is well known that polypharmacy is very common in elderly patients and increases the risk of adverse drug events (ADEs), potential drug–drug interactions and drug errors [4], in addition it has considerable impact on morbidity and mortality [5].

Health care providers must carefully investigate the use of drugs to identify the DRPs, and try to solve these DRPs, especially the elderly [6, 7]. Pharmacists are ideal medical team member to optimize drug therapy, adjust drug doses, conduct medication reconciliation, improve drug compliance, monitor laboratory indicators, conduct patient education where appropriate [8]. By performing medication review or medication therapy management (MTM), the pharmacist can identify and resolve the DRPs [9]. MTM services has been demonstrated positive effects on drug compliance, clinical effectiveness and safety [10-12]. The core elements of MTM services include medication therapy review (MTR), a personal medication record (PMR), a medication-related action plan (MAP), intervention and referral, and documentation and follow-up [13].

In order to determine the effectiveness of MTM services to identify DRPs in elderly patients (age [?] 65) in outpatients, we evaluated the incidence and characteristics of DRPs in outpatient patients conducted by a group of pharmacists. This study also examined clinical outcomes (blood pressure (BP), and lipids) pre- and post-intervention by pharmacist. Thus, the purpose of this manuscript is to assess the impact of pharmacist-led MTM for ambulatory patients.

2 Methods

2.1 Ethics approval

This study was approved by the institutional review boards of Beijing Chao-Yang Hospital affiliated to Capital Medical University (registration number: 2019-6-20-3).

2.2 Study design and setting

This was a retrospective cohort study conducted in a pharmacist outpatient clinic in a general hospital in Beijing, China. Consecutive patients were enrolled from January 2016 to June 2018. Four pharmacists from the hospital interviewed patients at the pharmacist outpatient clinic. The pharmacists conducted a comprehensive assessment of the patient's medication. These three MTM pharmacists had completed training program accredited by the American Pharmacists Association, with an average of 10 years of hospital practice experience. The other pharmacist had a physician certificate and was authorized to prescribe.

The inclusion criteria were patients aged [?] 65 years and with chronic diseases, such as cardiovascular diseases (including hypertension, hyperlipidemia, coronary artery disease and heart failure) or diabetes, osteoporosis, gout. Eligible subjects were performed with MTM services by the pharmacists and had clinical data for at least 2 clinic visits within a consecutive 12-month period after the first MTM visit. These patients were assigned into two groups (pre-intervention group and post-intervention group) based on the date when they accepted the first MTM services in the pharmacist outpatient clinic.

2.3 Description of the intervention

MTM was defined as analysis, education and monitoring services provided by pharmacists to optimize patient outcomes [14]. For this study, the MTM process included the following five steps: (1) collected clinical information of patients and recorded a comprehensive list of patients' medications, including previous and current medications and whether there was any adverse drug reactions (ADR) during the medication; (2)

identified DRPs, such as unnecessary, suboptimal or repeated medications, over- or under-dosing, toxicity or adverse reaction; (3) identified patient's understanding of his/her medications and diseases, and provided appropriate patient education based on the knowledge deficits discovered; (4) provided treatment advices, including those related to dosing and drug regimens based on the DRPs identified; and (5) performed individual follow-up of the achievements of drug treatment.

2.4 Data collection

The following information was documented: patients' demographic factors (age, gender), diseases factors (active or currently under treatment), therapeutic regimens (dosing, frequency, and treatment duration) of each medication. Additionally, BP level, heart rate, laboratory findings (such as lipid level, creatinine) and cost of medicines were collected.

2.5 Outcome measures

2.5.1 Detection of DRPs

The Detection of DRPs was the first outcome. The pharmacists were required to work as usual, using their professional knowledge to evaluate medication therapies. The DRPs were classified by the pharmacists who performed the medication reviews. The DRPs were recorded after evaluating the indication, dosage, adherence, adverse reactions, and therapeutic effects of each medication. It was recommended to optimize patients' drug therapy by the pharmacists. The DRPs and recommendations were evaluated using The Pharmaceutical Care Network Europe (PCNE) Classification for Drug related problems V8.03 regarding problem, causes, planned interventions and intervention acceptance [15].

2.5.2Clinical outcomes and cost-saving effect

The clinical outcomes and cost-saving effect were the secondary endpoints and compared on the first visit date (baseline) and the end of follow-up. The outcomes of BP was mean diastolic blood pressure (DBP)/ systolic blood pressure (SBP) of hypertensive patients on every visit. The outcomes of lipids was concluded total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG). The cost-saving effect outcome was average costs of medications per patient for every month. The drug costs were standardized over the study period.

2.6 Statistical analysis

All data analyses were performed using SPSS version 23.0 software. A descriptive analysis was conducted on patient's demographics, diseases characteristics, types of DRPs, and recommendations. Comparisons between the pre-intervention group and post-intervention group with regard to clinical outcomes were given. Continuous data was computed with mean ± standard deviation. Categorical variables were calculated with frequencies and percentages. Groups were compared by Student's T test for continuous variables, by the Mann-Whitney test for continuous variables with non-parametric distribution, and by the chi-square test or Fisher's exact tests for categorical data. Univariate analysis and multiple linear regression were used to determine factors related to the number of DRPs. A P value of <0.05 was considered to be statistically significant.

3 Results

3.1 Characteristics of study population

A total of 288 eligible patients were invited by the pharmacists to participate in the study during their daily outpatient visits, and 260 patients were recruited (participation rate 90.28%). A total of 244 patients completed all required follow-up and were included in our study (completion rate was 93.85%). The patients had a mean of 8.76±4.35 ongoing medications during patients' routine clinic visits. The most commonly seen comorbid conditions were hypertension (70.08 %), heart disease (56.56%), and hyperlipidemia (29.92%). The demographic and clinical characteristics of these patients are described in Table 1.

3.2 Detection of DRPs

As shown in Table 2, a total of 525 DRPs were identified during the study period. An average of 2.15 DRPs per patient was detected. Treatment effectiveness P1 (53.71%) was the most common problems of DRPs followed by treatment safety (33.90%). The main causes of DRPs were related to drug selection (71.43%) and dose selection (20.57%). These identified DRPs led to interventions proposed to prescribers in 96.19% of the cases. The most frequently recommended intervention was changing the drug (48.76%), followed by changing the dosage (24.76%) and starting a drug (11.62%). These interventions were accepted by the patients in 92.38% of the cases and were completely implemented in 90.48%.

The univariate analysis showed that the "number of drugs" and "number of chronic conditions" were the significant factors affecting the number of DRPs. In the multivariate analysis, only "number of drugs" was associated with the number of DRPs (P ¡0.0001), as described in Table 3.

3.3 Clinical outcomes and cost-saving effect

There were 171 patients with hypertension in the study. Post-intervention group showed lower levels in SBP and DBP compared to the pre-intervention group (SBP: 134.56 +- 12.38 vs 149.08 +- 19.75, P = 0.000; DBP: 78.01 +- 9.78 vs 84.56 +- 11.34, P=0.000). There were 73 patients with hyperlipidemia in the study. There were statistically significant changes in TC, LDL-C and TG between the pre-intervention group and the post-intervention group (Table 4).

The average costs of medications per patient for every month were 387.72+-168.48 Ren Min Bi (RMB) in the pre-intervention group and 355.17+-180.03 RMB in the post-intervention group. The cost of antihypertensive drugs was markedly declined (230.40+-138.14 vs 206.58+-112.74, P=0.001). However, the cost of lipid modifying agents was increased (181.12+-106.14 vs 242.67+-175.56, P=0.006; Table 5).

4 Discussion

To the best of our knowledge, this study was the first to evaluate the outcomes of pharmacist-led MTM services in ambulatory elderly patients in mainland China. This study showed that the proportion of patients with DRPs was high, with an average 2.15 per patient. Interventions by pharmacists significantly reduced the cost of medication and improved clinical outcomes (BP and lipids level). The average cost of medications per patient for every month decreased from 387.72 to 355.17 RMB in our study. It suggests that the pharmacist-led MTM services played an important role in improving health outcomes and saving medication cost.

To be able to perform MTM services with high quality, the pharmacists need to have full access to patient's medical and laboratory records. Compared with many other outpatient clinics, in order to obtain more comprehensive information, the pharmacists collected the medical records of each patient for 30-40 minutes, including previous medical history, previous medications, current medications, laboratory examination and other information. This was important, for example, to understand why a drug had been changed or to identify any adverse effect of earlier drugs.

In previous studies, the average number of DRPs per person was lower than the result in our study [16, 17]. A study from Australia reported that 130 DRPs were found in 73 patients (mean 1.8 DRPs per patient) [16]. Rhalimi et al revealed an average of 1.37 DRPs per patient in French community pharmacies [17]. There might be several explanations for why the number of DRPs in this study was higher than in other studies. First, our study was conducted in a tertiary hospital rather than a community pharmacy. Most of the patients who come to the pharmacist clinic had medication problems, so there were more DRPs than other studies. Second, there were several available tools to evaluate DRPs. We chose to use the PCNE V8.03 classification system, but other available assessment tools may differ slightly in some aspects, and therefore, other tools may observe different results.

Adverse drug event (possibly) occurring was quite common problems of DRPs in our study. This was also the most common pharmaceutical care problem in the Kwint's study [18]. This finding could give support to the hypothesis that pharmacists have adequately addressed patients' problems in the pharmacist outpatient

services. For example, it was well known that elderly people were at high risk of side effects from non-steroidal anti-inflammatory drugs (NSAIDs), such as gastrointestinal bleeding and renal toxicity, and that NSAIDs also increase the risk of hypertension and heart failure [19, 20]. High doses of dihydropyridines calcium-channel blockers often caused ankle edema, headache, flushing and tachycardia [21]. In order to reduce the occurrence of adverse reactions, the pharmacists may reduce the dose of the drug or switch it to another medicine according to the symptoms.

In our study, no or incomplete drug treatment in spite of existing indication was the main causes subtype of DRPs. For example, some patients did not receive the standard "ABCDE" method for secondary prevention of coronary artery disease: antiplatelet therapy, blood pressure management, cholesterol management, diabetes treatment, and exercise; it was recommended that it was often used to reduce the cardiovascular risk [22]. Although cardiac rehabilitation following a cardiovascular event is a Class I recommendation of the European Society of Cardiology, the American Heart Association and the American College of Cardiology, it remains vastly underutilized, accounting for 15% to 50% of the targeted population participating in such services [23-27]. Lack of awareness on the importance of those drugs and fear of ADRs were possible causes. The high incidence of incomplete drug treatment in our study highlights the need for pharmacists to conduct a MTM services in elderly patients to optimize drug treatment.

The overall acceptance rate of pharmacist interventions was relatively high (90.48%), which was higher than what has been reported in other studies [28, 29]. This is probably due to the fact that adequate training and experience in clinical pharmacy are important factors for meeting the specific challenges of MTM service.

Multivariate analysis showed that the number of drugs taken was associated independent risk factor for the number of DRPs, which was consistent with most previous studies [30-32]. Patients taking large amounts drugs tend to experience adverse drug reactions, potential drug–drug interactions, decreased compliance and drug selection problems [33-35]. It was recommended that patients could visit pharmacist clinic to conduct medication reorganization and reduce unnecessary drugs. Pharmacists can review medication history and identify medication issues in these patients. Pharmacists were familiar with not only medication but also the interaction between the drug and the disease. Therefore, it was recommended that pharmacists could provide MTM services for ambulatory patients who receiving long-term pharmacotherapy [36].

After one year MTM service, the improvements in several clinical outcomes among the patients were significant. Hypertension and hyperlipidemia increase the risk of fatal or non-fatal cardiovascular events [24-26]. Like other studies, our study also found that the MTM service improved BP and lipid level among patients [37-39]. Regarding cost-saving effect, the post-intervention group experienced a significant reduction in total costs of medications per patient for every month. This decrease in medication expenditures was similar to those reported in other MTM services studies [37, 40].

Some limitations of this study have to be taken into account. First, it was a retrospective study and the patient population in this study was small. This could lead to non-significant results. Second, all involved pharmacists performed comprehensive medication reviews as described in the methods section. Still, limitations in the inter-rater reliability cannot be ruled out. Finally, the lack of usual care group was a limitation of the present study, therefore, in terms of clinical outcomes and cost-saving effect, the self-comparison study of patients pre- and post- intervention were conducted.

5 Conclusions

This study described the number and type of DRPs in ambulatory patients and clinical and economic outcomes pre- and post-intervention by pharmacist-led MTM services. DRPs were commonly observed among ambulatory patients. We confirmed that pharmacists has a valuable role to perform MTM services for ambulatory elderly patients, not only in identifying and solving the DRPs, but also in improving clinical outcomes (BP and lipid level) and cost saving.

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Authors' contributions

XW and LHL designed the experiments. XW, XJY, HGW, JY and LHL carried out the experiments. XW, SHW and ZM collected and analyzed the data. XW wrote the article. All authors reviewed the article.

Conflict of interest statement

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

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Table 1 The demographic and clinical characteristics of 244 patients

Characteristics	**Total(N=244)**
Demographics (n = number of patients)	
Age, year, mean ± SD	72.54±9.96
65–79 years, n (%)	204(83.61%)?¿?
80 years, n (%)	40(16.39%)
Female, n (%)	143(58.61%)
Number of medications taken, mean ± SD	8.76±4.35
Active chronic conditions,n(%)	
Hypertension	171(70.08%)
Heart disease	138(56.56%)
Hyperlipidemia	73(29.92%)
Diabetes mellitus	70(28.69%)
Osteoporosis	42(17.21%)
Gout	36(14.75%)
Constipation	20(8.20%)
Chronic obstructive pulmonary disease	18(7.38%)
Gastric ulcer/gastritis	14(5.74%)
Gastroesophageal reflux disease	12(4.92%)
Insomnia	10(4.10%)
Kidney disease	8(3.28%)
Others	33(13.52%)
Anatomical therapeutic chemical classification,n(%)	
A: Alimentary tract and metabolism	
A02 Drugs for acid related disorders	82
A06 Drugs for constipation	69
A10 Drugs used in diabetes	122
A11 Vitamins	24
B: Blood and blood-forming organs	
B01 Anti-thrombotic agents	266
C: Cardiovascular system	
C01 Cardiac therapy	102
C02 Antihypertensives	684
C03 Diuretics	45
C04 Peripheral vasodilators	52
C05 Vasoprotectives	33
C07 Beta blocking agents	207
C08 Calcium channel blockers	143
C09 Agents acting on the renin-angiotensin system	245
C10 Lipid modifying agents	134

Characteristics	Total(N=244)
G: Genital urinary and sex hormones	
G04 Urologicals	15
M: Musculoskeletal system	36
N: Nervous system	
N05 Psycholeptics	45
(Anxiolytics, hypnotics, anti-psychotics i.e. neuroleptics)	
N06 Antidepressants	12
No ATC code	32

ATC, anatomical therapeutic chemical.

Table 2 Classification of DRPs identified according to PCNE V8.03 (N=525)

Code	Detailed classification
Problems	**Problems**
P1	Treatment effectiveness
P1.1	No effect of drug treatment
P1.2	Effect of drug treatment not optimal
P1.3	Untreated symptoms or indication
P2	Treatment safety
P2.1	Adverse drug event (possibly) occurring
P3	Other
P3.1	Problem with cost-effectiveness of the treatment
P3.2	Unnecessary drug-treatment
Causes	**Causes**
C1	Drug selection
C1.1	Inappropriate drug according to guidelines/formulary
C1.2	Inappropriate drug (within guidelines but otherwise contra-indicated)
C1.3	No indication for drug
C1.4	Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary su
C1.5	Inappropriate duplication of therapeutic group or active ingredient
C1.6	No or incomplete drug treatment in spite of existing indication
C2	Drug form
C2.1	Inappropriate drug form (for this patient)
C3	Dose selection
C3.1	Drug dose too low
C3.2	Drug dose too high
C3.3	Dosage regimen not frequent enough
C3.4	Dosage regimen too frequent
C3.5	Dose timing instructions wrong, unclear or missing
C4	Treatment duration
C4.2	Duration of treatment too long
Planned interventions	**Planned interventions**
I1	At prescriber level
I1.2	Prescriber asked for information
I1.3	Intervention proposed to prescriber
I1.4	Intervention discussed with prescriber
I3	At drug level
I3.1	Drug changed to

Code	Detailed classification
I3.2	Dosage changed to
I3.3	Formulation changed to
I3.4	Instructions for use changed to
I3.5	Drug paused or stopped
I3.6	Drug started
Intervention Acceptance	**Intervention Acceptance**
A1	Intervention accepted
A1.1	Intervention accepted and fully implemented
A1.3	Intervention accepted but not implemented
A2	Intervention not accepted
A2.2	Intervention not accepted: no agreement
A2.3	Intervention not accepted: other reason (specify)

DRPs, drug-related problems.

Table 3 Statistical analysis of factors associated with the number of DRPs

Variables	Univariate analysis	Univariate analysis	Univariate analysis	Multivariate analysis	Mu
	Unstandardized coefficients β	95% Confidence interval for β	P value	Unstandardized coefficients β	95% int
Age	0.044	0.036-0.138	0.273		
Gender	-0.191	-0.053 to 0.445	0.669		
Number of drugs	0.24	0.036-0.637	¡0.0001	0.24	0.0
Number of chronic conditions	0.286	0.094-0.344	0.005	0.177	0.1

DRPs, drug-related problems.

Table 4 Blood pressure and lipids outcomes of two groups

	Pre-intervention	Post-intervention	P
Hypertensive patients (n=171)			
SBP mean (mm Hg)	149.08±19.75	134.56±12.38	0.000
DBP mean (mm Hg)	84.56±11.34	78.01±9.78	0.000
Hyperlipidemia patients (n=73)			
TC (mmol L^{-1})	6.17±1.34	4.51±0.80	0.027
LDL-C (mmol L^{-1})	3.26±1.08	2.54±0.57	0.000
TG (mmol L^{-1})	2.47±0.93	1.69±0.90	0.000

SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides.

Table 5 Average cost of medications per patient for every month

	Pre-intervention	Post-intervention	P
Average drug cost per patient for every month (RMB)	387.72±168.48	355.17±180.03	0.009
Cost of antihypertensive drugs(RMB)	230.40±138.14	206.58±112.74	0.001
Cost of lipid modifying agents(RMB)	181.12±106.14	242.67±175.56	0.006

RMB, Ren Min Bi.