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Original Paper

Effects of medication reduction in outpatients with polypharmacy following medication review by pharmacists

Short running title: Medication use in outpatients with polypharmacy

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Abstract

Rationale, aims and objectives: Polypharmacy is a risk factor for the health and safety of elderly patients. To determine whether pharmacists could reduce the number of medications administered to patients with polypharmacy in a clinical setting via counselling and medical review.

Method: The assigned clinical pharmacists conducted a medication review of outpatients at the Showa University Hospital. When a medication-related risk was identified, the pharmacists counseled the patients. We retrospectively surveyed the medical records of 13 outpatients who received interventions (medication review and counseling) by clinical pharmacists between January 2017 and June 2017. Adverse events or changes in the physical conditions of patients were assessed for 6 months. The suitability of medications was assessed using the medication appropriateness index (MAI) by two pharmacists before the review and 6 months post-review.

Results: The number of coadministered medications was 17 (9–30) [median (range)] before the intervention; it significantly reduced to 8 (8–29) just after the intervention and to 13 (8–27) 6 months post-intervention. The MAI score was sustained for up to 6 months after the intervention (before vs. just after and 6 months after the intervention: 9

[3–23] vs. 4 [0–22] and 2 [0–23], $p < 0.005$). No adverse events were observed for 6 months.

Conclusions: Pharmaceutical counseling and medication review by clinical pharmacists reduced polypharmacy without any adverse events for at least 6 months despite limited number of assessments. Thus, interventions (medication review and counseling) by clinical pharmacists are a useful method to resolve polypharmacy in outpatients.

Keywords: pharmaceutical counseling; medication review; medication appropriateness index; pharmacist; pharmacy practice; polypharmacy

Introduction

In the 2015 Japan Geriatrics Society Guidelines for medical treatment and its safety in elderly patients, polypharmacy was defined as the simultaneous use of ≥6 medications (1). In 2018, the Ministry of Health, Labor and Welfare published guidelines on the appropriate use of medications in geriatric patients (2). The guidelines state that polypharmacy increases the risk of side effects associated with medications in patients taking many drugs and in such patients, a multidisciplinary consultation, including pharmacist consultation, is recommended with the need for a prescription review. The consequences of polypharmacy include drug–drug interactions, adverse reactions, drug-induced frailty, and prescribing cascade initiation (3-7). Polypharmacy in elderly individuals has been associated with potentially inappropriate medications (PIMs) and negative health outcomes, including an increased risk of hospital admission, adverse drug events, and mortality (8). In observational studies, PIM use has been associated with a 1.6-fold increase in the mortality rate in elderly individuals (9). Polypharmacy increases the risk of PIM administration, and as some PIMs may have cognition-impairing effects, prolonged polypharmacy may result in dementia (10).

Adverse events are known to occur more frequently in elderly patients than in younger patients owing to the diminishing physical strength that occurs with age. Although different criteria for the prevention of polypharmacy, such as the Beer's

criteria (11), STOPP/START criteria (12), and STOPP-J criteria (13, 14), have been introduced, the reduction in the number of medications is still challenging because of the patients' needs.

In Japan, medical fees associated with polypharmacy, such as antibiotics and benzodiazepines, were updated to reduce the health care cost. Currently, hospitals calculate reimbursement by reducing the number of medications administered to a patient by two or more (15). However, the outcomes of these actions have not been sufficiently assessed by clinical pharmacists. In this study, we retrospectively surveyed outpatients with polypharmacy in Showa University Hospital, who received a medication review and pharmaceutical counseling by clinical pharmacists to reduce medications.

Methods

Study subjects

We retrospectively enrolled 13 outpatients, who were charged medical fees and received medication review and pharmaceutical counseling by clinical pharmacists to reduce the number of medications, between January 2017 and June 2017. The study protocol was approved by the Ethics Committee of the Department of Pharmacy, Showa University,

Tokyo, Japan (No. 343). Adverse events or changes in the physical conditions of the patients were monitored for 6 months using the medical records. The suitability of administered medications before and after medication reduction or underprescribing was assessed using the medication appropriateness index (MAI) (16) by two pharmacists. The MAI consists of 10 questionnaire items. However, in this study, we used only nine items and excluded the medication cost because in Japan, the switch to low-cost medications (generic medication) is mainly overseen by community pharmacies according to the patients' needs. Laboratory data, including aspartate transaminase, alanine aminotransferase, and estimated glomerular filtration rate, were assessed just before the review and 6 months post-review. The adverse events associated with medication reduction were assessed throughout the monitoring period by pharmacists using laboratory data, and based on the changes in the physical conditions using the medical records.

Medication review and pharmaceutical counseling by clinical pharmacists

Pharmaceutical counseling was provided by the clinical pharmacists at Showa University Hospital in a clinical setting. The steps in pharmaceutical counseling were as

follows: (i) hyper-polypharmacy or duplicate gastrointestinal medications were identified using prescription data; (ii) physicians and clinical pharmacists conducted a medication review of the identified patients; and (iii) after receiving approval from the patients to adjust medications, physicians changed the prescriptions appropriately, or pharmacists provided pharmaceutical counseling (e.g., explained the risk of polypharmacy and advantages of medication reduction) for 10–30 min and changed the prescriptions appropriately.

Statistical analysis

Data are expressed as median with range. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R software (The R Foundation for Statistical Computing, Vienna, Austria) (17). We used EZR in R commander (ver. 1.38) for analysis. The laboratory data before and 6 months after pharmaceutical counseling were compared using a Wilcoxon signed-rank test. The MAI was compared before, just after, and 6 months after pharmaceutical counseling using the Friedman-Bonferroni test. The results with a p-value of less than 0.05 were considered significant.

Results

Thirteen outpatients (male/female: 1/12, median [range]: 69 [45–82] years) were included in our study (Table 1). The patients were diagnosed with hypertension (n = 6), diabetes mellitus (n = 5), dyslipidemia (n = 5), and chronic kidney disease (n = 5). For these patients, the number of coadministered medications was 17 (9–30) before medication review and pharmaceutical counseling. The number of medications significantly reduced to 8 (8–29) just after the medication review and counseling and to 13 (8–27) 6 months after medication review and counseling (Fig 1). The MAI score was sustained for up to 6 months after medication review and pharmaceutical counseling (before vs. just after and 6 months after the medication review and counseling: 9 [3–23] vs. 4 [0–22] and 2 [0–23]). The MAI score significantly decreased from the baseline (just after and 6 months after counseling: $p < 0.005$ and $p = 0.007$, respectively); however, no significant difference in the MAI score was observed just after and 6 months after counseling (N.S.) (Fig 1).

The reasons for medication reduction (Table 1) were as follows: a) incorrect indication (6 medications); b) non-effective (5 medications); c) incorrect dosage (2 medications); d) drug–drug interactions (6 medications); e) drug–disease interaction (1 medication); f) duplicated drugs (11 medications); g) inappropriate duration (0 medications); and h) high cost (0 medications). The above-mentioned inappropriate

medications belonged to the following medication categories: medications for peptic ulcer and gastro–esophageal reflux disease (8 medications), vitamins (4 medications), probiotic products (4 medications), hypnotics and sedatives (3 medications), medication for constipation (3 medications), and iron supplements (3 medications). Adverse events and changes in the physical conditions associated with medication reduction were not observed in any patient. There was no significant difference in the laboratory data owing to medication reduction before and after pharmaceutical counseling.

Discussion

In this study, we aimed to determine whether medication reduction after medication review and pharmaceutical counseling resolved polypharmacy in outpatients, without any adverse events. We found that polypharmacy was reduced without any adverse events for at least 6 months.

We had previously reported the prescription patterns by clinical pharmacists in 13 Tokyo-area hospitals in 2,075 patients aged ≥75 years (18, 19). The findings of these studies were as follows: a) clinical ward pharmacy services reduce polypharmacy and b) 58.6% of patients practice polypharmacy. These data led to a reduction in the number of medications and should be used to reduce polypharmacy in Japanese healthcare. A few

trials have reported clinical pharmacist interventions for reducing polypharmacy in inpatients (20-23). However, the efforts of clinical pharmacists at reducing polypharmacy in outpatients have not been sufficient. Therefore, in this study, we provided pharmaceutical counseling to outpatients at Showa University Hospital with a focus on medication reduction. We showed that pharmaceutical counseling by clinical pharmacists could partially resolve polypharmacy.

The number of medications was significantly decreased just after the interventions, but after 6 months, the number of medications increased. The reason was that patients with systemic lupus erythematosus had worsened symptoms. We believe that these were not medication-related problems because the MAI score for these patients was low. The reduction in the MAI and the number of medications was sustained for at least 6 months after the pharmaceutical counseling by clinical pharmacists (Table 1 and Fig. 1). Several studies have reported that interventions by the medical staff, including pharmacists, can reduce polypharmacy, and various responses were obtained for different durations, such as 1 month to 12 months (24-27). In our study, 6 months was considered an appropriate duration for monitoring the effects of medication review and counseling on polypharmacy.

In conclusion, pharmaceutical counseling and medication review by clinical pharmacists resolve polypharmacy without any adverse events for at least 6 months, despite the limited number of assessments. Thus, it can be suggested that intervention (medication review and counseling) by clinical pharmacists is a useful method to resolve polypharmacy in outpatients.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Ethical approval

The study protocol was approved by the Ethics Committee of the Department of Pharmacy, Showa University, Tokyo, Japan (No. 343).

Conflicts of Interest and Source of Funding

All authors declare that they have no conflicts of interest and received no funding

Figure legends

Fig 1. Changes in the A) medication appropriateness index and B) number of medications before and after 6 months of interventions by clinical pharmacists to our study outpatients

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303 Fig. 1

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