Effects of pharmacist intervention on polypharmacy in patients with type 2 diabetes in Japan

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Research note

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Effects of pharmacist intervention on polypharmacy in patients with type 2 diabetes in Japan

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Short running title: Effects of intervention by pharmacist on polypharmacy

Abstract

Objective

Investigation of polypharmacy in patients with type 2 diabetes revealed that the medications being administered according to the patient's symptoms and complaints strongly contributed to polypharmacy. We explored the effects of clinical ward pharmacy service, which evaluated the need for symptomatic treatment, therefore minimizing polypharmacy by reducing inappropriate medications.

Results

The number of drugs [hospitalization vs. discharge: 9 (1-17) vs. 7 (1-16), P < 0.001] and rate of PP (hospitalization vs. discharge: 75.4% vs. 61.1%, P < 0.001) were significantly lower at discharge. Since hospital admission, the number of drugs increased (n = 6, 11%), remained unchanged (n = 15,28%), decreased by 1 drug (n = 4,8%), decreased by 2 drugs (n = 3,6%), and decreased by more than 2 drugs (n = 25,5%). Daily drug costs were significantly reduced (hospitalization vs. discharge: $ 8.3 vs. $ 6.1, P < 0.001).

Keywords: polypharmacy, type2 diabetes, pharmacy service

38 # Introduction

39

40 In Japan, the number of patients with type 2 diabetes (T2DM) is steadily increasing[1].
41 Medication used for the management of diabetes and its complications such as
42 hyperglycemia, microvascular complications, pain, insomnia, and other symptoms may
43 improve target outcome but can also have side effects that lead to the addition of
44 unnecessary medications to the drug regimen[2]. We identified that this strongly
45 contributes to polypharmacy (PP) in these patients PP resulting in an increase risk of
46 adverse drug reactions, drug-interactions and medication non-adherence[3-9]. The
47 symptomatic treatment administered according to the patient's symptoms and
48 complaints, such as pain and insomnia, strongly affect PP[10]. Although there is an
49 urgent need to prevent PP, none of the devised methods have been put into practice at
50 many facilities.
51 After a patient’s admission at the hospital, a clinical ward pharmacist evaluates
52 inappropriate medications using a pharmaceutical approach and checks for PP. The
53 clinical ward pharmacy service is effective in eliminating PP, as reported in the United
54 States of America and in Europe[11–14]. But so far, no such observations have been

55 made in Japan. Therefore, we investigated how the clinical ward pharmacy service

56 affects the rate of PP in T2DM in Japan.

57

58 # Main text

59 ## Methods

60 An uncontrolled before-after study was conducted at Shimokitazawa Hospital. We

61 included patients who were newly admitted in November 2017. The exclusion criteria

62 were as follows: (1) type 1 diabetes, (2) age <18 years, and (3) the clinical ward

63 pharmacy service is not implemented. We reviewed medical records to retrieve the

64 patients' clinical information. Since PP is defined as taking six or more drugs, our

65 primary outcome was reducing these medications. Secondary outcome was changes in

66 drug costs per day from when the patient was hospitalized to the day of discharge.

67 Normally distributed numerical data is presented as means ± standard deviation.

68 Categorical variables were analyzed using Fisher's exact test and chi-square test and are

69 expressed as absolute numbers or percentages. Differences were regarded as significant

70 when $p < 0.05$. All statistical analyses were performed using the Stata software (version

71 10; Stata Corp, College Station, TX, USA). In this study, 1 dollar was converted to 100

72 yen. This study was conducted in accordance with ethical guidelines for medical and

health research involving human subjects. The ethics board of the Kitasato University approved the study (Control number: 17078).

Results

Table 1 shows the characteristics of 53 patients who met the selection criteria.

<Table 1>

Comparing the number of drugs and PP rate at hospitalization and discharge, the number of drugs [hospitalization vs. discharge: 9 (1-17) vs. 7 (1-16), $P < 0.001$] and PP rate (hospitalization vs. discharge: 75.4% vs. 61.1%, $P < 0.001$) were significantly lower at discharge (Fig 1).

<Fig 1>

Since hospital admission, the number of drugs increased (n = 6, 11%), remained unchanged (n = 15,28%), decreased by 1 drug (n = 4,8%), decreased by 2 drugs (n = 3,6%), and decreased by more than 2 drugs (n = 25,5%). Daily drug costs were

91 significantly reduced upon comparing cost on the day of hospital admission with that on

92 the day of discharge (hospitalization vs. discharge: $ 8.3 vs. $ 6.1, P < 0.001, Fig. 2).

93

94 <Fig 2 >

95

96

97 **Discussion**

98 The method used in our study is to extract factors that strongly affect PP using

99 multivariate analysis, and to intervene using the clinical ward pharmacy service, which

100 is an existing service. The results of this study indicate that by using only the clinical

101 ward pharmacy service, an existing service, without adding new medical resources, it

102 was possible to lower the rate of PP and the total drug costs per day.

103 In Japan, medical expenses are increasing not only for the aged but also for diabetes

104 patients. According to the statistics of the fiscal year 2019, it is over $12 billion in

105 Japan[15]. Therefore, there is an urgent need for its optimization, possibly by avoiding

106 unnecessary medication and by reducing polypharmacy and medical costs. However, in

107 chronic diseases such as hyperglycemia and hypertension, it takes a year to determine

108 the therapeutic effects of the medication, making it difficult to decide whether to

109 continue the drug during the patient's stay at the hospital. In contrast, with symptomatic
110 treatment, one can evaluate the effects of drug withdrawal in a short term. Medication
111 used for symptomatic treatment is strongly responsible for PP in patients with T2DM
112 and there are previous reports which show that drugs which have similar functions are
113 frequently stopped[16]. Thus, we believe that active intervention in symptomatic
114 treatment is effective in resolving PP. Although there was a reduction in drug costs of
115 about 1.7 dollars per day, it helped improve the quality of life (QOL) by reducing the
116 burden of continuing treatment.
117 Beers criteria and STPP criteria are used as a screening tool for potentially inappropriate
118 medications (PIMs) in PP[17,18]. Whereas, in Japan, "Guidelines for medical treatment
119 and its safety in the elderly" was proposed in 2005 by the Japan Geriatrics Society[19].
120 As these are screening tools for the elderly, they cannot be used for patients under 65
121 years of age with T2DM who also have a high risk of PP[10]. In our study, we extracted
122 risk factors using multivariate analysis, and we believe that this will be useful for
123 resolving PP in younger T2DM.
124 Efforts to eliminate PPs include the use of screening tools such as STOPP criteria and
125 the establishment of specialized outpatient clinics with a team of multi-specialties such
126 as doctors, nurses, and pharmacists who are focused on reducing PPs[20-24]. In a study

127 conducted in Japan that extracted PIMs using STOPP criteria and pharmacist
128 intervention, it was reported that 28.0% of the drugs that corresponded to STOPP
129 criteria were changed[22]. On the other hand, all drugs suggested by pharmacist
130 intervention were changed in this study. This is the reason why we do not recommend a
131 change in treatment using just criteria because based on the patient's subjective
132 symptoms, continuation of the drugs could be necessary. In addition, while criteria and
133 efforts to introduce new medical resources are effective in eliminating PP, at present,
134 many facilities cannot do the same. In fact, the New Health care Fee, which includes
135 these new services to stop PPs, covers only 16.5% of all hospitals[25]. Therefore, we
136 should consider a method that utilizes existing approaches without adding new medical
137 resources. In our study, pharamcist interventions for PP were conducted for all ages, the
138 PP rate was significantly reduced, and 53% of patients met the calculation requirement
139 for the The New Health care Fee by reducing two or more PIMs.
140

141 **Conclusions**

142 We believe that the results of this study will provide guidance because of its
143 effectiveness in eliminating PP in T2DM in Japan and Asia. In addition, by eliminating
144 PP, medical costs are reduced, and the number of drugs taken is reduced, which

145 increases patient satisfaction and contributes to improved treatment adherence. As a
146 result, it is speculated that it has an impact on clinical outcomes such as QOL and
147 Hemoglobin A1c, and thus we would like to investigate further.
148

149 ## Limitations

150 There are several limitations in this study. First, we did not compare this study with
151 cases where no intervention was performed, and we think it is necessary to examine the
152 details of the effectiveness of this approach in the future. Finally, since interventions are
153 centered on drugs for symptomatic treatment, there is still room for intervention in
154 PIMs.
155

156 ## Availability of data and materials

157 The datasets used and/or analyzed during the study are available from the corresponding
158 author on reasonable request.
159

160 ## List of abbreviations

161 PP: polypharmacy
162 T2DM: type 2 diabetes

163 QOL: quality of life

164 PIMs: potentially inappropriate medications

165

166 ## Declarations:

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Authors' contributions

TH designed the study and wrote the initial draft of the manuscript. KA assisted in the preparation of the manuscript. All other authors have contributed to data collection and interpretation and have critically reviewed the manuscript. All authors approved the final version of the manuscript, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Disclosure Statement: The authors declare that they have no conflict of interest.

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Ethics approval and consent to participate

199 This study was conducted in accordance with the ethical guidelines for medical and

200 health research involving human subjects. The ethics board of the T Kitasato University

201 approved the study (Control number: 17078).

202

203 **Consent for publication**

204 Not applicable.

205

206 **Competing interests**

207 The authors declare that they have no competing interests.

208

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289

290 **Tables**

291

292 Table 1. Patient characteristics

	Mean ± S.D. or Median (min-max) or n (%)
	Overall n =53
Male n (%)	27 (50.9)
Age (years)	68.8±14.0
HbA1c (%)	7.1 ± 1.6
BMI (kg/m^2)	22.2 ± 4.5
eGFR (mL/min/1.73m^2)	71.9 ± 64.1
Diabetes Duration (years)	7.9±5.9
Number of drugs	9 (1-17)
Polypharmacy n (%)	40(75.4)
Hospitalization days(days)	17.2 ± 2.5

293 HbA1c (hemoglobin A1c), BMI (body mass index), eGFR (estimated glomerular

294 filtration rate), Polypharmacy was defined as taking six or more drugs.

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301 Fig1. Changes in number of drugs and polypharmacy rate

302 The number of drugs [hospitalization vs. discharge: 9(1-17) vs. 7(1-16), P < 0.001] and

303 PP rate (hospitalization vs. discharge: 75.4% vs. 61.1%, P < 0.001) were significantly

304 lower at discharge (Wilcoxon signed rank test).

305

306

307 Fig2. Changes in the number of drugs and daily drug costs

308 Changes in the number of drug since admission were increased (6 patients, 11%),

309 unchanged (n = 15, 28%), decreased by 1 drug (n = 4,8%), decreased by 2 drugs (n = 3,

310 6%), decreased by more than 2 drugs (n = 25, 47%). Daily drug costs were significantly

311 reduced when comparing hospital admission and discharge (hospitalization vs.

312 discharge: $ 8.3 vs. $ 6.1, P < 0.001, 1 $ = 100yen, Wilcoxon signed rank test)

Figures

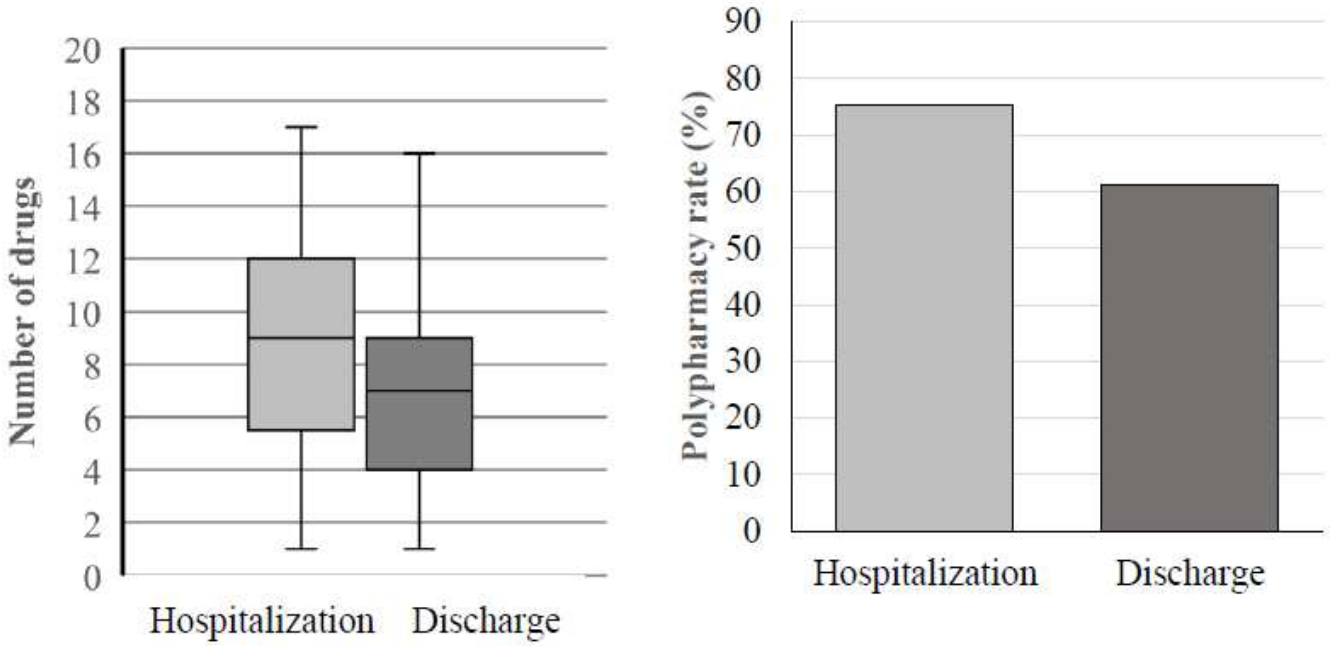

Fig1. Changes in number of drugs and polypharmacy rate

Figure 1

Changes in number of drugs and polypharmacy rate

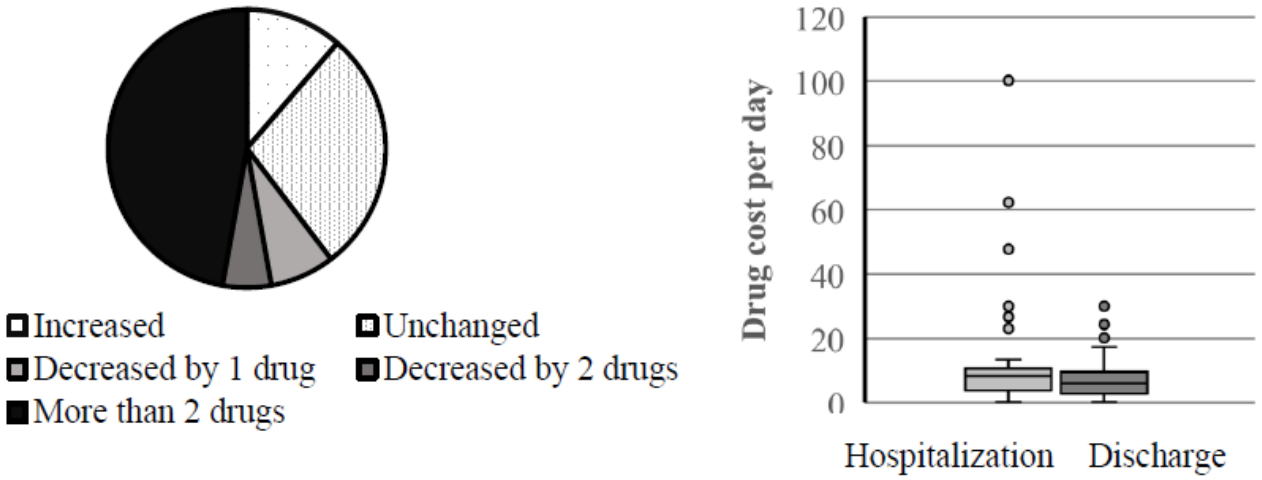

Fig2. Changes in the number of drugs and daily drug costs

Figure 2

Changes in the number of drug s and d aily drug costs