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Medical Economic Effect of Pharmaceutical Interventions by Board-Certified Pharmacists in Palliative Pharmacy for Patients with Cancer Using Medical Narcotics in Japan: A Multicenter, Retrospective Study

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Background: The Japanese Society for Pharmaceutical Palliative Care and Sciences specializes in pharmacology in the field of palliative medicine. More than 700 board-certified pharmacists in palliative pharmacy (BCPPP) are actively involved in palliative pharmacotherapy at various hospitals and pharmacies. The purpose of this study was to determine the economic effect of pharmaceutical interventions by BCPPPs.

Methods: This multicenter retrospective study included 27 medical centers and analyzed the medical economic effect of interventions by BCPPPs (17 pharmacists) and non-BCPPPs (24 pharmacists) on patients using medical narcotics for cancer pain in September 2021.

Results: The percentage of patients who received a pharmaceutical intervention and whose drug costs were reduced by pharmacist intervention was significantly higher in the BCPPP group than in the non-BCPPP group. Although there was no significant difference between the two groups in drug cost reduction per patient per month (BCPPP group: $0.89 [–$64.91 to $106.76] vs. non-BCPPP group $0.00 [–$1,828.95 to $25.82]; P = 0.730), the medical economic benefit of pharmacist intervention in avoiding or reducing adverse drug reactions was higher in the BCPPP group ($103.18 [$0.00 to $628.03]) than in the non-BCPPP group ($0.00 [$0.00 to $628.03]) ($P$ = 0.070). The total medical economic benefit—the sum of these—was significantly higher in the BCPPP group ($88.82 [–$14.62 to $705.37]) than in the non-BCPPP group ($0.66 [–$1,200.93 to $269.61]) ($P$ = 0.006).

Conclusion: Pharmacological intervention for patients with cancer using medical narcotics may have a greater medical economic benefit when managed by BCPPPs than by non-certified pharmacists in Japan. (J Nippon Med Sch 2024; 91: 59–65)

Key words: medical economic effect, palliative pharmacy, pharmaceutical interventions, opioids

Introduction

Early implementation of palliative care in patients with cancer not only relieves patient suffering, it also prolongs life[1,2]. Early palliative care in patients with cancer, simul-

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taneous with the initiation of standard treatment, is also recommended in the guidelines of the American Society of Clinical Oncology[3]. The role of the pharmacist is important in the safe, effective practice of pharmacotherapy in palliative care[4,5], and The American Journal of Health-System Pharmacy (AJHP) has established guidelines for the role of pharmacists in palliative care[6]. In Japan, the Japanese Society for Pharmaceutical Palliative Care and Sciences (approximately 3,900 members), which specializes in pharmacology in the field of palliative medicine, has been certifying board-certified pharmacists in palliative pharmacy (BCPPP) since 2009 to train pharmacists who, together with doctors, nurses, and other healthcare professionals, can contribute to palliative medicine. As of 2021, more than 700 BCPPPs are working in hospitals and insurance pharmacies, and they play a leading role in palliative drug therapy in various settings, including palliative care teams. However, there are no studies of the usefulness of pharmacological interventions by BCPPPs, particularly the health and economic effects of such interventions. Consequently, there are no additional fees for the reimbursement of BCPPP interventions.

Many recent studies in Japan have investigated the health economic effects of pharmacist interventions in avoiding adverse drug reactions[7–10]. The economics of side effect avoidance is estimated from the amount paid by the Pharmaceuticals and Medical Devices Agency (PMDA) to patients under the Relief Systems for Adverse Drug Reactions. In this study, we conducted a multicenter retrospective study of the health economic effects, including avoidance of side effects and drug cost reductions, of pharmaceutical interventions by BCPPPs in patients with cancer who used medical narcotics.

Methods

Certification of BCPPPs

The Japanese Society for Pharmaceutical Palliative Care and Sciences began to certify BCPPPs in 2009. Pharmacists are eligible to apply for certification if they satisfy the requirements, namely, working experience as a pharmacist for at least 5 years, attending courses (100 credits), presentations at conferences on palliative medicine (two presentations), experience in palliative medicine drug management and guidance (30 cases at hospital pharmacists or 15 cases at pharmacy pharmacists), and satisfactory performance on the certification examination[11].

Recruitment of participating pharmacists

The Japanese Society for Pharmaceutical Palliative Care and Sciences recruited pharmacists to participate in this study via its website and by email. A total of 41 pharmacists from 20 hospitals and seven pharmacies participated in the study.

Collection of patient information

Patients who used medical narcotics for the treatment of cancer pain and were served by participating pharmacists in the study at participating facilities from September 1 to 30, 2021, were included in the study. Patient information was collected from each center, excluding personally identifiable information and including pharmacist-led interventions, changes in side effects, and medications used before and after the intervention.

Calculation of medical economic effects

The medical economic effects of the pharmacist's intervention were evaluated in two ways: by calculating the amount of drug cost reduction and the avoidance/reduction of adverse drug reactions. Drug cost reductions per month were calculated based on drug prices in Japan in 2021 (Eq. 1).

Drug cost reductions = Drug cost reductions per day × 30 days … (Eq. 1)

The method used to calculate the medical economic effects from the avoidance/reduction of adverse drug reactions was based on the amount paid by the PMDA to patients under the Relief Systems for Adverse Drug Reactions[7–10]. The total amount paid under this program was ￥2,420,942,000 (approximately $21,720,000; 1$ = ￥111.46, September 30, 2021), and the number of payments was 1,342 during the 1-year period from April 1, 2020 to March 31, 2021 in Japan[12]. Thus, we calculated that avoidance or reduction of serious side effects would have an economic effect of $16,176 (￥1,803,000) per case. The medical economic benefits of avoiding or reducing side effects of cancer chemotherapy, high-risk drugs, and other drugs were calculated as $834 (￥93,000), $628 (￥70,000), and $413 (￥46,000), respectively. These amounts were calculated by multiplying the effectiveness of avoiding or reducing serious adverse effects by 5.21%, 3.91%, and 2.6%, respectively[7–10].

After calculating reduction in drug costs and benefits from avoidance or reduction of side effects for each pharmacist, these amounts were divided by the number of patients with cancer who used the narcotics for which they were responsible per month to arrive at the respective medical economic benefit per patient per month (Eqs. 2 and 3). In addition, these two medical economic benefits per patient per month were summed to obtain the total medical economic effect of the pharmacist's intervention per month and patient (Eq. 4).

Table 1 Pharmacist background

	non-BCPPP (N = 24)	BCPPP (N = 17)	*P* value
Years working as a pharmacist	10 (4-41) [a]	17 (9-33) [a]	*0.007* [b]
Work location			
Insurance pharmacy	4 (16.7%)	3 (17.6%)	>0.999 [c]
Hospital	20 (83.3%)	14 (82.4%)	
Jobs usually involved in			
Palliative care ward services	2 (8.3%)	3 (17.6%)	0.671 [c]
General ward services	17 (70.8%)	7 (41.1%)	0.058 [c]
Preparation of medicines	16 (66.7%)	11 (64.7%)	>0.999 [c]
Palliative care team	6 (25.0%)	10 (58.8%)	*0.028* [c]
Anticancer drug preparation	4 (16.7%)	4 (23.5%)	0.876 [c]
Pharmacy services for outpatients with cancer	2 (8.3%)	3 (17.6%)	0.671 [c]
At-home medical care	4 (16.7%)	4 (23.5%)	0.876 [c]
Number of medical narcotic use patients in charge (per month)	7 (1-26)	8 (1-44)	0.465 [c]

[a] median (min-max); [b] Mann-Whitney U test; [c] chi-square test.

Drug cost reductions = Sum of drug cost reductions achieved through pharmacist intervention (Eq. 1) / Number of patients served by a pharmacist in a month (September 2021) … (Eq. 2)

Medical economic effects from avoidance or reduction of adverse drug reactions = Sum of medical economic effects from avoidance or reduction of adverse drug reactions/Number of patients served by a pharmacist in a month (September 2021) … (Eq. 3)

Total medical economic effect of pharmacist intervention = Drug cost reductions (Eq. 2) + Medical economic effects from avoidance or reduction of adverse drug reactions (Eq. 3) … (Eq. 4)

"Patients served by a pharmacist" was defined as those interviewed by a pharmacist.

Statistical analysis

Statistical analysis was performed using the chi-square test or Mann-Whitney U test (StatView; Abacus Concepts, Berkeley, California, USA). For the chi-square test, Yates' correction was applied when the number of cases for each item was less than 5. A risk rate of less than 5% ($P < 0.05$) was considered significant.

Ethics approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. The requirement for informed consent was waived because of the retrospective nature of the study, and the official website of Kyushu University was used as an opt-out method. Ethical approval was provided by the Institutional Review Boards of Kyushu University Graduate School and Faculty of Medicine (Approval No. 21105, December 28, 2021), and permission to perform the study was obtained from the director of each participating institution.

Results

Pharmacist background

Of the 41 participating pharmacists, 17 were BCPPPs and 24 were non-BCPPPs (**Table 1**). Pharmacist work history was significantly longer in the BCPPP group than in the non-BCPPP group ($P = 0.007$). There was no significant difference between these groups with respect to work location, such as at hospitals or insurance pharmacies ($P > 0.999$). Regarding jobs, the BCPPP group had a significantly higher rate of pharmacists working on a palliative care team ($P = 0.028$). There were no significant differences between the two groups in the percentage of people involved in other jobs. In addition, there was no significant difference between the two groups in the number of patients with cancer using medical narcotics prescribed to them during the study period ($P = 0.465$).

Percentage of patients who benefited from pharmacist interventions

The percentage of patients receiving pharmaceutical interventions was higher in the BCPPP group than in the non-BCPPP group (**Table 2**, $P = 0.003$). Among patients served by pharmacists, the rate of patients whose drug costs were reduced by pharmacist intervention was also significantly higher in the BCPPP group ($P = 0.031$). There was no significant difference between the two groups in the percentage of patients with side effects that were avoided or reduced by pharmacist intervention ($P = 0.106$). In addition, the proportion of patients who had no or reduced constipation or delirium tended to be higher in the patient group treated by BCPPPs (**Table 3**; constipation, $P = 0.080$; delirium, $P = 0.099$). The percentage of patients who had no or reduced nausea, vomiting, somnolence, respiratory depression, and extrapyramidal

Table 2 Percentage of patients who benefited from pharmacist interventions

	non-BCPPP (N = 24)	BCPPP (N = 17)	*P* value
Percentage of patients receiving pharmaceutical intervention	16.2% (0.0%-100.0%)	66.7% (0.0%-100.0%)	*0.003*
Percentage of patients with reduced drug costs	5.3% (0.0%-66.7%)	20.0% (0.0%-20.0%)	*0.031*
Percentage of patients who avoided/reduced side effects	0.0% (0.0%-100.0%)	12.5% (0.0%-62.5%)	0.106

median (min-max), Mann-Whitney U test.

Table 3 Number and percentage of patients with avoided or reduced side effects

	Patients served by non-BCPPP (N = 196)	Patients served by BCPPP (N = 225)	*P* value
Constipation	5 (2.6%)	15 (6.7%)	0.080
Nausea/vomiting	10 (5.1%)	7 (3.1%)	0.301
Drowsiness	4 (2.0%)	1 (0.4%)	0.290
Respiratory depression	0 (0.0%)	0 (0.0%)	>0.999
Delirium	0 (0.0%)	5 (2.2%)	0.099
Cone external circuit symptoms	2 (1.0%)	3 (1.3%)	>0.999
Other side effects	8 (4.1%)	26 (11.6%)	*0.005*

chi-square test.

symptoms did not differ between the two groups. Regarding other side effects, significantly more were avoided in the patients cared for by BCPPPs ($P = 0.005$).

Medical economic effects of pharmacist intervention

There was no significant difference in drug cost reduction (per patient per month) between the BCPPP and non-BCPPP groups (**Fig. 1A**; BCPPP group −$0.89 [−$64.91 to $106.76] vs. non-BCPPP group $0.00 [−$1,828.95 to $25.82]; $P = 0.730$). In addition, there was a tendency for greater medical economic benefits from avoided or reduced adverse effects due to pharmacist intervention in the BCPPP group (**Fig. 1B**; BCPPP group $103.18 [$0.00 to $628.03] vs. non-BCPPP group $0.00 [$0.00 to $628.03]; $P = 0.070$). Furthermore, total medical economic benefits—the sum of these benefits—were significantly higher in the BCPPP group than in the non-BCPPP group (**Fig. 1 C**; BCPPP group $88.82 [−$14.62 to $705.37] vs. non-BCPPP group $0.66 [−$1,200.93 to $269.61]; $P = 0.006$).

Discussion

This study evaluated the medical economic effects of BCPPP intervention on cancer pain relief. The total pharmacoeconomic benefit, drug reductions plus avoided or reduced adverse drug reactions, was significantly higher in the BCPPP group than in the non-BCPPP group.

In Japan, the requirements for BCPPP certification include working as a pharmacist for at least 5 years, attending courses, presentations at conferences on palliative medicine, and experience in palliative medicine drug management and guidance. Thus, BCPPPs are expected to be able to provide substantially more advanced pharmaceutical palliative care. However, there are no data on the advantages of certified pharmacists, especially in terms of medical economics, and this study is the first to report such benefits.

Regarding the background of the present pharmacists, the BCPPP group had longer careers as pharmacists. This likely results in part from the fact that the certification requirement is a minimum of 5 years of pharmacist experience. Certified pharmacists are thus probably more likely to be included on palliative care teams because of their expertise. In addition, there were no significant differences in pharmacist background between the two groups, which was not considered a hindrance to conducting this study.

Although there was no difference in the number of patients treated by the certified and non-certified groups during the study period, the proportion of patients for whom the pharmacist identified problems and provided prescription intervention was significantly higher in the certified group, which suggests that pharmacological intervention was more aggressive in the BCPPP group. Among patients treated by a pharmacist, the percentage of patients with reduced drug costs was also higher in the BCPPP group. Uchida et al.[13] previously reported that BCPPP intervention reduces inappropriate prescription in patients with cancer and polypharmacy. Taken together,

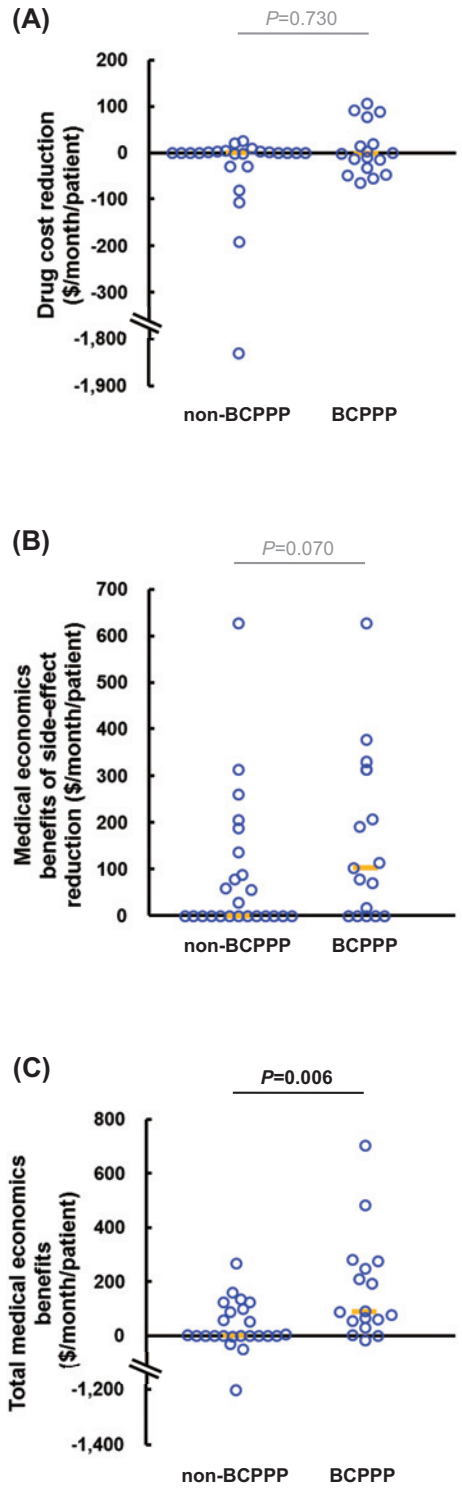

Fig. 1 Medical economic benefits of pharmacist interventions.
Drug cost reduction (A), medical economic benefits of side effect reduction (B), and total medical economic benefits (C) are shown. The total medical economic benefits were calculated by adding the drug cost reductions and medical economic benefits of side effect reduction. The blue circles and orange lines indicate data obtained from each pharmacist and the corresponding median, respectively. Statistical analysis was performed using the Mann-Whitney U test.

intervention by BCPPPs can be effective in reducing the use of drugs that are therapeutically unnecessary.

No significant difference was found in the percentage of patients with no or fewer side effects. However, with respect to individual side effects, improvements in constipation and delirium tended to be greater in patients cared for by BCPPPs. Delirium and extrapyramidal symptoms are reportedly induced by antiemetic, gastrointestinal, or hypnotic sedatives taken concomitantly with opioids, exacerbating adverse effects in these patients[14]. Because delirium involves factors other than opioids and other drugs[15], it is likely that certified pharmacists with more advanced pharmacological skills were able to achieve better results. Moreover, patients treated by the certified group had a significantly higher percentage of other side effects, suggesting that BCPPPs use a multifaceted approach. However, the response to major adverse events, such as nausea and vomiting, may have been standardized because of the development of guidelines for the palliation of cancer pain.

There was no significant difference in drug cost reduction between the two groups. However, the total medical economic effect of the pharmacist's intervention was significantly higher in the BCPPP group. Cost reductions are greater when fewer drugs are prescribed unnecessarily, whereas drug cost reductions are smaller when pharmacists actively suggest supportive care for side effects and titration for pain control. In some cases, opioid rotation can also increase drug costs. In this study, the BCPPP group actively engaged in pharmacological interventions, which is why drug cost reductions were not higher than those of the non-BCPPP group.

The median total health economic benefit (per patient per month) was $88.82 in the BCPPP group and $0.66 in the non-BCPPP group. In other words, it can be concluded that a pharmacist with certification treating one patient with cancer using a medical narcotic would be effective at approximately $88 per month.

This study evaluated the medical economic effects of pharmacist interventions in reducing drug costs and avoiding side effects. However, this study has several limitations. First, other factors may be involved in economic health effects. For example, although many studies reported that pharmacist interventions improved pain control[16,17], our study did not evaluate the medical economic effects of pain control. Because there were many cases in this study in which pain control was improved by BCPPP intervention, the actual medical economic benefit may be higher than the calculated $88.82. Second,

as mentioned above, there was a difference in years of pharmacist experience between the BCPPP and non-BCPPP groups. A more precise analysis with the same number of years of pharmacist experience may be necessary in the future. Third, the medical economic effects of the avoidance/reduction of adverse drug reactions in this study are indirect values because they are based on the amount paid by the PMDA to patients under the Relief Systems for Adverse Drug Reactions. They are also based on amounts paid from April 2020 through March 2021, so they may vary slightly from year to year. Moreover, the number of pharmacists participating in this study was small. However, because this was a multicenter study involving more than 20 facilities, we believe that the results are not influenced by the biased work environment of a single center; rather, they represent a situation that is universal throughout Japan. Furthermore, the participating pharmacists were recruited via website and email, so sampling bias is a concern. To compare the two groups more rigorously, a randomized, larger, comparative study is needed.

International reviews found that oncology pharmacists contribute to clinical care, patient education, and cost reduction[18]. Pharmacists specialized in palliative care are also active in the United States, and palliative care consultation by inpatient palliative care clinical pharmacy specialists in the United States decreased total health care expenditures, increased opioid use, and decreased subsequent hospitalizations and urgent care visits[4]. Training of pharmacists in palliative care is expected to lead to widespread provision of more advanced palliative care practices. However, no study has assessed whether BCPPPs in Japan contribute to medical economic benefits, and the present work is the first study conducted by an academic committee.

Pharmacological intervention for patients with cancer using medical narcotics may have a greater medical economic benefit when managed by BCPPPs than by non-certified pharmacists in Japan.

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Conflict of Interest: The authors declare no conflicts of interest.

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