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Omae, Takahito
Yotani, Nobuyuki
Sakashita, Akihiro
Kizawa, Yoshiyuki

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Number of Unused Medications at the Time of Last Admission: A Prospective Observational Study in a Single Palliative Care Unit

Takahito Omae, MD¹, Nobuyuki Yotani, MD, PhD², Akihiro Sakashita MD, PhD¹, Yoshiyuki Kizawa MD, PhD¹

*1 Department of Palliative Medicine Kobe University Graduate School of Medicine

*2 Department of Palliative Medicine National Center for Child Health and Development

Abstract

Background: Unused medications (UM) are an important issue, with the waste associated with UM a burden to the healthcare system. The aims of this study were to clarify the amount and costs of UM in advanced cancer patients at the time of their last admission to a palliative care unit, and to explore the factors contributing to the cost of UM and how patients dealt with UM. **Methods:** A prospective observational study was conducted in single palliative care unit. UM were classified into 6 categories, and the number and cost of UM by category calculated per patient. Patients were classified into 2 cost groups (high and low) based on the total cost of UM, and the number and cost of UM by category were compared between these 2 groups. **Results:** Of 194 consecutive hospitalized patients, data were analyzed for 90. The mean number and cost of UM per patient was 440 and USD 301, respectively. Opioids accounted for 47% of the cost of UM. Comparing costs by UM category, the proportion of opioids (51% vs. 21%; $P < .0001$) and oral anticancer drugs (14% vs. 3%; $P = .02$) was higher in the high than low cost group. **Conclusion:** Based on the results of the present study, the estimated annual waste cost of UM for deceased cancer patients in Japan was approximately USD 110 million. Interventions to educate patients regarding UM and to eliminate barriers to opioid use may help reduce the cost of UM, particularly opioids and anticancer drugs.

Keywords

unused medications, neoplasms, palliative care, opioid, oral anti-cancer drugs, drug disposal, medical cost

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Review

Introduction

The evaluation and management of unused medications (UM) are important because UM can have several undesirable outcomes, such as environmental pollution due to inappropriate drug disposal, drug intoxication due to misuse, especially by children, and illegal transaction of opioids.¹⁻¹² From another point of view, UM may indicate poor drug adherence, which is associated with the potential for decreased treatment efficacy, poor prognosis, and poor patient satisfaction.¹³⁻²³ In the past decade, cancer treatment has shifted from inpatient to outpatient clinics.²⁴⁻²⁶ This means that cancer patients need to manage many drugs, such as oral anticancer drugs, anti-emetics, analgesics, and opioids, by themselves.²⁷ UM are also an important issue from the viewpoint of medical economics.^{28,29} Because the costs and use of oral anticancer drugs have increased rapidly, UM cannot be overlooked. In the case of cancer patients, we believe that the best way to ascertain UM in this group is to investigate UM in deceased cancer patients, because this would reflect total UM during their life and cancer journey. However, to the best of our knowledge, only a few studies have investigated UM in an advanced cancer setting, and no prospective studies have investigated UM in deceased cancer patients.^{30,31} To investigate UM in deceased cancer patients, we need to ask bereaved family members about UM soon after the patient's death. However, such a study would be difficult to conduct for both ethical and practical reasons. Thus, instead of conducting a survey of family members of deceased cancer patients, we decided to conduct a prospective study to investigate UM at the time of cancer patients' last admission to a palliative care unit (PCU).

The primary aim of the present study was to clarify how many UM advanced cancer patients had left at home at the time of their last admission to the PCU. Secondary aims of the study were to explore the factors contributing to the cost of UM, as well as to determine how patients dealt with UM.

Methods

Study design and setting

The present study was a prospective observational study at an inpatient PCU in Hyogo Prefectural Kakogawa Medical Center (HPKMC) located in Kakogawa City, a provincial city in Hyogo Prefecture with a population of 265 000. Consecutive patients who were admitted to the PCU with a diagnosis of advanced incurable cancer between 1 October 2015 and 31 July 2016 were recruited to the study. We attempted to obtain written informed consent from the patients themselves, but if the patients no longer had

the capacity to make decisions, consent was obtained from their families or primary caregivers as surrogate decision makers. Patients were excluded from the study if we were unable to explain the nature and objectives of the study to them and their caregivers, or if the attending physicians deemed that the survey could cause psychological distress and was therefore inappropriate for the patients and their caregivers. In the present study, UM were defined as “the prescription drugs that were left over and not in use at the patient’s home”.

Data collection

Eligible participants were asked to bring in all the prescription drugs that were left over at home at the time of their last admission to the PCU. Hospital pharmacists immediately checked the UM and registered the name, number, and amount of UM in the patient’s medical record. Then, the UM were differentiated, counted, and recorded by 1 of the authors (TO). UM were classified into 6 categories: opioids, non-opioid analgesics, oral anticancer drugs, gastrointestinal drugs, psychotropic drugs, and others.

Opioids included strong opioids and weak opioids. The strong opioids were morphine (tablets, powder, and liquid), oxycodone (tablets and powder), fentanyl (extended-release patch and transmucosal tablets), and methadone (tablets), whereas the weak opioids were tramadol (tablets) and codeine (tablets and powder). Non-opioid analgesics included non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and gabapentinoids. Oral anticancer drugs included oral cytotoxic drugs and oral molecular target drugs, whereas gastrointestinal drugs included laxatives, antacids, and anti-emetics. Psychotropic drugs included benzodiazepines, antidepressants, and antipsychotics. The “others” category of drugs included cardiovascular system drugs, corticosteroids, drugs for the treatment of diabetes mellitus (including insulin injections), respiratory system drugs, antibacterial drugs, anti-allergy drugs, and anti-epileptics, among others. Drugs for external use, such as dermatologic pastes, eye drops, poultices, inhalants (including nebulized medication), fluids, and liquids for injection, were excluded from the calculation of the number of UM because counting these types of medications was complicated. Conversely, they were included in the calculations of costs in the “others” category.

The price of all the evaluated UM was then calculated by referring to standard price lists published by the Japanese Ministry of Health, Labor and Welfare (March 2016).³² We then determined the total number and cost of UM per patient for all participants and the respective number and cost of UM according to the different categories described above. In the present study, when calculating costs, the currency

conversion rate was set at USD 1 = ¥ 100. In addition, sociodemographic information was collected from patients' medical records, including age, sex, type of cancer, admission route (i.e. the last place where the patient received treatment and care before being admitted to the PCU), household composition (whether the patient was living alone or not), and whether medication had been prescribed by family physicians (including both primary care doctors and home-based palliative care doctors).

Patients were excluded from the analysis if they met any of the following criteria: (i) they had been discharged from the PCU alive and were not readmitted; (ii) they did not bring in UM from home, as requested; (iii) there was no information about UM on their medical record; (iv) they reported that a large amount of UM had been discarded just before their admission to the PCU; and (v) it was considered (by the researchers) that there was no UM at home. In addition, 1 of the authors (TO) conducted a structured interview to determine how patients dealt with UM. If the patients did not have sufficient decision-making capacity, the interview was conducted with the patient's family or caregiver. Patients (or family members or caregivers) were asked, "How did you deal with UM?" and were given the following answer options: (i) **not disposed of**; (ii) discarded UM in the trash; (iii) flushed them down the sink or toilet; (iv) requested physicians to adjust the prescription; (v) gave them away to someone; and (vi) "other". Multiple answers were allowed.

Statistical analysis

Demographic data were summarized using standard descriptive statistics. To investigate variables associated with high UM cost, patients were divided into 2 groups, namely a 'high cost group' and a 'low cost group', and several variables (i.e. proportion of cost of UM by category, results of interview, and demographic background) were compared between these 2 groups. The high cost group consisted of patients in the top 25th percentile of total UM cost, whereas the low cost group consisted of the remaining 75% of patients. The Mann–Whitney *U*-test was used to compare the proportion of cost of UM by category, whereas the Chi-squared or Fisher's exact test was used, when appropriate, to compare the interview results and demographic background. Statistical analyses were conducted using JMP v.10.0.2 (SAS Institute, Cary, NC, USA). Two-sided *P* < .05 was considered significant.

Ethical considerations

This study was approved by the Ethics Committee of Hyogo Prefectural Kakogawa Medical Center (Authorization no. 27–5, 27–12).

Results

Between 1 October 2015 and 31 July 2016, 194 consecutive patients were screened, but 69 were ineligible for inclusion in the study because informed consent was not obtained. The remaining 125 patients (64%) were enrolled the study. Of these, 35 were excluded from analysis: 11 because they were discharged from the PCU alive and were not readmitted, 10 because they lacked UM data in their medical records, 7 because they reported that a number of UM had been discarded just before their admission to the PCU, 5 because they did not bring in UM from home as requested, and 2 because they were considered to have no UM at home because they had been in other hospitals due to other disease for many years. This left 90 patients (46%) who were included in the analysis.

Patient characteristics and number and cost of UM

Patient characteristics and the frequency of patients who had UM according to drug category are summarized in Table 1. Mean patient age was 71 years, and 52% were male. The most common type of cancer was gastrointestinal (44%), followed by lung (19%). Twelve percent of patients lived alone, and 49% received medications from their family physicians. All family physicians were working without hospice input. Of the patients in the present study, 46 (51%) were managed by hospital physicians only, and 7 (8%) were co-managed by the palliative care consultation team in HPKMC. The most frequent category of UM was gastrointestinal drugs (96%), followed by non-opioid analgesics (74%), opioids (61%), psychotropic drugs (53%), and oral anticancer drugs (10%). Among the “other” type of UM, 53% of patients had cardiovascular system drugs at home, 26% had corticosteroids, and 14% had drugs for the treatment of diabetes mellitus.

Table 2 shows the number and cost of UM by category in all 90 participants. The total number of UM across all 90 patients was 39 628, with a mean number of 440 UM per patient. The total cost of UM across all 90 patients was USD 27 085, with a mean cost of USD 301 per patient. Regarding the number of UM by category in all patients, gastrointestinal drugs accounted for the largest proportion of UM in all patients (33%), followed by non-opioid analgesics (14%), and opioids (10%). Conversely, opioids accounted for the greatest cost of UM (47%), followed by gastrointestinal drugs (9%), and oral anticancer drugs (8%). With regard to unused opioids, the number and cost of long-acting opioids (LAO) were 1379 and USD 8200, respectively, compared with 1639 and USD 3800, respectively, for short-acting opioids (SAO). The total number of UM

per patient ranged from 16 to 1702 (interquartile range [IQR] 192–625), whereas the total cost of UM per patient ranged from USD 4 to USD 3190 (IQR USD 85–359).

Factors contributing to the cost of UM

The number and cost of UM by drug category in the high and low cost groups are summarized in Table 3. The mean number and cost of UM per patient in the high cost group were 719 and USD 780, respectively, compared with 350 and USD 146 in the low cost group. The proportion of opioids (16% vs. 7%; $P < .0001$) and oral anticancer drugs (4% vs. 0.3%; $P = .02$) was significantly greater in the high than low cost group. Conversely, the proportion of the “other” drug category was significantly lower in the high than low cost group (26% vs. 39%, respectively; $P = .04$). In terms of cost, opioids (51% vs. 21%; $P < .0001$) and oral anticancer drugs (14% vs. 3%; $P = .02$) accounted for a significantly greater proportion of cost in the high than low cost group. Comparing demographic variables between the 2 groups revealed that patients in the high cost group were more likely to have received medication from family physicians (68% vs. 43%; $P = .04$) and have been admitted to the PCU from home (77% vs. 51%; $P = .03$) than patients in the low cost group. There were no significant differences in age, sex, cancer type, and the proportion of patients living alone between the 2 groups.

How UM were dealt with

The interview with patients (or family members or caregivers) revealed that 62% of patients **did not dispose of** UM, 24% discarded them in the trash, 17% requested physicians to adjust prescriptions, 5% gave them away to someone else, and 9% reported some other way of dealing with UM. No patient reported flushing UM down the sink or toilet. Comparisons of the disposal of UM between the high and low cost groups are given in Table 4. Patients in the high cost group were significantly more likely to store UM at home (91% vs. 51%; $P = .0003$) or give them away to someone else (15% vs. 2%; $P = .05$) than patients in the low cost group. There were no significant differences in the proportion of patients who discarded UM in the trash, requested physicians to adjust prescriptions, or used some other method to deal with UM between the 2 groups.

Discussion

To the best of our knowledge, the present study is the first prospective study to investigate UM not only in the advanced cancer setting, but also in a PCU. The most important finding of the present study is that the wasted cost of UM left over in

individual homes was approximately USD 300 per cancer patient. In 2015, the Ministry of Health, Labor, and Welfare in Japan reported that there were 370 346 deaths annually due to cancer.³³ Based on these figures, we can estimate that, in Japan, the annual total cost of UM for cancer patients who die is approximately USD 110 million (¥ 10 990 017 550). The USD 110 million due to UM in cancer patients corresponds to 0.18% of total dispensed medication expenses in 2015.³⁴

Another important finding of the present study is that unused opioids account for almost 50% of the cost of UM by category and have the greatest impact on cost. In addition, comparing the high and low cost groups revealed that the proportion of UM accounted for by opioids and oral anticancer drugs, in terms of both their number and cost, was significantly higher in the high cost group. This indicates the need for the development of effective interventions focusing on the management of unused opioids and oral anticancer drugs in advanced cancer patients. With regard to opioids, incorrect knowledge of or misunderstanding about opioids, in addition to insufficient explanation about opioid use from health care provider, may result in poor drug adherence to opioids and the insufficient use of opioids. For example, previous studies have reported that 30%–40% of advanced cancer patients believed that opioids are addictive and/or shorten life.^{35–38} In addition, several studies have reported that patients possibly do not receive sufficient instruction as to how to manage unused opioids. For example, studies in the US found that, after surgery, 67%–92% of patients stored unused opioids for acute pain treatment at home and 42%–71% of unused opioids tablets were left at home, however 92% of patients reported not to have received disposal instruction of unused opioids.^{39–41} Previous studies have reported improvements in the safe use, storage, and disposal of opioids through education programs for both advanced cancer and non-cancer patients.^{8,42} To overcome the issues surrounding UM identified in the present study, it may be effective for health care providers to check any opioids remaining at each visit, and to educate patients how to effectively deal with any UM when prescribing opioids.^{8,14} From another perspective, the extent of unused opioids may be affected by physicians' prescription patterns. For example, prescriptions of rescue opioids for patients with limited prognosis may have contributed to the increase in unused SAO.³⁰

With regard to disposal of UM, the present study found that UM were most frequently simply not disposed of (just left at home; 62%), followed by being discarded in the trash (24%). This finding is consistent with studies conducted among cancer patients in the US, where 53% of cancer patients reported storing opioids and 35% reported discarding them in the trash or flushing them down the sink or toilet, even

though no one reported flushing opioids down the sink in the present study.^{7,43} In the present study, patients in the high cost group were significantly more likely **not to dispose of** UM than those in the low cost group (91% vs. 51%, respectively; $P = .0003$). Based on the findings of the present and previous studies, we hypothesize that patients, when dealing with higher-cost UM, such as opioids, tend to “store them at home” rather than “discarding them in the trash”. To prove this hypothesis, intervention studies using behavioral economics may be useful. **In addition, the medication disposal structure and regulations vary according to country and region. The US provides disposal guidelines for unused and expired medications from three governmental agencies (i.e. the US Food and Drug Administration, Environmental Protection Agency, and the Drug Enforcement Administration).**^{44–48} **Canada issues statements for the safe disposal of prescription drugs and manages national disposal programs.**^{49,50} **Most European countries also have special drug disposal schemes in order to prevent UM from ending up in the environment.**⁵¹ **However, there are no government-issued guidelines for the safe disposal of UM in Japan, with the exception of opioids, which are managed under a controlled drugs regulation. Future studies are needed to clarify differences in UM disposal practices according to different global geographical regions and different healthcare systems and regulations.**

The present study has several limitations. First, we could only obtain informed consent from 64% of eligible patients. Thus, the patients in the present study may not be representative of all deceased cancer patients in our PCU. Patients who were admitted to the PCU were usually coming to the end of their life and/or required intensive palliative care because they were suffering from severe symptoms. As a result, approximately one-third of patients and their families were not approached to participate in this study. Second, in the present study patients were asked to bring in all the UM they had at home. However, it is possible that the patients and their families did not bring in all the medications they had at home. Thus, we may have underestimated the true number and cost of UM.²⁸ Third, the study findings may not be generalizable to all cancer patients **or all cancer patients in PCUs in Japan** because the present study was conducted at a single PCU **located in a provincial city**. Mortality statistics for cancer patients in Japan in 2015 revealed that 11.6% died at a PCU, 10% died at home, and more than 75% died at hospital.⁵² Further prospective multicenter studies are needed to clarify the status of UM in advanced cancer patients. **Fourth, it may not be appropriate to extrapolate the results of the present study to other countries because healthcare systems, overall healthcare spending, payment structures for healthcare, and access to medication differ from country to country. Finally, we did not investigate the use of specialist palliative**

care services other than the palliative care team in HPKMC prior to the last admission, which could have contributed to the amount and cost of UM.

Conclusion

Based on the findings of the present study, the estimated annual waste cost of UM for deceased cancer patients in Japan is approximately USD 110 million. Unused opioids and oral anticancer drugs may have a significant impact on the high cost of UM among cancer patients. To overcome this issue, health care provider should: (i) focus on patients prescribed opioids and oral anticancer drugs; (ii) check the number of remaining drugs at each outpatient visit; (iii) communicate with patients to reduce the barriers to the effective use of opioids; and (iv) promote patient education with regard to how to deal with UM. A larger multicenter study in different settings is essential to clarify the actual situation of UM in advanced cancer patients.

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Declaration on Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Table 1. Patient Characteristics (n = 90) and Frequency of Unused Medications by Drug Category

Mean ($\pm$ SD) age (years)	71 $\pm$ 11
Male	47 (52)
Cancer type	
Gastrointestinal	40 (44)
Lung	17 (19)
Genitourinary	7 (8)
Breast	5 (6)
Other	13 (14)
Admission from home to the PCU	52 (58)
Living alone	11 (12)
Receiving medication from family physicians	44 (49)
No. patients with UM by drug category	
Gastrointestinal drugs	86 (96)
Antacids	74 (82)
Laxatives	71 (79)
Anti-emetics	34 (38)
Non-opioid analgesics	67 (74)
NSAIDs	61 (68)
Acetaminophen	28 (31)
Opioids	55 (61)
Strong opioids	45 (50)
Short-acting opioids	41 (46)
Long-acting opioids	40 (44)
Psychotropic drugs	48 (53)
Oral anticancer drugs	9 (10)
Others	81 (90)
Cardiovascular system drugs	48 (53)
Steroids	23 (26)
Drugs for diabetes mellitus	13 (14)

Unless indicated otherwise, data are presented as n (%).
NSAIDs, non-steroidal anti-inflammatory drugs; PCU, palliative care unit; UM, unused medications.

Table 2. Number and Cost of Unused Medications by Drug Category in All Patients

Drug category	No. UM ^A (%)	Cost (USD) of UM ^B (%)
Gastrointestinal drugs	13 004 (33)	2457 (9)
Non-opioid analgesics	5500 (14)	1406 (5)
Opioids	4417 (10)	12 727 (47)
Psychotropic drugs	2819 (7)	770 (3)
Oral anticancer drugs	365 (1)	2200 (8)
Others	13 823 (35)	7524 (28)
Total	39 628 (100)	27 085 (100)
Mean total per patient	440	301

^AIncludes tablets, packs, patches, and suppositories.

^BCurrency conversion: USD 1 = ¥ 100.

UM, unused medications.

Table 3. Comparison between 2 Groups (High and Low Cost) Based on the Total Cost of Unused Medications

	High cost group	Low cost group	P-value
	(n = 22)	(n = 68)	
Mean (±SD) age (years)	68 ± 10	72 ± 12	.18
Male	13 (59)	34 (50)	.46
Cancer type			
Gastrointestinal	9 (41)	39 (57)	.18
Lung	6 (27)	11 (16)	.25
Genitourinary	2 (9)	5 (7)	1.0
Breast	0 (0)	5 (7)	.33
Other	5 (23)	8 (12)	.29
Admission from home to PCU	17 (77)	35 (51)	.03
Living alone	2 (9)	10 (15)	.72
Receiving medication from family physicians	15 (68)	29 (43)	.04
% UM by category (95% CI)			
Gastrointestinal drugs	32 (25, 40)	35 (30, 40)	.76
Non-opioid analgesics	18 (10, 25)	12 (8, 15)	.06
Opioids	16 (10, 22)	7 (4, 10)	<.0001
Psychotropic drugs	4 (1, 7)	6 (4, 9)	.50
Oral anticancer drugs	4 (–2, 10)	0.3 (0, 1)	.02
Others	26 (19, 32)	39 (33, 46)	.04
% Cost of UM by category (95% CI)			
Opioids	51 (36, 66)	21 (14, 28)	<.0001
Oral anticancer drugs	14 (0, 28)	3 (0, 6)	.02
Gastrointestinal drugs	10 (3, 16)	18 (13, 22)	.02
Non-opioid analgesics	6 (2, 9)	7 (3, 10)	.56
Psychotropic drugs	2 (0, 3)	6 (3, 10)	.64
Others	18 (8, 29)	46 (37, 54)	.001

Unless indicated otherwise, data are presented as n (%).

The high cost group consisted of patients in the top 25th percentile of total unused medications (UM) cost. In this group, the mean number and cost of UM were 719 and USD 780, respectively. The low cost group consisted of the remaining 75% of patients and the mean number and cost of UM in this group were 350 and USD 146, respectively.

CI, confidence interval; PCU, palliative care unit; UM, unused medications.

Table 4. Methods of Disposal of Unused Medications (UM) in All Patients and in Patients Stratified According to the Total Cost (High and Low Cost^A) of UM

Disposal method	All patients	High cost group	Low cost group	P-value
Not dispose	49 (62)	19 (95)	30 (51)	.0003
Discard in the trash	19 (24)	6 (30)	13 (22)	.5
Request physicians to adjust prescription	13 (17)	3 (15)	10 (17)	1.0
Give away to someone	4 (5)	3 (15)	1 (2)	.05
Flush down the sink or toilet	0 (0)	0 (0)	0 (0)	–
Other	7 (9)	3 (15)	4 (7)	.4

Data are shown as n (%).

Patients (or families or caregivers) were asked to respond to the question, “How did you deal with UM?”

Respondents could provide multiple answers and some patients did not provide any answer.

^AThe high cost group consisted of patients in the top 25th percentile of total UM cost, whereas the low cost group consisted of the remaining 75% of patients.