[Short Report]

Enhancement of Medical Condition Assessment of Cancer Patients after the Introduction of an Audit System

Kensaku AWAJI,[*1] Shouhei FUKAO,[*1] Satomi NAKASE,[*1]
Erika TAKESHITA,[*1] Kazutoshi SUGAYA,[*1] and Hisamitsu TAKASE[*1]

[*1] Department of Pharmacy, Nippon Medical School Tama Nagayama Hospital

(Accepted September 30, 2021)

Abstract: A newly introduced audit system (AS) enhanced prescription proposals to benefit ward pharmacists who may be unfamiliar with chemotherapy. This study aimed to evaluate its utility. A weekly audit using the AS monitoring sheet and its medical records was conducted in patients with cancer who received chemotherapy or were taking opioids. The AS revealed that the rate of change in prescriptions was 82.9%. It resulted in a numerical rating scale score reduction for pain (5.0→3.3, $p < 0.00$), an increase in serum sodium levels (129 mEq/L→133 mEq/L, $p < 0.00$) and improvement in constipation and diarrhea. AS ensured appropriate medical intervention.

Key words: palliative care, audit system, education

INTRODUCTION

In Japan, pharmacists are recommended to be stationed in the ward to improve the efficiency of optimal drug administration of the in-patients. A drug management protocol was introduced in the wards of Tama Nagayama Hospital, Nippon Medical School, in 2014.

Patients with cancer experience multiple symptoms, including pain,[1] for which symptomatic treatment is often required. Not all ward pharmacists are familiar with palliative care or the clinical symptoms associated with chemotherapy.

The knowledge regarding assessment of symptoms varies from person to person. A previous study assessed the utility of auditing an entire hospital for evaluating its pain management protocol and providing feedback to the medical staff.[2] However, only a few studies have described the utility of auditing to evaluate the protocols for managing of symptoms other than pain.[2–4]

In January 2017, we introduced an audit system (AS) in our hospital. In this study, we report the utility of this AS in cancer patients.

METHODS

This study was conducted between January 2017 to December 2018 and included patients with cancer who received chemotherapy or were taking opioid medications with consultation by a ward pharmacist. Out of the 211 patients included in the study, 21 were discharged before obtaining their AS response and were thus excluded from study. Among the patients who underwent the Audit, those who were re-introduced to AS after readmission were treated as separate patients.

Corresponding Author: Hisamitsu Takase, Department of Pharmacy, Nippon Medical School Tama Nagayama Hospital, 1–7–1, Nagayama, Tama-shi, Tokyo 206–8512, Japan
E-mail: h-takase@nms.ac.jp

The AS team consisted of two pharmacists who were qualified for cancer guidance and palliative drug therapy certification (years of experience: 34) and cancer drug therapy certification (years of experience: 8). The team conducted a weekly audit using an AS monitoring sheet (Fig. 1), drug management guidance records, and medical records. The detailed auditing process is depicted in the flowchart (Fig. 2).

The ward pharmacist fills in the “check items” for pain evaluation, meal information, and defecation status, while the AS team fills the “problems to be checked” and “advice on evaluation” sections.

The AS team and the ward pharmacist share information on the given problem through the AS monitoring sheet. After reviewing the process, the AS monitoring sheet is used as an educational tool to train the ward pharmacist.

This study was approved by the Ethics Committee of our hospital, and patient data was handled after being anonymized (Ethics Committee Approval Number: Nippon Medical School Tama Nagayama 536).

1. AS evaluation methods

The primary endpoint was the rate of prescription change to confirm the details of ward pharmacist intervention through AS. Based on the number of cases for which prescription changes were proposed (A) and made (B) through the AS, the rate of prescription change was calculated with the formula:

$$(B) / (A) \times 100\ (\%)$$

The prescription changes included the following: 1) indiscriminate medicines; 2) blood test values; 3) opioid dose; 4) side effects; and 5) the other five types.

The secondary endpoints were evaluated with the

Patient ID		Age years old		Control number
Patient Name		Body weight kg		
Audit	Number of continuous evaluations; times		Evaluation date	
Problems			Correspondence contents	
Check items	・Carcinoma: ・Anti-cancer drug treatment (Regimen:)			
	・Opioid (mg/day) Rescue drug ( )			
	・Pain evaluation NRS (/10) ・Number of times the rescue drug was used ___times/day			
	・Meal (Form: , Intake: %) ・Defecation status (Number: ___times/day, Properties:)			

Fig. 1 AS monitoring sheet. The ward pharmacist fills in the "check items" for pain evaluation, meal information, and defecation status, while the AS team fills the "problems to be checked" and "advice on evaluation" sections.

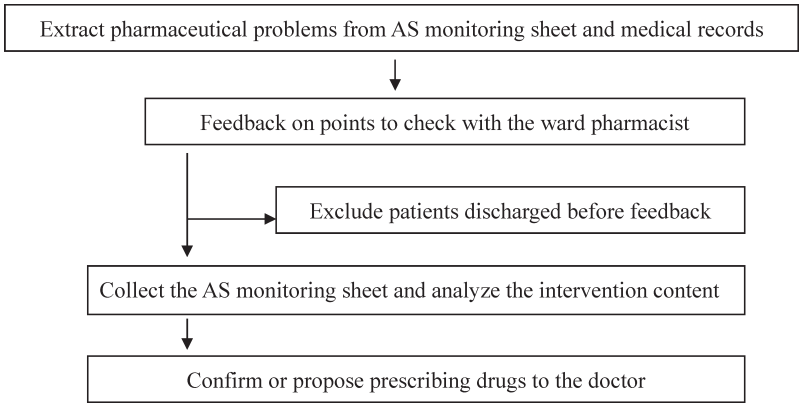

Fig. 2 Flowchart about AS. The AS team and the ward pharmacist share information on the given problem through the AS monitoring sheet. After reviewing the process, the AS monitoring sheet is used as an educational tool to train the ward pharmacist.

Table 1 BS score and as per stool examination

Type 1: Separate hard lumps, like nuts (hard to pass)
Type 2: Sausage-shaped but lumpy
Type 3: Like a sausage but with cracks on its surface
Type 4: Like a sausage or snake, smooth and soft
Type 5: Soft blobs with clear-cut edges (passed easily)
Type 6: Fluffy pieces with ragged edges, a mushy stool
Type 7: Watery, no solid pieces (entirely liquid)

BS score: stools are classified into 7 types.[5]
Diarrhea: loose stools (BS score: 6/7) at least three times a day.[6]
Constipation: stools passed less than three times a week (0.4 times per day).[7]

Table 2 Standard concentrations of electrolytes

Serum sodium: 138–145 mEq/L
Serum potassium: 3.6–4.8 mEq/L

Facility standard of Nippon Medical School Tama Nagayama.

following scales: the numerical rating scale (NRS) for pain, World Health Organization definition of diarrhea, Rome Ⅳ criteria, and Bristol stool form scale (BS score) for defecation (Table 1).[5–7]

Electrolyte concentrations were estimated using blood tests, and the standard electrolyte values of our hospital were used as references (Table 2).

For statistical analysis, JMP Pro version 13.2 (SAS Institute, Cary, NC, United States) was used, and the significance level was set a $p<0.05$ with the paired t-test.

RESULTS

Lung cancer was the most common intervention and anticancer drug treatment, followed by gastrointestinal

Table 3 AS-intervened patient age, carcinoma, opioids, and anti-cancer drugs ($n = 190$)

Age			
Mean ± S.D.		69.0 ± 9.7	
Range		37–90	
Carcinoma			
Lung		88	
Gastrointestinal		77	
Myeloid/Lymphocyte		15	
Other		10	
Opioid			
(Regulatory drugs)		(Rescue drugs)	
Oxycodone	60	Oxycodone	34
Fentanyl	29	Morphine	10
Morphine	4		
Laudanum	1		
(Injection)			
Oxycodone	10		
Fentanyl	4		
Morphine	6		
Anti-cancer drugs regimen			
(Lung)			
Taxane-containing		17	
Anti PD-1 antibody drugs		10	
EGFR tyrosine kinase inhibitor		10	
Pemetrexed-containing		7	
Etoposide-containing		6	
Irinotecan-containing		6	
Cisplatin + Vinorelbine		6	
Amrubicin		2	
Other		3	
(Gastrointestinal)			
Fluorinated pyrimidine antimetabolite-containing		23	
Gemcitabine-containing		14	
(Myeloid/Lymphocyte)			
Rituximab-containing		8	
Bortezomib		2	
Other		4	
(Other)			
Trastuzumab-containing		2	
Other		4	

PD-1: Programmed Cell Death Receptor.
EGFR: Epidermal Growth Factor Receptor.
SD: Standard deviation.

cancer. Oxycodone administration was the most frequent opioid administered (Table 3).

The AS revealed that the rate of change in the proposed prescription was 34/41 (82.9%). Most changes were for the 6 patients who had discontinued prochlorperazine therapy for 2 weeks or more, and the patients undergoing electrolyte correction for hyponatremia (Table 4). In some patients, symptoms worsened after the prescription was changed.

Audit intervention significantly reduced pain and diarrhea defecation frequency and increased constipation defecation frequency. Mean serum sodium levels in patients with hyponatremia also approached acceptable levels (Table 5).

DISCUSSION

Epidemiological data indicated that patients undergoing chemotherapy for lung cancer have been increasing in recent years in Japan[10] with oxycodone being the most commonly used opioid for pain relief.[11] Our findings show a similar trend.

We note that the ward pharmacist was unable to anticipate problems in case of frequent prescription changes. The high number of prescription changes by AS is a spillover to education that involves discussing the process of anticipating problems and methods to address. The prescription proposal through AS was not proposed by the ward pharmacist alone. Even if it is not actually adopted, the proposal can instill a follow-up awareness in the ward pharmacist about the item. This is also considered to be an index that spreads to clinical education. It may not have a direct effect on the patient, but it is important to consider the prescription proposal rate. Audit has also been introduced at Kameda General Hospital in Japan, and there is a report[12] that it helped alleviate symptoms in patients who have difficulty in

Table 4 Clinical trends before and after prescription changes and intervention

1) Indiscriminate medicines

Before	Prescription proposal details	Prescription change Yes/No	After	AS follow count#	Number
Prochlorperazine, 2 weeks or longer administration to prevent nausea	Discontinuation	Yes	Avoiding akathisia without nausea	1	6
Antiflatulent, continuous administration for no abnormal defecation	Discontinuation	Yes	No change	1	2
Acetaminophen-ineffective pain (NRS: 8/10)	Acetaminophen discontinuation	Yes	Avoiding liver damage without a change in pain	1	2
Continuous administration during chemotherapy discontinuation i) Hangeshashinto for oral mucositis ii) Olanzapine for nausea	Discontinuation	i) Yes ii) Yes	i) No recurrence of oral mucositis ii) Avoiding elevated blood sugar without nausea	i) 1 ii) 1	i) 1 ii) 1
Fungizone-gargling, 2 weeks or longer use after oral candidiasis improvement	Discontinuation	Yes	No recurrence of oral candidiasis	1	1
Mecobalamin, 16 weeks administration for peripheral neuropathy	Discontinuation	Yes	Peripheral neuropathy unchanged	1	1

2) Blood test values

Before	Prescription proposal details	Prescription change Yes/No	After	AS follow count#	Number
Decreased serum sodium level i) Less than 125 mEq/L ii) 125–130 mEq/L	Sodium correction	i) Yes ii) No	i) Increased to 128–132 mEq/L ii) Maintained 125 mEq/L or higher without sodium correction for treatment of heart failure, cancerous edema, and hypothyroidism	i) 1 ii) 1	i) 3 ii) 3
PT-INR extension (3.0) for elderly patients (70s)	Warfarin potassium dose reduction (3.5 mg/day → 3.0 mg/day)	Yes	Decrease in PT-INR (2.0)	1	1
Flurbiprofen administration to patient with renal impairment (Creatinine Clearance less than 30 mL/min)	Change to acetaminophen	Yes	Recovery to Creatinine Clearance 43 mL/min, no worsening of pain (Face Scale: 3/5)	1	1

3) Opioid dose

Before	Prescription proposal details	Prescription change Yes/No	After	AS follow count#	Number
Fentanyl-ineffective pain (NRS: 8/10)	Gradually increased dose (0.1 mg/day → 0.3 mg/day)	Yes	Mild relief (NRS: 7/10)	1	1
Fentanyl for 4 weeks for postoperative analgesia	Used was discovered for itching, gradually reduced dose and discontinuation	Yes	No pain	4	1
Ineffective pain with rescue morphine (NRS: 7/10)	Increased rescue dose (5 mg → 10 mg)	Yes	Pain relief (NRS: 4/10)	1	1

Table 4 (Continued)

4) Side effects

Before	Prescription proposal details	Prescription change Yes/No	After	AS follow count#	Number
Refractory oral mucositis	Irsogladine[8] ‡ or loperamide gargling[9] ‡ addition	Yes	Oral mucositis and pain improvement	2	2
Delirium	Amitriptyline or prednisolone discontinuation	Yes	Delirium improvement	1	2
Muscle pain (Face Scale: 4/5)	Celecoxib addition	Yes	Muscle pain improvement (Face Scale: 3/5)	1	1
Oral candidiasis	Itraconazole addition	Yes	Oral candidiasis improvement	1	1
Constipation	Butylscopolamine discontinuation	Yes	Ileus Onset	1	1
Thirst	Oxycodone dose reduction (30 mg/day → 20 mg/day)	Yes	Improvement of thirst also worsened pain (NRS: 2/10 → 7/10)	1	1
Akathisia	Metoclopramide and prochlorperazine discontinuation	Yes	Akathisia improved and nausea disappeared	1	1
Nausea	Lubiprostone discontinuation	Yes	Nausea improved	1	1

‡ Informed consent was provided by the patient for off-label use of drugs, and the prescribing doctor stated the same in the medical record.

5) Other

Before	Prescription proposal details	Prescription change Yes/No	After	AS follow count#	Number
Fatigue	Dexamethasone addition	No	Not added to prevent infection, no change	1	2
Nausea caused by decreased gastrointestinal motility	Metoclopramide addition	Yes	Fasted without improving nausea	1	1
Radiation site pain	Mefenamic acid addition	No	Radiation therapy finished and pain improved	1	1
Starting central venous nutrition	Starting intravenous nutrition in advance	No	No refeeding syndrome	1	1
Fever and procalcitonin positive	Antibiotics addition	Yes	Fever improvement and procalcitonin negative	2	1

PT-INR: Prothrombin time-international normalized ratio.

One week after proposing the prescription, the AS team followed up again. The number of follow ups is indicated as "AS follow count."

dealing with pain and side effects and who are undergoing unintervention palliative care. This report shows similar results.

Prochlorperazine has been reported to cause late-onset akathisia after continuous administration for 6 months.[13] It should be maintained for 2 weeks from commencement until resistance to the opioid develops.[14]

Asymptomatic chronic hyponatremia is observed at sodium levels below 125 mEq/L.[15] Treatment with drugs correcting hyperglycemia/hypertriglyceridemia and water restriction[16] is expected to result in improvement. It is necessary to monitor sodium supplementation through a prescription for hyponatremia and, at the same time, watch for symptoms of hyponatremia to prevent changes in plasma osmolality. It is essential to identify whether the hyponatremia is hypertonic, isotonic, or hypotonic. Sodium should be supplemented judiciously after considering plasma osmolality and fluid volume. Regular feedback of the evaluated parameters to ward pharmacists contributes to their education.

In some patients, symptoms deteriorated after a prescription change which was attributed to the fact that

Table 5 Transition of secondary endpoints by AS intervention

Major	sub	Before	After	*n*	*p*-value
Pain	NRS	5.0 ± 2.8	3.3 ± 2.5	58	< 0.00
Constipation	Defecation frequency[§]	0.1 ± 0.1	0.7 ± 0.7	15	< 0.00
Diarrhea	Defecation frequency[§]	6.4 ± 2.7	3.9 ± 2.0	7	0.03
	BS score	6.7 ± 0.5	6.1 ± 0.5	7	0.05
Electrolytes	Hyponatremia	129 ± 6.1	133 ± 4.6	18	< 0.00
	Hypokalemia	2.9 ± 0.1	3.6 ± 0.5	3	0.10
	Hyperkalemia	5.0 ± 0.6	5.3 ± 0.2	4	0.10

Mean ± S.D.
Evaluate the progress 1 week after AS intervention.
[§]Calculate the number of defecations per day in 1 week.

the ward pharmacist reduced medication to a level under the required dose and re-evaluation was not performed immediately. The AS was conducted weekly, and detailed intervention was not possible without the approach of the ward pharmacist. The limitation of the AS used is that it revealed limited patient information.

The introduction of AS enhanced the medical assessment of cancer patients. It also ensured timely intervention and appropriate initiation of medicinal treatment through prescription proposals provided by ward pharmacists. This suggests that AS is useful for evaluation of pharmacists' work.

Conflict of interest: The authors declare no conflict of interest.

REFERENCES

1) World Health Organization. Cancer, WHO definition of palliative care. https://www.who.int/cancer/palliative/definition/en/, cited 3 January, 2017.
2) Goldberg GR and Morrison RS. Pain management in hospitalized cancer patients: A systematic review. J. Clin. Oncol. 2007; 25: 1792–1801.
3) Bookbinder M, Coyle N, Kiss M, et al. Implementing national standards for cancer pain management: Program model and evaluation. J. Pain Symptom Manage. 1996; 12: 334–347.
4) Morrison RS, Meier DE, Fischberg D, et al. Improving the management of pain in hospitalized adults. Arch. Intern. Med. 2006; 166: 1033–1039.
5) Mearin F, Lary BE, Chang L, et al. Bowel disorders. Gastroenterology 2016; 150: 1393–1407.
6) World Health Organization. Diarrhoea. https://www.who.int/topics/diarrhoea/en/, cited 3 January, 2017.
7) Simren M, Palsson OS, and Whiteheal WE. Update on Rome Ⅳ criteria for colorectal disorders: Implications for clinical practice. Curr. Gastroenterol. Rep. 2017; 19: 15.
8) Takase H, Futagami K, Sueta T, et al. Irsogladine maleate reduces radiotherapy or chemoradiotherapy oral mucositis in patients with head and neck cancer. Jpn. J. Pharm. Palliat. Care Sci. 2014; 7: 71–76.
9) Taguchi N, Shutoh M, and Shimoyama N. Potential utility of peripherally applied loperamide in oral chronic graft-versus-host disease related pain. Jpn. J. Clin. 2008; 38: 857–860.
10) Yamaguchi T and Nishiura H. Predicting the epidemiological dynamics of lung cancer in Japan. J. Clin. Med. 2019; 8: 326.
11) Foundation for Promotion of Cancer Research. CANCER STATISTICS IN JAPAN—2017. Narcotics for Medical Use. Trends in usage of morphine, fentanyl, and oxycodone in Japan [Ministry of Health, Labour and Welfare (2016)] https://ganjoho.jp/data/reg_stat/statistics/brochure/2017/cancer_statistics_2017_date_J.pdf, cited 2 December, 2018.
12) Kawana M, Hashizawa K, Nagai J, et al. Hospital-wide "opioid surveillance" audit led by palliative care team pharmacists to monitor pain management with opioids. Palliat. Care Res. 2015; 10: 149–154.
13) Takahashi M, Hosoda M, and Koyama T. Akathisia causing secondary severe depression in a cancer patient. Prim. care companion. J. Clin. Psychiatry 2010; 12: PCC.09l00935.
14) Tsukuura H, Ando Y, Gyawali B, et al. Opioid-induced nausea and vomiting: A questionnaire survey among Japanese physicians. J. Palliat. Med. 2015; 18: 977–980.
15) Sahay M and Sahay R. Hyponatremia: A practical approach. Indian J. Endocrinol. Metab. 2014; 18: 760–761.
16) Rondon H and Badireddy M. Hyponatremia. 2020. StatPearls, Treasure Island.