Effects of a nurse-led medication self-management programme in cancer patients: a mixed-method randomised controlled trial

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Abstract

Background : Despite patient convenience and better tolerability, treatment challenges have become evident compared with conventional chemotherapy. This study evaluated the effects of a patient-centred medication self-management support programme in patients with metastatic breast cancer undergoing oral anticancer treatment. We also evaluated the programme's effectiveness based on the perceptions of intervention nurses. **Methods:** This trial was a two-phased mixed-method approach, with a prospective randomised, parallel-group, two-arm, open-label, four-centre study, followed by a qualitative study using a focus-group interview. Eligible participants were 155 patients with metastatic breast cancer who had been newly prescribed an oral chemotherapy or a targeted therapy agent. The intervention group received the patient-centred medication self-management support programme conducted by trained nurses. Primary outcome was adherence to medication at three months after the commencement of oral chemotherapy or target therapy, calculated as Medication Possession Ratio (MPR). Patients were defined as being adherent if MPR was equal to or greater than 90%. Secondary outcomes included the Japanese version of the General Self-Efficacy (GSE) Scale, Functional Assessment of Cancer Therapy-Breast (FACT-B), Kessler 6 (K6), M.D. Anderson Symptom Inventory (symptom severity and symptom interference), and patient satisfaction score. **Results:** Primary outcome ($MPR \geq 0.9$ at three months) was not significantly different in the intervention group (59/64 patients: 92%) and control group (54/59 patients: 92%). There was no significant difference in secondary outcomes except for GSE ($p = 0.026$). In the qualitative study, comments about the intervention programme of 20 participating nurses were positive. They also felt a patient's enhanced self-efficacy by reassurance or endorsement. **Conclusions:** The patient-centred medication self-management support programme in patients with metastatic breast cancer undergoing oral anticancer treatment did not improve medication adherence because the adherence rate was high in both groups. Nevertheless, this study offers suggestions to design future studies for optimal adherence to oral medication therapy, including focusing on patients with high risk of non-adherence and the effect of involvement of other healthcare providers.

Background

Although oral anticancer agents improve patient convenience and tolerability, numerous treatment challenges have become evident compared with conventional chemotherapy [1, 2]. The complexity of regimens, including dosage, frequency, intermittent schedules, toxicity-based dose modifications, and individual tolerance, is a common challenge [3]. In addition, unknown benefit of delayed disease progression may affect medication-taking behaviours [4].

Oral medication therapy requires self-management. Barriers to self-management includes symptom distress, a lack of knowledge about cancer trajectory, and feelings of abandonment and isolation [5, 6]. As patients with metastatic breast cancer often face a lack of control and concern over side effects, poor self-efficacy in medication management, and decision making are pointed out, healthcare providers should focus on building patient-centred and sustainable relationships to ensure adequate adherence [7].

The present study focused on adherence to oral chemotherapy and targeted therapy in patients with metastatic breast cancer. A patient-centred medication self-management support programme was developed based on patient preferences and problem solving through follow-up counselling by nurses under the concept of concordance and shared decision making [8]. We conducted a randomised controlled trial to determine the effects of a patient-centred medication self-management support programme. Participants were patients with metastatic breast cancer undergoing oral anticancer treatment. We also evaluated the programme's effectiveness based on the perceptions of intervention nurses.

Methods

Study Design

This trial was a two-phase mixed-method approach, with a prospective randomised, parallel-group, two-arm, open-label, four-centre study. This study also employed a qualitative approach using focus group interview. Details of the study design and protocol have been published previously [8].

This study was approved by the internal review board of the Faculty of Nursing and Medical Care, Keio University (No. 218), three cancer centres, and one university hospital. We received a verbal and written informed consent from all participants.

Phase I: An intervention study

Participants and Recruitment

Eligible participants were patients with metastatic breast cancer who had been newly prescribed an oral chemotherapy or a targeted therapy agent. They were identified from outpatient lists by primary physicians and recruited by nurse investigators before the commencement of oral chemotherapy at the outpatient clinics of three cancer centres and one university hospital in Japan. Originally, three cancer centres were planned in the protocol. However, we added a university hospital to meet the recruitment goal. After the research objectives and outline were given, consented participants were enrolled from April 2015 to March 2018, and followed up until July 2018. They completed surveys at baseline and at two- and three-month after the commencement of oral chemotherapy or target therapy.

Randomisation and Group Allocation

Participants were randomised to either the medication self-management programme group (intervention group) or conventional care group (control group) at a 1:1 ratio. Randomisation was carried out using a computerised random number generator at the Joint Center for Researchers, Associates, and Clinicians

(JCRAC) Data Center, an independent, non-profit organisation with extensive experience in conducting clinical trials. Randomisation was stratified according to age (<40 vs. ≥ 40), treatment regimen (Capecitabine vs. Capecitabine and Lapatinib vs. Tegafur/gimeracil/oteracil [TS-1]), and facility. Because of the open-label study, patients, nurses, and investigators were not blinded.

The intervention group received two sessions of the patient-centred medication self-management support programme conducted by trained nurses at one and two months after the commencement of oral chemotherapy or target therapy. The patient-centred medication self-management support programme aims at improving adherence to medication and self-management [8], consisting of information giving using teach-back, patient preference, and follow-up by a nurse under the concept of concordance and shared decision making [9–12]. The control-group participants received conventional care, including explanation and instructions on oral chemotherapy, and information on treatment-related toxicity.

Measurement

The primary outcome of this study was adherence to medication at three months after the commencement of oral chemotherapy or target therapy. Patients were defined as being adherent if their medication possession ratio (MPR) was equal to or greater than 90% [13]. Secondary outcomes were assessed by four measures: the Japanese version of the 10-item General Self-Efficacy (GSE) Scale measured on a 4-point scale [14], the Japanese version of the 36-item Functional Assessment of Cancer Therapy-Breast (FACT-B) measured on a 5-point scale to assess quality of life [15–17], the Japanese version of the 6-item Kessler 6 (K6) measured on a 5-point scale to assess psychological distress [18, 19], and the Japanese version of the 13-item M.D. Anderson Symptom Inventory measured on a numerical rating scale to assess perceived symptom severity and interference [20–22]. In addition, a self-designed patient satisfaction with the programme was measured on a 5-point scale by two questions developed for this study: 1) Are you satisfied with the medication self-management support programme? and 2) Do you want to continue to receive support from healthcare professionals?

Demographic characteristics and baseline measures were assessed at one month after the commencement of oral chemotherapy or target therapy. Health service visit, including emergency department visits, and admissions were collected from medical records. Only treatment change (discontinuation/dose reduction/oral chemotherapy free interval) was described in a case report form.

Data Collection and Management

Research nurses at individual facilities collected raw data from all participants and stored them in a locked shelf at the outpatient clinic or nursing department. Input and data cleaning were carried out by two trained data managers at the JCRAC Data Center. Central Monitoring was conducted, and a monitoring report was issued every three months by the JCRAC Data Center.

Phase 2: A qualitative study

After the completion of Phase 1 intervention study, we conducted a qualitative study in intervention nurses at the participating facilities to explore the role and challenges of nurses in the patient-centred medication self-management support programme. Nurse investigators recruited more than four intervention nurses from each facility. Written consent was obtained from all participating nurses before the start of each focus group. All focus group discussions were tape recorded. Thematic analysis was used.

Statistical Analysis

An intention-to-treat approach was used for the primary analysis that compared the two groups. Mantel-Haenzel test with adjustments made for allocation factors was used to compare the difference in the primary outcome, the proportion of patients who maintained $\geq 90\%$ MPR in each group at three months. For the secondary outcomes, summary statistics were calculated at each measurement time point in each group and compared between groups using generalised linear models with robust estimates. The significance level was set at 0.05.

The sample size and power calculation were based on the primary outcome. The study protocol assumed an evaluable sample of least 200 patients (100 per group) to provide 80% power (effect size at an alpha level of 0.05 [13, 23]. However, we were not able to achieve the target enrolment because of unanticipated delays, despite the addition of one participating institution. The final sample size consisted of an evaluable sample of 155 patients (78 and 77 in the intervention and control group, respectively).

Results

Participants

Figure 1 shows the study enrolment, randomisation, follow-up, and reasons of withdrawal. A total of 155 participants with metastatic breast cancer were randomised (78 and 77 to the intervention and control group, respectively).

Baseline Characteristics

The baseline characteristics of the study participants are presented in Table 1. Mean age was around 58 years in both intervention and control groups. About 70% were married/partnered, and nearly 90% lived with their families. About a quarter of the participants were employed. Around 80% of the participants graduated from high school or less in both groups. Capecitabine was the most common regimen in both

intervention (68.0%) and control (68.4%) groups, followed by TS-1 (27.0% vs 28.0%), and Capecitabine and Lapatinib (5.1% vs 4.0%).

Medication Adherence

At baseline, median (range) medication adherence measured by the MPR was 102% (78%–108%) in the intervention group and 102% (59%–115%) in the control group. Median (range) medication adherence at three months was 100% in both intervention (82%–150%) and control (47%–111%) groups. Primary outcome was the percentage of patients achieving adherence at three months after the commencement of oral chemotherapy or target therapy, defined as equal to or greater than 90%. After three months, medication adherence (MPR ≥ 0.9) was recorded in 59/64 patients (92%) in the intervention group and 54/59 patients (92%) in the control group. There was no significant difference in both groups (Table 2).

The results of analyses of secondary outcomes are shown in Table 3. GSE was significantly different in the two groups ($p = 0.026$). There was no significant difference in the changes in the FACT-B, K6, M.D. Anderson Symptom Severity, M.D. Anderson Symptom Interference, and patient satisfaction score between the two groups ($p = 0.566, 0.473, 0.94, 0.128$ and $p = 0.226$, respectively).

In Phase 2, 20 intervention nurses participated in the focus group interviews. At the individual facilities, a facilitator (HK or KY) conducted an interview (40–57 min.) in 4–7 nurses using a semi-structured interview guide. The mean age of the intervention nurses was 47.7 (range 34–60) years, and the mean duration of oncology nursing experience was 22.4 years.

Comments of participating nurses about the intervention programme were positive. They reported that the intervention programme helped them to review patient's daily medication behaviours, and they felt his/her enhanced self-efficacy by reassurance or endorsement. They realised that the intervention programme is feasible for not only oncology nurse specialists but also general nurses because information on when and what they should do is clear. The shortage of outpatient nurses and time are a challenge to use this programme in clinical settings. Multiple nurses reported that they were rewarded and more interested in nursing by consultation with and proposal to a patient within the limited time of outpatient care in the intervention programme and receiving feedback from patients.

Discussion

In this prospective randomised, parallel-group, two-group, open-label study, there was no significant difference in medication adherence between the intervention and control groups at three months.

There are several potential explanations for our negative results. First, participants of this study might influence the high adherence rate above 90% in both intervention and control groups. The previous study reported that adherence was very high among patients with metastatic cancer, particularly breast cancer, because the women were concerned about the evolution of the disease; adherence was 88.3% for

metastatic colon cancer, 90.4% for non-metastatic colon cancer, 94.3% for rectal cancer, and 96.2% for metastatic breast cancer [24]. Future studies should target patients who are at risk of non-adherence to treatment.

Second, the same nurses were involved in data collection and adherence check in both intervention and control groups. Consequently, an awareness of being observed (Hawthorne effect) [25] might be generated and of adherence might be increased in not only the intervention group but also the control group. As the four participating facilities were designated cancer hospitals and nurses were well trained, including communication with cancer patients, specific care for cancer patients by nurses might affect the results.

Third, as patients with recurrence and advanced cancer were targeted, some patients reduced the dose or discontinued medications according to the change of the condition in both groups. These patients had opportunities for explanation and support about the dose reduction or discontinuation from the physician and nurse at outpatient visit other than the intervention that might enhance adherence regardless of the intervention.

Regarding secondary outcomes, only GSE was significantly different in the two groups. However, this main effect is qualified by possible interaction effects, requiring a further study. Positive comments were obtained from the qualitative study among the intervention nurses. Multiple nurses felt the effects of the programme, particularly on self-efficacy. As among the nurses said that enhanced self-efficacy leads to adherence to treatment, self-efficacy is an important factor of medication adherence [26]. The use of this programme may help outpatient nurses to enhance patients' self-efficacy and has a potential to contribute to better self-management and medication adherence.

Limitations

This study has several limitations. First, we extended the recruitment period but failed to reach our target number of participants that might affect the null results of the study. Recruiting patients who met the inclusion criteria was difficult because of rapid progression of the disease and metastasis. Second, we did not rule out whether the patient received support healthcare providers other than the intervention nurses. We cannot deny that healthcare providers, including pharmacists, outpatient nurses who did not receive the training for self-management support programme, and physicians other than the attending physician, were individually involved in their patients' self-management as usual care.

Conclusions

The patient-centred medication self-management support programme in patients with metastatic breast cancer undergoing oral anticancer treatment did not improve medication adherence because the adherence rate was high in both intervention and control groups. Nevertheless, this study offers suggestions to design future studies for optimal adherence to oral medication therapy in patients with

metastatic breast cancer, including focusing on patients with high risk of non-adherence and the effect of involvement of other healthcare providers.

Abbreviations

FACT-B: Functional Assessment of Cancer Therapy-Breast cancer

GSE: General Self-Efficacy

JCRAC: Joint Centre for Researchers, Associates and Clinicians

K6: Kessler 6

MPR: medication possession ratio

Declarations

Competing interests

The authors declare that they have no competing interest.

Authors' contributions

HK and KY contributed to the design and conception of the study as well as drafting of this manuscript. TY conducted the statistical analysis. AM, HK, NM, and OH were involved in the data acquisition and quality control of data. KT were involved in the data acquisition. All authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are including in this published article. The data analyzed during the study are available from corresponding author on reasonable request in a deidentified form.

Ethics approval and consent to participate

This study was approved by the internal review board of the Faculty of Nursing and Medical Care, Keio University (No. 218), three cancer centres, and one university hospital. We received a verbal and written informed consent from all participants.

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Tables

Table 1. Patient Characteristics at Baseline

Characteristic	Intervention (n = 78)	Control (n = 76)
Age (y), mean (SD)	57.0 (12.2)	59.4 (11.6)
Married/with a partner, n (%)	57 (73.1%)	54 (71.1%)
Lived with family, n (%)	69 (88.5%)	66 (86.8%)
Employed, n (%)		
Full-time, Part-time	22 (28.2%)	19 (25.0%)
Educational attainment, n (%)		
High school or below	61 (78.2%)	61 (82.4%)
College or above	17 (21.8%)	13 (17.6%)
Regimen, n (%)		
Capecitabine	53 (68.0%)	52 (68.4%)
Capecitabine and Lapatinib	4 (5.1%)	3 (4.0%)
Tegafur/gimeracil/oteracil (TS-1)	21 (27.0%)	21 (28.0%)

NOTE: Numbers may not always round up to 155 because of missing data.

Table 2. Primary outcome

	Intervention	Control	Proportion (95%CI) and p-value	
Variable	(n=64)	(n= 59)		
MPR $\geq$ 90% at 3 months*	59/64 (92%)	54/59 (92%)	0.8 (-10.0, 12.0)	p=0.869
*MPR: medication possession ratio				

MPR $\geq$ 90% at 3 months after the commencement of oral chemotherapy or target therapy

Table 3. Secondary outcomes

	Baseline		2M		3M		Treatment- by-Time Interaction
	Intervention	Control	Intervention	Control	Intervention	Control	
	(n= 78)	(n= 75)	(n= 75)	(n= 69)	(n= 64)	(n= 62)	p-value
Variable	mean (SE)	mean (SE)	mean (SE)	mean (SE)	mean (SE)	mean (SE)	
General self-efficacy	26.7 (0.6)	25.7 (0.8)	26.4 (0.7)	26.5 (0.7)	27.4 (0.6)	25.6 (0.7)	0.026
Functional assessment of cancer therapy-breast cancer (Total)	90.3 (2.4)	92.6 (2.1)	91.0 (2.4)	92.2 (2.5)	93.9 (2.4)	93.7 (2.2)	0.566
Kessler 6	5.0 (0.5)	5.3 (0.5)	5.1 (0.5)	5.0 (0.6)	5.3 (0.6)	4.8 (0.5)	0.473
M.D. Anderson Symptom Severity	2.2 (0.2)	2.2 (0.2)	2.4 (0.2)	2.4 (0.2)	2.3 (0.2)	2.3 (0.2)	0.94
M.D. Anderson Symptom Interference	2.8 (0.3)	2.5 (0.3)	3.1 (0.3)	2.9 (0.3)	2.4 (0.2)	2.7 (0.3)	0.128
Patient satisfaction	4.0 (0.1)	4.1 (0.1)	4.2 (0.1)	4.0 (0.1)	4.2 (0.1)	4.1 (0.5)	0.226

Figures

Figure 1. The flow of patients throughout the study following the CONSORT 2010 flow diagram

Figure 1

The flow of patients throughout the study following the CONSORT 2010 flow diagram