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Effect of progressive muscle relaxation on symptom clusters in breast cancer patients receiving chemotherapy: A quasi-experimental controlled trial

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1. Introduction

Breast cancer (BC) remains a major disease worldwide. Globally, there are approximately 1.7 million new BC cases per year, [1]. In Thailand, BC is the most common type of cancer in women and the number of breast cancer patients continues to increase annually. In 2006, the prevalence of BC in Thailand was 26.4 per 100,000 and it increased to 32.8 per 100,000 in 2014 [2].

Recently, there has been a significant improvement in the life expectancy of women with BC because of early detection and improved treatment methods. Chemotherapy is commonly used to treat all stages of the disease [3]. However, most antineoplastic agents result in varying degrees of toxicity and a range of adverse effects in patients such as insomnia, fatigue, loss of appetite, pain, nausea, and vomiting. In some cases, anxiety and depression, and reduced psychological well-being may also affect patients' quality of life [4,5].

Patients with cancer often experience multiple symptoms—which may occur in groups or clusters—from the disease itself *and* from treatment throughout the duration of the illness [6]. Symptom clusters (SCs) often occur as a group of two or more symptoms concurrently, but they can also occur independently. SCs may or may not have a common etiology or underlying mechanism [7,8]. Symptoms in the same cluster tend to amplify one another. When one symptom becomes particularly severe, other symptoms in the cluster are also exacerbated [7,9]. For example, in the symptom cluster of "pain, fatigue, and nausea", the pain could be perceived as being considerably worse in the presence of fatigue *or* nausea; in the presence of both symptoms, the pain could be even more severe [10]. Consequently, cancer patients often suffer symptom clusters that are caused by all types of discomfort from both the disease and the treatment side effects. This can affect physical, mental, emotional, social, and spiritual functions. These in turn result in a reduced quality of life for the patient [11]. Thus, studying symptom clusters may lead to a better understanding of patients' needs, which may contribute to improved care and disease management.

Currently, non-pharmacological interventions are being introduced to address the symptoms experienced by cancer patients and to reduce complications caused by treatment side effects [12]. Progressive muscle relaxation (PMR) is one promising example of a non-pharmacological intervention that is being used in cancer patients, especially those with breast cancer [5,13–15]. This method is based on the mind-body strategies and the control of muscles via the mind to relax the body [16–18]. By achieving muscle relaxation, the sympathetic nerve activities and neuroendocrine function are diminished; causing a reduction in cortisol level [19] and pro-inflammatory cytokines such as tumor necrosis factor (TNF)-alpha and interleukin (IL)-6 which can decrease physical and psychological stress [20]. PMR is relatively simple and convenient, and can be performed at any time by the patient with few complications. It requires no special equipment and can be done in as little as 15 min to achieve the desired effects [13].

Review of the literature in this field showed that PMR can significantly reduce anxiety levels [21,22] and other side effects of chemotherapy such as loss of appetite, fatigue, nausea, mucositis, cough, and back pain [5,14,23–25]. A study by Yilmaz and Arslan confirmed that PMR increased the level of comfort in BC patients who were receiving chemotherapy [15]. However, such studies primarily tested the effectiveness of PMR solely on one symptom, therefore the effect on symptom clusters remains unknown.

Previous studies have focused on examining single symptoms rather than symptom clusters because assessing SCs is more complicated [26]. At present, limited knowledge is available on the characterization of symptom clusters, especially among patients with breast cancer undergoing chemotherapy in Thailand. To our knowledge, there are no published studies investigating the effectiveness of PMR for symptom clusters specific to patients with breast cancer receiving chemotherapy. A better understanding of symptom clusters would be beneficial for all health care providers. It would be advantageous to consider clustering

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symptoms when recommending plans for symptom management, and the positive effect of PMR on those symptom clusters might be a useful nursing intervention that could diminish suffering in patients with breast cancer receiving chemotherapy.

The primary aim of this study was to identify symptom clusters in Thai patients with breast cancer who were undergoing chemotherapy. The secondary aim was to examine the effect of PMR on symptom clusters among breast cancer patients undergoing chemotherapy.

2. Materials and methods

2.1. Research design and participants

A quasi-experimental trial was designed with pre- and post-test control. Participants were breast cancer patients who first underwent chemotherapy at a university hospital—which provides specialist oncology care to people throughout northern Thailand—between March 2016 and March 2017. After finishing chemotherapy, patients who met the following criteria were invited to participate in this study: 1) older than 20 years; 2) able to speak and understand Thai language; 3) willing to participate in the study; and 4) received permission from their doctors to participate. Exclusion criteria were: 1) muscular or skeletal problems such as Parkinson's disease or osteoporosis, which may affect PMR training; 2) received previous PMR training; 3) received muscle relaxant or anti-anxiety drugs within 4 h of the study. The study was approved by the Institutional Review Board of the Faculty of Nursing, Chiang Mai University (IRB No. 2559–03853). Informed consent was obtained from all participants.

The sample size was calculated based on two-sided $\alpha = 0.05$, power analysis = 0.80 [27], and effect size based on previous PMR study = 0.60 [5]. The sample size was 44 persons for each group (88 participants total). With an anticipated 8.57% non-compliance/adherence [5], and to ensure adequacy of final sample size, 48 patients were selected per group.

2.2. Instruments

A short questionnaire was administered to patients to collect demographic information including age, marital status, religion, education, income, as well as prior chemotherapeutic agents used during cancer treatment. Symptoms and severity experienced by patients were evaluated using the Edmonton Symptom Assessment Scale (ESAS). Symptom severity was evaluated by scores on an 11-point scale, with 0 referring to “not present” and 10 referring to “as bad as you can imagine”. The Thai version of the ESAS was validated in a sample of 37 cancer patients and it achieved good levels of face validity; the Cronbach's alpha was 0.89 [28]. A treatment logbook designed by the researcher was provided to participants, who were asked to record each time a symptom occurred. The experimental group recorded the time of day in which PMR was used and made immediate recordings of symptom(s) severity using the ESAS immediately before and after treatment. A PMR manual was created and included an explanation on PMR, its health benefits, guidance on how to self-prepare for PMR, and the sequence of the PMR technique. PMR instructions were evaluated by five experienced physical therapists, who along with ten patients provided feedbacks on whether the instructions were easy to listen and

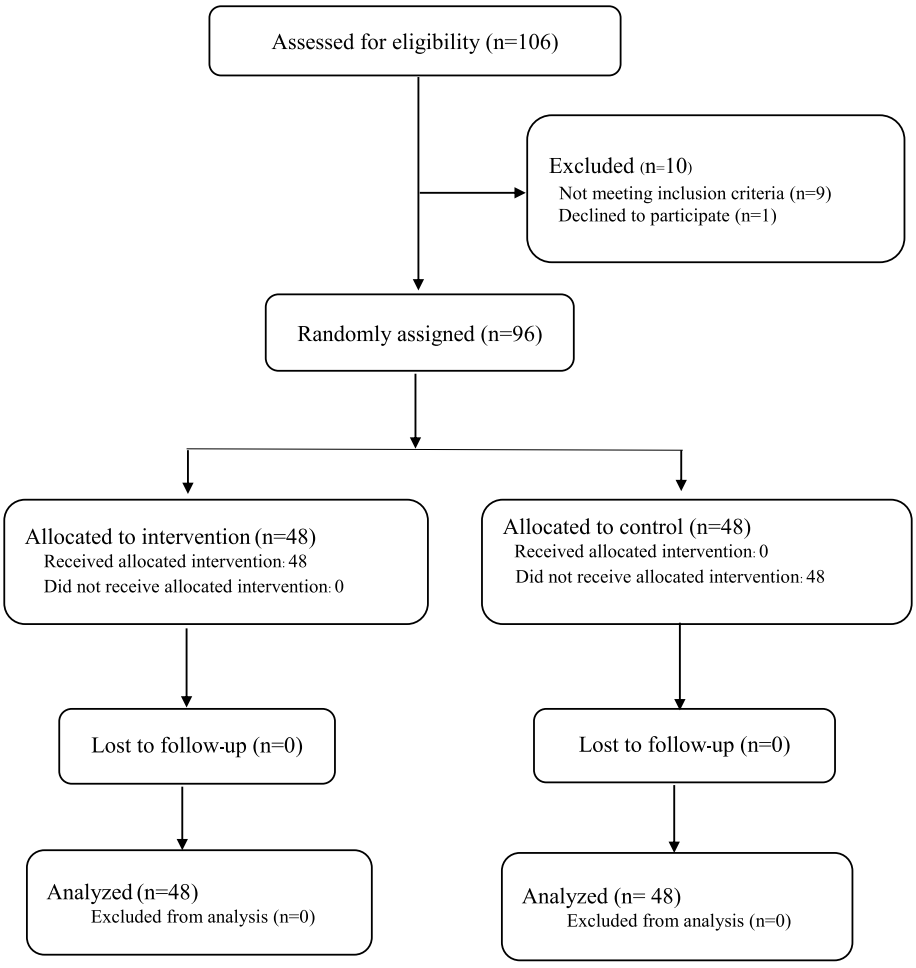

Fig. 1. Flow diagram of this study.

follow. The final PMR instructions were voiced on a CD. A CD player and earphones were provided to participants in the experimental group.

2.3. Data collection

Participants were randomly assigned to the experimental group or the control group using block sizes of four (See Fig. 1).

2.3.1. The experimental group

Participants in the experimental group first received PMR training at the hospital where the entire PMR process was demonstrated and explained from a CD developed by the researchers. The entire duration of the instruction was approximately 25 min. Participants were instructed to perform the PMR technique, which involves tensing and relaxing their eleven muscle groups (the forearms and upper arms, lower legs and front thighs, lower legs and rear thighs, buttocks, lower back, upper back, shoulders, neck and throat, forehead, cheeks and nose, periorbital area and lower jaws). Participants were asked to focus on any present feelings associated with contracting the muscle groups and to maintain tension for 20 s followed by relaxing the muscles for 40 s. This cycle of tensing and relaxing is performed twice for each muscle group. Patients were instructed to perform PMR at bedtime every night for seven days after discharge, and whenever they experienced symptoms.

The researcher demonstrated how to use the CD player and earphones, and participants gave return demonstration. The researcher asked the participants to keep a logbook each time PMR was used and to record the severity of symptoms before and after PMR.

2.3.2. The control group

In this group, participants received routine care, including home medications such as: antiemetic and pain relief drugs, and discharge advice following chemotherapy. Similar to the experimental group, participants were instructed to keep a logbook of all symptoms and their severity.

Table 1
Demographic characteristics of participants.

Characteristics	Experimental group (n = 48) n (%)	Control group (n = 48) n (%)	*P*-value
Age (years): (Mean ± SD)	50.7 ± 9.1	52.4 ± 10.0	0.44[a]
Marital status			
Married	27 (56.3)	35 (72.9)	0.24
Single	16 (33.3)	5 (10.4)	
Divorced/widow	5 (10.4)	8 (16.7)	
Religion			1.00[b]
Buddhist	47 (97.9)	47 (97.9)	
Other	1 (2.1)	1 (2.1)	
Education attainment			0.31
None	1 (2.1)	2 (4.2)	
Primary school	18 (37.5)	15 (31.2)	
Secondary school	7 (14.6)	14 (29.2)	
College or more	22 (45.8)	17 (35.4)	
Income (Baht)			0.13
< 20,000	33 (68.8)	29 (60.4)	
20,000–40,000	11 (22.9)	8 (16.7)	
> 40,000	4 (8.3)	11 (22.9)	
Chemotherapeutic agents			0.56
Taxane	43 (89.6)	41 (85.4)	
Herceptin	5 (10.4)	7 (14.6)	
PMR experienced			1.00[b]
Never	48 (100.0)	48 (100.0)	

SD = standard deviation.
[a] Mann-Whitney *U* test.
[b] Fisher's exact probability test.

2.4. Data analysis

Descriptive statistics on the number, percentage, mean, and standard deviation were used to present the descriptive characteristics of the participants in the experimental and control groups. The Chi-square test was used to compare the categorical data. Symptom data based on occurrence and severity ratings were examined using Exploratory Factor Analysis. The varimax orthogonal rotation method was utilized to approximate multivariate normal data and to assess covariance between symptoms. The number of factors (clusters) was determined based on an eigenvalue higher than 1.0; only significant correlations were accepted. Potential symptom clusters were also required to be non-overlapping. The Wilcoxon signed-rank test was used to assess the mean scores of symptom clusters before and after the intervention within each group. The difference between participants' mean scores of symptom clusters before and after the intervention was assessed using the Mann-Whitney *U* test due to data distribution. A p-value of 0.01 was considered as statistically significant for tests.

3. Results

3.1. Characteristics of study participants

A total of 96 patients took part in the study, including 48 in the PMR group and 48 in the control group. There were no statistically significant differences in demographic characteristics between the experimental and control group participants in terms of age, marital status, religion, education attainment, income, chemotherapeutic agents, and PMR experience ($p > 0.05$) (Table 1).

3.2. Symptom clusters

Eight symptoms occurred simultaneously. The most prevalent symptom was pain, followed by anxiety, fatigue, lack of appetite, emotional distress, drowsiness, depression, and nausea. We conducted an exploratory factor analysis, which is the most common approach to examine the relationship among a number of variables [29], using the principle component method with varimax orthogonal rotation, and eigenvalues greater than 1.00. Four symptom clusters were identified with 58.12% of the total variance explained. Cluster 1 was comprised of anxiety and emotional distress; Cluster 2 consisted of nausea and pain; Cluster 3 included drowsiness and fatigue; and Cluster 4 was composed of depression and lack of appetite. Four clusters were loaded and explained 18.04%, 14.44%, 12.92%, and 12.72% of the factor variance, respectively (Table 2).

Table 2
Factor matrix[a] with Component Loading Factors.

Symptoms	Cluster 1	Cluster 2	Cluster 3	Cluster 4
1. Anxiety	**0.75**	–	–	–
2. Emotional distress	**0.61**	–	–	–
3. Nausea	–	**0.78**	–	–
4. Pain	–	**−0.62**	–	–
5. Drowsiness	–	–	**0.77**	–
6. Fatigue	–	–	**0.56**	–
7. Depression	–	–	–	**0.83**
8. Lack of appetite	–	–	–	**0.60**
Eigenvalues	1.44	1.16	1.03	1.02
% of variance explained	18.04	14.44	12.92	12.72
% Total variance explained	18.04	32.48	45.41	58.12

Note: Cluster 1 = (anxiety, emotional distress).
Cluster 2 = (nausea, pain).
Cluster 3 = (drowsiness, fatigue).
Cluster 4 = (depression, lack of appetite).
[a] Principal components analysis with varimax orthogonal rotation.

Table 3
Effect of progressive muscle relaxation on symptom clusters severity.

Symptom cluster	Experimental group (n = 48)			Control group (n = 48)			Treatment
	Before	After	Group	Before	After	Group	Effect,
	M ± SD	M ± SD	Diff.,	M ± SD	M ± SD	Diff.,	p-value
			p-value			p-value	
Cluster 1	4.46 ± 2.83	3.33 ± 1.53	0.29	3.87 ± 1.71	2.12 ± 0.63	0.11	0.20
Cluster 2	5.32 ± 2.41	4.33 ± 2.02	0.07	4.55 ± 2.28	3.69 ± 2.48	0.04	0.54
Cluster 3	4.42 ± 1.87	2.85 ± 1.38	< 0.01	4.29 ± 1.65	3.20 ± 1.53	< 0.01	0.26
Cluster 4	4.89 ± 1.76	4.20 ± 2.27	0.08	4.65 ± 1.89	3.65 ± 1.72	< 0.01	0.56

M ± SD, mean plus/minus standard deviation.

3.3. The effect of PMR on symptom cluster severity

Within the experimental group, the mean scores of Cluster 3 significantly decreased after PMR treatment ($p < 0.01$). When comparing the mean scores of the control group, there was a statistically significant reduction in Cluster 3, and 4 ($p < 0.01$). For all clusters, there were no significant differences between the mean scores of the PMR and the control group before and after treatment ($p > 0.05$) (Table 3).

4. Discussion

Our first research objective was to identify symptom clusters in Thai breast cancer patients receiving chemotherapy. The results revealed that all participants experienced eight symptoms simultaneously, which were pain, anxiety, fatigue, lack of appetite, emotional distress, drowsiness, depression, and nausea. Average symptom severity ranged from mild to moderate. This finding was consistent with previous findings that breast cancer patients being treated with chemotherapy reported experiencing a variety of symptoms that can be physical and psychological, which resulted from both the primary disease and from the treatment used [4,5,13–15,21–25]. The most prevalent physical symptoms were loss of appetite, constipation, nausea, vomiting, fatigue, and diversity of pain [4,5,25,26]. Moreover, drowsiness, emotional distress, sleep disturbance, anxiety, and depression [21–24] were the common psychological symptoms.

Based on the guidelines for factor analysis in a symptom cluster study, four symptom clusters were identified in our study. Symptom cluster 1 consisted of anxiety and emotional distress. Cluster 2 was nausea and pain. Cluster 3 included drowsiness and fatigue, and Cluster 4 included depression and lack of appetite. The reason why these symptom clusters have not been previously described may lie in the unique features of our patients, the different assessment times, and different evaluation methods used by other investigators. Additionally, Jimenez et al. found that age, sex, and the primary type of tumor influenced symptom clusters [30].

Furthermore, a review of 19 studies from Sullivan et al. found that specific symptoms within each symptom cluster were highly variable [31]. Molassiotis et al. also described that clusters are dynamic constructs reflecting complex relationships [32]. There was a relative stability of the clusters across time, with some 'secondary' symptoms changing over time at each stage of the disease and the treatments. Similarly, Sullivan et al. concluded in their literature review that across eight longitudinal studies, only 37.5% found the symptom clusters to be relatively stable over time [31].

Interestingly, fatigue and depression were grouped into different clusters instead of a single cluster in this study. Hsu et al. explained that because the symptom clusters were obtained by a statistical method, symptoms in some clusters may have had different pathophysiological causes or shared a common etiology [33]. Our study did not find significant difference between two groups in mean scores of all clusters before and after treatment ($p > 0.05$). It may be due to the symptom scores for the experimental group that were higher than the control group before intervention. Although score severity decreased after PMR intervention, this was not statistically significant.

As for the effectiveness of the PMR technique in managing symptoms, the study showed positive effects of this technique in reducing severity of symptom clusters. When comparing the mean score of Cluster 3 [drowsiness, fatigue]—before and after treatment—a significant decrease was shown in the experimental group ($p < 0.01$). This finding coincides with those of earlier studies suggesting a positive effect in fatigue management in patients undergoing chemotherapy [5,34]. Cancer patients are often physically and emotionally stress affected by the disease and the side effect of treatments. During stress, the sympathetic nervous system induces increased levels of catecholamine, norepinephrine, and epinephrine. Meanwhile, the hypothalamic-pituitary-adrenal axis induces the production of cortisol and pro-inflammatory cytokines resulting increase tension in body muscles. PMR may ease the resulting bodily tension through mind-body concentration and deep relaxation of muscles, which may reduce the stress hormones [19,20]. The resulting production of endorphin, encephalin, and serotonin may also ease bodily pain and fatigue, and possibly increase quality of sleep [5]. The results add to the body of evidence that PMR is a systematic technique that can be used to achieve a deep state of relaxation [35]. It is effective not only for physical, but also for mental health [23].

Several limitations of this study should be noted. First, all participants were recruited from only one hospital, most patients had received Taxane for chemotherapy, and PMR was only used for seven days. For these reasons, the results are not generalizable to all patients with breast cancer undergoing chemotherapy. Second, the randomization seems to have failed to produce groups with similar levels of symptoms. Finally, although participants reported that they practiced PMR as instructed, the researchers were not able to verify whether participants performed PMR in full each time. However, the strength of this study was the quasi-experimental design.

5. Conclusion

These findings suggest that PMR might be a useful nursing intervention to alleviate symptoms in breast cancer patients undergoing chemotherapy. Further studies are needed to verify the effect of PMR in reducing symptom clusters.

Conflicts of interest

The authors declare no conflict of interest.

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