Symptom Experience and Symptom Clusters of Thai Women with Breast Cancer Receiving Chemotherapy

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Abstract: Women with breast cancer experience multiple co-occurring symptoms and symptom clusters associated with chemotherapy. Understanding these symptom clusters will help to improve the effectiveness of symptom management. The purposes of this study were to explore symptom experience, symptom clusters, and to compare similarities and differences in symptom clusters based on severity and distress. Three hundred and twenty-two Thai women with breast cancer receiving chemotherapy were recruited from eight hospitals in Thailand. The instruments consisted of a Demographic and Clinical Data Form and the Thai-Memorial Symptom Assessment Scale. Data were analyzed using descriptive statistics and factor analysis.

The five most common symptoms reported by these women were hair loss, lack of energy, lack of appetite, change in the way food tastes, and nausea. Lack of appetite was the most frequent symptom, and hair loss was the most severe and distressing symptom. Based on the analysis of severity and distress ratings, four symptom clusters were identified that were labeled emotional, gastrointestinal, image, and discomfort. The four symptom clusters based on severity or distress explained 49.49% and 54.51% of the variance in all of the symptoms, respectively. Similarity rates between the symptom clusters created using severity and distress ratings ranged from 33.33% to 100.00%. These findings suggest that symptom clusters are relatively similar regardless of the dimension evaluated. Nurses and other health care providers should assess these symptom clusters and provide appropriate symptom management interventions for these women.

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Introduction

Breast cancer is the most common cancer in women worldwide.[1] In Thailand, the incidence continues to increase each year. For example from 20.5 to 28.5 new cases per 100,000 women from 1998 to 2012.[2] Chemotherapy is one of the most important treatments that increases survival and decreases disease recurrence in these women.[3] The chemotherapy for early and locally advanced stage disease is commonly given in

outpatient units every three weeks for four to six cycles; lasts for four to six months; and consists of multiple agents.[4] Women with breast cancer experience multiple symptoms or symptom clusters during chemotherapy.[5-15]

Multiple symptoms and symptom clusters have a negative impact on women's quality of life (QOL) and functional status.[16] A symptom cluster is defined as "three or more concurrent symptoms that are related to each other".[17(p465)] However, it is not entirely clear whether symptom clusters remain stable over time or across groups of patients.[18] To be considered congruent, 75% of the symptoms between clusters should be the same and the core symptoms should be present in both clusters.[18]

Knowledge of symptom clusters in women with breast cancer is limited and the findings are inconsistent. Only a limited number of studies have evaluated symptom clusters in these women using various dimensions of the symptom experience including: occurrence,[5-6] frequency,[7-8] severity,[6, 8-12] distress,[7,8,10,13] or combined frequency, severity, and distress.[14-15] Across these studies, the number of clusters and number of symptoms within each cluster were inconsistent. Moreover, most of these studies identified symptom clusters based on only one symptom dimension. Two studies compared similarities between symptom clusters identified using ratings of severity and distress[10] and ratings of occurrence and severity.[6] Given the paucity of research, additional studies that compare symptom clusters across symptom dimensions are needed. This information will enable health care providers to improve their assessment and management of these multiple co-occurring symptoms.

Literature Review

The Theory of Symptom Management (TSM)[16] and relevant literature guided this study. The TSM is composed of three inter-related dimensions: symptom experience, management strategies, and outcomes.

According to Humphreys et al.,[16] a symptom refers to the subjective experience of an individual about changes in biopsychosocial functioning, sensation, or cognition. The symptom experience dimension is composed of perception, evaluation, and response to the symptom. When a symptom is perceived, a person evaluates its frequency, severity, and distress.[16] Symptoms can have an impact on a variety of outcomes including: symptom status, functional status, costs, morbidity and co-morbidity, and QOL.[16] Symptom management aims to alleviate or delay negative symptom outcomes.[16] It may involve both patients and his/her family members.

In this study, we focused on the symptom experience dimension especially symptom perception and evaluation which included symptom frequency, severity, and distress. *Frequency* refers to the number of times that an event occurs within a given period.[19] *Severity* refers to "the fact or condition of something being extremely bad or serious."[20] *Distress* is defined as "the degree or amount of physical or mental upset, anguish, or suffering experienced from a specific symptom".[21] The TSM was selected as the framework for this study because it can be used to explain the experience of multiple co-occurring symptoms.[16]

Across the studies of symptom clusters in women with breast cancer in other countries, the number of symptom clusters varied from two[7-9,11] to six[6] and the number of symptoms within each cluster ranged from two[5-8,14] to eight.[14] Across these studies, the types of symptom clusters varied based on the symptom dimension used. Based on occurrence, fatigue; perceived cognitive impairment; and mood clusters were identified in one study.[5] In another study, psychological, hormonal, nutritional, gastro-intestinal, and epithelial symptom cluster were reported.[6] Based on frequency, a gastro-intestinal and a treatment-related cluster[7-8] were found. Based on severity, two to six clusters related to gastro-intestinal,[6,8,11] psycho-neurological or emotion,[6,9] neurocognition,[12] emotion and nausea,[12] hormonal, epithelial,[6] treatment,[8-9] fatigue and anorexia,[12]

neuropathy,[6] and pain related symptom[6] were identified. For distress, two to five clusters related to gastro-intestinal,[7-8,11-12] and treatment,[7-8] symptom were found. In two studies, symptom burden, based on frequency, severity, and distress was used to create the symptom clusters.[14-15] Emotional and gastro-intestinal were the common symptom clusters reported in both studies.[14-15] Two more clusters were identified namely an unwellness[11] and a physical[15] symptom cluster. The inconsistent findings across these studies may relate to differences in the instruments used to assess the symptom clusters (i.e., number of symptoms included varied from 8 to 38[6-8]) and the statistical approaches used to create the symptom clusters.

Moreover, only one study compared symptom clusters based on two symptom dimensions.[6] The emotional-, psychological-, hormonal- gastro-intestinal -, and body image-related symptom clusters were identified based on occurrence and severity.[6] In addition, neuropathy cluster was identified using severity.[6] However, the specific symptoms within each cluster were not identical.[6] For example, the hormonal cluster based on occurrence included difficulty sleeping. However, when severity was used, difficulty sleeping was not included in any symptom cluster.[6]

In terms of research on symptom clusters in Thai women with breast cancer, only two studies were reported that the number of symptom clusters ranged from four[10] to five[13] and the number of symptoms within each cluster ranged from two[13] to nine.[10] Emotional or mood-, gastro-intestinal-, image-, pain- or pain and discomfort- related symptom clusters were identified based on severity[10] and distress.[10,13] In addition, an oral related symptom cluster was identified using distress.[13] Only one study examined the similarities between symptom clusters identified using ratings of severity and distress.[10] Emotional-, gastro-intestinal-, and image- related symptom clusters were identified.[10] Some specific symptoms within each cluster were not identical.[10] For example, while pain and neuropathy were included in the pain and discomfort symptom cluster based on severity, these symptoms were included in the emotional, pain, and discomfort symptom cluster based on distress.[10] Additional research is warranted that evaluates for congruence in the number and types of symptom clusters identified using different dimensions of the symptom experience.[6, 10] Identical symptom clusters and identical symptoms within clusters may help to prioritize symptom management interventions. Therefore, this study aimed to evaluate the occurrence, frequency, severity, and distress of multiple symptoms in Thai women with breast cancer receiving chemotherapy and evaluate for similarities in symptom clusters that were identified based on ratings of severity and distress.

Methods

Design

A cross-sectional, descriptive design was used in this study.

Sample and Setting

A sample size estimation of five to 20 participants per variable, is suggested for factor analysis.[22] The calculation for this study was based on the rule of ten.[23] Since the MSAS is composed of 32 symptoms, 320 participants were needed. As suggested by a prior study in Thailand,[10] an additional 10% (i.e., 40 participants) was added for attrition. Three hundred and seventy participants were approached; ten chose not to participate because it was inconvenient. Of the 360 participants who consented to participate, 322 (89.44%) completed the study questionnaires.

The research team members recruited participants using purposively sampling from one-day chemotherapy units located in one general, five regional, and two university hospitals in northern Thailand during 2014-2015. The inclusion criteria were: a woman of at least 18 years of age, newly diagnosed with stage I to III breast cancer, had received at least one chemotherapy treatment in the outpatient department, and was able to communicate in Thai. The exclusion

criteria included: recurrent or metastatic breast cancer and receipt of concurrent radiotherapy.

Ethical Considerations

Ethics approval for this study was obtained from the Institutional Review Board (IRB) of the Faculty of Nursing (FON), Chiang Mai University, and the six hospitals. One general and one university hospital approved and accepted the IRB from the FON. All participants were informed about the research objectives and their right to participate or withdraw from the study and to refuse to answer any questions without penalty or any impact on them or their health care services. Privacy, anonymity, and confidentiality were assured. A member of the research team began data collection after participants provided written consent.

Instruments

1. Demographic and Clinical Data Form was developed by the principal investigator (PI). Demographic data included: age, education, marital status, religion, occupation, income, and health expenditure. Clinical data included: menstrual status, co-morbidity, types of breast surgery, stage of cancer, chemotherapy regimen, and number of chemotherapy cycles, hemoglobin, white blood cell count, absolute neutrophil count, and pre-medications.

2. Thai Memorial Symptom Assessment Scale (Thai-MSAS)[10] is a questionnaire that measures symptoms related to cancer and its treatment. The original English version, developed by Portenoy et al.[24] was translated into the Thai language by Suwisith[10] The questionnaire evaluates the occurrence, frequency, severity, and distress of 24 symptoms, and evaluates occurrence, severity, and distress of 8 symptoms during the past week. For occurrence, participants were asked to respond yes (1) or no (2). For frequency, severity, and distress, symptoms were rated on a Likert scale. For frequency, the scale ranged from 1 (rarely) to 4 (almost constantly). For severity, the scale ranged from 1 (slight) to 4 (very

severe). For distress, the scale ranged from 0 (not at all) to 4 (very much). The participants were asked if they had each symptom (e.g., pain) during the past week. If they responded yes, they were asked "how often did you have it?", how severe was it usually?", and "how much did it distress or bother you?". When calculating the symptom scores, a score of 0 was used for all dimensions of a symptom if the patient did not experience the symptom. However, if participants experienced a symptom, the severity, distress, and frequency scores were calculated.[24] In a previous report[10] the Thai MSAS had a Cronbach's alpha of 0.96.[10] In another study, the Cronbach's alphas were 0.96 for symptom severity and 0.93 for symptom distress.[13] In this study, the Cronbach's alphas were 0.89, 0.93, and 0.94 for frequency, severity, and distress, respectively.

Data collection

Participants were identified from medical records and those who met our inclusion criteria were approached. The PI or research assistants (RAs) met the participants at the one day chemotherapy unit and informed them about the objectives of the study and the time needed to complete the questionnaires. After obtaining written informed consent, the Demographic and Clinical Data Form was completed. Participants received the Thai-MSAS in a postage paid envelope. They were asked to complete the Thai MSAS on day seven in their home. The PI or RAs expressed appreciation to the participants with gift sets valued at 150 Bahts (approx. $4.41 US) after the first meeting. Six days after enrollment, the PI or RAs called the participants to remind them to complete the Thai-MSAS by themselves. The participants were asked to answer the Thai-MSAS by day seven and return it to the PI using a postage paid envelope.

Data analysis

Descriptive statistics were used to describe demographic and clinical characteristics and symptom dimensions. Exploratory factor analysis (EFA) was

used to identify symptom clusters based on severity and distress. The specific technique used was Principle Component Analysis (PCA) with oblique rotation. The criteria for determining the optimal number of factors were in accordance with theoretical[22-23] and prior studies,[13] namely: 1) eigenvalue of 1.2[7-8,10,13] 2) scree plot;[22-23] 3) factor loading of >0.4;[7,9-10] 4) a few items with cross loadings;[9] 5) a factor had at least three items;[9] and 6) the factor had clinical or theoretical plausibility.[9]

The assumptions of factor analysis were tested including normality, interval data, and linearity. Symptoms that were not normally distributed (i.e., swelling of arms or legs, problems with sexual interest or activity, and diarrhea) were excluded. Factorability was tested to evaluate multicollinearity[22-23] including Bartlett's test of sphericity, the Measure of Sampling Adequacy (MSA), both overall, and for each variable. The Bartlett's test of sphericity rejecting the null hypotheses in both datasets, meant that both symptom dimensions were appropriate for factor analysis (i.e., for symptom severity, the chi-square =3854.924, df=406, p<.001, for symptom distress, the chi-square =4786.718, df=406, p<.001). The MSA was used to measure intercorrelations among the variables in the study[23] (i.e., "compare the magnitudes of correlation coefficients to the partial correlation coefficients"). If true factors exist in the data, the partial correlation or "the correlation that is unexplained when the effects of other variables are taken into account" should be small.[22-23] The overall MSA can use the Kaiser-Meyer-Olkin (KMO) and the value should be > 0.80. The MSA of each variable used the anti-image correlation (AIC), which should be > 0.70.[23] In this study, the overall KMO values were 0.906 for symptom severity and 0.930 for symptom distress. The AIC for each variable ranged from 0.801 to 0.963 for symptom severity and 0.826 to 0.967 for symptom distress.

Results

Demographic and clinical characteristics of the sample

The age of the participants ranged from 41 to 60 years with a mean age of 51.97 (SD=9.20) and 76.4% were married. The majority of participants attended primary school (56.5%) and almost all (99.1%) were Buddhist. About one-third were farmers (28.9%). Most of them (77.0%) had a monthly family income of up to 25,000 Baht (730 US Dollars) and 66.8% used the Universal Coverage Scheme as their health payment. In terms of clinical characteristics, 55.0% were post-menopausal and 51.2% had no comorbid condition. Fifty-seven percent had Stage II breast cancer and 82.3% had undergone a modified radical mastectomy. The majority of the participants received a 5 fluorouracil, adriamycin, and cyclophosphamide (FAC)(43.8%) or an adriamycin and cyclophosphamide (AC)(36%) regimen. About 59% received three to six cycles of chemotherapy. With regards to the antiemetic premedication received, the majority of them (83.9%) received dexamethasone and ondansetron. Fifty-eight percent had Grade I anemia (i.e., hemoglobin of 10-12 gm%), 73.3% had white blood cell counts within normal limits, and all of them had an absolute neutrophil count within normal limits.

Symptom experience

Table 1 provides information on the occurrence, frequency, severity, and distress of the 32 MSAS symptoms. Total number of symptoms ranged from 3 to 32 (mean =18.62, SD=8.21). In the total sample, the five *most common* symptoms were: hair loss (92.6%), lack of energy (87.3%), lack of appetite (82.0%), change in the way food tastes (81.7%), and nausea (78.9%). The *symptom frequency* mean scores ranged from 0.31 (problems with sexual interest or activity) to 2.21 (lack of appetite). The *symptom severity* mean scores ranged from 0.29 (problems with sexual interest or activity) to 3.20 (hair loss). The *symptom distress* mean scores ranged from 0.15 (problems with sexual interest or activity) to 1.89 (hair loss).

Table 1 Summary of Symptoms Experience (n=322)

Symptom	Occurrence		Frequency (1-4)		Severity (1-4)		Distress (0-4)	
	N	%	Mean	SD	Mean	SD	Mean	SD
Difficulty concentrating	198	61.5	1.14	1.08	0.98	0.97	0.72	1.05
Pain	194	60.2	1.19	1.19	1.05	1.08	0.87	1.13
Lack of energy	281	87.3[2]	2.06[2]	1.17	1.77[4]	1.04	1.46[3]	1.28
Cough	122	37.9	0.58	0.88	0.48	0.71	0.32	0.71
Feeling nervous	183	56.8	1.14	1.14	0.99	1.06	0.85	1.15
Dry mouth	217	67.4	1.55[5]	1.35	1.24	1.13	0.84	1.10
Nausea	254	78.9[5]	1.85[3]	1.27	1.59	1.12	1.46[3]	1.27
Feeling drowsy	221	68.6	1.50	1.25	1.20	1.05	0.81	1.09
Numbness/tingling in hands/feet	161	50.0	1.10	1.36	0.85	1.03	0.65	1.06
Difficulty sleeping	232	72.0	1.74[4]	1.36	1.44	1.21	1.23[5]	1.27
Feeling bloated	176	54.7	1.25	1.35	1.09	1.22	0.88	1.20
Problems with urination	139	43.2	0.84	1.14	0.73	1.00	0.57	0.98
Vomiting	181	56.2	1.31	1.36	1.14	1.22	1.07	1.32
Shortness of breath	148	46.0	0.93	1.18	0.78	0.10	0.62	0.97
Diarrhea	93	28.9	0.44	0.77	0.39	0.71	0.25	0.62
Feeling sad	155	48.1	0.93	1.14	0.84	1.06	0.69	1.05
Sweats	143	44.4	0.88	1.17	0.76	1.04	0.49	0.89
Worrying	189	58.7	1.19	1.22	1.05	1.11	0.92	1.15
Problems with sexual interest or activity	70	21.7	0.31	0.69	0.29	0.64	0.15	0.51
Itching	130	40.4	0.76	1.08	0.61	0.89	0.39	0.79
Lack of appetite	264	82.0[3]	2.21[1]	1.37	1.91[3]	1.27	1.46[3]	1.34
Dizziness	218	67.7	1.49	1.26	1.24	1.11	0.98	1.13
Difficulty swallowing	155	48.1	1.04	1.28	0.89	1.12	0.72	1.15
Feeling irritable	207	64.3	1.39	1.24	1.16	1.10	0.94	1.14
Mouth sores	172	53.4	NA	NA	0.99	1.16	0.78	1.09
Change in the way food tastes	263	81.7[4]	NA	NA	1.98[2]	1.28	1.50[2]	1.29
Weight loss	182	56.5	NA	NA	1.08	1.18	0.61	0.99
Hair loss	299	92.6[1]	NA	NA	3.20[1]	1.21	1.89[1]	1.61
Constipation	194	60.2	NA	NA	1.30	1.36	1.03	1.33
Swelling of arms or legs	84	26.1	NA	NA	0.36	0.72	0.22	0.67
"I don't look like myself"	232	72.0	NA	NA	1.74[5]	1.40	1.29[4]	1.36
Changes in skin	239	74.2	NA	NA	1.50	1.24	0.98	1.20
Total number of symptoms	Range 3 to 32, Mean=18.62, SD=8.21							

NA: Not applicable

Bold: Five most common symptoms

Symptom clusters

Four symptom clusters were found using ratings of severity (Table 2) and distress (Table 3). Based on severity ratings, the four symptom clusters explained 49.49% of variance for the entire set of symptoms. These clusters were named "Emotion related", "Gastro-intestinal and energy related", "Image and nutrition related", and "Pain and discomfort related". Based on distress ratings, the four symptom clusters explained 54.51% of variance for the entire set of symptoms. These clusters were named "Emotional, energy, and pain related", "Gastro-intestinal related", "Image related", and "Discomfort, nutrition, and elimination related". Across the eight symptom clusters, the largest amount of variance explained by severity and distress were for the "Emotion related", followed by the "Emotion, energy, and pain related" with explained variances of 32.51% and 38.68%, respectively.

Table 2 Summary of Symptom Clusters Using Symptom Severity (n=322)

Factor	Name	Symptoms	Factor Loading	Item-Total Correlation	Cronbach Alpha	Total Variance
1	Emotion related symptom cluster	Worrying	.889	.724		
		Feeling sad	.798	.680		
		Feeling nervous	.724	.671		
		Feeling irritable	.605	.628		
		Difficulty sleeping	.594	.480		
		Difficulty concentrating	.491	.537		
		Feeling drowsy	.445	.492		
		Sweats	.422	.474		
	Total	8			0.847	32.51
2	Gastro-intestinal and energy related symptom cluster	Nausea	-.869	.646		
		Vomiting	-.833	.610		
		Difficult swallowing	-.488	.657		
		Feeling bloated	-.423	.598		
		Dizziness	-.415	.540		
		Lack of energy	-.412	.538		
		Shortness of breath	-.396	.583		
		Lack of appetite	-.360	.548		
	Total	8			0.850	7.10
3	Image and nutrition related symptom cluster	Changes in skin	.721	.539		
		Hair loss	.659	.428		
		"I don't look like myself"	.645	.560		
		Mouth sores	.520	.518		
		Change in the way food tastes	.514	.493		
		Weight loss	.490	.490		
		Constipation	.347	.424		
		Dry mouth	.342	.535		
	Total	8			0.791	5.31
4	Pain and discomfort related symptom cluster	Pain	.710	.471		
		Numbness/tingling in hands/feet	.606	.493		
		Itching	.583	.445		
		Problems with urination	.466	.395		
		Cough	.377	.323		
	Total	5			0.670	2.57
Total		29 Symptoms			0.922	49.49

Table 3 Summary of Symptom Clusters Using Symptom Distress (n=322)

Factor	Name	Symptoms	Factor Loading	Item-total Correlation	Cronbach Alpha	Total Variance
1	Emotion, energy, and pain related symptom cluster	Worrying	.875	.725		
		Feeling sad	.805	.676		
		Feeling nervous	.738	.660		
		Difficulty sleeping	.687	.555		
		Feeling irritable	.667	.666		
		Difficulty concentrating	.597	.671		
		Lack of energy	.576	.592		
		Feeling drowsy	.504	.632		
		Pain	.440	.464		
		Numbness/ tingling in hands/ feet	.391	.451		
		Shortness of breath	.375	.603		
		Sweats	.348	.514		
	Total	12			.884	38.68
2	Gastro-intestinal related symptom cluster	Nausea	−.850	.699		
		Vomiting	−.790	.641		
		Difficulty swallowing	−.437	.621		
		Lack of appetite	−.414	.617		
		Dizziness	−.360	.551		
	Total	5			.828	6.60
3	Image related symptom cluster	"I don't look like myself"	−.547	.729		
		Changes in skin	−.541	.646		
		Hair loss	−.520	.649		
	Total	3			.813	5.07
4	Discomfort, nutrition, and elimination related symptom cluster	Itching	.731	.434		
		Mouth sores	.694	.563		
		Constipation	.645	.593		
		Dry mouth	.518	.608		
		Problem with urination	.478	.544		
		Weight loss	.449	.444		
		Cough	.421	.448		
		Feeling bloated	.382	.590		
		Change in the way food tastes	.367	.575		
	Total	9			.803	4.16
Total		29 Symptoms			.884	54.51

A comparison of symptom clusters based on severity and distress ratings

Some similarities and differences were found when the symptoms clusters based on severity and distress ratings were compared (Table 4). First, eight symptoms were identical in the Emotion-related symptom cluster based on severity and the Emotion, energy, and pain related symptom cluster based on distress (similarity rate based on severity was 100%, similarity rate based on distress was 66.7%). The following four symptoms were only in the distress cluster: lack of energy, pain, numbness/tingling in hands/feet, and shortness of breath.

Table 4 Comparison Symptom Clusters Based on Severity and Distress

Factor	Symptom Severity	Symptom Distress	Similar Rate Based on Severity	Similar Rate Based on Distress
1	Emotion−related (8 Symptoms) Worrying Feeling sad Feeling nervous Difficulty sleeping Feeling irritable Difficulty concentrating Feeling drowsy Sweats	Emotion, energy and pain related (12 Symptoms) Worrying Feeling sad Feeling nervous Difficulty sleeping Feeling irritable Difficulty concentrating Feeling drowsy Sweats Lack of energy Pain Numbness/Tingling in hands/feet Shortness of breath	**100% Similar** (8 of 8)	**66.7% Similar** (8 of 12)
2	Gastro−intestinal and energy related (8 Symptoms) Nausea Vomiting Difficulty swallowing Dizziness Lack of appetite Feeling bloated Lack of energy Shortness of breath	Gastro−intestinal related (5 Symptoms) Nausea Vomiting Difficulty swallowing Dizziness Lack of appetite	**62.5% Similar** (5 of 8)	**100% Similar** (5 of 5)
3	Image and nutrition related (8 symptoms) Changes in skin Hair loss "I don't look like myself" Mouth sores Change in the way food tastes Weight loss Constipation Dry mouth	Image related (3 symptoms) Changes in skin Hair loss "I don't look like myself"	**37.5% Similar** (3 of 8)	**100% Similar** (3 of 3)
4	Pain and discomfort related (5 symptoms) Pain Numbness/ tingling in hands/ feet Itching Problems with urination Cough	Discomfort, nutrition, and elimination related (9 Symptoms) Itching Problems with urination Cough Dry mouth Mouth sores Weight loss Constipation Feeling bloated Change in the way food tastes	**60% Similar** (3 of 5)	**33.3% Similar** (3 of 9)

Second, five symptoms were identical in the gastro-intestinal and energy related symptom cluster based on severity and the gastro-intestinal related symptom cluster based on distress. The similarity rate based on severity was 62.5% and for distress, 100%. The symptoms of feeling bloated, lack of energy, and shortness of breath were identified only in the symptom cluster based on severity.

Third, three of the symptoms were identical in the image and nutrition related symptom cluster based on severity and the Image related symptom cluster based on distress. The similarity rate based on severity was 37.5%. The similarity rate based on distress was 100%. Five additional symptoms were included only in the severity-based cluster (i.e., mouth sores, change in the way food tastes, weight loss, constipation, and dry mouth).

Fourth, the same three symptoms were found in the pain and discomfort related cluster based on severity and the discomfort, nutrition, and elimination related cluster based on distress. The similarity rate based on severity was 60.0%. The similarity rate based on distress was 33.3%. Two symptoms (i.e., pain and numbness/tingling in hands/feet) were identified only in the cluster based on severity. Six additional symptoms (i.e., dry mouth, mouth sores, weight loss, constipation, feeling bloated, change in the way food tastes) were identified only in the cluster based on distress ratings.

Discussion

Findings from this study suggest that Thai women with breast cancer receiving chemotherapy experience multiple co-occurring symptoms and symptom clusters. In this study, the most common symptoms were not necessarily the most severe or distressing. For example, hair loss, lack of appetite, lack of energy, "I don't look like myself" were rated as both severe and distressing symptoms. However, while difficulty sleeping and nausea were rated as

distressing, they were not the most severe symptoms. Compared to studies of Thai women with breast cancer receiving chemotherapy,[10, 13] none reported nausea as one of the five most common, frequent, severe, or distressing symptoms. Compared to a sample of Thai women who were similar to the current study in terms of stage of disease, similar chemotherapy regimens, and number of chemotherapy cycles,[13] all of the women in the previous study received a combination of potent antiemetics[25] which may explain the lower rate of nausea. In the current study, potent antiemetic drugs were given to only 83% of participants.

Symptom experience

The five most common symptoms in this study were: hair loss, change in the way food tastes, nausea, lack of energy, and lack of or change in appetite. *Hair loss* or alopecia is a common symptom[10, 13] that occurs 2 to 4 weeks after the start chemotherapy.[26] Chemotherapy disrupts the division and proliferation of cells and hair follicles.[27] Cyclophosphamide, doxorubicin, paclitaxel, and methotrexate that are used to treat breast cancer cause the most frequent and severe hair loss.[28] Because hair plays an important role in women's appearance and personality,[26] hair loss influences a women's sense of attractiveness, femininity, and body image and can decrease her self-esteem and self-confidence.[27]

Change in the way food tastes can occur within 4 to 6 days after receiving chemotherapy and may decline over the cycle.[29] Taste changes occur through direct effects of the chemotherapy on the epithelial cells of the taste receptors or neurotoxicity.[30] Cyclophosphamide and taxane can induce a metallic sensation.[31] It is a common symptom reported by individuals with breast cancer.[6,10, 13]

Nausea or vomiting occurs because chemotherapy acts on the chemoreceptor trigger zone, as well as on the release of serotonin and substance P from cells that line the gastric mucosa.[25] Individually, cyclophosphamide, doxorubicin, and taxanes are associated with moderate emetic risk. When combined, they have a high level

of emetogenicity.[32] Nausea is a common symptom reported during chemotherapy for breast cancer.[5,9] However, in recent studies, it was not found among the five most common symptoms.[6,13] These inconsistent findings may be related to differences in the anti-emetic regimens used across the various studies.[13]

The symptom of *lack of energy* on the MSAS is more commonly referred to as fatigue.[33] Fatigue occurs between 3 and 7 days after receiving chemotherapy. Its severity increases during the first cycle and becomes more severe in later cycles.[34] Fatigue is associated with sleep problems, depression, and pain. Lack of energy is a common symptom reported during chemotherapy treatment for breast cancer.[6,10,13]

Lack of or change in appetite is "...a sensation related to the maintenance of eating and a desire for specific foods".[30] This desire may not correlate with a liking for certain foods and may change due to depression, psychosocial stress, nausea, constipation, taste alterations, and/or pain.[35] It occurs prior to or during the first three cycles of chemotherapy and is associated with decreases in energy intake.[33] Lack of appetite is a common symptom reported during chemotherapy for breast cancer.[10,13]

Symptom clusters

All of the symptom clusters identified in this study are similar to previous reports[6-15] The *emotional cluster* based on severity in this study, was similar to the previous studies that reported emotional- related symptom clusters.[6-12] The *emotional, energy, and pain cluster* in this study based on distress was similar to the emotional-,[10] mood,[13] or treatment[7-8] related symptom clusters reported in previous studies. While the number of symptoms, as well as, the specific symptoms in these clusters were not identical, the fact that a mood related cluster was identified across studies suggests that this cluster warrants careful evaluation in women with breast cancer. The emotional cluster may be related to the disease itself, its treatment, and associated physical symptoms. The diagnosis of breast cancer is a significant life stress event that

causes emotional and/or psychological symptoms from the time of diagnosis to at least four months after diagnosis.[36] Cytokine-induced sickness behavior was suggested as a mechanism that underlies the emotion-related symptoms (e.g., anxiety, depression), as well as fatigue, cognitive impairment, gastro-intestinal problems, pain, and wasting.[37] Cancer, immune, and nervous system cells secrete pro-inflammatory cytokines and chemokines that act on various brain regions and alter the release of serotonin, as well as prostaglandins and substance P. At the same time, the hypothalamic-pituitary-adrenal (HPA) axis is activated.[37]

The gastro-intestinal and energy cluster based on both severity and distress in this study, was similar to previous reports.[6-13] Nausea and lack of appetite were the common symptoms found in both the severity[6-12] and distress[7,8,10,13] clusters. The gastro-intestinal cluster in this study may be related to the chemotherapy and antiemetics that the women received. The chemotherapy agents or their metabolites act directly on the chemoreceptor center.[26] Moreover, in this study, the receipt of highly emetogenic chemotherapy without potent prophylactic antiemetic drugs may contribute to nausea and vomiting. Only 83.9% of the participants in our study received potent antiemetic drugs as recommended in international guidelines.[26]

The image and nutrition cluster based on severity, in this study was similar to a previous report.[6,10] Hair loss and skin changes were the common symptoms in both studies.[6, 10] Our image cluster based on distress included symptoms that were found in "image related cutaneous",[10] and "psychologically related self-images"[13] related symptom clusters in previous studies. Body image changes in women with breast cancer after diagnosis[38] and surgery[39] are related to the loss of a breast and/or surgical scarring. A person who had a mastectomy tends to have a lower body image compared to an individual who had a lumpectomy.[39] In addition, doxorubicin, cyclophosphamide, and paclitaxel can cause severe alopecia.[28] Alopecia was one of most common symptoms associated with

chemotherapy.[10,13] Women with breast cancer report body image changes following surgery and chemotherapy.[39,40]

The *pain and discomfort cluster* based on severity in this study was similar to the previous studies that identified neuropathy-,[6] and pain and discomfort-,[10] related symptom clusters. *The discomfort nutrition, and elimination cluster* based on distress, in this study was similar to emotional-,[10] disturbed mood-,[13] and discomfort-[13] related symptom clusters found in previous studies. However, the specific symptoms within these clusters varied across studies. Based on severity, pain and numbness/tingling in hands/feet in this study were similar to a previous report.[6,10] In contrast, itching, problems with urination, and cough were not identified.[10] Based on distress, problems with urination, constipation, and feeling bloated were included in the discomfort cluster[13] and dry mouth and mouth sores were in an oral cluster in a previous report.[13] Constipation, dry mouth, mouth sores, and change in the way food tastes were in the image-related symptom cluster in a previous study.[10]

A comparison of symptom clusters based on severity and distress

In this study, similarities in the number and types of symptom clusters were partially supported. These findings are consistent with only one report,[10] where the calculated similarity rates ranged 36.4 to 100%.[10] In the emotion cluster, in this study and the previous study,[10] seven symptoms (i.e., worrying, feeling sad, feeling nervous, feeling irritable, difficulty sleeping, difficulty concentrating, sweats) were identical.[10] Three symptoms (i.e., nausea, lack of appetite, dizziness) were identical symptoms within the gastro-intestinal cluster.[10] For the image-related symptom cluster, two symptoms were identical, namely hair loss and changes in skin.[10]

One possible explanation for the different symptoms within the symptom clusters based on severity and distress is that severity and distress represent distinct dimensions of an individual's symptom experience. Ratings of symptom severity and distress rely on an individual's subjective experiences or perceptions that interpreted or evaluated.[16]

In a recent publication, Sullivan et al. reported on similarities in symptom cluster in women with breast cancer undergoing chemotherapy using ratings of occurrence and severity.[6] The similarity rates ranged between 0% for the chemotherapy neuropathy cluster to 100% for the psychological, hormonal, epithelial, and chemotherapy neuropathy cluster. Similar to our emotion cluster, Sullivan et al., identified a psychological symptom cluster. Worrying, feeling sad, feeling nervous, and feeling irritable were the common symptoms in both clusters. In addition, the gastro-intestinal cluster in this study, was labeled a nutrition cluster.[6] Both of these clusters included the symptoms of nausea and lack of appetite. Finally, an image-related symptom cluster that included hair loss and changes in skin was found in both studies[6] While different dimensions of the symptom experience were used to create the symptom clusters, these consistent finding suggest that these three clusters warrant additional investigation.

Limitations

The purposive sampling from eight hospitals in the northern part of Thailand is a limitation of this study as the findings may not generalize to Thai women with breast cancer in other regions of the country.

Conclusions and implications for nursing science and nursing practice

This study provides evidence that women with breast cancer who are receiving chemotherapy have multiple co-occurring symptoms and symptom clusters that can be identified based on severity and distress ratings. Different symptoms were identified based on different dimensions of the symptom experience (i.e.,

occurrence, frequency, severity, and distress). Therefore, nurses should assess patients using on multidimensional instrument, that includes the most common symptoms that can occur during cancer treatments.

In this study, for both the severity and distress dimensions, the number of clusters identified, as well as the types of symptom clusters were relatively similar. Our findings are consistent with a previous study and suggest that three specific symptom clusters (i.e., emotional, gastro-intestinal, and image- related) warrant assessment and management in women receiving chemotherapy for breast cancer. These types of focused assessment can guide the development of more target symptoms management interventions for these patients. Future studies need to identify the common and distinct mechanisms associated with each of these symptom clusters. Additional research needs to evaluate the impact of these symptom clusters on patient outcomes.

Acknowledgements

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ประสบการณ์อาการและกลุ่มอาการของสตรีไทยที่เป็นมะเร็งเต้านมที่ได้รับการรักษาด้วยเคมีบำบัด

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บทคัดย่อ: สตรีที่เป็นมะเร็งเต้านมมักมีประสบการณ์การเกิดอาการหลายอาการเกิดขึ้นพร้อมกันและกลุ่มอาการหลายกลุ่มจากการรักษาด้วยเคมีบำบัด ความเข้าใจเกี่ยวกับกลุ่มอาการจะช่วยในการจัดการให้มีประสิทธิผล การศึกษาครั้งนี้มีวัตถุประสงค์เพื่อศึกษาประสบการณ์การเกิดอาการ กลุ่มอาการและเปรียบเทียบความเหมือนหรือความต่างของกลุ่มอาการที่ใช้ความรุนแรงหรือความทุกข์ทรมานต่ออาการเป็นเกณฑ์ กลุ่มตัวอย่างเป็นสตรีไทยที่เป็นมะเร็งเต้านมที่รักษาด้วยเคมีบำบัด 322 คนจากโรงพยาบาล 8 แห่ง เครื่องมือที่ใช้เก็บข้อมูลได้แก่ แบบบันทึกข้อมูลส่วนบุคคลและการเจ็บป่วย และแบบบันทึกอาการ การวิเคราะห์ข้อมูลใช้สถิติเชิงพรรณาและการวิเคราะห์ปัจจัย

ผลการศึกษาพบว่า อาการที่พบบ่อย 5 อาการได้แก่ ผมร่วง ไม่มีแรง เบื่ออาหาร การรับรสเปลี่ยนแปลง และคลื่นไส้ และพบว่าเบื่ออาหารเป็นอาการที่พบบ่อยที่สุด ผมร่วงเป็นอาการที่รุนแรงและทุกข์ทรมานที่สุด เมื่อวิเคราะห์โดยใช้ความรุนแรงหรือความทุกข์ทรมาน พบว่ากลุ่มอาการ มี 4 กลุ่มได้แก่กลุ่มอาการด้านอารมณ์ กลุ่มอาการด้านทางเดินอาหาร กลุ่มอาการด้านภาพลักษณ์และกลุ่มอาการด้านความไม่สุขสบาย กลุ่มอาการทั้ง 4 ตามความรุนแรงหรือความทุกข์ทรมานสามารถอธิบายความแปรปรวนของอาการได้ร้อยละ 49.49 และ 54.51 ตามลำดับ การระบุความคล้ายคลึงกันของกลุ่มอาการทั้ง 4 อยู่ในช่วง ร้อยละ 33.33 -100 ผลวิจัยดังกล่าวแสดงให้เห็นถึงความคล้ายคลึงกันของกลุ่มอาการแม้จะใช้มิติของอาการที่ต่างกันในการประเมิน พยาบาลและบุคลากรทีมสุขภาพควรประเมินกลุ่มอาการเหล่านี้และให้การพยาบาลเพื่อจัดการกับกลุ่มอาการอย่างเหมาะสม ในสตรีที่เป็นมะเร็งเต้านมและได้รับเคมีบำบัด

คำสำคัญ: ประสบการณ์อาการ กลุ่มอาการ สตรีไทย มะเร็งเต้านม เคมีบำบัด

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