นิพนธ์ต้นฉบับ ▪ Original Article

กลุ่มอาการและผลของการผ่อนคลายกล้ามเนื้อแบบก้าวหน้าในผู้ป่วยมะเร็งตับชาวไทยที่ได้รับยาเคมีบำบัดผ่านทางหลอดเลือดแดง

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Symptom Clusters and Effects of Progressive Muscle Relaxation in Thai Patients with Hepatocellular Carcinoma Undergoing Transarterial Chemoembolization

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หลักการและวัตถุประสงค์: กลุ่มอาการที่เกิดขึ้นในผู้ป่วยมะเร็งทำให้เกิดความทุกข์ทรมาน การศึกษากลุ่มอาการและจัดการกลุ่มอาการจึงมีความสำคัญ การผ่อนคลายกล้ามเนื้อแบบก้าวหน้าถูกนำมาใช้เพื่อบรรเทาอาการในผู้ป่วยมะเร็งมากขึ้น เนื่องจากสามารถปฏิบัติได้ง่าย สะดวก การวิจัยครั้งนี้มีวัตถุประสงค์เพื่อศึกษากลุ่มอาการในผู้ป่วยมะเร็งตับชาวไทยที่ได้รับยาเคมีบำบัดผ่านทางหลอดเลือดแดง และประเมินผลเบื้องต้นของการผ่อนคลายกล้ามเนื้อแบบก้าวหน้าต่อกลุ่มอาการที่เกิดขึ้น

วิธีการศึกษา: เป็นการศึกษาแบบกลุ่มเดียววัดก่อนหลังการทดลอง ในผู้ป่วยมะเร็งตับที่เข้ารับการรักษาในโรงพยาบาลมหาวิทยาลัยแห่งหนึ่งในเขตภาคเหนือของประเทศไทย จำนวน 30 ราย

ผลการศึกษา: จากการวิเคราะห์ปัจจัยพบกลุ่มอาการในผู้ป่วยมะเร็งตับ 2 กลุ่มอาการ กลุ่มอาการที่หนึ่ง ประกอบด้วย แน่นท้อง ปวดหลัง และปวดไหล่ และกลุ่มอาการที่สอง ประกอบด้วย ปวดเอว และ ปวดท้อง คะแนนเฉลี่ยของกลุ่มอาการที่หนึ่งและกลุ่มอาการที่สองลดลงหลังการผ่อนคลายกล้ามเนื้อแบบก้าวหน้าอย่างมีนัยสำคัญตามลำดับ ($Z=-6.84$, $p<0.001$; $Z=-5.35$, $p<0.001$).

สรุป: ผลการวิจัยนี้สนับสนุนบุคลากรผู้ให้การดูแลด้านสุขภาพใช้การผ่อนคลายกล้ามเนื้อแบบก้าวหน้าเพื่อลดกลุ่มอาการจาก

Background and objectives: Symptom clusters cause suffering in cancer patients. The study of symptom clusters as well as symptom clusters management is important. Progressive muscle relaxation (PMR) is used to alleviate symptoms in cancers due to it can be performed simply and convenient. This research aimed to investigate the symptom clusters in Thai patients with hepatocellular carcinoma (HCC) undergoing transarterial chemoembolization (TACE) and to preliminarily evaluate the effects of progressive muscle relaxation (PMR) on those symptom clusters.

Methods: The study used a one-group, pre- and post-test design. Thirty participants were recruited from a university hospital in northern Thailand.

Results: Two symptom clusters emerged from factor analysis. The first symptom cluster consisted of abdominal distension, upper back pain, and shoulder pain. The second symptom cluster was lower back and abdominal pain. The mean score of symptom cluster 1 and 2 from pre- to post-PMR significantly decreased ($Z=-6.84$, $p<0.001$; $Z=-5.35$, $p<0.001$, respectively).

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การได้รับยาเคมีบำบัดผ่านทางหลอดเลือดแดงในผู้ป่วยมะเร็งตับ

คำสำคัญ: การผ่อนคลายกล้ามเนื้อแบบก้าวหน้า กลุ่มอาการ มะเร็งตับ การให้ยาเคมีบำบัดผ่านทางหลอดเลือดแดง การพยาบาล

Conclusions: It is recommended that health care providers should encourage the use of PMR in HCC patients undergoing TACE to minimize their symptom clusters.

Keywords: Progressive muscle relaxation, Symptom clusters, Hepatocellular carcinoma, Transarterial chemoembolization, Nursing

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Introduction

Hepatocellular carcinoma (HCC) is the second most common cause of cancer mortality among men and sixth among women, resulting in between 250,000 and one million deaths globally per annum[1]. Men are affected 2-4 times more frequently than women, and the incidence rates are highest in developing countries of Sub-Saharan Africa and Southeast Asia where the incidence of chronic hepatitis B is high[2]. In Thailand, HCC ranks as the number one cancer in men and fourth in women, and is a leading cause of death in both genders[3].

HCC is frequently diagnosed in the advanced stages and prognosis is generally poor when the tumor is unresectable. Transarterial chemoembolization (TACE) is the recommended treatment for patients with advanced and unresectable HCC, which uses radiological techniques to block a hepatic artery in combination with the administration of chemotherapeutic agents (most often with doxorubicin and cisplatin) mixed with lipiodol (an oily contrast agent)[4]. Injection through a catheter is done through the hepatic artery directly into the tumor. Subsequently, the artery will be blocked or embolized with a gelatin sponge or other occluding agents. This renders the tumor ischemic, depriving it of nutrients and oxygen, and resulting in a temporary decrease in tumor growth. However, TACE can often lead to several undesirable symptoms including pain, fever, abdominal discomfort, nausea, and vomiting[5,6].

Patients with cancer often experience multiple concurrent symptoms which derived from the disease itself or the treatment side-effects. Those simultaneous symptoms can be categorized in groups or clusters, named "symptom cluster"[7-10]. Symptoms in the same cluster tend to amplify one another. Specifically, when one symptom becomes severe, other symptoms in the cluster are also exacerbated[7,8]. For example, in the symptom clusters of "pain, fatigue, and nausea," the pain could be perceived considerably worse in the presence of fatigue or nausea; in the presence of both symptoms, the pain could be proportionally more severe[11]. Consequently, cancer patients often suffer symptom clusters that caused all types of discomfort which affect physical, mental, emotional, social, and spiritual functions. These HCC in turn, lead to a reduced quality of life for the patient[12,13].

Currently, non-pharmacological interventions have been introduced to address the symptoms experienced by cancer patients and to reduce complications caused by treatment side effects[14]. Progressive muscle relaxation (PMR) is one aspect of non-pharmacological interventions that have been used in cancer patients with encouraging results. This method is based on the mind-body treatments and the control of muscles via the mind to relax the body[15-17]. This method is relatively simple and convenient and can be performed at any time by the patient with little complications. It requires no special equipment and can be done in as little as 15-30 minutes to achieve the desired effects.

Previous studies have focused on examining a single symptom rather than symptom clusters, which is more complicated to assess. At the present, limited knowledge is available on the characterization of symptom clusters, especially among liver cancer patients in Thailand.

Study purpose

The primary aim of this study was to investigate the symptom clusters among Thai HCC patients undergoing TACE. As the secondary intention, the researchers preliminarily evaluated the effects of non-pharmacological interventions using PMR in managing those symptom clusters.

Methods

Research design and participants: This is a descriptive study of one group pre- and post-test design. Participants were HCC patients who first underwent TACE at a university hospital in northern Thailand between September 2015 and April 2016. Patients who met the following inclusion criteria were invited to participate in this study: 1) older than 20 years, 2) able to speak and understand the Thai language, 3) willing to participate in this study, and 4) received permission from their doctors to participate. For this study, the researchers analyzed the data from 30 patients. The study was approved by the Institutional Review Board of the Faculty of Nursing, Chiang Mai University.

Instruments: The research instruments consisted of 1) A short questionnaire was designed for this study to obtain information on the patient demographics (age, gender, religion, education, and PMR experience) and clinical characteristics (months since diagnosis, Child-Pugh class, stage of HCC, and co-morbid diseases), 2) The Edmonton Symptom Assessment Scale-Thai version was used to assess patients' symptoms. Severity for each symptom 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 Cronbach's alpha in the validation of scale was 0.89[18], 3) Treatment log book designed by the researcher-Each participant was instructed to keep a log each time PMR was used by recording the time of day when using PMR and immediate pre- and post-treatment symptom severity using the log book scale, 4) A Manual on PMR, and 5) CD on PMR, CD player and earphones

Data collection: On the first day of the admission, a) the researcher introduced the purpose of the study to patients who were interested. Eligible patients provided signed written informed consent and retained a copy. The researcher then gathered the demographic data by interviewing patients; b) the researcher provided a manual on PMR and the entire PMR process was demonstrated using a CD player for about 25 minutes. Then, the participants were allowed to practice until they could do it correctly by themselves. The researcher demonstrated how to use the CD player and earphones, and participants gave return demonstration; c) the researcher taught the participants to keep a log each time PMR was used until each participant was able to correctly record in the treatment logbook on their own.

On the second day of inpatient status, a) the researcher met with the participants and inquired on any problems relating to using PMR and the log book. In addition, the researcher re-trained any participants who required repeated demonstration; b) the participants were advised to use the PMR technique at home and to record the severity of symptoms before and after PMR.

On the third day of inpatient status (the day of discharge), a) the researcher met with the participants and confirmed that after patient discharge the researcher would make follow-up phone calls within 48 hours to check on any concerns about using the PMR, operating the CD, or completing the logbook. A phone call would also be made every week until the participants return for follow-up by the 6-week period of their outpatient clinic visits.

At the 6-week outpatient clinic, the research team retrieved the CD player, earphones and log book. The participants were remunerated and received a new PMR CD as compensation for their time and effort.

Data analysis: Descriptive statistics were used to analyze personal characteristics. Symptom data based on severity ratings were examined using Exploratory Factor Analysis, and the varimax orthogonal rotation method was utilized for approximately multivariate normal data to assess covariance between symptoms. The number of factors (clusters) was determined based on an eigenvalue higher than 1.0. Additionally, Wilcoxon signed rank was used to determining the differences among pre- and post-test symptoms score. A p-value of <0.001 was considered statistically significant.

Results

Participants' characteristics: As shown in Table 1 and 2, participants ranged in age from 42 to 82 (M= 57.08, S.D.= 8.39). Most were male (83.33%), Buddhist (90.00%), and completed primary school (50.00%). None had previously experienced PMR. The majority of participants had intermediate stage HCC (93.33%) with Child-Pugh class A (93.33%). Time since being diagnosed with HCC was less than 6 months (56.67%), and all participants had pre-existing cirrhosis.

Symptom prevalence and severity: After TACE, the most frequently recorded symptom was the pain (81.58%), which included pain in the upper back (43.33%), abdomen (30.00%), lower back (16.67%),

Table 1 Demographic characteristics of patients (n=30).

Characteristic	n (%)
Age	
Mean (S.D.)	57.08 (8.39)
Range	42-82
Gender	
Male	25 (83.33)
Female	5 (16.67)
Religion	
Buddhist	27 (90.00)
Other	3 (10.00)
Education completed	
Primary school	15 (50.00)
Secondary school	7 (23.33)
College or more	8 (26.67)
Experienced in PMR	
Never	30 (100)

and shoulder (13.33%) (Table 3). Abdominal distention was also reported in some participants (23.33%). Most participants (70.00%) experienced multiple symptoms, while 6.67% reported none. Symptoms were considered significant when participants rated the severity of symptoms greater than 0 in the log book scale. The most severe symptom was lower back pain (4.72±0.82), followed by shoulder pain (4.45±0.65), upper back pain (4.33±0.45), abdominal distention (3.88±0.86), and abdominal pain (3.80±0.64).

Symptom clusters: Two symptom clusters were identified with 55.40% of the total variance explained. Three symptoms (abdominal distension, upper back pain, and shoulder pain) were loaded on Cluster 1, which explained 30.63% of the factor variance. Cronbach's alpha coefficient of 0.82 suggests that these symptoms within the cluster occurred at high rate with a homogenous pattern. Two symptoms (lower back pain, abdominal pain) were loaded on cluster 2, which explained 24.77% of the variance. For cluster 2, Cronbach's alpha coefficient was 0.61, which also indicated a homogenous group (Table 4).

The effects of PMR on symptom clusters severity:

Table 2 Clinical characteristics of patients (n=30).

Characteristic	n (%)
Stage HCC	
Intermediate	28 (93.33)
Advanced	2 (6.67)
Child-Pugh class	
A	28 (93.33)
B	2 (6.67)
Months since diagnosis	
<6	17 (56.67)
6-12	5 (16.67)
>12	8 (26.66)
Co-morbid disease	
Cirrhosis	30 (100.00)

Table 3 Symptom prevalence and severity (n=30).

Symptoms	Prevalence N (%)	Severity Mean (SD)
Upper back pain	13 (43.33)	4.33±0.45
Abdominal pain	9 (30.00)	3.80±0.64
Abdominal distension	7 (23.33)	3.88±0.86
Lower back pain	5 (16.67)	4.72±0.82
Shoulder pain	4 (13.33)	4.45±0.65
Total symptoms		
No symptoms	2 (6.67)	-
One symptom	7 (23.33)	-
Two or more	21 (70.00)	-

The changes in symptom ratings from pre- to post-PMR were significant (Table 5). Mean scores of cluster 1 decreased from 4.22 (S.D.= 0.30) pre-treatment to 3.00 (S.D.=0.66) post-treatment (Z= -6.84, p<0.001). The mean scores of cluster 2 decreased from 4.26 (S.D.=0.64) pre-treatment to 3.25 (S.D.=0.80) post-treatment (Z=-5.35, p<0.001).

Discussion

Results from this study showed that HCC patients undergoing TACE experienced multiple symptoms

Table 4 Factor matrix† with Component Loading Factors (n=30).

Symptoms	Cluster 1	Cluster 2
1. Abdominal distension	0.788	-
2. Upper back pain	0.708	-
3. Shoulder pain	0.618	-
4. Lower back pain	-	0.707
5. Abdominal pain	-	0.604
Cronbach's alpha	0.823	0.609
Eigenvalues	1.590	1.180
% of variance explained	30.63	24.77
% Total variance explained	30.63	55.40

† Principal components analysis with varimax rotation

Note: Cluster 1 = (abdominal distension, upper back pain, and shoulder pain)

Cluster 2 = (lower back pain, abdominal pain)

fever, nausea and/or vomiting[5,6], fatigue, dry mouth, and lack of appetite[20]. This current finding is consistent with a study of Jung and colleagues[21], which reported 66.7% of patients experienced pain after TACE. However, the participants in this study reported concurrent pain at multiple body sites. To our knowledge, there have been no published studies describing sites of pain in which HCC patients who underwent TACE manifest.

Additionally, the results indicated that HCC patients experienced at least two sites of pain, and two symptom clusters emerged from factor analysis. The main characteristics of Cluster 1 were abdominal distension, upper back pain, and shoulder pain. This presented cluster was associated with consequent symptoms of HCC disease, especially in intermediate and advanced stages.

The finding of Cluster 2 included symptoms of lower back and abdominal pain. It is possible that abdominal pain was recognized in a post-embolization

Table 5 Determination and comparison of the differences in the mean scores of symptom cluster severity before (pre-test) and after PMR (post-test).

Symptom	Experiment group (n=30)		Z (Wilcoxon signed rank test)
	Pre-test Mean ± SD	Post-test Mean ± SD	
Cluster 1	4.22 ± 0.30	3.00 ± 0.66	-6.84*
Abdominal distension	3.88 ± 0.86	2.52 ± 0.72	
Upper back pain	4.34 ± 0.45	2.73 ± 0.33	
Shoulder pain	4.45 ± 0.65	3.75 ± 0.82	
Cluster 2	4.26 ± 0.64	3.25 ± 0.80	-5.35*
Lower back pain	4.72 ± 0.82	3.81 ± 0.60	
Abdominal pain	3.80 ± 0.64	2.68 ± 0.83	

*p<0.001

simultaneously. Significant pain was reported in the shoulder, upper and lower back, and in the abdomen. These findings were consistent with the literature and previous studies of HCC patients who received TACE. Such symptoms resulted from visceral involvement originating from the primary or metastatic lesion of the abdomen[19]. HCC patients may also manifest fatigue, loss of appetite, and ascites[20]. Moreover, following TACE, a post-embolization syndrome can occur in 80-90% of patients. It often involved abdominal pain, abdominal distension, low-grade

symptom because this treatment reduces the oxygen-rich blood supply to the tumor. Lack of oxygen causes pain in any tissue, while lower back pain may occur from positioning during the procedure and during bed rest after TACE[22].

This study also examined the effect of PMR on distressing symptom clusters of HCC patients undergoing TACE. Six weeks after TACE, symptom cluster levels were found to be markedly reduced with the use of PMR. This result may be explained based on the theory of the psycho-biological state.

PMR has been found to activate the parasympathetic nervous system and this can reduce blood pressure, heart rate, breathing, and even lower levels of anxiety and pain[8-10,17]. Progressive muscle relaxation has been used to reduce the number of symptoms in cancer patients, such as pain, fatigue, anxiety, nausea[12], and sleep disturbance[13]. Similarly, Gupta, et al[23] demonstrated that PMR was highly effective in reducing severe pain among cancer patients receiving chemotherapy. Our study showed a significant difference in the mean scores between pre- and post-PMR. Since all of our patients have cirrhosis, pain management with traditional analgesics such as NSAIDs will be contraindicated due to the increased risk for renal failure and GI bleeding. Fortunately, participants in this study reportedly experienced mild pain level, therefore non-pharmacological intervention such as PMR may be particularly useful.

This study has several limitations. First, the patient sample size was relatively small, homogeneity and was derived from only one hospital, thus the results may not be generalizable to all HCC patients undergoing TACE. Larger future studies will be needed to clarify the difference in symptom clusters among those patients. Second, the study used a one group pre- and post-test design. Additional studies with randomized controlled trials will be required since they are the gold standard in providing clinical evidence to determine the true relative efficacy of an intervention.

Conclusion

This study demonstrated that there are two symptom clusters in HCC patients who underwent TACE, and PMR technique was effective in reducing those symptom clusters. The findings of this study suggests positive outcomes from the use of PMR among HCC patients undergoing TACE to minimize their symptom clusters.

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