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Can Progressive Muscle Relaxation (PMR), as an adjunctive therapy, effectively reduce depression symptoms in cancer patients?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

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ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether or not Progressive Muscle Relaxation (PMR) is an effective adjunctive therapy in reducing depression symptoms in cancer patients.

STUDY DESIGN: Systematic review of three randomized controlled trials (RCTs), one being modified and used a case series, from peer reviewed journals, published in 2015, 2016 and 2018.

DATA SOURCES: The studies compare the effectiveness of PMR versus other therapies such as routine nursing care and weekly visits with psychologists. All studies were found using PubMed and Cochrane Library.

OUTCOMES MEASURED: Depression symptoms perceived by the patient and measure by the Zung self-rating depression scale, Beck Depression Inventory and Hospital Anxiety and Depression scale.

RESULTS: In the single-blind RCT conducted by Charalambous, et al., there was a reduction of depression symptoms with a mean change in baseline of 7.7. These results were statistically significant with a p-value of <0.0001. In the RCT, being used as a case series, conducted by Liao et al., there was a reduction of depression symptoms with a mean change in baseline of 2.86. These results were statistically significant with a p-value of <0.05. In the single-blind RCT conducted by Zhou et al., showed a statistically significant decrease in posttest depression symptoms with a p-value <0.0001 and an F score of 20.31.

CONCLUSION: The three studies in this systematic review showed a statistically significant decrease in depression symptoms in the cancer patients studied; however, the results remain inconclusive as they could be skewed by the adjunct therapies of music listening and guided imagery. Further research needs to be conducted in order to prove the effects are truly from PMR as an adjunct, such as using PMR and music therapy or guided imagery as the treatment group, and music therapy or guided imagery alone as the control group.

KEYWORDS: Progressive Muscle Relaxation, Cancer, Depression

INTRODUCTION

Cancer is an unregulated division of cells in tissues that have the ability to invade surrounding tissues and organs and metastasize to other areas in the body. Cancer does not only impact the body physically but can have a profound impact mentally and emotionally. Along with many other risk factors, those who undergo a significant life event, such as a cancer diagnosis, are at high risk for developing depression.[1,2]

As life expectancies continue to grow, cancer rates will concomitantly rise as well. In 2020, approximately 1.8 million people will be diagnosed with cancer in the United States and 606,500 will die because of this disease.[1] Due to the various types of cancer, mortality rates and age distributions, depression rates among cancer patient are difficult to define. However, one study showed that about 15-25% of patients with cancer will experience depression.[3] Cancer patients suffering with depression accumulate 113% more health care charges yearly compared to patients without depression.[4] It is difficult to accurately identify how many health care visits patients with cancer and depression accrue, but in 2016, cancer accounted for 24.7 million healthcare visits and 9.3% of patients had a depression diagnosis on their medical chart. [5]

Depression does not discriminate and can virtually affect anyone. There are no discrete criteria regarding who it affects, however, there are conditions that may predispose an individual. Family history, significant life events, environmental factors such as socioeconomic status or child abuse, personality types and alterations in brain chemistry are risk factors for depression. Depression is not just being sad or down, but a coalition of symptoms that affects how one thinks, lives and makes decisions. The gold standard of treatment for depression is the use of selective serotonin reuptake inhibitors (SSRIs).[6] Among these are escitalopram, sertraline, fluoxetine, citalopram and paroxetine. Selective norepinephrine reuptake inhibitors (SNRIs),

tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs) and bupropion are other medications used if there are contraindications to SSRIs.[6] Cognitive behavioral therapy (CBT) is often used in conjunction with medications, focusing on a problem-solving approach.[6] In refractory depression, electroconvulsive therapy (ECT) can be used.[6]

Progressive muscle relaxation (PMR) is an adjunctive therapy often used to cope with mental health symptoms.[7] It works by alternatively tensing and relaxing certain muscle groups in hopes that patients will benefit by acknowledging when they are in certain situations that make them tense and relax accordingly.[7] PMR is being further investigated in cancer patients due to the fact that in prior research, this population has had improved mental health symptoms with the use of psychological intervention.[8]

OBJECTIVE

The objective of this selective evidence-based medicine (EBM) review is to determine whether PMR is an effective adjunctive therapy in reducing depression symptoms in cancer patients.

METHODS

The clinical question posed sought to investigate PMR; therefore, PMR with either GI, CM or music listening used by primary researchers were considered for this review. The intervention method in this study was PMR with Guided Imagery (GI) or Chinese Medicine five element music (CM) or music listening, in comparison to routine nursing care, and weekly meetings with the health center psychologist. Improvement in depression symptoms based on their severity of symptoms at baseline and after treatment were determined for effectiveness of therapies. The studies selected for this systematic review consisted of three RCTS, with Liao et

al. being used as a case series, to investigate the effect of PMR on depression symptoms in cancer patients.

The three articles included were peer reviewed and published in journals using the following databases: Cochrane Library and PubMed. The keywords used to search articles pertaining to the topic were PMR, cancer, depression, RCT and all articles were published in English. These articles were selected based on their relevance to the topics and patient oriented evidence that matters (POEMs). The criteria of the articles researched included RCTs, English and human studies and excluded animal studies and children's studies. The summary of statistics was reported using an F score and the mean change from baseline. The demographics and characteristics of each study is shown in Table 1.

OUTCOMES MEASURED

The outcome of depression symptoms was measured by three separate entities. The Beck Depression Inventory-II (BDI-II) is a 21 item self-report measure on scale of zero (no depression symptoms) and three (severe depression symptoms).[7] A score of 0-13, 14-19, 20-28 or greater than 29, suggest minimal, mild, moderate and severe depression respectively.[7] The Hospital Anxiety and Depression scale (HADS) is a seven-question survey with answers ranging from zero to three.[8] A score of 0-7, 8-10, or 11-21 indicate no depression, borderline and depression respectively.[8] Lastly, the Zung Self-Rating Depression Scale (ZSDS), a 20 item self-report measure on a scale of zero (no depression symptoms) and four (severe depression symptoms).[9] A score of below 50, 50-59, 60-69 and greater than 70 indicate no depression, minimal to mild, moderate to marked and severe to extreme depression respectively.[9]

RESULTS

A single blinded RCT was conducted in the country of Cyprus by Charalambous et al., where 236 participants were randomly assigned by a 1:1 ratio to a control group or an intervention group.[7] Participants included in this study were over 18 years of age with an active breast or prostate cancer diagnosis and were receiving chemotherapy. Further inclusion and exclusion criteria are mentioned in Table 1. Out of the 236 participants, 208 completed the study.

Table 1. Demographics and Characteristics of Included Studies

Study	Type	# Pts	Age	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Charalambous, et al. 2016[7]	RCT	236	>18 yrs old	Dx of breast or prostate CA, receiving chemo, experiencing fatigue, pain, N/V, depression or anxiety	Patients with visual/hearing/ cognitive impairment, xerostomia and/or oral mucositis	28	4 weekly supervised and daily unsupervised sessions of PMRT
Liao et al. 2018[8]	RCT (using as case series)	30	> 18 yrs old	Pts histologically and cytologically confirmed as cancer regardless of tumor type/disease staging HADS score between 7-15 Primary school education and Karnofsky performance status no less than 60	Patients with psychiatric disease, intellectual disability or deafness and expected survival <3 months	1	20 minutes of PMRT followed by 20 minutes of CM five element music
Zhou et al. 2015[9]	RCT	170	25-65 yrs old	Female, Dx of breast cancer with arranged radical mastectomy	Patients with voice sensitive epilepsy, not preferred to music listening or refused to give written consent	0	PMRT for 30 minutes once in the morning and once at nighttime until discharge

Participants in the intervention group, received four weekly supervised and daily unsupervised sessions of PMR followed by a guided imagery session (GI) and a control group, who had weekly meetings with the health center psychologist.[7] Patients were assessed at baseline and the end of four weeks using the Beck Depression Inventory-II (BDI-II) scale.[7]

After four weeks of treatment, the mean change from baseline in the intervention group was 7.7 with a p-value of <0.0001.[7] Shown in Table 2 below, patients in the intervention group mean baseline score on the BDI-II was 27.3 ± 7.6, while the mean follow up score was 19.6 ± 8.6. In comparison, patients in the control group saw a mean change in baseline of -7.0 with a p-value of <0.0001.[7] In accordance with the BDI-II, 35 patients in the intervention group were classified as moderately depressed at baseline.[7] This number decreased to 15 patients following the four weeks of intervention.[7] In comparison, the incidence of moderate depression increased by 42% in the control group, p-value 0.02.[7] These results show a statistically significant decrease in depression symptoms with the use of PMR followed by GI.[7] There was no mention of adverse events occurring in this study.

Table 2. BDI-II Mean ± SD Change in Depression Symptoms at Baseline and 4 Weeks Post-Intervention Between Control and Intervention Groups (Charalambous et al. 2016[7])

	Baseline	**Post-Intervention**	**Δ**	**p-value**
PMR + GI	27.3 ± 7.6	19.6 ± 8.6	7.7 ± 6.9	<0.0001
Psychologist	28.2 ± 9.4	35.2 ± 12.0	-7.0 ± 7.8	<0.0001

A second study was conducted in two hospitals in Beijing, China by Liao et al. Thirty participants were assigned to a treatment group. One participant was lost to follow up. Refer to the methods section regarding the use of this RCT as a case series.[8] Participants were required to be over 18 years of age, have an active cancer diagnosis, primary school education, and a Karnofsky Performance Status score of no less than 60.[8] Further inclusion and exclusion criteria are mentioned in table 1. The intervention group received 20 minutes of PMR followed by 20

minutes of Chinese Medicine Five Element Music.[8] The group was then assessed at baseline and after eight weeks of therapy using the Hospital Anxiety and Depression Scale (HADS).[8]

After eight weeks of treatment, the mean change from baseline was 2.86 with a p-value of <0.05.[8] Demonstrated in Table 3, patients initially scored 6.55 ± 3.08 on the HADS at baseline and decreased to 3.68 ± 1.97 after eight weeks.[8] The use of PMR and CM showed a statistically significant decrease in depression scores after eight weeks of treatment in comparison to baseline.[8] There was no mention of adverse events occurring in this study.

Table 3. Hospital Anxiety & Depression Scale Mean ± SD Change in Symptom Scores at Baseline and at 8 Weeks of Treatment (Liao et al. 2018[8])

	Baseline	8 Weeks	Δ	p-value
PMR + CM	6.55 ± 3.08	3.69 ± 1.97	2.86	<0.05

Zhou et al. conducted a single-blind RCT in Xi'an, China, in which 170 participants were randomly assigned to a control group or an intervention group and all of them completed the study.[9] To be included in this study, participants required an active breast cancer diagnosis and have undergone radical mastectomy. Further exclusion criteria are mentioned in table 1. Participants in the intervention group simultaneously received PMR and music listening for 30 minutes in the morning, and 30 minutes at night.[9] Patients in the control group received routine nursing care which included vital signs, tube drainage, functional exercise on the side of surgery, and post op complication monitoring.[9] Patients were assessed using the Zung Self-Rating Depression Scale (ZSDS) at baseline and post mastectomy, until discharge from the hospital.[9]

After treatment, the control groups pretest depression scores decreased from 38.01 ± 6.65 to posttest depression scores of 33.40 ± 5.30.[9] For the intervention group, the pretest depression scores decreased from 37.47 ± 5.66 to posttest depression scores of 30.21 ± 3.3.[9] The PMR with music listening showed a statistically significant decrease in depression symptoms with a p-value

of 0.001 (Table 4).[9] With this data, an F score was calculated as 20.31.[9] There was no mention of adverse events occurring in this study.

Table 4. Comparison of Pre-test and Post-Test Depression Scores on the Zung Self-Rating Depression Scale Between Intervention and Control Groups (Zhou et al. 2015[9])

	Pre-test	Post-test	F Score (Univariate analysis)	P-value
PMR + Music	37.47 ± 5.66	30.21 ± 3.31	20.31	<0.001
Nursing Care	38.01 ± 6.65	33.40 ± 5.30		

DISCUSSION

Though there have been outstanding improvements in diagnosing and treating cancer, it is still a deadly disease that has a profound impact both physically and mentally. It requires many visits to healthcare offices and hospitals which can eventually take a toll on patients. This three-study systematic review evaluates the efficacy of PMR as an adjunctive therapy in hopes to reduce depression symptoms in cancer patients. As mentioned above, PMR aims at reducing tension throughout the body by contracting and then relaxing certain muscle groups in order, which aims at reducing mental health symptoms.[7] Charalambous et al. and Liao et al. demonstrated a decrease in depression symptoms with a mean change in baseline of 7.7 and 2.89 respectively.[7,8] Both studies showed statistical significance with p-values of <0.0001 and <0.05 respectively.[7,8] Zhou et al. utilized a general linear model with univariate analysis and calculated a statistically significant F score of 20.31 ($p<0.001$) which showed a statistically significant decrease in the intervention group compared to the control group.[9] Although these three studies had a statistically significant reduction in depression symptoms, it is not clear whether PMR directly played a role in this reduction.

The three studies in this review had numerous limitations. In Charalambous et al., creating a double-blind study was not possible due to the techniques of using PMR and GI. During the unsupervised sessions, researchers were not confident that patients were in an

environment free of external stimuli or completed the full sessions.[7] This study took place in the country of Cyprus and consisted of only breast and prostate cancer patients which limits the generalizability. In Liao et al., the absence of a control group and small sample size of patients, 29, limited the study. The generalizability was also limited due to one of the two hospitals used in this study, being a geriatric hospital. Finally, the study conducted by Zhou et al, did not contain the physiologic data regarding depression and the reduction in symptoms may have been attributed to increased attention towards the intervention group.[9] Furthermore, the generalizability of the study was low due to its location in only one province in China, and all participants being female with breast cancer after radical mastectomy.

As therapies continue to improve and life expectancies rise, cancer rates will increase as well along with the myriad of symptoms cancer entails, such as depression. PMR is a technique that was developed in the 1920s, initially for anxiety, but its indications have expanded greatly since its birth.[10] It is a form of therapy that focuses on the voluntary and thoughtful contraction and subsequent relaxation of 14 different muscle groups.[10] The aim of this therapy is to teach the patient to recognize situations when they are tense and to relax accordingly, leading to the improvement of their mental health.[10] PMR is a technique that takes practice and may not yield results immediately. When recommending PMR to patients, it is important to assess their motivation to determine whether PMR may benefit them.

CONCLUSION

The aim of this systematic review was to determine whether PMR is effective as an adjunctive therapy in reducing depression symptoms in cancer patients. Based on the analysis of the three studies, the results of this review are inconclusive. Although the groups treated with PMR as an adjunct showed a statistically significant reduction in depression symptoms[7,8,9], it

cannot be determined if PMR played a part in this reduction. In order to further evaluate the efficacy of PMR, more specific studies should be conducted evaluating PMR as an adjunct. For example, using PMR paired with music therapy or guided imagery as the treatment group, and music therapy or guided imagery alone as the control group. By doing this, we will be able to further evaluate the effect PMR plays in reducing depression symptoms. Furthermore, increasing sample sizes, extending treatment time, and ensuring the quality of the PMR may help to strengthen the validity of future studies. Cancer is a devastating disease that can profoundly impact one's mental health and using adjunctive therapies such as PMR may help alleviate some of these symptoms which in turn, will improve patient's lives.

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