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Progressive muscle relaxation as a supportive intervention for cancer patients undergoing chemotherapy: A systematic review

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ABSTRACT

Background: Many cancer patients use a wide variety of techniques to improve their physical and mental well-being, including relaxation therapy and, specifically, Progressive Muscle Relaxation (PMR). However, there is no strong evidence that supports the efficacy of this technique.

Objective: Our aim was to review the evidence regarding the use of PMR as a supportive intervention for cancer patients undergoing chemotherapeutic treatment.

Method: Six databases were electronically searched: AMED, the Cochrane Library, MEDLINE, PsychINFO, Scopus, and the Web of Science. After removing duplicates, 700 publications were screened and 57 identified as potentially relevant. The flow of information from record identification to study inclusion was conducted in accordance with the PRISMA statement. Original articles published in peer-reviewed journals that studied the use of PMR as an intervention, were randomized or included a matched control group, and that included patients receiving chemotherapy were included. Studies that combined PMR with other interventions were excluded. The methodological quality of included trials was assessed using the Jadad Scale and the CONSORT guidelines.

Results: A total of 5 of the 57 papers fulfilled the preset criteria and were included in our systematic review. Our findings indicate that PMR might improve comfort and reduce the anxiety levels and side effects caused by chemotherapy, with the exception of vomiting. Nonetheless, the quality of all the included studies was extremely low.

Significance of results: There is evidence that PMR might have a few benefits for patients undergoing chemotherapy. Still, the small number of studies included and their poor quality limit the significance of our results. Despite the fact that pharmaceutical approaches for controlling side effects might be reaching their full potential and that there might be further usefulness for such integrative treatments as PMR, the need to run more high-quality trials testing the efficacy of this technique is warranted before suggesting its adoption as part of standard cancer care.

KEYWORDS: Anxiety, Cancer, Chemotherapy, Progressive muscle relaxation, Side effects

INTRODUCTION

Due to its high incidence, cancer poses a major threat to most parts of the developed world, including the European Union, the United States, Canada, Australia, and Japan (Australian Institute of Health and Welfare, 2013; Ferlay et al., 2013; Katanoda et al., 2015; Kachuri et al., 2013; Siegel et al., 2016), while less-developed countries are also threatened by increasing cancer rates (Jemal et al., 2010). A global outburst of this cancer epidemic is expected by 2030, almost doubling new disease cases based on

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2008 statistics (Bray et al., 2012). Therefore, cancer should be regarded as a worldwide public health hazard.

Thanks to earlier diagnosis and advancements in the field of chemotherapy, this increased incidence has been countered by prolonged survival of cancer patients (DeVita & Chu, 2008). Nevertheless, patients receiving chemotherapeutic treatment are threatened by such disturbing side effects as nausea and vomiting (Mustian et al., 2011) and cognitive impairment (Moore, 2014), as well as such common mental disorders as anxiety, depression, and sleep disorders, triggered by both the disease and the applied therapies (Dickerson et al., 2014; Die Trill, 2013; Nakash et al., 2014). There is thus an urgent need to intervene in order to address these patients' needs.

Many cancer patients hoping to improve their physical and mental well-being employ complementary and alternative medicine (CAM). Relaxation therapies are one of the most common CAM techniques used (Huebner et al., 2014; Molassiotis et al., 2005). Most of the patients practicing relaxation therapies start after being diagnosed (Molassiotis et al., 2005). Progressive muscle relaxation (PMR) is a CAM intervention (Park et al., 2013) that includes repetitive cycles of tensing and relaxing of major muscle groups combined with breathing exercises (Jacobson, 1938).

Regarding the effect of PMR in noncancer patient populations, there is evidence from several systematic reviews suggesting that it is an effective technique. For example, it has been shown to decrease elevated blood pressure (Rainforth et al., 2007), to manage the pain of osteoarthritis (Morone & Greco, 2007), and to improve the mental state and subjective well-being of persons suffering from schizophrenia (Vancampfort et al., 2013). Additionally, PMR has demonstrated efficacy in decreasing depressive and anxiety symptoms in the general population (Jorm et al., 2008; Manzoni et al., 2008).

To date, the effects of this intervention on cancer patients receiving chemotherapy have been reported in a few sporadic publications. A recent case study found that the development of panic disorder in a 54-year-old breast cancer patient receiving eight cycles of adjuvant chemotherapy was blocked by the practice of PMR (Koumarianou et al., 2015). According to a bold study comparing two different interventions to counter anxiety and depression, the efficacy of PMR was found to be almost equivalent to receiving 0.5 mg of the triazolobenzodiazepine alprazolam three times daily (Holland et al., 1991). Despite these data, the appropriate way to come to a conclusion about a treatment's efficacy is to test an intervention condition against a control by applying a randomized trial, or even by using well-formulated and matched subject groups (Robson, 2002).

The present study evaluates the efficacy of PMR in improving the mental and physical well-being of cancer patients receiving chemotherapeutic treatment by reviewing all the relevant PMR trials.

METHODS

Registration

Our systematic review was registered in the PROSPERO database (registration no. CRD42016043111). There were no violations of the original protocol during any stages of the research.

Literature Search

All three authors participated in the literature search process. A search for English-language papers published from January of 1990 until July 3, 2016 was carried out in AMED, the Cochrane Library, MEDLINE, PsychINFO, Scopus, and the Web of Science databases. The combinations utilized were "progressive muscle relaxation" AND (cancer OR oncology OR chemotherapy). In addition, a snowball technique was employed in order to include any potential studies not revealed through this process. Issues of related journals, reference lists of included studies, and other relevant papers in the field were rummaged through in an attempt to locate possible records. The flow of information from record identification to inclusion followed the principles of the PRISMA statement (Moher et al., 2009).

Study Selection

Regarding study selection, the inclusion criteria were as follows: (1) original articles published in peer-reviewed journals; (2) two-arm trials with matched or randomized intervention and control groups; (3) using only PMR as an intervention; and (4) including cancer patients currently receiving chemotherapeutic treatment. The exclusion criteria were as follows: studies combining PMR with other interventions (e.g., psychoeducation). Identified abstracts were stored using Zotero reference management software. All authors participated in the study selection process.

Data Extraction

The extracted data from these papers included: study authors, country, total number of patients, patient gender, primary tumor, duration of PMR sessions, duration of the intervention, frequency of practice, average adherence rate, follow-up, variables

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examined, measures used, main findings, and qualitative reports.

The quality of trials was estimated by using the Jadad Scale and the CONSORT guidelines. The Jadad Scale is a brief (score range = 0–5 points) instrument used to rate the quality of a trial (Jadad et al., 1996). Randomization and double blinding were given two points each, while reporting withdrawal and dropout reasons received a single point. The CONSORT statement is a checklist including a variety of items concerning the quality of each separate section of a published trial (Schulz et al., 2010) (see Appendix I).

Both the data extraction process and trial evaluation were carried out by the first author and cross-checked by the second author. Disagreements were resolved through discussion or with the help of the third author.

RESULTS

The literature search conducted led to 700 unique potentially relevant records, of which 643 were not searched since their title was irrelevant to the scope of the specific systematic review, so that 57 abstracts were accessed.

As for the 57 studies whose abstracts were accessed, most did not meet the eligibility criteria of the systematic review: 4 were not in peer-reviewed journal publications, 14 used PMR along with another intervention, 11 included no cancer- nor chemotherapy-related populations, 21 were not two-armed trials with matched or randomized intervention and control groups, and 2 did not use PMR as an intervention. Therefore, five studies were finally included in our systematic review (Arakawa, 1995; 1997; Demiralp et al., 2010; Song et al., 2013; Yilmaz & Arslan, 2015). The information flowchart is depicted in Figure 1.

Four of these studies were randomized controlled trials (Arakawa, 1995; 1997; Demiralp, 2010; Yilmaz & Arslan, 2015), while one used matched subjects (Song et al., 2013). The participants in all studies were measured at baseline, those in the intervention group were provided with a PMR session practiced during the full length of follow-up, and all were measured during an endpoint assessment. In total, 255 patients were analyzed. Apart from the large range of sample sizes (8–100), there was also a discrepancy across studies regarding their specific characteristics (e.g., the measures used). These characteristics are detailed in Table 1.

The quality of trials was found to be low since four out of five of the studies were given a rating of zero points on the Jadad Scale (Arakawa, 1997; Demiralp, 2010; Song et al., 2013; Yilmaz & Arslan, 2015), while one was rated 1 due to reporting of participants' reasons for dropping out (Arakawa, 1995). The appraisal using the CONSORT guidelines also found a low trial quality (see Appendix I). As indicated, there were several weak points, such as not describing the mechanism used to implement random allocation and research blinding (in all trials) and sample size determination (in four of five trials).

Due to the small number of included studies, their small sample sizes, and their heterogeneity regarding several characteristics (tumor type, gender, measures used, and outcomes assessed), pooling of results was not considered to be a wise option. Thus, all five eligible studies are presented narratively in the following section.

Summaries of Included Studies

Arakawa (1995) examined the effects of PMR in a sample with various primary tumors. Sessions included tense/release of 16 muscle groups and deep breathing (for a total of 15 minutes) twice a day. Anxiety and side effects were recorded before and after chemotherapy using the State–Trait Anxiety Inventory (STAI) and the Morrow Assessment of Nausea and Emesis, respectively. Eight patients completed the endpoint assessments. The average adherence rate of the practice reached 98%, recorded by the investigator through direct observation of each individual practicing the technique once a day. The frequency and duration of nausea and state anxiety were decreased in the intervention group, while vomiting and trait anxiety were unaffected. With regard to self-reports in that group, they recounted being able to eat more and maintain a more optimal mobility level at the last chemotherapy session compared to the previous one.

The second trial (Arakawa, 1997) tested the effectiveness of the same intervention in a larger sample of patients ($N = 60$) diagnosed with different tumor types and receiving a variety of different chemotherapeutic agents and antiemetics. Intervention group participants were advised to practice a 25-minute PMR session twice a day, while control group participants were contacted for 10–15 minutes daily in an attempt to equalize the placebo effect. The average adherence rate reached 85.8%, recorded by the investigator through direct observation of each individual practicing the technique once a day. Assessments were carried out one week before initiation of their initial course and 72 hours after receiving the standard chemotherapy treatment. As measured by the STAI and the Rhodes Index of Nausea and Vomiting–Form 2, both scores were significantly reduced in the intervention group. However, subscale analyses indicated that vomiting was not significantly decreased, possibly due to the extremely low incidence in both groups.

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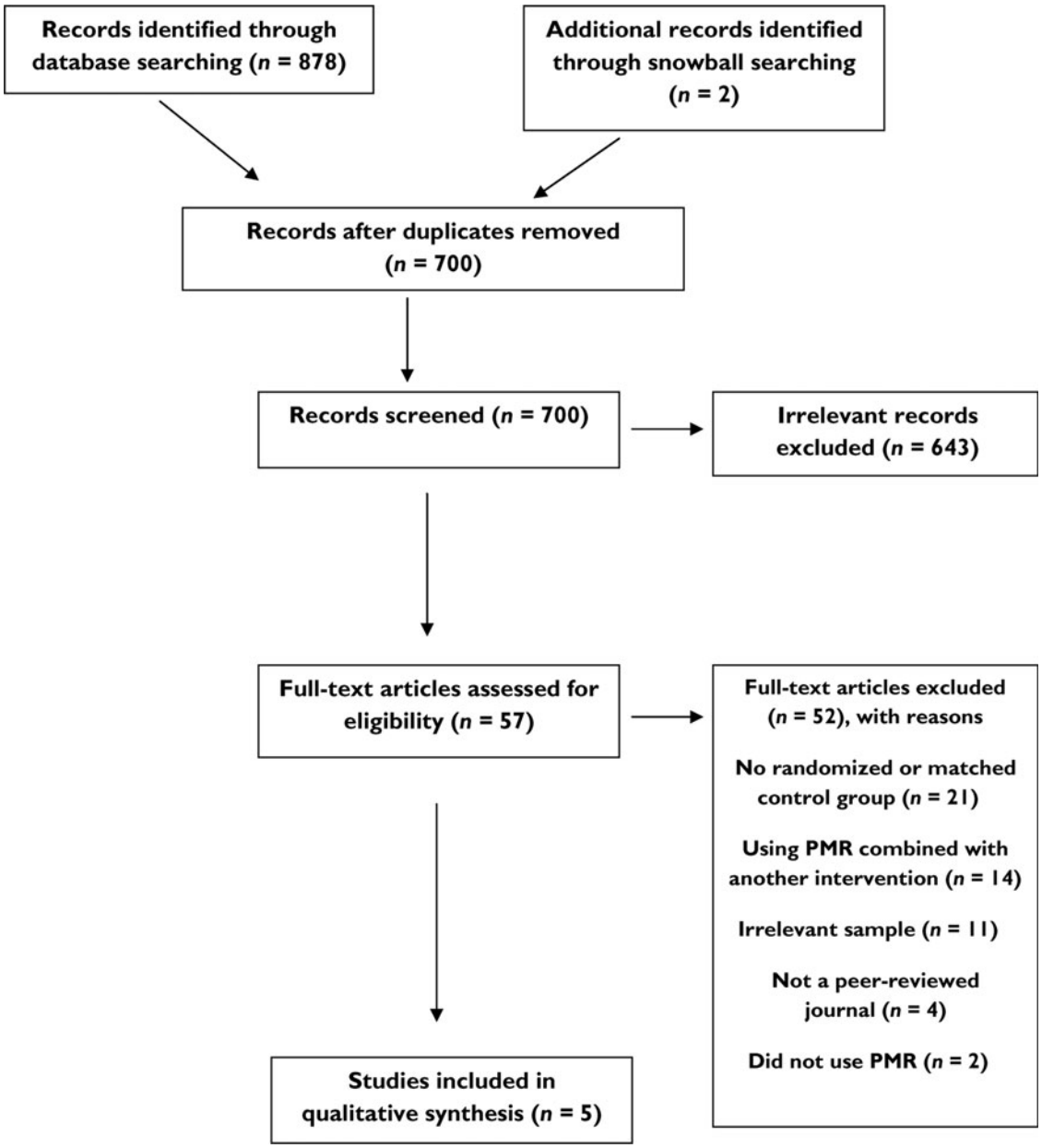

Fig. 1. Information flowchart

The third study (Demiralp et al., 2010) reported a prospective repeated-measures randomized trial with 27 total participants (intervention group, $n = 14$; control group, $n = 13$). Patients in the intervention group were assigned a 25- to 30-minute PMR session and were advised to practice this technique on a daily basis. Four repeated measures from day 1 until day 90 after the beginning of chemotherapy were used. The Pittsburgh Sleep Quality Index and the Piper Fatigue Scale (PFS) were utilized to measure sleep quality and fatigue, respectively. The results indicated that overall sleep was improved in the third and fourth measurements and that several subcomponents of sleep quality (e.g., habitual sleep efficiency) were improved in some post-intervention measurements. Similarly, the PFS score was also reduced in the intervention group ($p = 0.014$).

The fourth study (Song et al., 2013) examined the effects of PMR on 100 female breast cancer patients receiving chemotherapy. Patients were divided into two equal-sized groups matched by age, level of education, and tumor stage. The STAI, the Rotterdam Symptom Scale, and self-reported symptoms were employed to assess severity of anxiety, cancer discomfort, and chemotherapy-related symptoms,

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Table 1. *Extracted data*

Study	Country	Total *N*	*n* Gender	Primary tumor	Duration of PMR session	Duration of intervention	Frequency of Practice	Average adherence rate	Follow-up	Variables examined	Measures used	Main findings	Qualitative reports
Arakawa (1995)	Japan	8	4 males/ 4 females	Various types	15 minutes	Unknown	Twice a day	98%	Unknown	Anxiety, nausea, and vomiting	STAI, Morrow Assessment of Nausea and Emesis	Decrease of state anxiety, reduction of nausea	Improved mood, appetite, and mobility
Arakawa (1997)	Japan	60	36 males/ 24 females	Various types	25 minutes	72 hours	Twice a day	85.8%	72 hours after treatment	Anxiety, nausea, and vomiting	STAI, Rhodes Index of Nausea and Vomiting–Form 2	Anxiety and nausea reduction, vomiting wasn't reduced	NA
Demiralp et al. (2010)	Turkey	27	Females	Breast cancer	25–30 minutes	90 days	Everyday	Unknown	4 repeated measures from day 1 to day 90 after start of chemotherapy	Sleep quality, fatigue	Pittsburgh Sleep Quality Index, Piper Fatigue Scale	Sleep quality improve-ment, decrease of fatigue	NA
Song et al. (2013)	China	100	Females	Breast cancer	Unknown	Full duration of adjuvant chemotherapy	Unknown	Unknown	After chemotherapy	Cancer discom-fort, anxiety, side effects	Rotterdam Symptom Scale, STAI, self-reported side effects	Cancer discom-fort, side effects, and anxiety reduction	NA
Yilmaz & Arslan (2015)	Turkey	60	Females	Breast cancer	Unknown	3 weeks	3 times per week	Unknown	After 3 weeks	Cancer discom-fort, anxiety	General Comfort Questionnaire, STAI	Cancer discomfort and anxiety reduction	NA

N = number of patients; NA = not applicable; PMR = progressive muscle relaxation; STAI = State–Trait Anxiety Inventory.

respectively (loss of appetite, lack of energy, nausea, acid reflux, mouth ulcers, cough, and back pain). All of these scores were significantly lower in the intervention group after practicing the technique.

The final trial (Yilmaz & Arslan, 2015) examined the effects of the technique on 30 experimental and 30 control patients. The intervention group took part in four supervised sessions and were provided with a CD to help them practice the technique on their own three times a week, as suggested. The pre- and posttest outcomes were anxiety (measured by the STAI) and cancer discomfort (assessed by the General Comfort Questionnaire). While patients did not differ regarding these variables at baseline, both anxiety ($p > 0.0001$) and general comfort ($p > 0.0001$) were reduced in the intervention group after practicing the technique.

DISCUSSION

The present systematic review is the first study in the literature that clearly focuses on the effect of PMR in cancer patients undergoing chemotherapy. Its findings indicate that this technique may decrease a variety of side effects (including nausea), improve sleep quality, reduce anxiety levels, and provide a few additional episodic benefits (e.g., amelioration of diet) (Arakawa, 1995; 1997; Demiralp et al., 2010; Song et al., 2013; Yilmaz & Arslan, 2015). Three of the included studies concerned breast cancer patients (Demiralp et al., 2010; Song et al., 2013; Yilmaz & Arslan, 2015), while the other two looked at mixed cancer populations (Arakawa, 1995; 1997). As indicated in Table 1, with the exception of the STAI being used in three trials (Arakawa, 1995; 1997; Yilmaz & Arslan, 2015), there was heterogeneity of self-reporting tools, which resulted in no directly comparable results. Apart from the study by Song et al. (2013), in which 100 patients were included, the remaining studies had a relatively small sample size (Arakawa, 1995; 1997; Demiralp et al., 2010; Yilmaz & Arslan, 2015). Even though extracting data from available trials is important, it could be considered worthless if this evidence is not further analyzed. In that context, several parameters of the specific systematic review results are narratively discussed in the following subsections.

Feasibility

As reported in the studies included in our systematic review, PMR has been shown to be a feasible intervention. Participant adherence was measured in only two of the included trials, where the average adherence rates were 98 and 85.8%, respectively (Arakawa, 1995; 1997). The high adherence rates reported could be attributed to the cultural characteristics of the patients included in those two trials, which could influence adherence to health professionals' guidelines. In addition, the high acceptance of CAM therapies by cancer patients in Japan might have influenced this high adherence rate (Eguchi et al., 2000; Hyodo et al., 2005). As to adverse events, no side effects related or possibly caused by practicing PMR were reported in any of the included trials (Arakawa, 1995; 1997; Demiralp et al., 2010; Song et al., 2013; Yilmaz & Arslan, 2015). Even though there is no solid evidence from well-designed clinical studies that practicing PMR has its hindrances, it is logical to assume that the absence of side effects and the relatively high adherence rate make PMR a feasible intervention for cancer patients undergoing chemotherapeutic treatment.

Comparison with Similar Scoping Interventions

The evidence of our paper highlights the potential efficacy of PMR in countering anxiety and some chemotherapy-related side effects. Even though advanced pharmacological approaches have tackled the huge impact of nausea and vomiting, these side effects remain a major problem in cancer care (Glare et al., 2011; Kamen et al., 2014). Such nonpharmacological interventions as acupuncture and acupressure may also play a role in moderating these side effects (Garcia et al., 2013; Roscoe et al., 2003). Compared to these techniques, PMR has the advantages of benefiting both the physical and mental well-being of patients and that it can be easily practiced with the aid of playing a CD at home, without requiring extra visits with another health professional.

The comparison of the effect of PMR as opposed to other interventions has been explored by few studies to date. One such study compared the efficacy of PMR and music therapy (Lee et al., 2012). Yet, these studies have been excluded from specific systematic reviews whose purpose was to compare the efficacy of PMR and usual care. The comparison of an intervention with usual care is a one-way matter when searching for the effect of interventions that are not part of usual care practices (Thompson & Schoenfeld, 2007). Since the purpose of our study was to evaluate the efficacy of PMR compared to usual care, any comparison with another intervention should be part of other analyses.

External and Internal Validity

The five identified studies were conducted in three different countries (Japan, China, and Turkey), thus involving patients with different cultural backgrounds, nationalities, religions, and access to healthcare

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facilities (Arakawa, 1995; 1997; Demiralp et al., 2010; Song et al., 2013; Yilmaz & Arslan, 2015). In addition, both of Arakawa's studies (1995; 1997) included patients with several types of common cancers (e.g., lung, colorectal, breast), thus forming an inhomogeneous sample quite representative of the general cancer population. For these reasons, the external validity of the results of our systematic review should be considered to be relatively high. In contrast, its level of internal validity is in doubt due to the low trial quality (as indicated by both the Jadad Scale and the CONSORT criteria), thus raising concerns about the reliability of the reported efficacy. The main problem with the internal validity of all the included studies is a lack of specific information about patient randomization. Also, no patients nor outcome investigators were blinded in any of these studies. In addition, sample size estimation was carried out only in one trial (Yilmaz & Arslan, 2015). Since most study samples were small, this could lead to type I error. Hence, the internal validity of the studies included in our systematic review is fairly low.

Implications for Further Research

The small number of included studies indicates that there is a need for more extensive research regarding the effect of PMR on patients undergoing chemotherapeutic treatment. Although many trials were found that employed PMR as an adjunct to chemotherapy, the majority combined PMR with other interventions. Another minor category included studies that applied different PMR relaxation techniques. There is an urgent need to design clinical trials that could establish the role of PMR as a single nonpharmacological intervention to improve the well-being of cancer patients receiving chemotherapy.

In addition, there is a need for higher methodological quality. It is of concern that all except one study scored zero points on the Jadad Scale. The main reason for this failure arose from the difficulty in blinding patients who received the intervention. A major challenge for every CAM intervention is to establish its effects through a placebo-controlled trial (Lewith, 2002). Such trials pose serious obstacles to research on the effect of such CAM interventions as magnetic therapy (Carpenter et al., 2002), while other interventions (e.g., acupressure) have successfully passed this test (Roscoe et al., 2003).

In the case of PMR, sham sessions could be constructed by teaching participants to inhale and exhale at a usual pace and continuously repeating an exercise—such as tensing the same muscle or making any other body part move, instead of tensing all muscle groups one by one. The same timeframe for PMR sessions would also be essential. This type of pseudo-session is based on the philosophy of the placebo needle employed in acupuncture research (Streitberger & Kleinhenz, 1998) and could possibly lead to effective patient blinding.

Consonance with Recent Trends in Cancer Care

A growing body of literature focuses on how to transform traditional healthcare delivery into an more integrative process, resulting in a model where both conventional and CAM therapies are applied aimed at improving and promoting the patient's mental and physical health (Maizes et al., 2009). Cancer care should not be unaffected by this trend. To date, there are only a few studies that combine and test the use of different conventional techniques together with CAM interventions, including PMR, on patients receiving chemotherapy (Mahendran et al., 2015; Pelekasis et al., 2016). Since these programs aim to prove that they are clinically applicable, the background of their interventions must be extremely solid, meaning that each of the techniques under study must have proven benefits for patients. Thus, intensifying the research on the effects of PMR would not only benefit the reliability of this technique but also that of integrative cancer care programs that include PMR as part of their interventional regimen.

CONCLUSIONS

Preliminary results on PMR have shown that this method tackles anxiety and improves some of the side effects caused by chemotherapy (e.g., nausea, fatigue). Nonetheless, due to the limited number of studies and their low quality, it is premature to strongly support these statements and suggest the adoption of PMR as part of standard cancer care. The technique deserves further investigation in the context of randomized controlled trials.

CONFLICTS OF INTEREST

The authors hereby state that they have no potential conflicts of interest to declare.

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SUPPLEMENTARY MATERIALS AND METHODS

To view supplementary material for this article, please visit https://doi.org/10.1017/S1478951516000870.

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