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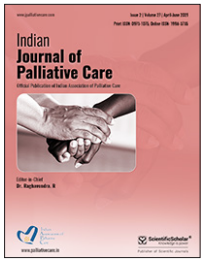

Review Article

Progressive Muscle Relaxation and Guided Imagery in Breast Cancer: A Systematic Review and Meta-analysis of Randomised Controlled Trials

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ABSTRACT

Breast cancer affects the mental well-being of patients who may need psychological support. The combined practice of progressive muscle relaxation (PMR) and guided imagery (GI) is known to improve psychological health. Its effect has been studied in patients with breast cancer. We need to systematically review and analyse the available data to outline its role in various stages of disease management. We wanted to evaluate the effect of the combined practice of PMR and GI on stress, anxiety, depression and mood. We also wanted to study the impact on quality of life and chemotherapy-related adverse effects. A systematic search and evaluation of the literature was performed. Five randomised controlled trials were selected for data extraction and construction of forest plots. The intervention was effective for stress and anxiety. It positively improved the quality of life but saw no significant improvement in chemotherapy-related adverse effects.

Keywords: Breast cancer, Guided imagery, Integrative therapy, Progressive muscle relaxation, Relaxation techniques

INTRODUCTION

Description of the condition

For a patient with breast cancer, the treatment journey is psychologically demanding.[1] The uncertainty of survival, a sense of worthlessness to near and dear ones and treatment-related hardships compromise the mental well-being. The change of body image following the surgery and adverse effects of chemotherapy further add to the problem. Multiple hospital visits for external beam radiotherapy or isolation following brachytherapy worsens the situation.[1-3] The survivors need long-term follow-up and complex assessments, which affect the quality of life.

They need coping strategies and a positive outlook on the scenario. Good family support and empathetic approach of physicians, nurses and staff improve the coping response of the patients to the disease. Integrative therapies such as yoga, meditation and mental relaxation are increasingly gaining importance. The exact mechanism by which they work is largely unknown. It is a general belief that these techniques help by reducing stress, restoring sympathetic and parasympathetic

balance and restoring the hormonal balance. Progressive muscle relaxation (PMR) and guided imagery (GI) are two different techniques that are often advised in combination with the hope of an overall better outcome.

Description of the intervention

PMR

PMR is a deep relaxation technique that was first described by Edmund Jacobson in the 1920s.[4] It is based on a principle that the physical sense of relaxation is associated with mental calmness. The sessions are usually of 10–20 min duration. In this, one group of muscle is tightened for nearly 5–10 s and then is relaxed for 10–20 s. The participants are advised to feel the release of tension while relaxing. One can start it from the head or toe region and then progress downward or upward, respectively. It induces relaxation and is helpful in stress, anxiety and chronic pain. The technique is easy to learn, and it has been tested in a variety of clinical conditions.[5]

GI

GI encourages patients to imagine things with an alternative perspective, thought or behaviour to improve their coping skills and reduce stress. Here, verbal instructions are given to direct the participant's attention to visual or auditory sensations that lead to a positive psychological response. Instructions are delivered either directly by a person or provided by a media. It is a type of mind-body intervention, and in clinical practice, it is commonly used as an adjunct to other treatment modalities. It has shown benefits in coronary artery diseases and conditions of chronic pain. It is helpful in chemotherapy-induced nausea and vomiting, and it also improves immune functions.[6,7]

Why it is important to review the combined use of PMR+GI

PMR+GI is in practice for a long and have been studied independently in various condition.[8] The combined practice of both interventions is an old practice. Their effects complement each other and give promising results in multiple clinical scenarios. Recently, a review of eight randomised control trials has been published in cancer patients, which reported a positive impact on the mental state as well as on chemotherapy-induced nausea and vomiting. However, it was not specific for breast cancer and also no attempt was made to perform the meta-analysis.[9]

As breast cancer is the most common cancer of women worldwide, we need to understand the role of the combined practice of PMR+GI in its management.[10] The disease is mainly limited to the female population, and therefore, the results can be specific. The meta-analysis will help in estimating the impact on different aspects of mental health and in understanding its limitations. This will give information on the present status of this intervention in breast cancer management and will also help in defining the scope of further research.

MATERIALS AND METHODS

Objectives

We wanted to study the effect of the combined practice of PMR+GI on stress, anxiety, depression and mood of the patients during breast cancer management. Our secondary objective was to evaluate its effect on common chemotherapy-related complications and quality of life.

Criteria for selecting studies

We included in our study all randomised controlled trials, in which the combined practice of PMR+GI was studied in patients with breast cancer. The articles in which the study population included cases other than breast cancer were excluded from the study. We also excluded studies in which the outcome measure did not have psychological effects or chemotherapy-related adverse effects. The study protocol was registered with PROSPERO with registration number-CRD4202019622.

Search strategy

We searched the electronic databases of PubMed/Medline, CENTRAL and CINAHL (EBSCO) from April to May 2021. We also searched the ClinicalTrials.gov registry. The articles were searched irrespective of language and year of publication. We searched PubMed using the search strategy: ("*Autogenic Training*" *[Mesh] OR* "*Imagery, Psychotherapy*" [*Mesh*]) *AND* "*Neoplasms*" [*Mesh*]. A similar search strategy was used for searching articles in the CENTRAL database. We searched CINAHL with the search strategy "*Progressive muscle relaxation OR Guided Imagery AND neoplasm*" without selecting fields. Terms "*Progressive muscle relaxation*" and "*Guided Imagery*" were separately searched in the ClinicalTrials.gov registry for the completed projects. The "*related articles*" function of PubMed was used to broaden the search. We also searched the reference list of selected articles and some of the reviews manually. The relevant references were further searched in Google Scholar also. The whole process was conducted in accordance with the protocol of the preferred reporting item for systematic reviews and meta-analysis.

Data extraction

A pre-designed pro forma was used to extract the data from eligible studies. The authors' MS and AB extracted the data and discussed the discrepancies. We collected

information about the place and year of study, participants characteristics (number of breast cancer patients), nature of the intervention, measurement tools, the outcome and a summary of the results.

Methodological quality assessment

Authors MS and AB assessed the risk of bias independently, and any disagreement was resolved by the third assessor MG. The bias was assessed for random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting and other sources of bias. According to criteria given in the Cochrane handbook, the studies were graded as having low risk of bias, high risk of bias or unclear risk of bias. Risk of bias summary was prepared.

Data synthesis and statistical analysis

We extracted the data on mean and standard deviation from the studies. The extracted data were continuous and belonged to different scales. The summary statistics were prepared using a standardised mean difference (SMD) approach. They were entered into the Review Manager 5.4, and forest plots were constructed. We used the fixed effect model for the construction of forest plots if the value of I^2 was less than 50%, and for others, the random effect model was used. The heterogeneity was assessed using I^2 and t^2 statistics. I^2 values of 25%, 50% and 75% were defined as low, moderate and high heterogeneity, respectively. $P < 0.05$ was considered statistically significant.

Measurement of treatment effect

For repeated measures value, we took the last recorded value for calculation. For studies with more than 2 intervention groups, we included the data of the arms with PMR+GI and controls only. We carried out analysis on intention to treat basis and included all the participants randomised to each group for analysis. We divided the studies into radiotherapy and chemotherapy subgroups based on the treatment stage. This was done for subgroup analysis.

RESULTS

Description of studies

We identified a total of 935 records [Figure 1]. We removed the duplicates and excluded the studies that were not related to cancer or were not randomised controlled trials. After this exclusion, we were left with 49 full-text articles. Out of these, in 35 studies, the combined practice of PMR+GI was not performed, and in two studies (Eremin *et al*., 2009; Walker *et al*., 1999), the outcome measures were different.[11,12] In four studies (De Paolis *et al*., 2019, León-Pizarro *et al*., 2007,

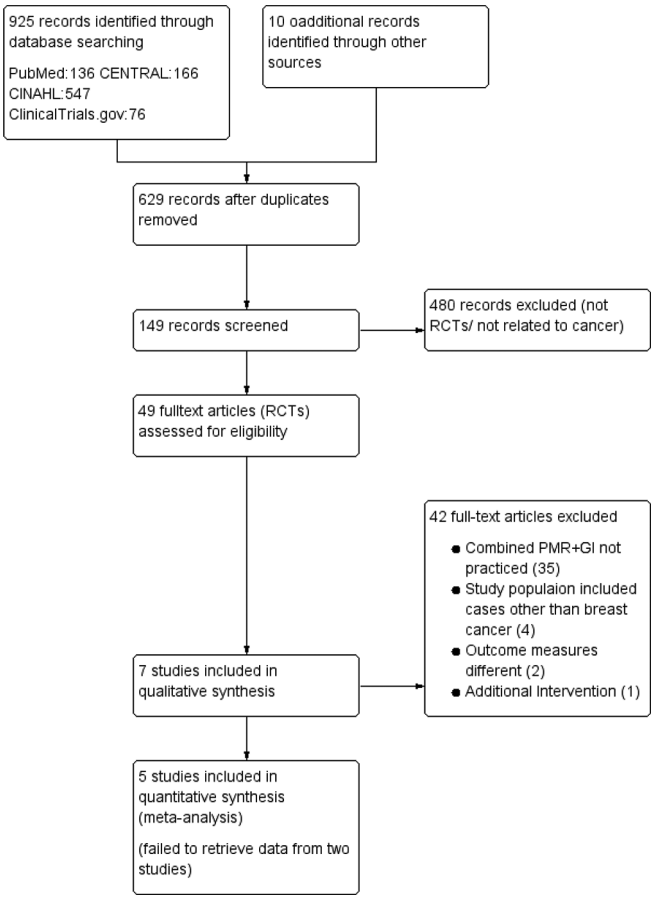

Figure 1: The study flow diagram.

Charalambous *et al*., 2015, and Shahriari *et al*., 2017), the population was heterogeneous and included cases other than breast cancer.[13-16] In one study (Elias *et al*., 2015), the intervention had spirituality and PMR+GI.[17] We excluded all these studies from further analysis and were left with seven studies for qualitative synthesis. We failed to retrieve data from two studies (Molassiotis, 2000; Molassiotis *et al*., 2002), and finally, five studies were selected for quantitative synthesis.[18,19] All included studies were in English literature.

Characteristics of included studies [Table 1]

The included studies were from the United Kingdom, Taiwan, South Korea and Brazil. Three studies were conducted on patients receiving chemotherapy and two on patients receiving radiotherapy.[20,21,22,23,24]

Training and practice of PMR+GI were not exactly the same in all the studies. In some of the studies, a single session training was given at the hospital, and then, instructional CDs were given for practice at home (Bridge *et al*., 1988; Chen *et al*., 2015). In the other three studies, either multiple sessions of training were organised in the beginning or they

Table 1: Characteristics of the included studies

Author	Year	Place	Sample Size	Phase of management	Intervention	Measuring tool	Frequency	Main findings
Bridge et al.[20]	1988	UK	89 PMR+GI=43 Control=46	Radiotherapy	Instructions at hospital and then practice at home PMR 4 min. then GI 16 min	Leeds scale for the self-assessment of depression and anxiety	Baseline, 6 weeks	Mood disturbance was significantly less in PMR+GI group
Walker et al.[21]	1999	UK	96 (48 in each group)	Chemotherapy	First 5 training sessions at hospital then practice daily at home once, maintain diary of compliance. For 18 weeks PMR+GI of host defenses destroying cancer cells	EPQ-L, CECS, GQOL, MRS, HADS	Assessment schedule spread from -1 week to 18 weeks	Quality of life was better and the emotional suppression was less in PMR +GI group
Yoo et al.[22]	2005	South Korea	60 (30 in each arm)	Chemotherapy	6 sessions at hospital 1 hour before chemo. First two sessions only PMR then PMR +GI. After chemotherapy practice at home for at least 3 days	MAACL, FACT-B, ANV, PNV	MAACL after PMR + GI but before Chemo *6 cycles FACT- B 0,3and 6 month, Others 12 times within 3 days of chemo*6 cycles	less anxious depressive and hostile, less ANV and PNV at 6-month post chemo higher QoL
Nunes et al.[23]	2007	Brazil	34 PMR+GI=20 Control=14	Radiotherapy	30 min session of PMR+GI at hospital after Radiotherapy, (Hospital – 24 group sessions). Practice twice daily at home	ISSL, STAI, BAI, BDI, salivary cortisol, peripheral blood	0,24 days	Attenuate the emotional distress
Chen et al.[24]	2015	Taiwan	65 PMR+GI=32 Control=33	Chemotherapy	1-hour training before chemotherapy then practice 20 min daily at home for 7 days	HADS, SDS	0, 7day	Anxiety and depression reduced significantly

Abbreviations: PMR+GI, progressive muscle relaxation and guided imagery; EPQ, Eyesenck Personality Questionnaire; CECS, Courtald emotional control scale; GQOL= Global self-rated quality of life; MRS, Mood rating scale; HADS, Hospital anxiety depression scale; MAACL, multiple affect adjective checklist; FACT- B, Functional assessment of chronic illness therapy- breast; ANV, anticipatory nausea and vomiting; PNV, post chemotherapy nausea and vomiting; ISSL=Inventory of Stress Symptoms Lipp for adults; STAI=State Trait Anxiety Inventory; BAI=Beck Anxiety Inventory; BDI, Beck Depression Inventory; SDS, symptom distress scale; Beck Depression Inventory-II.

were evenly spread over a long duration. Instructional CDs were given to patients for practice at home in all studies.

In one study (Nunes *et al*., 2007), patients were advised to practice the PMR+GI twice daily at home. In others, they were recommended for the same once daily. Walker, 1999, used patients' diary for checking the compliance to instructions. Methods for checking the same were not elaborated in other studies.

A variety of scales was used in different studies to assess pain, mood, stress, anxiety, depression, nausea and vomiting and quality of life. The day on which these scales were recorded was also different.

Assessment of risk bias

Assessment of the risk bias in included studies was done as per the guidelines given in the Cochrane handbook of systematic reviews and meta-analysis.[25]

Allocation

Random sequence generation was used in all studies. Allocation concealment was described in only one study (Walker *et al*., 1999).

Blinding

The intervention was non-pharmacological in nature, therefore, blinding of the participants was difficult. However, this was not described in two studies (Yoo *et al*., 2005; Nunes *et al*., 2007), and we categorised them as having an unclear risk of bias. Blinding of the outcome assessment was mentioned in the study of Bridge *et al*., 1988.

Incomplete outcome data

We could not find data on attrition in two studies (Walker, 1999; Yoo *et al*., 2005), and they were assigned a high risk of bias in this category.

Selective reporting bias

We evaluated each of the studies for the possible risk of selective reporting bias. We agreed that this was high in the study by Nunes *et al*., 2007.

Other sources of bias

We assessed other sources of bias. We checked for care provider experience and a standardised intervention protocol. Based on common consensus, we assigned the study of Bridge *et al*., 1988, as having lesser risk of bias.

The data were entered into Review Manager 5.4, and a methodological quality summary and graph were prepared [Figure 2].

Effects of intervention

Stress

Five studies, including a total of 344 patients, reported the effect on stress. Three studies measured stress during chemotherapy and two during radiotherapy. The time of score measurement ranged from the 7th day to 15th week. The heterogeneity was minimal, and a fixed effect model was used for analysis. The stress was significantly lower in intervention group (SMD, −0.38; 95% CI, [−0.59, −0.16]; I^2 = 8%, P < 0.001). However, this reduction was not significant in radiotherapy subgroup [Figure 3a].

Anxiety

Five studies with 344 patients reported the effect on anxiety. Three studies reported anxiety during chemotherapy and two during radiotherapy. We used a fixed effect model for analysis as the heterogeneity was small. The period range for the measurement of scores was from the 7th day to 18th weeks. In one study (Nunes *et al*., 2007), the anxiety in the intervention group was more than that in the control group. Overall, PMR+GI was found effective in reducing the anxiety (SMD, −0.30; 95% CI, [−0.51, −0.09]; I^2 = 24%; P = 0.006). However, a significant reduction in anxiety was not seen in radiotherapy subgroup [Figure 3b].

Depression

Five studies reported the effect on depression. A total of 363 patients were evaluated. The period range for score measurement was from the 7th day to 18 weeks. There was a significant heterogeneity in the reported outcome, and therefore, random effect model was used for analysis. PMR+GI reduced depression but this was not statistically significant (SMD, −0.37; 95% CI, [−0.81, 0.07]; I^2 = 76%; P = 0.1) [Figure 3c]. Significant improvement in depression was not observed in either the radiotherapy or the chemotherapy subgroups.

Mood

Only one study (Walker *et al*., 1999) reported mood on a total of 96 patients. Mood rating score was assessed at the 18th week in patients receiving chemotherapy. This study showed improvement in the mood of the patients. The effect was not significant (SMD, 0.13; 95% CI, [−0.27, 0.53]; P = 0.51) [Figure 3d].

Quality of life

Two studies reported quality of life on a total of 294 patients. The studies were on chemotherapy patients, and the effect was measured at the 6th week and 6th months. There was no heterogeneity, and therefore, a fixed effect model was used for analysis. The quality of life was significantly better in patients with PMR+GI (SMD, 0.60; 95% CI, [0.28, 0.92]; I^2 = 0%; P = 0.0002) [Figure 3e].

Nausea

Two studies reported the effect on nausea on a total of 125 patients. Both the studies were on patients receiving chemotherapy. The time range of reporting was at the 7th day and at the 18th weeks. There was a significant heterogeneity in the reported outcome; therefore, random effect model was used for analysis. Nausea was less in patients receiving intervention, but this was not statistically significant (SMD, −0.50; 95% CI, [−1.07, 0.06]; I^2 = 79%; P = 0.08) [Figure 3f].

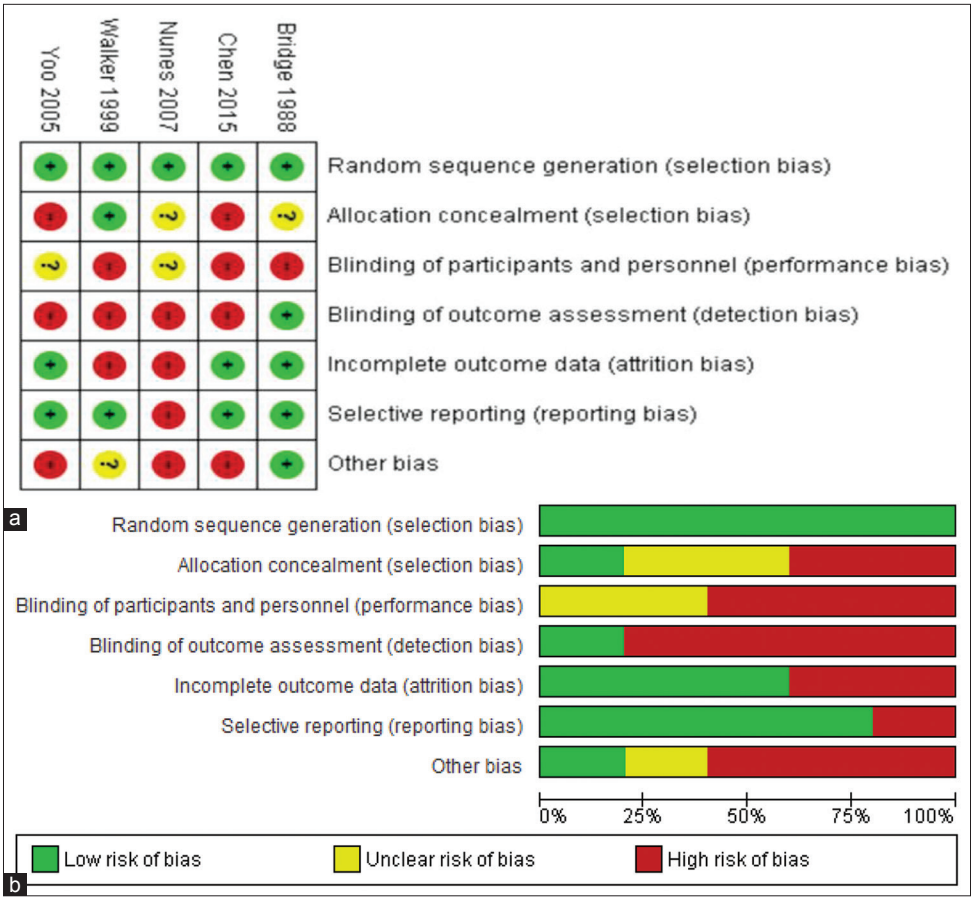

Figure 2: Quality assessment of included studies. (a) Methodological quality summary. (b) Methodological quality graph.

Pain

Only one study (Chen *et al.*, 2015) reported an effect on pain. The result was studied on the 7th day, on 65 patients receiving chemotherapy. Pain on the subjective scale was lesser in groups receiving the intervention, but the difference was not statistically significant (SMD, –0.35; 95% CI, [–0.84, 0.14]; $P = 0.16$) [Figure 3g].

Fatigue

Only one study (Chen *et al.*, 2015) reported an effect on fatigue. The effect was studied on the 7th day on 65 patients receiving chemotherapy. Fatigue was less in the group receiving intervention, but this was not statistically significant (SMD, 0.14; 95% CI, [–0.35, 0.63]; $P = 0.57$) [Figure 3h].

Subgroup analysis

There were two studies in the radiotherapy subgroup, and they reported the effect on stress, anxiety and depression. No significant improvement was observed on subgroup analysis following the intervention [Figure 3a-c].

DISCUSSION

This meta-analysis summarises the impact of PMR+GI on breast cancer patients. We analysed stress, anxiety, depression, mood and quality of life. We also observed its effect on nausea and vomiting, pain and fatigue during chemotherapy. Only randomised controlled trials were included in the study. Stress, anxiety and quality of life improved significantly in the intervention group. No significant effect on depression, mood or chemotherapy-related adverse effects was observed. Furthermore, on subgroup analysis, the improvement in stress and anxiety was not significant during radiotherapy. Our analysis of the impact on mood, pain and fatigue was based on the single study data.

The quality of included studies was not uniform. The intervention was non-pharmacological in nature and therefore blinding of the patients and the provider was difficult. The assessor blinding was missing in the majority of the studies. Similarly, data on attrition and compliance to practice at home were not mentioned in most of the studies. Furthermore, we could not find any harmful effects of the intervention. Only one article has reported that organising this program was difficult for the elderly and dependents

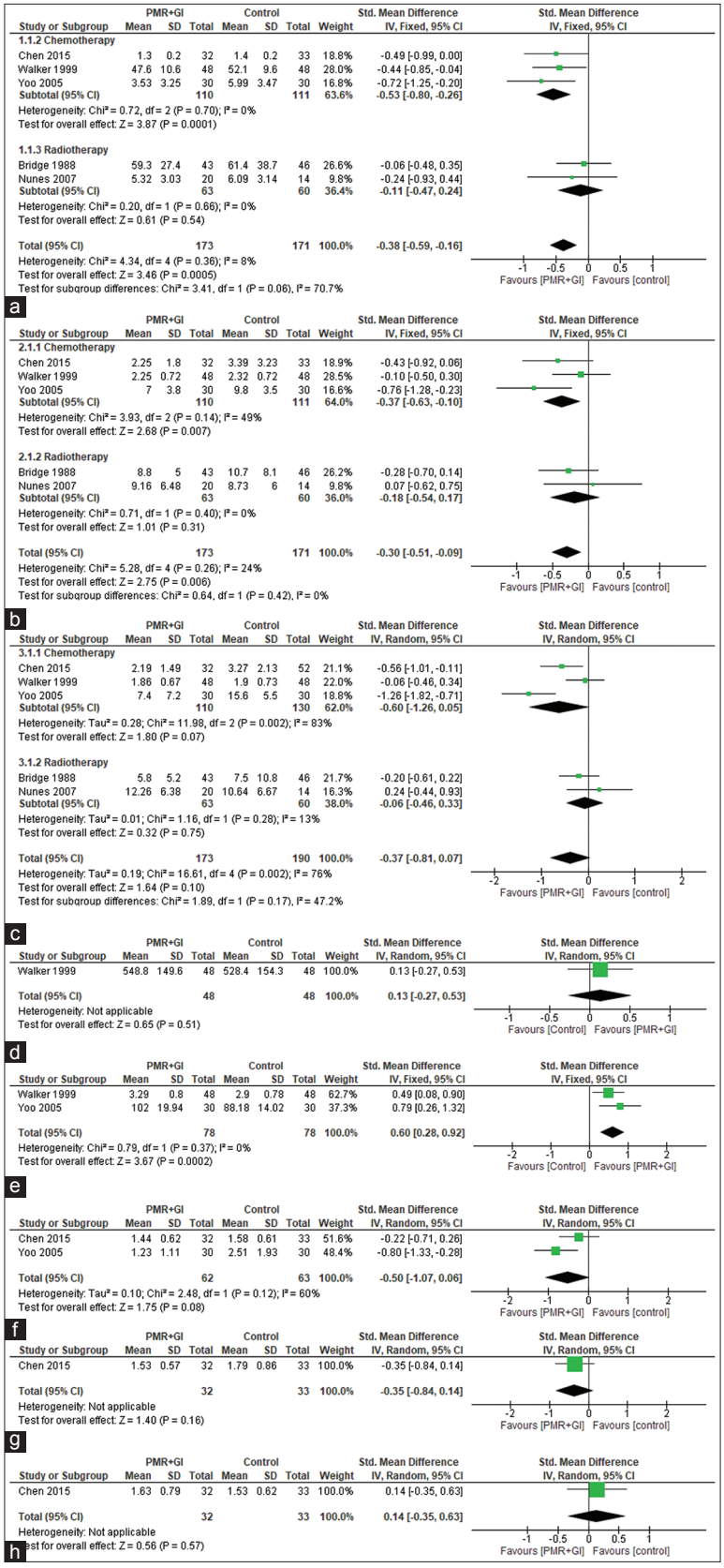

Figure 3: Forest plot of comparison showing effect on: (a) Stress, (b) anxiety, (c) depression, (d) mood, (e) HRQol, (f) nausea and vomiting, (g) pain, (h) fatigue.

(Yoo *et al.*, 2005). We observed that the patient training and practice advice were not similar in all studies. Measuring tools and the time when they were instituted also differed.

Yoga Nidra is a guided meditation of eight stages. The stage of "rotation of consciousness" and "breathe awareness" resembles PMR, and the stage of "image visualisation" is similar to GI.[26] Thus, technically, yoga Nidra resembles the combined practice of PMR+GI closely. Still, we have not included it in this review because there is no RCT to evaluate its effect on breast cancer.

Implications for practice

Based on the small number of randomised controlled trials, it appears that the combined practice of PMR+GI is a valuable intervention. This improves the psychological health of the patient, especially during the period of chemotherapy. In the long term, patients experience a better quality of life. However, the effect on chemotherapy-induced nausea, pain and fatigue may not be significant. This intervention may be of limited use during radiotherapy.

Implications for research

Breast cancer negatively impacts the psychology of the patient. This can be reduced by PMR+GI, especially during chemotherapy. More high-quality randomised controlled trials are needed for better evidence. Effect on chemotherapy-related side effects needs further evaluation. Furthermore, the role of this intervention during the follow-up period should be evaluated. The research methodology should include novel measures for checking patient compliance. The research should also report the difficulties in the technical implementation of the program. More well-planned studies are required to explore its impact on tumour pathology and immunity status.

CONCLUSION

The combined practice of progressive muscle relaxation and guided imagery reduces the stress and anxiety during the chemotherapy phase of treatment. It also elevates the mood and in long term improves the quality of life. Its effect on chemotherapy related adverse effects like nausea and vomiting, pain and fatigue are less studied. We need more well designed randomized controlled trials to further understand its role in breast cancer.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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