



Original Article

Effect of Music Therapy with Periorbital Massage on Chemotherapy-Induced Nausea and Vomiting in Gastrointestinal Cancer: a Randomized Controlled Trail

Behrouz Dadkhah¹, Elham Anisi^{1*}, Naser Mozaffari¹, Firouz Amani², Mehdi Pourghasemian³¹Department of Nursing, Faculty of Nursing and Midwifery, Ardabil University of Medical Sciences, Ardabil, Iran²Department of Epidemiology and Biostatistics, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran³Department of Internal Medicine, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

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*Corresponding Author:

MSc in Nursing, Email: elhamanisi
1370@gmail.com

ABSTRACT

Introduction: Music and massage therapy are among the approaches of complementary medicine. Patients with cancer have been hugely encouraged in recent years to use complementary medicine to relieve chemotherapy-induced nausea and vomiting. The present study was conducted to determine the effect of music and periorbital massage therapy on chemotherapy-induced nausea and vomiting in patients with gastrointestinal cancers.

Methods: The present single-blind clinical trial study was conducted on 60 patients with gastrointestinal cancer undergoing chemotherapy who were randomly assigned to control and music plus massage therapy groups. Two interventions were concurrently carried out on patients in music plus massage therapy group while receiving chemotherapy medication, but the control group received no intervention. Rhodes questionnaire was used to assess nausea and vomiting before and 24 hours after chemotherapy. Data were analyzed using descriptive and analytical statistical tests (Chi-square and t-tests).

Results: Music plus periorbital massage therapy significantly reduced nausea and vomiting in patients undergoing chemotherapy compared to the control group.

Conclusion: According to the results, using music plus periorbital massage improves nausea and vomiting in patients undergoing chemotherapy, and can be considered as a complementary medicine method in conjunction with other medicinal therapies to relieve symptoms of patients with cancer.

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Introduction

Today, cancer, with its growing prevalence, is one of the biggest health problems threatening human life around the world. It is anticipated that cancer-induced death rate may increase by about 45% in developed countries by 2035.^{1,2} Gastrointestinal cancer is one of the most common cancers accounting for 30% of cancer cases and 32% of cancer-induced deaths.³ Gastrointestinal cancer also accounts for nearly half of the common cancers in Iran. Gastric cancer is the second most common cancer.⁴ Over the past 30 years, the prevalence of gastric cancer has increased in Iran, especially in Azarbaijan and Ardabil, with the highest incidence rates in the country.⁵

Chemotherapy is one of the common treatments for GI cancer. Nausea and vomiting are two important digestive complications that people experience after chemotherapy for several days.⁶ Inappropriate control of these complications can significantly impair quality of life, nutritional status, and physical activity of individuals, and impose direct and indirect costs on them.⁷ The prevalence of chemotherapy-induced nausea and vomiting is 90% in people who receive highly emetogenic chemotherapy (HEC) and between 30% and 90% in people who receive moderately emetogenic chemotherapy (MEC).⁸ Despite the availability of new anti-nausea medications, the full control of these complications is not achieved yet, such that about 50% of people suffer from this condition despite

receiving anti-nausea medications, and reducing the incidence of these complications has become a challenge.⁹

In a qualitative study on the experiences of patients undergoing chemotherapy, patients were experiencing fatigue and exhaustion due to failure to control nausea properly, resulting in prolonged intervals between chemotherapy courses.¹⁰

Since pharmacological interventions have not completely controlled nausea and vomiting of chemotherapy, non-pharmacological methods have been used along with pharmacological therapies to control it.¹¹ Alternative therapies have a special place in controlling the symptoms of diseases in cancer patients.¹² Research has shown that cancer patients have a tendency to use alternative medicine along with standard treatments to control their disease.¹³ One of the approaches of complementary medicine to control chemotherapy-induced nausea and vomiting is music plus massage therapy. Music is a kind of complementary medicine that affects the central nervous system, making the patient feel relaxed and recovered.¹⁴ Music therapy means the regular use of music to maintain, provide and improve physical and mental health, such that the music therapist creates the desired changes in the patient's behavior and emotions by playing music in a therapeutic or stressful environment.¹⁵ The key point in music therapy interventions is the choice of desired, attractive music that is consistent with the individual's culture and taste.¹⁶ Anxiety is currently

recognized as an important factor for exacerbating nausea and vomiting. Hence, relaxation techniques such as music and massage are used to improve these side-effects.¹⁷ Many clinical trials have investigated the effect of music on chemotherapy-induced nausea and vomiting over the last decade, for example; in their study, Gimeno *et al.*, concluded that music plus visualization led to reduced chemotherapy-induced nausea and vomiting, but not significantly.¹⁸ Karagozolu *et al.*, reported the positive effect of music and visualization on anxiety, nausea and vomiting.¹⁹ However, a study by Moradian (2015) showed that music therapy had no effect on these side-effects.²⁰ Our previous study also showed that music reduced nausea in patients with gastrointestinal cancer, but had no effect on their vomiting.²¹ Review of literature shows that few studies investigated the effect of music therapy interventions on chemotherapy-induced nausea and vomiting in patients with gastrointestinal cancer undergoing chemotherapy with the most nauseating medications, and a definitive answer to the question about the effect of music on nausea and vomiting is yet to be found. However, many patients still suffer from chemotherapy-induced nausea and vomiting, and there is a need for evaluating another method to improve this complication.

As a complementary medicine technique, massage therapy enhances blood flow and oxygenation of tissues, and thus creates a peace of mind and relaxation.²² Massage therapy can be performed both manually and electronically. Many studies have examined the effect of different acupressure techniques on chemotherapy-induced nausea and vomiting; for example, subcutaneous stimulation of P6 using an electronic device,²³⁻²⁵ or direct pressure on P6.²⁶ Moreover, the effect of muscle relaxation on chemotherapy-induced nausea and vomiting has been investigated in many studies.²⁷⁻²⁹ One of the tools currently used for massage is the electronic eye massager, which simultaneously uses bio-magnetic and acupressure properties.³⁰ According to bio-magnetic studies, creating magnetic field on the acupressure points improves the performance of that part.³¹ The eye massager has a vibrating massage function and a warm airbag at the acupressure points around the eye, and the occipital and temporal regions that can provide more blood flow and oxygen to the brain tissue, facial muscles and the eye, with subsequent relaxation and reduced anxiety and stress. In their study, Adnan *et al.*, investigated the effect of eye therapies on the brain function via EEC waves, and concluded that using eye massager significantly increased alpha and beta waves.³² Alpha waves are known to be associated with relaxation modes and physiological balance of the body, and beta waves are associated with concentration and attention. Therefore, using the eye massager can effectively reduce anxiety and stress levels.

The eye massagers consist of a pair of magnetic pieces and a mask. The mask components are made of hard materials and the magnetic piece contains a steady magnet that produces a magnetic field. An eye massager is an inexpensive tool with a simple application, and functions by exerting a uniform pressure at a constant rhythm. In the

present study, a new complementary technique plus music therapy was used to explore the effects of the combination of these methods on chemotherapy-induced nausea and vomiting in patients with gastrointestinal cancer. So far, the impact of music on chemotherapy-induced nausea and vomiting has been measured globally, but the impact of two interventions of music and massage together has been less well-documented. As we searched about the effect of different complementary and bio-magnetic techniques on chemotherapy-induced nausea and vomiting, did not find a similar study in this regard. Thus, the present study was conducted to investigate the effect of music therapy plus periorbital massage on chemotherapy-induced nausea and vomiting in patients with gastrointestinal cancer undergoing chemotherapy.

Materials and methods

This randomized controlled trial study was conducted in the hematology department of Imam Khomeini Hospital in Ardabil after obtaining approval letter and the code of ethics (IR.ARUMS.REC.1395.1) from the Ethics Committee of the Research Deputy of Ardabil University of Medical Sciences. This study also was registered with the registration code of IRCT2016062528628N1 in the Iranian Registry of Clinical Trials. Furthermore, the principles of Helsinki Declaration were observed. The researcher provided participants with a verbal explanation about the study stages, answered their questions, and obtained their written informed consents. In this single blind randomized clinical trial, 60 patients were randomly assigned to the intervention (music plus massage therapy) and control groups. The randomization method consisted of the use of two colored cards, each representing a group, and 30 cards from each group were put in an opaque box. Then, each participant was asked to take a card, which was discarded once the group type was determined. This continued until cards were finished, and thus 30 people were assigned to control group and 30 to the massager group.

Sampling was performed in the Hematology Department of Imam Khomeini Hospital of Ardabil University of Medical Sciences in Iran from June 7, 2016, to January 4, 2017. Convenience sampling was initially used, and all patients with gastrointestinal cancer undergoing chemotherapy at this center were assessed for eligibility to take part in the study. The approximate sample size was estimated at 60 patients according to the Altman chart with 80% power, 61% ratio and 4% deviation from previous studies,^{19,33} which was divided into two groups of 30 patients. In this study, 145 people were first assessed for eligibility, of which 85 were excluded from the study for various reasons. Finally, 60 participants had inclusion criteria, which were randomly assigned to two groups. Study flow diagram for recruitment and allocation to study groups is shown in Figure 1. The inclusion criteria were age of 18 to 70 years old, having cancer of the upper gastrointestinal tract (stomach, esophagus), or lower gastrointestinal tract (colorectal), no gastrointestinal or metabolic diseases

causing nausea and vomiting, no psychiatric disorders, receiving the first chemotherapy session, no history of music and massage therapy, no visual or hearing impairments, and willing to take part. The exclusion criterion was receiving medications or therapy methods other than prescribed medications for reducing nausea and vomiting.

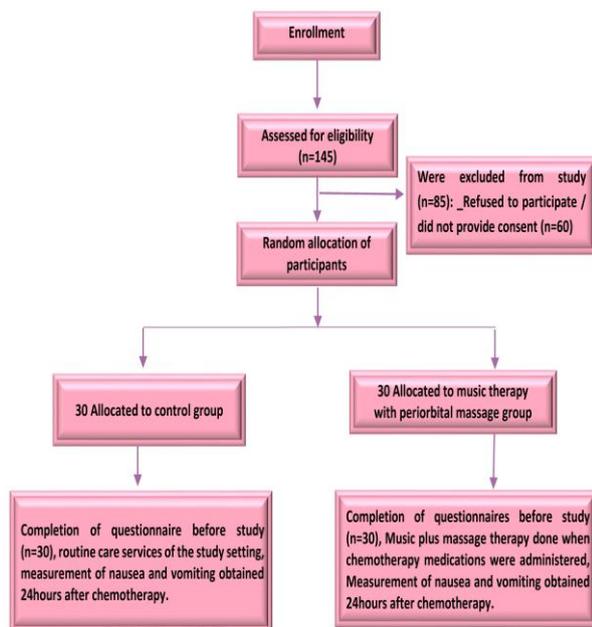


Figure 1. Consort flow chart

The procedure was as follows. In the Hematology Department of Imam Khomeini Hospital in Ardabil, chemotherapy regimen comprised Cisplatin (60mg/m²) for stomach and esophagus cancers, and Oxaliplatin (85mg/m²) for colorectal cancer. Antiemetic medications administered were 3mg of Granisetron (Kytril) and 8mg of Dexamethasone in colorectal cancer cases, and 3mg of Kytril, 8mg of Dexamethasone, and 80mg capsule of Aprepitant in stomach and esophagus cancer cases, which were administered before commencement of chemotherapy. Two nurses independently performed the intervention and assessed nausea and vomiting to ensure the blinding. Eligible people were included in the study a day before administration of chemotherapy medications, and were provided with verbal explanations about the study stages and answers to their questions. Once fully informed, participants were asked to sign the informed consent form. Then, they were randomly assigned to the massage plus music group and control group. The nausea and vomiting questionnaire was completed for the subjects by the first evaluator before chemotherapy.

This questionnaire was completed at patients' bedside, where questions were verbally explained for the patient and their answer was ticked. The second evaluator performed the intervention when chemotherapy medications were administered. The second evaluator had already been trained on periorbital massage and its

duration by the researcher. Music therapy was performed using relaxing music including classical, traditional, and the works by Beethoven containing slow and consistent rhythmic and melodic pieces. These pieces, selected by a professional musician who knows the musical beats, according to previous studies^{34,35} were played for 45 minutes during chemotherapy via MP3player and headphone. The control group patients received the routine cares on the day of chemotherapy including administration of antiemetic medications to control nausea and vomiting. An electronic eye massager (irest manufacturing Company, China) was applied to the patient's eyeball (according to manufacturer's instructions) for 15 minutes during chemotherapy. The massager has vibrating function and massages through a warm airbag. After the intervention, the first evaluator was asked to assess nausea and vomiting 24 hours after administration of chemotherapy medications.

Nausea and vomiting were assessed using Rhodes questionnaire. This questionnaire assesses nausea and vomiting index over the last 12-24 hours with eight items based on Likert scale from zero to four points, with the total score ranging from 0 to 32 points.³⁶ Our intervention was performed on patients admitted to the oncology department. The questionnaire was filled in at two different times for all patients: the first day of admission (before receiving chemotherapy to obtain the baseline amount of nausea and vomiting) and 24 hours after taking the chemotherapy drug while they were hospitalized. The score obtained is interpreted by calculating and comparing mean scores of nausea and vomiting indices in both groups. In this study, we used test-retest reliably using internal correlation coefficient, that Cronbach's alpha was 0.85. Also Moradian et al., used standard 'forward-backward' translation procedure to translate the original version of the INVR questionnaire into Persian for use in Persian-speaking cancer patients and reported a Cronbach's alpha of 0.88 for inter-item correlation.³⁷Data were analyzed by a statistician in SPSS version 13 (IBM, Armonk, NY, USA).

For normality of data we used KS test. After confirmed the normality, we used t-test for compare mean between two quantitative variables and chi-square test for determine the relationship between qualified variables. Demographic data were analyzed using t and chi-square tests. Mean and standard deviation of nausea and vomiting were reported in the two groups, independent t-test and paired t-test was used to compare them. P<0.05 was considered significant

Results

Mean and standard deviation of patients' age was 56 (8.84) years in the intervention group and 53.86 (12.68) years in the control. The majority of participants were men (58.3%), married (95%), illiterate (60%) and self-employed (46.7%). Independent t-test showed no significant difference between intervention and control groups in terms of age (P>0.05). Also, Chi-square test showed no significant difference between the two groups

in terms of demographic details (gender, education, marital status, and occupation) ($P>0.05$). (Table 1). With regard to the type of cancer, stomach cancer (43.3%), colon (41.7%), and esophagus (15%) were the most frequent respectively, and no significant difference was found between the two groups ($P>0.05$) (Table 1) Using the independent t-test showed no significant difference between the two groups in the level of nausea and vomiting before administration of chemotherapy medications (Tables 2 and 3), and they matched in terms of anticipatory nausea and vomiting ($P>0.05$). Using paired t-test before and after chemotherapy showed that there was a significant difference between the mean of nausea and vomiting before and after chemotherapy in the control group but this difference was not significant

in the intervention group (the P-value of nausea score in control and intervention group was 0.000 and 0.19 and vomiting score in both groups was 0.002 and 0.64, respectively, Table 2 and 3).

Acute nausea and vomiting level was also measured by independent t-test in both groups a day after administration of chemotherapy medications. According to Table 2, the level of nausea was higher in the control group compared to the massage group ($P= 0.000$). Also, the control group experienced a higher level of vomiting compared to the massage group ($P= 0.004$, Table 3) and there was a significant difference between the two groups in nausea and vomiting after chemotherapy.

Table 1. Personal/social details of patients with gastrointestinal cancer in intervention and control groups

Variable	Control	Music plus massage therapy	Total (60 patients)	P
Age ^a	53.86 (12.68) [29-70]	56 (8.84) [34-70]	54.93 (10.89) [29-70]	0.453 [*]
Gender				0.793 ^{**}
Male	17(56.7)	18 (60%)	35 (58.3%)	
Female	13(43.3)	12 (40%)	25 (41.7%)	
Education				0.181 ^{**}
Illiterate	20 (66.7)	16(53.3%)	36(60%)	
Sixth grade and below diploma	4 (13.3)	10(33.3%)	14(23.3%)	
Diploma and higher	6 (20)	4(13.4%)	10(16.7%)	
Marital status				0.554 ^{**}
Married	28 (93.3)	29 (96.7)	57 (95)	
Single	2 (6.7)	1 (3.3)	3 (5)	
Occupation				0.924 ^{**}
Housewife	11 (36.7)	11 (36.7)	22 (36.7)	
Employee	1 (3.3)	2 (6.7)	3 (5)	
Unemployed	4 (13.3)	3 (10)	7 (11.6)	
Self-employed	14 (46.7)	14 (46.7)	28 (46.7)	
Type of cancer				0.732 ^{**}
Stomach	14 (46.7)	12 (40)	26 (43.3)	
Esophagus	5 (16.7)	4 (13.3)	9 (15)	
Colon	11 (36.7)	14 (46.7)	25 (41.7)	

^aThe difference in age was compared with t –test and reported by using mean(M) and standard deviation(SD), also ^{**}Chi-square test was used to compare the other of the demographic characteristics and reported by using number and percent.

Table 2. Mean difference in patients' nausea score in intervention and control groups before and after chemotherapy

Nausea level	Control Mean (SD)	Music plus massage Mean (SD)	P-value ^a
Before chemotherapy	1.33 (0.41)	0.93 (0.32)	0.89
After chemotherapy	5.43 (0.60)	1.53 (0.43)	<0.0001
P-value ^b	<0.0001	0.19	

^aThe difference in nausea score between two group was compared with t –test and reported by using mean(M) and standard deviation(SD), ^bpaired t-test was used to compare the nausea score before and after chemotherapy and reported by using mean(M) and standard deviation(SD).

Table 3. Mean difference in patients' vomiting score in intervention and control groups before and after chemotherapy

Vomiting level	Control Mean (SD)	Music plus massage Mean (SD)	P-value ^a
Before chemotherapy	1.03 (0.32)	0.73 (0.34)	0.91
After chemotherapy	3.13 (0.56)	0.93 (0.33)	0.004
P-value ^b	0.002	0.64	

^aThe difference in vomiting score between two group was compared with t –test and reported by using mean(M) and standard deviation(SD), ^bpaired t-test was used to compare the vomiting score before and after chemotherapy and reported by using mean(M) and standard deviation(SD)

Discussion

The purpose of the present study was to investigate effectiveness of combined music and periorbital massage method as a non-medicinal intervention on nausea and vomiting in patients with gastrointestinal cancer undergoing chemotherapy over a short period. The results showed that combination of music and periorbital massage was able to reduce nausea and vomiting in patients undergoing chemotherapy. In the present study, more than half of the participants had stomach and esophagus cancer and received Cisplatin, which is the most nauseating chemotherapy medication. However, despite a significant difference between the two groups in terms of type of cancer, the control group patients experienced more nausea and vomiting, indicating effectiveness of music plus massage method in controlling chemotherapy-induced acute nausea and vomiting.

Many studies have investigated the effect of relaxation techniques on the prevention and control of chemotherapy-induced nausea and vomiting. For instance, the results obtained by Moradian et al., showed that music therapy has no effect on chemotherapy-induced nausea and vomiting in patients with breast cancer.²⁰ A study by Sadat-Husseini on the effect of music on nausea and vomiting in children with malignancy showed that music reduced patients' nausea, but had no effect on their vomiting.³³ This difference might be due to differences in the type of cancer and the type of chemotherapy medications. According to a study conducted by Moradian, in terms of nausea, the medication regimen used in breast cancer was moderately high emetogenic, which is different from the cisplatin regimen that is among the most nauseating chemotherapy medications. However, people's inclination toward non-pharmacological interventions used also affects its response, so that in Moradian's study, the majority of participants felt uncomfortable with the required intervention. In a study conducted by Husseini, there was no limitation on the type of cancer, and patients with a variety of malignant tumors entered the study, which can somehow affect the results. Some studies have mentioned the analgesic and anxiolytic effect of music therapy on cancer patients. For example, Karacozoglu reported that music therapy reduces anxiety, nausea and vomiting in patients undergoing chemotherapy.¹⁹ In a study by Ezzone et al. on the effect of music on nausea and vomiting in patients undergoing chemotherapy, the group receiving music therapy experienced less nausea and vomiting compared to the control group.³⁸ Gurkan reported that music therapy reduces anxiety of patients with cancer by making them relaxed and peaceful and distracting their attention from the disease, treatment and the surrounding environment.³⁹ In a clinical trial, Standley also found that people undergoing music therapy experience less nausea and vomiting.⁴⁰ The eye massager is an alternative therapy tool that is easy to use for individuals and helps them maintain their independence in using it. This was a preliminary study showing that the use of a simple and

cost-effective tool along with music therapy facilitated the improvement of nausea and vomiting in cancer patients. If further findings can support our research results, it can turn into an opportunity to provide an eye massager as a simple and inexpensive tool along with other therapies to help people with cancer. Therefore, it provides a strategy for improving the quality of life in patients. Although numerous studies were conducted to investigate the effect of relaxation techniques on chemotherapy-induced nausea and vomiting during the last two decades, this study was the first to examine the palliative effect of eye massager on nausea and vomiting and no similar study was not found in this area. In line with our research, Shin's study on patients with gastric cancer revealed that massage of the Nei Guan (P6) spot reduced nausea and vomiting in patients undergoing chemotherapy.²⁶ A clinical trial on the impact of Nei Guan spot massage on nausea and vomiting in women with breast cancer by Molassiotis reflected the positive impact of the intervention.⁴¹ In contrast, studies by Genç, Zhang, and Basac showed that massage has no effect on nausea and vomiting.⁴²⁻⁴⁴ These differences may be due to the different types of massage methods, chemotherapy drugs, and anti-nausea regimens received. The study conducted by Genç had certain differences, including the fact that it was conducted on patients with lung cancer, different combination of treatments used on the genital tract, and the lack of blinding, which can affect the results. In Zhang's study, the lack of intervention effect in the acute phase of nausea and vomiting was considered to be due to the better effect of ondansetron (as a strong anti-nausea medication) on the first day of chemotherapy in both control and intervention groups, which had largely reduced nausea and vomiting in both groups. In Zhang's study, serum dopamine and 5-HT₃ levels were measured in the acute phase after administration of ondansetron, and found to have significantly reduced in both groups.

In Besac's study, patients were treated with TAC regimen (Taxotere, Adriamycin, Cyclophosphamide), which had lower nauseating strength than Cisplatin used in the present study. No information was provided about vomiting assessment tool in Besac's study. Concerning the combination of two alternative therapies, Gimeno et al. indicated that music and visualization reduced the frequency of nausea and vomiting in patients undergoing chemotherapy, but this decrease was not significant.⁴⁵ In another study by Sahler, music and visualization reduced nausea in patients,⁴⁶ which was consistent with the present study. In line with the present study, the results of Suh's study on the effect of massage and nursing counseling on chemotherapy-induced nausea and vomiting showed that co-administration of these two methods is more effective in controlling the complications in patients with breast cancer.⁴⁷ Many studies are required to clarify the combined effect of music therapy and periorbital massage. Moreover, more comprehensive studies on larger populations are needed to achieve stronger results. No study is without limitations, as such, the present study limitations include small sample size and not assessing nausea and vomiting

in the delayed phase. Another issue that should be considered in reducing patients' nausea and vomiting is whether this reduction is due to the effect of music or massage alone, or combination of the two, which was not investigated in the present study.

Conclusion

Generally, the results showed that music plus periorbital massage reduce nausea and vomiting in patients with gastrointestinal cancer. Hence, as an inexpensive, simple, and available method with no side-effects, music therapy plus periorbital massage in conjunction with medication therapy can be considered as an effective method for controlling nausea and vomiting.

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Ethical issues

None to be declared.

Conflict of interest

The authors declare no conflict of interest in this study.

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