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Effect of music therapy on chemotherapy-induced nausea and vomiting in
gastrointestinal cancer: A systematic review and meta-analysis

Zhong FP *et al.* Music therapy for CINV

Abstract

BACKGROUND

Chemotherapy is the primary treatment for patients with advanced gastrointestinal cancer, but it has many adverse reactions, particularly nausea and vomiting. Music therapy can reduce anxiety symptoms, avoid the response to the human body under various stress conditions through psychological adjustment, and improve the adverse reactions of chemotherapy.

AIM

To investigate the impact of music therapy on relieving gastrointestinal adverse reactions in chemotherapy for patients with digestive tract cancer by meta-analysis.

METHODS

Embase, Pubmed, Ovid, WOS, CNKI, CBM (China Biology Medicine disc), and VIP database were all used for searching relevant literature, and the efficacy after treatment was combined for analysis and evaluation.

RESULTS

This study included seven articles. The results of meta-analysis indicated that music therapy could reduce the nausea symptom score of patients after chemotherapy [mean difference (MD) = -3.15, 95% confidence interval (CI): -4.62 to -1.68, $Z = -4.20$, $P < 0.0001$]. Music therapy could reduce the vomiting symptom score of patients after chemotherapy (MD = -2.28, 95%CI: -2.46 to -2.11, $Z = -25.15$, $P < 0.0001$). Furthermore, music therapy could minimize the incidence of grade I and above nausea or vomiting in patients after chemotherapy (odds ratio = 0.38, 95%CI: 0.26-0.56, $Z = -4.88$, $P < 0.0001$). Meta-regression analysis found that publication year was not a specific factor

affecting the combined results. There was no significant publication bias ($P > 0.05$).

CONCLUSION

Music therapy can significantly improve the scores of nausea and vomiting symptoms in patients with digestive system cancer during chemotherapy and reduce the incidence of grade I and above nausea and vomiting after chemotherapy, making it an effective psychological intervention method worthy of clinical promotion.

Key Words: Music therapy; Gastrointestinal cancer; Nausea and vomiting; Gastrointestinal reactions

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Core Tip: Music therapy bases on the theories and methods of psychotherapy. It helps human body to react positively under various stress conditions through psychological adjustment, interest improving, and anxiety symptoms reduction. Music therapy plays a role in improving the negative emotions of cancer patients. However, whether it could reduce nausea and vomiting caused by chemotherapy still remains unknown. In this meta-analysis, we searched the public databases for relevant articles and pooled the results of the symptom scores and incidence of chemotherapy-induced nausea and vomiting to further discussion.

INTRODUCTION

The basic types of gastrointestinal malignant tumors include esophageal cancer, liver cancer, and pancreatic cancer. Surgery is the first option for the

treatment of the disease. However, most patients are in the late stage of the tumor at the time of treatment and lose the chance of surgical treatment. Chemotherapy has become the standard treatment, but many adverse reactions, such as bone marrow suppression, gastrointestinal reactions, neurotoxicity, *etc*, directly affect the digestion and absorption function of patients, resulting in malnutrition. Chemotherapy-induced nausea and vomiting gastrointestinal reactions are among the most common adverse reactions during chemotherapy in cancer patients^[1,2]. Various clinical data confirmed that even if the latest antiemetics are used during chemotherapy, 60% of chemotherapy patients experience nausea and vomiting. Severe nausea and vomiting reduce the quality of life of cancer patients and affect the progress of chemotherapy courses^[3]. Therefore, timely and effective prevention and relief of nausea and vomiting caused by chemotherapy are of great significance to improving the quality of life of cancer patients and ensuring the smooth progress of chemotherapy. Music therapy can reduce anxiety symptoms, avoid the response to the human body under various stress conditions through psychological adjustment, and has a positive effect on improving the adverse reactions of chemotherapy^[4,5]. Music therapy has been used in treating primary cancers such as lung cancer and breast cancer and plays a huge role in relieving anxiety before surgery and reducing the dosage of anesthetics^[6,7]. However, the research on nausea and vomiting caused by chemotherapy for gastrointestinal cancer remains controversial. Thus, we implemented this meta-analysis study as it is an effective method to resolve the above controversy.

MATERIALS AND METHODS

Databases and keywords

The relevant articles on this topic were obtained in October 2022 by searching Embase, Pubmed, Ovid, WOS, CNKI, CBM (China Biology Medicine disc),

and VIP database and selecting the publication deadline of October 2022. The keywords used in the search strategy were “music therapy”, or “music intervention”, or “audio program”, or “chemotherapy-induced nausea and vomiting”, or “CINV”.

The following literature was included based on the PICOS principle: (1) Study types: randomised controlled trials were preferred, but a retrospective cohort study was also performed; (2) Study subjects: Gastrointestinal cancer was the primary disease of all study subjects, which could be any of esophageal cancer, colorectal cancer, and pancreatic cancer, where patients were treated with chemotherapy; (3) Intervention group: music therapy, which was adopted could be performed before chemotherapy, or throughout the chemotherapy process, and the selected repertoire, duration, and treatment methods were different according to different studies, and other relaxation methods could be superimposed, such as massage, aroma therapy, and other relaxation methods; (4) Control group: Routine intervention was adopted; (5) Outcome indicators: The scores of nausea and vomiting symptoms assessed using the scale as well as the number and proportion of nausea and vomiting grade I and above after chemotherapy^[8].

Literature exclusion criteria

Patients with non-primary gastrointestinal cancer, such as lung cancer, breast cancer, uterine cancer, *etc*, non-chemotherapy patients; literatures in which music therapy is not used in the intervention measures, or music therapy is only used as an adjuvant will be excluded; study types of investigation, case analysis, and review were excluded.

Literature quality evaluation and bias risk assessment

The risk of bias in the literature was evaluated using the Cochrane risk of bias V2.0^[9] provided by Cochrane Collaboration, which included six levels, with

each level assigned “low”, “some concern of risk” and “high” for risk evaluation.

Data extraction

Two authors independently extracted data, which included title, author name, publication year, number of participants, gender, grouping, and outcome indicators. Gastrointestinal reactions were graded in some studies as follows: (1) Grade 0: No nausea or vomiting; (2) Grade I: Mild nausea and vomiting, no effect on eating, vomiting frequency not more than once a day; (3) Grade II: Significant nausea and vomiting, affecting eating, vomiting frequency 2-5 times a day; (4) Grade III: Severe nausea and vomiting, persistent attacks, unable to eat, vomiting frequency > 5 times a day; and (5) Grade IV: Nausea and vomiting could not be controlled. The number of cases of nausea and vomiting in grade I and above shall predominate in the statistical results.

Synthetic analysis

Odds ratio (OR) was used for dichotomous variables, and SMD was used for continuous variables as the analysis statistic. Descriptive statistics were compared using forest plots. For heterogeneity, the Q test was used. For $P < 0.05$, heterogeneity among studies was considered. The I^2 test was used for quantitative analysis of inconsistency among different studies. If $I^2 < 50\%$, a fixed effect model was used, else the random effect model was used. Subgroup analysis method is adopted to investigate the heterogeneity, and if there is no heterogeneity, a descriptive method is used to investigate the heterogeneity between articles. Investigating factors meaningful for effect size by using meta-regression. The articles were eliminated one by one, and the combined effect size of the remaining articles was calculated to determine the greatest impact on the results. Egger's test was used to detect the publication bias, and a funnel plot was used for the presentation.

RESULTS

Literature retrieval results

Finally, seven articles were screened by search. Figure 1 depicts the retrieval results, whereas Table 1 presents the baseline information of these articles.

Quality evaluation

The article was grouped by ¹ order of admission and did not strictly follow the random sequence process^[15], and there may be a large bias. All other articles described the generation method of random sequence. The allocation concealment method and blinding method were not described in those articles^[11-14,16], and there was a potential bias of “deviation from established intervention”. Except for one article^[10], no dropout cases were recorded as there may be data assessment bias shown in Figure 2.

Meta-analysis results

Effect of music therapy on reducing nausea symptom scores: Among the reports^[10,16], nausea symptom score after the intervention was reported in two articles, with statistical heterogeneity between them ($I^2 = 98\%$, $P < 0.01$). Meta-analysis indicated that music therapy could reduce nausea symptom scores after chemotherapy [mean difference (MD) = -3.15, 95% confidence interval (CI): -4.62 to -1.68, $Z = -4.20$, $P < 0.0001$] by random effect model, as shown in Figure 2A.

Effect of music therapy on reducing vomiting symptom scores: Among the reports^[10,16], vomiting symptom score after the intervention was found in two articles, without statistical heterogeneity ($I^2 = 15\%$, $P = 0.28$). Meta-analysis indicated that music therapy could reduce vomiting symptom scores after

chemotherapy in patients (MD = -2.28, 95%CI: -2.46 to -2.11, $Z = -25.15$, $P < 0.0001$) by fixed effect mode, as shown in Figure 2B.

Effect of music therapy on reducing the incidence of nausea and vomiting (grade I and above): Five articles reported the incidence rate of grade I nausea or vomiting or above after intervention, without statistical heterogeneity between articles ($I^2 = 0\%$, $P = 0.46$)^[11-15]. Meta-analysis indicated that music therapy could reduce the incidence rate of grade I nausea or vomiting or above after chemotherapy (OR = 0.38, 95%CI: 0.26-0.56, $Z = -4.88$, $P < 0.0001$) by fixed effect mode, as shown in Figure 2C.

Investigation of heterogeneity: Subgroup analysis could not be performed due to the small number of articles. The two included articles showed heterogeneity in the statistics of nausea symptom scores, which could be attributed to the different scales adopted by the two articles for nausea and vomiting symptoms.

Meta-regression analysis: In analyzing the incidence of nausea and vomiting indicators, we used the “publication year of the literature” to regress pooled effect size. We found that this factor had no statistically significant effect on the results ($P = 0.68$), implying that the results of this indicator were not related to the publication year and month of the literature, as shown in Figure 4.

Sensitivity analyses: No significant deviations were found after removing each study during the analysis of incidence indicators of nausea and vomiting, indicating that the final pool results were stable.

Publication bias analysis: Egger's test was used to detect the publication bias during the analysis of nausea and vomiting incidence indicators, $t = -1.20$, $P = 0.30$. There was no asymmetry in the funnel plot, as shown in Figure 5.

DISCUSSION

Music therapy is not yet a well-defined science that uses music to promote physical and mental health based on its practical functions^[17,18]. Chemotherapy is one of the important means to treat malignant tumors. Chemotherapy kills tumor cells while also bringing many adverse physical and psychological reactions to patients, such as bone marrow suppression, nausea, vomiting, anxiety, and depression, reducing the quality of life of patients^[19]. Psychosocial intervention helps to alleviate the adverse reactions of chemotherapy and improve the quality of life of patients. Music therapy is a psychological intervention method that can improve the physical and mental health of cancer patients without causing adverse reactions^[20-22].

Seven articles were included in this study to explore the effect of music therapy on adverse reactions during chemotherapy for primary cancer of the digestive system. The results indicated that music therapy could significantly improve nausea and vomiting symptom scores during chemotherapy of patients with digestive system cancer and reduce the incidence of nausea and vomiting after chemotherapy (grade I and above), which was a good psychological intervention method.

The frequency, rhythm, and regular acoustic vibration of music are physical energies that can produce harmonious resonance phenomena in human tissue cells, resulting in excitation or inhibition of the corresponding organs. Simultaneously, music can improve the excitability of God meridian cells and secrete some beneficial and healthy hormones, enzymes, acetylcholine, and other substances *via* neurohumoral regulation, all of which contribute to improved blood circulation and strengthening metabolism. Furthermore,

music stimulation can inhibit adjacent pain centers while stimulating the auditory center and reducing pain because the auditory center on the cerebral cortex is adjacent to the pain center. Music can also stimulate the body to release endorphins, increase the content of endorphins in the blood, and achieve the effect of relaxing the body and mind and relieving pain^[23,24]. Subcortical centers like the hypothalamus control emotions such as joy, anger, mourning, and music, as a special language, can act directly on subcortical centers such as the hypothalamus through the auditory system plays a role in regulating emotions^[25,26]. Music stimulation of the limbic system of the brain can also cause people to remember or consider related events, resonate in music therapy, and release adverse emotions and catharsis. Therefore, the psychological effects of music therapy on people mainly achieve a good psychological state of patients by regulating emotions^[27]. Relaxation training with light music can counteract ² the negative effects of psychological and physical stress, restore balance and coordination of people's physical and psychological spirits, which help individuals deal with life challenges more healthily, make involuntary reactions of the human body, such as heartbeat, respiration, and blood pressure, and epinephrine secretion in spontaneous control, and reduce the severity of adverse reactions caused by chemotherapy^[28].

The music can be chosen by the healer or by the patient himself. Some studies suggest that music therapy should be patient-centered, and music selection should be individualized to meet everyone's preference for music. The included article adopted the method used in this study where the investigators selected music primarily, whereas the patients self-selected music as a supplement and achieved good results^[11]. Music therapy can also be combined with other intervention methods, such as progressive music and muscle relaxation training^[11]. Aromatherapy is applied in music therapy in

another study^[13], and the group music therapy model is also adopted^[16], combined with moderate aerobic exercise.

Although the results of the combined analysis indicated that music therapy had a significant effect on adverse reactions to chemotherapy, it must be recognized that music therapy is only a psychological intervention rather than a treatment for adverse reactions such as nausea and vomiting and patients receiving chemotherapy for moderately and highly emetogenic cancer, drugs such as 5-HT₃ receptor antagonists should be given before chemotherapy to prevent serious gastrointestinal reactions.

Furthermore, this study has limitations due to insufficient evidence. First, too few included studies were related to the current low number of reports on this topic. Second, there were inconsistencies in the reported indicators. Some articles used the incidence of gastrointestinal reactions as an indicator, others used the symptom score as an indicator, and some others used the quality of life as an evaluation indicator. Although the articles, Dadkhah *et al*^[10] and Li^[16] reported the symptom scores of nausea and vomiting in patients after the intervention, the scoring tables adopted were different, which made the results heterogeneous. Only one of the seven included articles had a low risk of bias, indicating that the rest are of poor quality and have a high risk of bias. Therefore, further research on this topic is required. Music therapy could significantly improve nausea and vomiting symptom scores in patients with digestive system cancer during chemotherapy and reduce the incidence of grade I and nausea and vomiting after chemotherapy, making it an effective psychological intervention method.

CONCLUSION

This meta-analysis included a total of 726 patients in 7 articles. The result is that music therapy can significantly improve the score of nausea and vomiting symptoms in patients with digestive system cancer during

chemotherapy, reduce the incidence of nausea and vomiting at grade I and above after chemotherapy, and is a good psychological intervention method. However, due to the small number of articles included in this study, the evidence is not good enough. This subject still needs to be further explored by larger number of randomized controlled studies.

ARTICLE HIGHLIGHTS

Research background

Music therapy can reduce anxiety symptoms, avoid the response to the human body under various stress conditions through psychological adjustment, and has a positive effect on improving the adverse reactions of chemotherapy. Music therapy has been used in treating primary cancers such as lung cancer and breast cancer and plays a huge role in relieving anxiety before surgery and reducing the dosage of anesthetics.

Research motivation

Music therapy plays a role in improving the negative emotions of cancer patients. However, whether it could reduce nausea and vomiting caused by chemotherapy still remains to be explored.

Research objectives

To explore whether music therapy has a positive impact on the improvement of nausea and vomiting symptoms in patients with gastrointestinal cancer during chemotherapy.

Research methods

A few relevant articles of this subject have been searched from the public databases. The data of the outcome indicators have been extracted from the articles. A meta-analysis has been performed for the pooling results.

Research results

Music therapy could reduce the nausea and vomiting symptom score of patients after chemotherapy, also it could reduce the incidence of grade I and above nausea or vomiting in patients after chemotherapy.

Research conclusions

Music therapy is a good adjuvant therapy for improving the adverse reactions of chemotherapy.

Research perspectives

Indicators for chemotherapy-induced nausea and vomiting have been determined and a meta-analysis has been performed for the pooling results of the indicators. The evidence was withdrawn from the process.

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SIMILARITY INDEX

PRIMARY SOURCES

1

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