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MUSIC INTERVENTIONS ON CANCER-RELATED FATIGUE DURING CHEMOTHERAPY: MUSIC FOR ALLEVIATING SYMPTOMS (MUSAS) TRIAL RATIONALE AND PROTOCOL

INTERVENÇÕES MUSICAIS NA FADIGA RELACIONADA AO CÂNCER NA QUIMIOTERAPIA: RACIOCÍNIO E PROTOCOLO DO ESTUDO MÚSICA NO ALÍVIO DE SINTOMAS (MUSAS)

Camila Siqueira Gouvêa Acosta Gonçalves[1]
Paula Karina Hembecker[2]
Thais Abreu de Almeida[3]
Willian Felipe Hadiak Amalio de Souza[4]
Percy Nohama[5]
Audrey Tieko Tsunoda[6]

ABSTRACT

Background: Cancer-related fatigue is the most reported symptom of cancer treatment, especially chemotherapy, and is associated with psychological symptoms. Non-pharmacological interventions are recommended for symptom management, including music-based interventions. **Methods**: The proposed Music for Alleviating Symptoms (MusAS) study is a single-center, non-blind, randomized controlled trial with three parallel arms (two experimental and one control, with usual care) to verify the efficacy of distinct music listening approaches for diminishing adverse events during chemotherapy. A sample of 25 participants per group will be recruited, including women with breast cancer in stages 1 to 3 at a Brazilian oncologic referral hospital. The Music Therapy group will have an individualized interview with a music therapist, who will tailor a personalized playlist to each participant, whereas the Music Medicine group will listen to a standard playlist. The primary outcome is cancer-related fatigue (FACT-F), and the secondary outcomes are health-related quality of life (FACT-G), adverse events, (PRO-CTCAE), anxiety and depression symptoms (HADS), mood (VAMS), and the biological markers of inflammation (CRP, IL-6, IL-10, and Interferon-gamma). **Results**: The results will inform the potential integration of music-based interventions in clinical practice for managing cancer-related fatigue and other associated symptoms. **Conclusions**: The strengths of MusAS are the inclusion of a homogeneous population and the incorporation of biomarkers as an objective measure. To our knowledge, this is the first 3-arm trial with music in oncology from Latin America. It is registered in the Brazilian Register of Clinical Trials (ensaiosclinicos.gov.br), code RBR-68w9xsy.

Keywords: Breast cancer. Emotional distress. Music therapy. Biomarkers. Adverse drug reactions.[7]

[1] Doctoral Graduate from the Graduate Program in Health Technology, Pontifical Catholic University of Paraná (PPGTS/PUCPR), Curitiba, PR, Brazil. E-mail: mt.camilasgagoncalves@gmail.com
[2] Postdoctoral Researcher, Graduate Program in Health Technology, Pontifical Catholic University of Paraná (PPGTS/PUCPR), Curitiba, PR, Brazil. E-mail: pkhembecker@gmail.com
[3] Clinical staff of Clinical Oncology at Erasto Gaertner Hospital, Curitiba, PR, Brazil. E-mail: thaisaalmeida@gmail.com
[4] Technical manager at Hadiak Laboratory and partner at W.F. Laboratories, LCA - Laboratórios Clínicos Associados group, Curitiba, PR, Brazil. E-mail: willianhadiak@gmail.com
[5] Head of the Graduate Program in Health Technology, Pontifical Catholic University of Paraná (PPGTS/PUCPR), Curitiba, PR, Brazil. E-mail: percy.nohama@pucpr.br
[6] Professor at the Graduate Program in Health Technology, Pontifical Catholic University of Paraná (PPGTS/PUCPR), Curitiba, PR, Brazil. E-mail: audrey.tsunoda@pucpr.br
[7] This protocol was previously presented at Centro de Estudos do IPUB/UFRJ (2023), at AMT-PR Music Therapy Forum (2024) and at IAMM & ISfAM Congress (2024). The latest two venues had short abstract publications.

RESUMO

Contexto: A fadiga relacionada ao câncer é o sintoma mais relatado do tratamento, especialmente na quimioterapia, associada a sintomas psicológicos. Intervenções não farmacológicas são recomendadas para manejar sintomas, incluindo intervenções baseadas em música. **Método**: O proposto estudo Música no Alívio de Sintomas (MusAS) é um estudo controlado, randomizado, não cego, de centro único, com três braços paralelos (dois experimentais e um controle, de tratamento padrão) para verificar a eficácia de abordagens distintas de audição musical para diminuir as reações adversas na quimioterapia. Será recrutada uma amostra de 25 participantes por grupo, mulheres com câncer de mama nos estágios 1 a 3 em um hospital oncológico brasileiro de referência. O grupo Musicoterapia terá entrevista individualizada com musicoterapeuta, que customizará uma *playlist* personalizada para cada participante, enquanto o grupo Música e Medicina escutará uma *playlist* padronizada. O desfecho primário é fadiga relacionada ao câncer (FACT-F), e os secundários são qualidade de vida relacionada à saúde (FACT-G), reações adversas (PRO-CTCAE), sintomas de ansiedade e depressão (HADS), estados de humor (VAMS) e marcadores biológicos de inflamação (CRP, IL-6, IL-10 e Interferon-gama). **Resultados**: Os resultados informarão a possível integração de intervenções baseadas em música na prática clínica para manejar a fadiga relacionada ao câncer e outros sintomas. **Conclusão**: Pontos fortes são a inclusão de uma população homogênea e a incorporação de biomarcadores como medida objetiva. Até onde sabemos, esse é o primeiro estudo de três braços com música na oncologia da América Latina. Ele está registrado no Registro Brasileiro de Ensaios Clínicos (ensaiosclinicos.gov.br), código RBR-68w9xsy.

Palavras-chave: Câncer de mama. Estresse emocional. Musicoterapia. Biomarcadores. Reações adversas.

BACKGROUND

Breast cancer is the most diagnosed cancer worldwide and the leading cause of cancer death among women (Sung et al., 2021). In Brazil, the National Institute of Cancer estimates there will be 74,000 new breast cancer cases in women for the three-year period 2023-2025 (INCA, 2022). Despite the safety and efficacy of current treatment options, patients often experience long-lasting physical, physiological, and psychological symptoms post-treatment (So et al., 2021).

CRF, a multidimensional symptom encompassing physical, cognitive, social, and emotional components, is the most reported adverse effect of cancer treatment (Berger et al., 2015). Defined as a persistent feeling of tiredness not proportional to recent activity and impacting functionality, CRF is particularly linked to chemotherapy in breast cancer patients and is associated with emotional symptoms like depression and anxiety (Berger et al., 2015; Kuhnt et al., 2019). This underscores the need for non-pharmacological interventions to mitigate fatigue and related psychological symptoms during cancer care (Berger et al., 2015; Sleight et al., 2022).

Music-based interventions have been implemented in oncology for various outcomes across different types of cancer treatment modalities and settings (Bradt et al., 2021; Nguyen et al., 2022; Qi et al., 2021). These interventions fall into two main

categories: Music Therapy (MT) and Music Medicine (MM). MM involves healthcare personnel using pre-selected recorded music to assist patients during medical procedures, while MT involves a trained therapist providing a wider range of music-based interventions tailored to the patient's preferences and needs informed by an assessment, treatment and evaluation process within a therapeutic relationship (Bradt et al., 2021; Wheeler et al., 2019).

The latest Cochrane review with meta-analyses showed a small effect of music interventions on fatigue, with low certainty evidence (SMD −0.28, 95% CI −0.46 to −0.10, P = 0.002) (Bradt et al., 2021). Sensitivity analysis revealed evidence of effect for MT (SMD −0.36, 95% CI −0.61 to −0.12, P = 0.004, I2 = 0%), but not for MM (Bradt et al., 2021). However, trials were heterogeneous in terms of cancer type, stage, and treatment modality.

Regarding the chemotherapy treatment, Nguyen et al. (2022) pooled the results from nine trials on music interventions in chemotherapy, finding a medium-size effect on anxiety (SMD: −0.29, 95% CI−0.50 to−0.08, p=0.006, I 2=62%) and no significant effect for depression. Although Qi et al. (2021) found a significant effect of music interventions on CRF in a meta-analysis (SMD −0.88, 95% CI −1.49 to −0.26, P = 0.005), their sensitivity analysis involving women with breast cancer did not find evidence of effect.

Given the association of CRF and emotional symptoms with chemotherapy (Berger et al., 2015; Sleight et al., 2022), non-pharmacological interventions are essential to alleviate the adverse effects of cancer treatment (Berger et al., 2015). Although music-based interventions have shown promise, the heterogeneity of samples and the limited number of trials, specifically during chemotherapy, highlight the need for further research. To our knowledge, no trials have investigated CRF outcomes using multiple music intervention groups.

Therefore, the Music for Alleviating Symptoms (MusAS) trial aims to assess the efficacy of music listening during chemotherapy for CRF in two experimental groups and one control group. The first group will use a personalized playlist tailored by a music therapist (MT group); the second group will use a standard playlist (MM group); and the third group will be a wait-list control group receiving usual care.

This manuscript proposes the rationale and methods of the MusAS study, based on the Reporting Guidelines for Music-based Interventions (Robb et al., 2010) and on

the Standard Protocol Items: Recommendations for Intervention Trials (SPIRIT) by Chan et al. (2013).

CONCEPTUAL FRAMEWORK

This study is informed by the 3-P conceptual model for CRF, which identifies predisposing, precipitating, and perpetuating factors for this symptom (Sleight et al., 2022). Poor quality of sleep, pain, depression, and neuroticism are considered predisposing factors for CRF, chemotherapy and inflammation are amongst precipitating factors, and poor nutrition and sedentarism are perpetuating factors (Sleight et al., 2022). For minimizing CRF during oncologic treatment, therapies focusing on the patient's sense of self-efficacy are recommended (Sleight et al., 2022).

Enhancing self-efficacy reduces fatigue, depression, and anxiety in oncologic patients (Merluzzi et al., 2019). Additionally, preferred music listening is related to reduced stress (Burns et al., 2018), improved pain control (Linnemann et al., 2015) and to analgesia due to perceived choice (Howlin et al., 2022).

Furthermore, music stimulates the reward system, reducing psychophysiological symptoms (Chen et al., 2020). Whether as a distraction, a comfort, or a pleasant stimulus, preferred music listening can offer safety and predictability to oncologic patients (Bradt et al., 2014). So, music listening can enhance agency and sense of control for the MT group or provide relaxation and distraction for the MM group, aiding symptom management (Nguyen et al., 2022).

Design and Setting

MusAS is a single-site, three-arm, randomized controlled trial at Erasto Gaertner Hospital, a referral oncologic center in the city of Curitiba, Brazil. The hospital treats 75% of cases from the Brazilian unified health system annually (LPCC, 2022). The chemotherapy unit consists of five rooms with around 5 to six armchairs each, organized by the infusion duration. Breast cancer patients usually have their chemotherapy in the fast chemo room, with their procedures lasting from one and a half to two hours.

Ethics

This study received approval from the Institutional Ethics and Research Review Commission for human participant research under the number 62711822.4.0000.0098. The trial is also registered at the ReBEC portal, the Brazilian Register of Clinical Trials (ensaiosclinicos.gov.br), under the code RBR-68w9xsy.

Patient Population

Eligible participants are women aged 18 or over, diagnosed with initial or locally advanced breast cancer, and referred to chemotherapy. They must have adequate hearing and cognitive function to understand the study's aims and interact with auditory stimuli. Exclusion criteria include undergoing palliative care treatment, having a treatment plan of fewer than six total cycles of chemotherapy, or having significant comorbidities that would limit participation in the study (such as psychotic episodes or severe intellectual disability).

Sample Size Calculation

The sample size was determined using G*Power 3.1.9.7, considering repeated measures ANOVA design with three groups and three time points (baseline, post-intervention, and follow-up). The calculation was guided by previous studies on music interventions in oncology, particularly Lima et al. (2020), which evaluated the impact of music listening on quality of life, anxiety, and depression in breast cancer patients undergoing chemotherapy.

Although Lima et al. (2020) did not explicitly report the effect size, we estimated Cohen’s d = 0.81 based on their reported means and standard deviations. Given this evidence, we set f = 0.35 for the power calculation. Using $\alpha = 0.05$ and 80% power, the G*Power analysis recommended a minimum of 21 participants per group (total N = 63). To account for potential dropout and variability in real-world clinical settings, we increased the sample size to 25 participants per group (total N = 75), ensuring robustness while maintaining feasibility within the study constraints.

Randomization and Stratification

Patients will be randomized in a 1:1:1 ratio to a MT intervention group, a MM intervention group, and a usual care group, using block randomization. Randomization will be conducted using the website Randomizer (randomizer.org). For allocation concealment purposes, the randomized sequence will be with a MusAS researcher not involved in data collection – immediately contacted upon recruitment.

The sample will be is stratified into four groups: starting neoadjuvant chemotherapy (before surgery and 0 to 3 chemotherapy sessions completed), middle or end of neoadjuvant chemotherapy (before surgery and four or more chemotherapy sessions completed), starting adjuvant chemotherapy (after surgery and 0 to 3 chemotherapy sessions completed), and middle or end of adjuvant chemotherapy (after surgery and four or more chemotherapy sessions completed).

Data Collection

Data will be collected at three times. Time one (T1) will be recruitment, baseline assessments, randomization, and MT interview (for the MT group).

Time two (T2) will occur within 2 to 7 days after T1, in the participant's scheduled chemotherapy. Participants of experimental groups will receive their assigned playlist, a hardcopy list of the tunes' titles and composers, will use headphones, and will receive instructions to skip, repeat, or change tunes, and to adjust the volume. Mood scales will be used for pre and post-intervention assessments. The Control group will be assessed with the same scales within a 45-minute interval during chemotherapy.

Time three (T3) will occur within 7 to 21 days after T2, before or after the participant's scheduled oncology consultation or blood sample collection – usually 2 to 7 days before their next chemotherapy session. Participants will be assessed with the same measures as baseline assessments and will be given space for questions and orientations, such as on external and free MT services for continued treatment. The Control group will also receive the standard playlist to listen to during their next chemotherapy session if they wish.

The Table 1 shows the data collection summary of the MusAS trial.

Table 1 - MusAS Study Flowchart

Data Collection MusAS Trial				
T1 Oncologist or Nursing Orientation Consultation	Recruitment	Medical record screening; invitation, explanation about the study; consent form signed		
	Assessment	Demographics & Clinical Data Scales: FACT-G, FACT-F, PRO-CTCAE, HADS		
		Blood Sample: Lab		
	Randomization	Block Randomization		
	Interview	Control Group (CT)	Music Medicine Group (MM)	Music Therapy Group (MT)
		--	--	Music therapy interview
2-7 day interval		--	--	Music therapist taylors playlist
T2 Chemotherapy	Assessment	CT VAMS pre & post 45 min	MM VAMS pre & post 45 min playlist	MT VAMS pre & post 45 min playlist
	Intervention	Usual Care	Standard playlist	Personalized playlist
	Recommendation	--	Daily Music Listening	Daily Music Listening
7-21 day interval				
T3 Oncologist Consultation or Blood Test or Phone Interview	Assessment	CT Scales: FACT-G, FACT-F, PRO-CTCAE, HADS	MM Scales: FACT-G, FACT-F, PRO-CTCAE, HADS	MT Scales: FACT-G, FACT-F, PRO-CTCAE, HADS
		Blood sample: Lab	Blood sample: Lab	Blood sample: Lab
		CT: receives standard playlist	--	--
	Closure	Feedback & final orientations	Feedback & final orientations	Feedback & final orientations

Obs: FACT-G: Functional Assessment of Cancer Therapy- General; FACT-F: Functional Assessment of Cancer Therapy- Fatigue; PRO-CTCAE: Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events; HADS: Hospital Anxiety and Depression Scale.

Music Therapy Intervention Rationale

The MT arm will involve a personalized playlist tailored by a music therapist after an assessment interview with each participant. The rationale for this intervention is based on participant-led, meaningful stimuli to elicit positive feelings (Burns et al., 2018; Chanda & Levitin, 2013). Furthermore, the MT interview is intended to provide the participant with a sense of control and personal agency (Burns et al., 2018; Merluzzi et al., 2019) and allows the music therapist to understand the emotional characteristics of the music according to the participant's criteria (Rossetti, 2014). Building trust during the interview may help participants focus more on the musical materials (Witte et al., 2021), leading to more positive responses.

Music Therapy Intervention Description

Participants in the MT group will complete the Music Profile Assessment form, which includes questions about musical background, preferences, and dislikes, as well as the functions and uses of music in their daily lives. This form was specifically created for this trial, based on existing music background questionnaires (Hanser & Mandel, 2010; Meadows et al., 2015; Magee et al., 2023).

Following this, participants will be interviewed by a music therapist. The interview will explore the participant's relationship with music, positive memories associated with favorite tunes, and interpersonal relationships linked to musical materials. The therapist will also discuss how the participant copes with the treatment, and their expectations for the "chemotherapy with music" day. This interview aims to build a positive therapeutic relationship and trust, which can contribute to positive emotional changes (Witte et al., 2021).

The music therapist will ask about the participant's goals for the music playlist and listen to their preferences and symbolic associations. The participant will be asked to suggest a title for the playlist. This process provides opportunities for decision-making and control, enhancing the participant's sense of self-efficacy and agency, which are protective factors against cancer-related fatigue (Sleight et al., 2022; Witte et al., 2021).

The music therapist will also provide orientations on how the participant can listen to the personalized playlist during her chemotherapy. The professional may give

instructions on breathing with the music, reading or remembering the lyrics, imagining a safe and calm place, etc., according to the participant's goals. These orientations are based on Burns et al. (2008) study, where the music therapist added an educational component for music imagery and relaxation for participants undergoing chemotherapy.

The music therapist will then select music from the participant's preferences and data from the MT interview for a 45-minute collection. The selection will use The Music Characterization System (Rossetti, 2014), considering the arousal-valence model (Vuilleumier & Trost, 2015) and the participant's goals. The music therapist will select the tunes according to their salience for the participant and determine the degree of relaxation-activation for each tune according to their music elements, as Rossetti (2014) recommended. The professional will arrange the tunes so the ones with more activation components start, gradually moving to the ones with more relaxation components and progressively moving to the ones with activation components.

The music therapist will also prepare a letter for each participant, listing the titles and artists of each tune and providing personalized listening recommendations. This strategy targets the participant's goals and choices to enhance their self-efficacy during treatment (Merluzzi et al., 2019).

Music Medicine Intervention Rationale

The rationale for the MM arm is based on music as distractive and relaxing stimuli for managing pain and stress (Huang & Huang, 2023). Soft music with low arousal is recommended for symptom relief (Chanda & Levitin, 2013; Linnemann et al., 2015).

Previous reviews have shown that pre-selected music provides more benefits for symptom management, such as reduced anxiety, than participant-selected (Nguyen et al., 2022). So, a standard playlist was chosen for relaxation and distraction, replicating stimuli from other MM studies (Bulfone et al., 2009; Lima et al., 2020).

Music Medicine Intervention Description

The playlist consists of a 45-min music selection of nine tunes from previous studies with similar population and settings (Bulfone et al., 2009; Lima et al., 2020). The titles are: "Suite from the Man Who Planted Trees" (Paul Winter Consort);

“Nature’s Harmony Just Before DayBreak” (Glorious Sunrise); “Small Steps to the Moon” (Cecilia Chailly); “Far Away” (Yiruma); “River Flows in You” (Yiruma); “Heart” (Yiruma); “Hello / Lacrimosa” (The Piano Guys); “In the Arms of the Angel” (Sarah McLachlan); and “An Ocean of Memories” (Jamos Horner).

Interventionists and Treatment Fidelity

The MusAS trial has a team of eight researchers for data collection, including four undergraduate medicine students, one physiotherapist graduate student, one statistician, and two music therapists with over 15 years of experience. One of the music therapists, who holds a bachelor's degree in MT, a master's degree in Creative Arts Therapy - Music, and is a doctorate scholar, will conduct the interviews and tailor the playlists for the MT group. To ensure treatment fidelity, she will train the entire team through meetings, videos, written materials, and ongoing onsite supervision. Furthermore, interventions will be discontinued upon participant’s request at any given time.

Efficacy Outcomes and Measures

Despite the challenges subjective measures may have in their validation processes (Sijtsma, 2009), our team determined the scales based on recommended guidelines (Bower et al., 2024; Fabi et al., 2020), their application length, their previous implementation in music-based trials in oncology (Bradt et al., 2021) and their routine use in the research site. Additionally, MusAS trial includes objective measures (biomarkers). They are presented as follows.

Primary Outcome

The primary efficacy outcome of the MusAS trial is the change in cancer-related fatigue, measured by the Functional Assessment of Cancer Therapy-Fatigue scale (FACT-F) at baseline versus 7 to 21 days after one chemotherapy session across the three groups. The FACT-F is a tool with excellent psychometric properties (Seyidova-Khoshknabi et al., 2011), recommended by Oncology societies (Bower et al., 2024; Fabi et al., 2020), validated in Brazilian Portuguese (Ishikawa et al., 2010) and previously used in a Brazilian cohort (Alcântara-Silva et al., 2018). Fatigue was

determined as the primary endpoint due to its high prevalence as a symptom from oncologic treatment (Berger et al., 2015).

Secondary Outcomes

Secondary efficacy outcomes of the MusAS trial include health related quality of life, symptoms of anxiety and depression, adverse effects from chemotherapy, biomarkers of inflammation, and mood states.

Health-Related Quality of Life is measured by the Functional Assessment of Cancer Therapy – General (FACT-G), a validated assessment with good responsiveness (Luckett et al., 2010), with a Brazilian Portuguese validated version (Ishikawa et al., 2010). Symptoms of Anxiety and Depression are assessed by the Hospital Anxiety and Depression Scale (HADS), a validated screening tool widely used in oncologic settings (Vodermaier & Millman, 2011) and recommended for screening emotional symptoms (Mitchell et al., 2010). There is a validated Brazilian Portuguese version of HADS (Botega et al., 1995).

Adverse Effects from Chemotherapy are evaluated by the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE), a validated and reliable tool for assessing adverse symptoms (Basch et al., 2014; Dueck et al., 2015) and previously used in a Brazilian cohort (Lima et al., 2020). Five items will be measured: nausea, vomiting, headache, insomnia, and fatigue, as these are frequently experienced during infusion and associated with cancer-related fatigue (So et al., 2021).

Biomarkers of Inflammation include interleukin (IL-6), interleukin (IL-10), C-reactive protein (CRP), and Interferon-gamma. These biomarkers were selected for their potential to predict fatigue levels and their association with fatigue-related depression due to inflammatory processes in the central nervous system (Bower, 2019; Sleight et al., 2022). They have been used in previous studies to verify their association with fatigue and depression levels (Lengacher et al., 2019; Liu et al., 2012).

Lastly, mood states are assessed by Visual Analogue Mood Scales (VAMS), validated by Stern et al. (1997) and widely used in research settings (Machado et al., 2019; Rijsbergen, 2012), including oncologic music-based trials worldwide (Dalli et al. 2023; Harper et al., 2023) and in Brazil (Doro et al., 2016). Six mood categories are measured: happiness, sadness, calmness, tension, energy, and tiredness. These

scales will be used pre- and post-music listening during chemotherapy for the experimental groups and within a 45-minute interval for the control group. This timing is chosen due to VAMS's ability to assess the present moment and ease of use (Machado et al., 2019; Rijsbergen, 2012).

Other Measures

Given that music can be a source of both pleasantness and discomfort (Murakami, 2021) the MusAS trial will monitor adverse events during chemotherapy. Researchers are trained to ask participants about their comfort with the music and to register any adverse symptoms.

Additionally, self-report forms will document how each group listened to the playlist (e.g., skipping or repeating tunes), the frequency of music listening between T2 and T3, and participants' perceptions of their experience in T2 (comfort, relaxation, and passage of time). These questionnaires will help assess the safety of the music-based interventions and compare participants' experiences across different groups.

Data Analysis

All collected data will be entered into a Google Sheets document linked to the study's official email by one researcher. To ensure accuracy, a second researcher will independently review the data before proceeding with statistical analysis. To maintain blinding, groups will be coded using letters instead of intervention/control labels.

Statistical analyses will be conducted using JAMOVI (version 2.3.36, The Jamovi Project, 2022). Baseline characteristics of the three groups will be compared using the χ^2 test or Fisher’s exact test for categorical variables and one-way ANOVA or Kruskal-Wallis test for continuous variables, depending on data normality, which will be assessed using the Kolmogorov-Smirnov test. A significance level of $\alpha = 0.05$ will be adopted for all statistical tests.

The efficacy analysis will follow an intention-to-treat (ITT) approach, including all participants who attended at least one intervention session. To assess the impact of the intervention on dependent variables – including cancer-related fatigue (FACT-F), health-related quality of life (FACT-G), adverse effects (PRO-CTCAE), symptoms of anxiety and depression (HADS), and mood states (VAMS) – a repeated measures ANOVA will be employed. This model will evaluate within-group changes over time and

between-group differences at multiple time points (T1 and T3). For post hoc comparisons, Tukey's test will be conducted to explore significant differences identified by repeated measures ANOVA.

Results will be interpreted in terms of both clinical and statistical significance. Findings will be presented using tables and graphical visualizations to illustrate trends over time and differences between groups. The discussion will contextualize results in relation to existing literature and the study hypotheses.

DISCUSSION

This protocol outlines the rationale and methods of the MusAS study, a three-arm randomized controlled trial comparing music listening in two intervention groups (personalized and standard playlist) and a control group. Methodological strengths include applying music-based interventions specifically to women with non-metastatic breast cancer and providing a rationale for using different music methods for the two experimental groups. Additionally, to our knowledge, this may be the first study using CRP, IL-6, IL-10, and interferon-gamma as biomarkers in music interventions during chemotherapy. Additionally, this may be the first three-arm RCT using music in oncology from Latin America. This is particularly relevant as the targeted group may be underrepresented in research and collectivistic societies may have different criteria for music preferences and functions than individualistic societies (Schäfer et al., 2012).

Limitations

The MusAS trial protocol has some limitations. Firstly, it is a single-site study, which may impact generalizability of its results (Kahn et al., 2012). Secondly, it is a non-blinded study, meaning that researchers collecting the data will know to which group each participant belongs after randomization. Although masking is not possible at T2 due to the intervention's characteristics (Bradt et al., 2021), masking researchers responsible for the assessments at recruitment and at the end of the data collection would ensure more quality to the study (Costa et al., 2017). This decision for a non-blinded study was influenced by data collection schedules and the researchers' scholarships periods.

Lastly, another limitation of the MusAS study is that each participant in the experimental groups will listen to a playlist during a single chemotherapy session.

Although this provides only a snapshot of the participants' experience during chemotherapy cycles, it was necessary to establish this frequency for the feasibility of the study. The literature supports changes in cancer-related fatigue and related outcomes after a single session (Qi et al., 2021).

Innovation

Despite the limitations, the MusAS trial is innovative in comparing interventions based on MT and MM principles during chemotherapy. Similar studies have been conducted with cancer patients before surgery (Palmer et al., 2015) and undergoing other oncologic treatments (Bradt et al., 2014), comparing active and receptive methods (i.e. using live and recorded music). In this trial, the focus is on comparing the same method – music listening – with different delivery approaches: one standardized and easily replicable and the other personalized and mediated by a trained music therapist.

CONCLUSION

The results of the MusAS trial will demonstrate the effectiveness of music listening in alleviating cancer-related fatigue, improving health-related quality of life, reducing adverse effects, alleviating symptoms of anxiety and depression, enhancing mood, and influencing inflammatory biomarkers in women with breast cancer undergoing chemotherapy. This trial is expected to contribute significantly to the fields of MM and MT, highlighting the potential of music as non-pharmacological interventions in infusion settings.

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Disclosure Statement

The fourth author is a business partner of the lab in charge of the biological analyses. There are no other conflicts of interest to declare.

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