



Music therapy reduces fatigue in patients undergoing autologous hematopoietic stem cell transplantation

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ABSTRACT

Introduction: Autologous hematopoietic stem cell transplantation (HSCT) is a therapeutic medical treatment for various neoplastic hematologic, congenital, genetic, or acquired disorders. In this procedure which combines high-dose chemotherapy and/or radiotherapy and has a high degree of cytotoxicity, the patient experiences solitary confinement, which causes psychological distress, anxiety, mood disorder, fatigue, nausea, and pain and can lead him/her to depression. Objective: Evaluate the effectiveness of music therapy intervention for fatigue in patients undergoing autologous hematopoietic stem cell transplantation. Methods: This is a randomized clinical trial patients (n=151) were selected randomly were selected for the Experimental Music Therapy Group (EMG, n=76) which received the intervention, and for the Control Group (CG, n=75) which received only standard treatment. Interventions of live music were made using music therapy methods and techniques by a qualified music therapist. For assessment and quantification, the visual analog scale (VAS), and piper fatigue scale (PFS) were used. Results: The analysis and statistical tests applied were considered statistically significant. (PFS) Score Total (EMG) Baseline 7.1 (CG) 6.7 p=0.30 follow up (EMG) 2.4 (CG) 5.7=2.4 p<0.001 (VAS) before intervention 6.45 p=0.89 after intervention 2.52 p<0.001. Conclusion: Music therapy reduces fatigue of the undergoing autologous hematopoietic stem cell transplantation, providing bio-psychosocial welfare.

Keywords: music therapy; fatigue; hematopoietic stem cell transplantation; transplantation, autologous.

INTRODUCTION

Hematopoietic Stem Cell Transplantation (HSCT) is a therapeutic clinical treatment that consists of replacing hematopoietic stem cells of the diseased¹, or deficit bone marrow with healthy cells². This procedure combines high doses of chemotherapy, and radiotherapy and has a high degree of toxicity, causing damage to the quality of life, of patients for 100 days after transplantation³. Organic toxicity causes heart problems, osteoporosis, infections, cataracts, and infertility. In addition, pulmonary

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Declaration of conflicts: nothing to declare



This is an open access article distributed under the terms of the Creative Commons Attribution License © 2025 The authors and other organ complications occur⁴. Highlighting the patient's infection in the face of a malignant disease such as certain types of lymphoma, leukemia, and multiple myeloma, fatigue related to hematologic cancer represents one of the most reported undertreated and debilitating symptoms in patients treated with autologous stem cell transplantation⁵.

Currently, around the world, it is possible to perceive through publications in scientific journals, an approximation of contemporary medicine with the use of music as a form of therapy for hospitalized patients due to a wide range of diseases. In recent years, the use of music therapy as a therapeutic method has expanded its field of application. In the medical field, it is used as an alternative complementary source that aims to reduce stress, anxiety, tension, fatigue, and fear of death, both for patients and family members. The practice of music therapy, with its easy acceptance and emotional involvement, can also act in humanization, so the effectiveness of music therapy in the hospital environment is a trend to be followed by the area of contemporary medicine⁶.

The inclusion of new protocols, in the routine for therapeutic assistance, with groups of patients and family members are possibility, for relevant and promising approaches, in the hospital context, in oncology services, and in transplant centers. There are countless works involving music therapy to relieve human suffering. An investigation was conducted to reduce psychophysiological stress in adolescent cancer patients during the hospitalization period. The results found by the authors demonstrate that music therapy was beneficial in coping with stress during hospitalization. Furthermore, a reduction in suffering was identified through the inclusion of moments of relaxation, entertainment, tranquility, and physical and emotional well-being⁷.

A systematic review and meta-analysis were conducted in Türkiye about the effects of music therapy interventions on fatigue, in patients with hematological cancers and the authors describe what they found below. The findings of the meta-analysis indicated that music therapy interventions made important and positive contributions to reducing fatigue in patients with hematological cancer. Music therapy interventions are a convenient method to reduce fatigue because they are comfortable and noninvasive. It is recommended that music therapy interventions applied to patients diagnosed with hematological cancer be considered interventions that can be used together with other nonpharmacological or pharmacological methods to reduce fatigue⁸.

However, in the hospital context, the premise that music alone does not have the same reach as it can have when applied with the specific knowledge of music therapy and the competence of the music therapist1 is considerable. In Brazil, hospital institutions at a national level still lack the effectiveness of music therapy as a profession. At the same time, research publications related to music therapy in journals with respected scientific impact are increasingly rising to the top of current therapeutic modalities. Therefore, the contribution of this specialty to the patient's psycho-emotional balance can be more effective, as it provides comfort, welcome, and a reduction in morbidity, inherent to the treatment and, consequently, an improvement in quality of life.

This study is also justified by the perspective of more humanized care, and in the context of bone marrow transplantation, music therapy has enabled patients to conduct this treatment that causes so much suffering, with greater emotional balance and biopsychosocial well-being.

Music therapy was applied through an investigation in patients undergoing allogeneic hematopoietic stem cell transplantation, at the clinical hospital complex of the federal University of Paraná, and the results demonstrated improved mood, reduced anxiety, and pain relief¹.

The objective of this study was to evaluate the effectiveness of music therapy intervention for fatigue in patients undergoing autologous hematopoietic stem cell transplantation.

METHODS

It is a randomized clinical trial conducted in Erasto Gaertner Hospital Bone Marrow Transplant Unit with adult patients undergoing autologous hematopoietic stem cell transplantation (HSCT). Randomization was made before starting the research, 170 numbers were randomized using the program (www.randomizer.org).

The random selection, for allocation of the patient into the groups, took place as follows. After the patient agrees to participate in the research and has signed the free and informed consent form, (ICF). The envelope was opened in front of the patient, and it was agreed that the "even" number would comprise the group that would receive the music therapy intervention, referred to as the experimental music therapy group (EMG), and the 'odd' number will make up the Control Group (CG). The group that will not receive the music therapy intervention.

Statistical Analysis

The Piper scale was calculated in its final value and in three dimensions as stated in the author's article: Final score: average of twenty-two items Behavioral dimension: average of items two to seven Affective dimension: average of items eight to twelve sensory dimension /psychological: average of items thirteen to twenty-three. Analysis of the Gaussian distribution of continuous variables. The final Piper scales and respective dimensions were checked for the Gaussian distribution of the data based on the histogram format, mean and median, skewness, and kurtosis. The variation (difference between follow-up and baseline) of the Piper scales was also calculated and analyzed in the same way.

Among these variables, all were considered to have a normal distribution, considering parsimony in data presentation and the Central Limit Theorem. Comparison between the intervention and control groups Continuous variables were compared between groups using the unpaired t-test and categorical variables were compared using the Chi-square test. Subgroup analysis for the main outcome (Piper Scale) assessed whether the variation in the Piper scale (follow-up – baseline) differed in the respective subgroups. To evaluate whether any of the categories were effect modifiers, a linear regression was performed with the addition of an interaction term between the variable in question and the group (intervention/control).

Evolution of visual analog scales, firstly, the evolution of fatigue, scales before the intervention was compared at each visit between the intervention and control groups. The idea was to evaluate the existence of a persistent effect of the intervention throughout hospitalization. For this analysis, a mixed-effect longitudinal regression model was performed to compare the trajectories of the scales throughout the visits between the groups. Given the two-phase trajectory of the scales, time (visit) was included in the model as a quadratic function (visit and visit squared). The trajectories were compared between groups including a group-visit and group-visit interaction term squared and a Wald test was performed under the null hypothesis that both interaction terms are equal to zero. Variation in visual analogue scales of fatigue, with the intervention. The Piper scale was calculated in its final value and in three dimensions as guided by the PFS manual: final score: average of twenty-two items behavioral dimension: average of items two to seven affective dimension: average of items eight to twelve Sensory/ psychological dimension: average of items thirteen to twenty-three. Statistical significance was p<0.05 and Stata software version 15.0 (StataCorp. College Station, Texas) was used.

Application of music therapy

Music therapy services began pre-transplanting, from the moment the patient was accommodated in the room, with the appropriate catheter, to begin conditioning, which is high-dose chemotherapy. From this stage onwards, music therapy interventions began, until eight sessions were completed. The music therapy interventions were coordinated and executed by a graduated and qualified professional music therapist, in a welcoming environment, and directed through the principles, methods, and techniques of music therapy, in a process of interactive participation.

Interactive participation occurs when the participant interacts with the music therapist by recreating and singing a song from their cultural environment, with rhythmic production activities that will make it possible to follow the rhythm of the songs even while lying in bed, using easy-to-use percussion instruments, such as the tambourine, the rattle (egg), the triangle, bongos. During periods of spinal cord aplasia (low immunity), to avoid contagion problems, in certain cases, contact with musical instruments was replaced by body rhythmic production, such as clapping in time with songs. The music therapy interventions were individual, conducted in the room where the patient was hospitalized, with each participant allocated to the Experimental Music Therapy Group, during eight sessions, held three times a week, lasting approximately 30 minutes. The session times were limited to the afternoon, a time when the flow of care from other specialties was lower and the patient was alone in the room, sometimes with the presence of a family member, who also participated in this process. However, with the advent of the COVID-19 pandemic, these visits were vetoed as a precaution.

The student t-test analysis applied, (p<0001) was considered statistically significant when comparing the groups (EMG versus CG), significantly reducing fatigue in the experimental group (EMG)

Inclusion criteria

Each patient, submitted to Autologous Hematopoietic Stem Cell Transplantation (HSCT), and aged between 18 and 70 years, were invited to participate in this study. If the patient, the patient agrees to participate in the study, he/she signs the Free and Informed Consent Form (ICF).

Exclusion criteria

All the patients undergoing allogeneic and syngeneic hematopoietic stem cell transplantation were excluded.

Activity procedure

Live music was applied through music therapy techniques, taught by a qualified music therapist, interpreting popular songs that are part of the patients' social/musical/cultural identity. For example: The music therapist and the patient sang the participant/patient's favorite songs together, accompanied by guitar, with the patient following the rhythm of the music with percussion instruments, such as a bongo, tambourine, bells, triangle, or maracas, among others, in an interactive process. The sessions were individual and took place at the patient's bedside, three times a week, with each session lasting 30 minutes. Eight sessions were applied for each patient.

Materials

The visual analog scale⁹ is a kind of ruler where each number from 0 to 10 has a corresponding face. For example, 0 to 3 corresponds to mild symptoms and a happy face, 4 to 7 for moderate symptoms and a worried face, and 8 to 10 for intense symptoms and a sad face. This scale was then shown to the patient by the evaluator at 30 centimeters, so the patient did not need to touch anything. Visual Analog Scale (VAS) The visual analog scale is one-dimensional and was used in this study to assess the dependent variable fatigue, referring to the patient's subjective responses. It was applied pre and post-intervention, in the experimental music therapy group (EMG) during eight music therapy sessions. Subjective

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responses about fatigue from patients assigned to the control group (CG) were also collected during eight evaluations. This scale was used because it is easy for patients to understand. After all, the bone marrow transplant environment is controlled.

The Piper Fatigue Scale (PFS)¹⁰ is a multidimensional scale that is divided into three dimensions; behavioral, affective, and sensory dimensions. The three dimensions are divided into 22 questions about fatigue. In each question, the patient chooses a number ranging from 0 to 10, which corresponds to the degree of fatigue he/she is feeling at that moment. This scale was applied before the first music therapy session and right after the eighth music therapy session.

Demographic Questionnaire Clinical: personal and clinical patient data were also collected, such as age, gender, religion, education, social class, diagnosis, and cell source.

Music therapy questionnaire: the music therapy form was created to collect information regarding the musical preferences of the patient and the patient's family. With the musical information in hand, the music therapist created a unique repertoire for each patient and thus conducted the process of attending music therapy interventions using the method of recreating songs according to each patient's preferences. Prior and informed consent form (PICF): Signed by all patients who participated in the study.

Ethical approval, approved by the ethics committee in the research of the Erasto Gaertner Hospital Certificate of Ethical Presentation and Appreciation (CAAE) number 82882017.6.0000.0098 and (REBEC) Registration Brazilian Clinical Trials RBR 3h4csb http:// www.ensaiosclinicos.gov.br/rg/RBR-3h4csb/

Sample Calculation

Considering a standard deviation of 1.6 in each of the groups, for the difference between before and after, a significant level of 5% and a power of 85%, it would take 72 cases in each group to identify a clinically significant difference of 0,8 between the two groups in the variation between before and after.

RESULTS

For each of the qualitative variables analyzed, we evaluated the null hypothesis of equal distribution of ratings in both groups: experimental music therapy group (EMG) and control group (CG) versus the alternative hypothesis of different distributions.

The analysis and statistical tests applied were considered statistically significant. (PFS) Score Total (EMG) Baseline 7.1 (CG) 6.7 p=0.30 follow up (EMG) 2.4 (CG) 5.7=2.4 p<0.001 (VAS) before intervention 6.45 p=0.89 after intervention 2.52 p<0.001.

Table 1 shows the profile, social class, and other characteristics of the population submitted to autologous hematopoietic stem cell transplantation. The age was categorized; as young people from eighteen to thirty years old, adults from thirty-one to fifty-nine years old, and the elderly from sixty years old and older (Table 1 and Figure 1).

Table 1: Clinical Demographic Data

	(EMG)	(CG)				
	n=76	n=75				
Gender						
Male, n (%)	53 (69.7%)	44 (58.7%)	p=0.16			
Female, n (%)	23 (30.3%)	31 (41.3%)	p=0.10			
AGE, n (%)						
Yang	11 (14.5%)	8 (10.7%)				
Adult	35 (46.1%)	38 (50.7%)	p=0.74			
Elderly	30 (39.5%)	29 (38.7%)				
Education, n (%)						
Illiterate	1 (1.3 %)	1 (1.3 %)	p=0.53			
First Degree	24 (31.6%)	28 (37.3%)				
Hugh School	20 (26.3%)	24 (32.0%)	μ=0.55			
Third Degree	31 (40.8%)	22 (29.3%)				
Social Class, n (%))						
Low Social Class	21 (27.6%)	(/	n 0.05			
Midle Social Class	55 (72.4%)	43 (57.3%)	p=0.05			
Religion, n (%)						
Evangelical	25 (32.9%)	29 (38.7%)				
Catholic	49 (64.5%)	39 (52.0%)	p=0.12			
Others	2 (2.6 %)	7 (9.3 %)				
Diagnosis, n (%)						
No Hodgkin Lymphoma	17 (22.4%)	21 (28.0%)				
Multiple Myeloma	40 (52.6%)	37 (49.3%)				
Testicle Tumor	3 (3.9 %)	2 (2.7 %)				
Hodgkin Lymphoma	12 (15.8%)	10 (13.3%)				
Blastic Lymphoid Leukemia	1 (1.3 %)	0 (0.0 %)	p=0.81			
Amyloidosis	0 (0.0 %)	1 (1.3 %)	p=0.01			
Ewing's Sarcoma	1 (1.3 %)	1 (1.3 %)				
Mental Lymphoma	1 (1.3 %)	2 (2.7 %)				
Meduloblastoma	1 (1.3 %)	0 (0.0 %)				
T Lymphoma	0 (0.0 %)	1 (1.3 %)				
Cell Source, n (%)						
Bone Marrow	32 (42.7%)	. ,	p=0.40			
Peripheral Blood	43 (57.3%)	48 (64.0%)				



Figure 1: Flow Chart of the Research

Table 2 shows the values of the Piper Fatigue Scale (PFS) calculated in its final value and in three dimensions according to the operating manual by the PFS: Final score: average of twentytwo items, behavioral dimension: average of items two to seven. Affective dimension: average of items eight to twelve. Sensory/ psychological dimension: average of items thirteen to twentythree. In comparison between the experimental music therapy group and control group, variables continuously were compared between groups using the unpaired t-test (Table 2) and (Figure 2).

Table 3 in the intervention group, the mean variation (95% confidence interval) of each scale at each visit, was evaluated to test whether the effect varied between visits, a longitudinal regression model was performed with analysis of response profiles assuming as a null hypothesis that the effect was the same in all visits (Table 3) and (Figure 3).

DISCUSSION

Follow UP

Baseline

Follow UP

Affective Domain Baseline

Follow UP

Baseline

Follow UP

Sensory Domain

Behavioral Domain

Change from Baseline

Change from Baseline

Change from Baseline

Change from Baseline

This investigation was motivated by music therapy sessions applied in a previous study, developed at the bone marrow transplant service of the clinical hospital complex of the Federal University of Paraná, located in the city of Curitiba, capital of State Paraná, Brazil. In the previous study, fatigue disorder was not investigated, but patients reported that music helped to reduce fatigue because

(EMG)

n=76

 2.4 ± 1.8

-4.6 ± 1.8

 7.1 ± 2.2

 2.5 ± 1.9

-4.5 ± 1.8

 7.3 ± 2.3

 2.6 ± 1.9

-4.7 ± 1.8

70 + 2.1

 2.3 ± 1.7

-4.7 ± 1.9

(CG)

n=75

5.7 ± 2.4

-1.0 ± 2.5

 6.7 ± 2.3

5.7 ± 2.5

 -0.9 ± 2.5

 $\textbf{6.9} \pm \textbf{2.4}$

 5.9 ± 2.6

-1.1 ± 2.5

6.6 + 2.3

 5.6 ± 2.4

-1.0 ± 2.5

p=0.30

p<0.001

p<0.001

p=0.34

p<0.001

p<0.001

p=0.29

p<0.001

p<0.001

p=0.31

p<0.001

p<0.001

the musical experience provided relaxation. So, we decided to conduct this scientific investigation on fatigue disorder.

Patients diagnosed with a neoplastic hematological disease undergo great emotional, physical, psychological, and social suffering. We noticed that patients experience a lot of fatigue, pain and mood disturbances, nausea, insomnia, and fear of death.

The interactive musical experience approached the patient closer to their cultural universe, leading them to a process of remembering covering moments experienced through music, distancing themselves from hospital problems and the disease itself, leading the patient to a musical sound experience, providing relaxation, which allowed improvement of their symptoms. The presence of the music therapist in an interactive activity with the patient, singing and playing a percussion instrument, accompanied by a guitar, listening to musical expressions, and enhancing the patient's experience, made a real difference, in addition to providing presence, acceptance, care and follow-up of the patient during this journey towards a successful treatment. Live music has power and vibratory energy that create a greater emotional impact on the environment. Furthermore, the human presence of the music therapist makes the patient welcome, in a relationship of attention, care, resonance, and appreciation of the patient's feel interactive expressions. Music therapy interventions reduced the symptoms and side effects of the treatment, recovering the socio-cultural-sound



Figure 2: Changes in Piper Fatigue Scale from baseline to followup according to Allocated group.

Table 3: Visual Analogue Scale (VAS) Investigated Variable: fatigue before and after intervention in the groups: Experimental Music Therapy Group (EMG) e Control Group (CG)

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Means of the visits	
	n=76	n=76	n=76	n=76	n=76	n=76	n=76	n=76	n=76	
Fatigue										
Before intervention	$\textbf{6.30} \pm \textbf{2.20}$	$\textbf{6.28} \pm \textbf{2.07}$	6.64 ± 2.29	6.62 ± 2.25	6.79 ± 2.36	6.61 ± 2.55	$\textbf{6.63} \pm \textbf{2.69}$	5.72 ± 2.79	$\textbf{6.45} \pm \textbf{1.79}$	
After intervention	2.53 ± 1.94	2.51 ± 1.74	2.62 ± 1.93	2.58 ± 1.63	2.51 ± 1.54	2.58 ± 1.83	2.89 ± 1.89	1.91 ± 1.67	$\textbf{2.52} \pm \textbf{1.08}$	
Control group	6.51 ± 2.45	6.01 ± 2.65	6.37 ± 2.39	$\textbf{6.39} \pm \textbf{2.44}$	6.84 ± 2.24	6.72 ± 2.21	$\textbf{6.39} \pm \textbf{2.49}$	6.04 ± 2.82	$\textbf{6.41} \pm \textbf{1.87}$	
Value expression in means + standard deviation p<0.001										

Value expression in means ± standard deviation. p<0.00

Total Score Baseline 7.1 ± 2.2 6.7 ± 2.3

Table 2: Evolution Fatigue Scale of Piper





contact, through the recreation of the songs, of their cultural environment, and by reducing the feeling of social confinement imposed by the autologous hematopoietic stem cells transplantation. In this randomized experimental study, the visual analog scale (VAS) and the Piper fatigue scale (PFS) were used to assess fatigue-dependent variables, which were statistically treated with the choice of Student's t-tests, to calculate the meaning in the comparison of the groups (EMG x CG) resulting in a significant decrease in fatigue symptoms. Therefore, the music therapy intervention was effective, contributing to the humanization of the hospital environment and resulting in biopsychosocial well-being for patients. However, there are few studies with the theme of music therapy, evaluating fatigue.

The Japan Journal of Nursing Science brings a recent publication of a systematic review and meta-analysis from January 2024, demonstrating in its results that the meta-analysis of the population included in the study showed that musical intervention for patients undergoing HSCT was associated with improved quality of patients' lives and resulted in a reduction in depression/anxiety and fatigue compared to patients without musical intervention¹¹.

In the study association between music therapy techniques and moderate to severe fatigue reported by patients in adults hospitalized with cancer, the American Society of Clinical Oncology published in 2020, active music therapy was applied where the patient is part of the process by singing and playing an instrument and they also applied passive music therapy where the patient only listens to music. The results were positive for the reduction of fatigue in the active music therapy group and non-significant in the passive music therapy group. It is an interesting study that shows the path to be taken by music therapy to achieve improvements for patients with fatigue. The strength of the study is in demonstrating which technique is best to achieve the reduction of this symptom. In this case, active or interactive music therapy as we call it here in Brazil due to the patient's participation in singing, producing rhythm within their possibilities, and in passive music therapy where the patient just listened to music, there was no improvement in fatigue¹².

The strong point of our study is the number of patients researched, the strength of live music and the interaction created by the music therapist and patient, and the number of sessions applied, eight sessions per patient in the intervention group, which we obtained 76 patients, eight times sessions that resulted in a total of 608 music therapy sessions administered over three years. As a limiting force of the study, we highlight the nonpossibility of implementing double-blind, with music this was impossible.

We hope that this study fills a gap and that more music therapists can replicate this study. This contributes to the affirmation of the results around this theme, so recurrent in this population, but little researched, and thus, also obtaining greater credibility and validity for this therapeutic modality; "music therapy."

Conclusion

According to the objective of the study, the data collected were treated statistically and the results indicate that the music therapy intervention was able to reduce the fatigue of patients admitted undergoing autologous hematopoietic stem cell transplantation.

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