

CLINICAL RESEARCH

Effects of music therapy on pain and oxidative stress in oocyte pick-up: A randomized clinical trial[☆]



Yavuz Orak^{a,*}, Suleyman Murat Bakacak^b, Asli Yaylalı^c, Fatma Inanc Tolun^d, Hakan Kırın^b, Omer Faruk Boran^a, Akif Hakan Kurt^e, Adem Doganer^f

^a Kahramanmaraş Sutcu Imam University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Onikişubat, Turkey

^b Kahramanmaraş Sutcu Imam University, Faculty of Medicine, Department of Obstetrics and Gynecology, Onikişubat, Turkey

^c Kahramanmaraş Sutcu Imam University, Faculty of Medicine, Histology Department, Onikişubat, Turkey

^d Kahramanmaraş Sutcu Imam University, Faculty of Medicine, Department of Biochemistry, Onikişubat, Turkey

^e Bolu Abant İzzet Baysal University, Faculty of Medicine, Medical Pharmacology, Bolu, Turkey

^f Kahramanmaraş Sutcu Imam University, Faculty of Medicine, Biostatistics and Medical Informatics, Onikişubat, Turkey

Received 17 June 2019; accepted 17 April 2020

Available online 21 July 2020

KEYWORDS

Oocyte retrieval;
Music therapy;
Pain;
Oxidative stress

Abstract

Background and objective: The aim was to investigate the effects of Turkish classical music on pain and oxidative stress in patients undergoing oocyte pick-up.

Methods: The study was a randomized, controlled trial. The groups included Group NM (Non-Music), control group; Group PM, which comprised patients who listened to music before the operation; and Group CM, which comprised patients who listened to music both before and during the operation. Blood was drawn prior to the operation to measure the oxidative stress values. Pain, hemodynamic parameters, oxidative stress values were assessed postoperatively.

Results: The number of patients requiring additional propofol was higher in Group PM than in Groups NM and CM ($p=0.003$). The postoperative Visual Analog Scale (VAS) score were lower in Groups PM and CM than in Group NM ($p=0.001$, $p=0.007$) in the 1st and 60th minutes. The postoperative VAS score was lower in Group CM than in Group NM ($p=0.045$) in the 5th minute. The postoperative additional analgesic requirements were lower in Groups PM and CM than in Group NM ($p=0.045$). The postoperative blood glutathione peroxidase values were significantly higher in Groups PM and CM than in Group NM ($p=0.001$). The postoperative catalase values were significantly higher in Groups PM and CM than in Group NM ($p=0.008$ and $p<0.001$). The preoperative malondialdehyde values were significantly lower in Groups PM and CM than in Group NM. The preoperative nitric oxide values were higher in Groups PM and CM than in Group NM ($p<0.001$), whereas the postoperative nitric oxide values were lower in Groups PM and CM than in Group NM ($p<0.001$).

[☆] This prospective, randomized, controlled study was performed between November 15, 2017, and June 1, 2018 in Faculty of Medicine, Kahramanmaraş Sutcu Imam University.

* Corresponding author.

E-mail: dryavuzorak@hotmail.com (Y. Orak).

PALAVRAS-CHAVE

Aspiração folicular;
Musicoterapia;
Dor estresse oxidativo

Conclusion: Turkish classical music has beneficial effects on pain and oxidative stress in oocyte pick-up patients.

© 2020 Sociedade Brasileira de Anestesiologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Efeitos da musicoterapia sobre dor e estresse oxidativo na aspiração folicular: um estudo clínico randomizado

Resumo

Justificativa e objetivo: O objetivo deste estudo foi investigar os efeitos da música clássica turca sobre a dor e o estresse oxidativo em pacientes submetidas a aspiração folicular.

Método: Estudo randomizado controlado. Os grupos foram: grupo controle NM, sem música; Grupo PM, com pacientes que ouviram música antes da cirurgia; e Grupo CM, com pacientes que ouviram música antes e durante a cirurgia. Foi coletado sangue antes da cirurgia para avaliar os valores de estresse oxidativo. Dor, parâmetros hemodinâmicos e valores de estresse oxidativo foram avaliados após a cirurgia.

Resultados: O número de pacientes que necessitou de propofol adicional foi mais alto no Grupo PM do que nos Grupos NM e CM ($p=0,003$). A pontuação da Escala Visual Analógica (EVA) pós-operatória foi mais baixa nos Grupos PM e CM do que no Grupo NM ($p=0,001$; $p=0,007$) no 1° e 60° minutos. A pontuação da EVA pós-operatória foi mais baixa no Grupo CM do que no Grupo NM ($p=0,045$) no 5° minuto. A necessidade de analgesia pós-operatória adicional foi mais baixa nos Grupos PM e CM do que no Grupo NM ($p=0,045$). Os valores pós-operatórios de glutathione peroxidase no sangue foram significativamente mais altos nos Grupos PM e CM do que no Grupo NM ($p=0,001$). Os valores pós-operatórios de catalase foram significativamente mais altos nos Grupos PM e CM do que no Grupo NM ($p=0,008$ e $p<0,001$). Os valores pré-operatórios de malondialdeído foram significativamente mais baixos nos Grupos PM e CM do que no Grupo NM. Os valores pré-operatórios de óxido nítrico foram mais altos nos Grupos PM e CM do que no Grupo NM ($p<0,001$), ao passo que valores pós-operatórios de óxido nítrico foram mais baixos nos Grupos PM e CM do que no grupo NM ($p<0,001$).

Conclusão: Música clássica turca exerce efeito benéfico sobre a dor e estresse oxidativo em pacientes na aspiração folicular.

© 2020 Sociedade Brasileira de Anestesiologia. Publicado por Elsevier Editora Ltda. Este é um artigo Open Access sob uma licença CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

In Vitro Fertilization (IVF) is an important advanced procedure for the treatment of infertility and involves controlled stimulation of the ovaries with drugs, ultrasound-guided transvaginal oocyte aspiration from the ovaries, fertilization, and embryo transfer to the uterus.¹ The collection of oocytes (eggs) using transvaginal ultrasound in IVF requires little time to accomplish. Puncturing the vaginal skin and ovarian capsule to aspirate the oocytes causes discomfort, which resembles deep menstrual pain.^{2,3}

Oxidative Stress (OS) is the result of an imbalance between the formation of Reactive Oxygen Species (ROS) and antioxidants. Oxidative stress biomarkers are important in assessing the disease state and health-promoting effects of antioxidants.⁴

OS affects a woman's entire reproductive life and even after the reproductive life ends. Enzymatic antioxidants, also referred to as natural antioxidants, neutralize excess ROS and prevent damage to cellular structures.⁵ Studies have shown that OS is a factor responsible for female infertility.⁶

Music therapy is considered an inexpensive, safe, and efficacious non-pharmacological and anxiolytic approach because of its effects on the perception of pain and anxiety.⁷ During music therapy, the patient's experience with music, along with his or her cultural habits, personality type, and music preferences, needs to be considered.^{8,9} Turkish classical music is a genre of national and traditional music that Turkish people like to listen to. Our study focused on the Ace-masiran mode of Turkish classical music. It affects the brain and bones and promotes a body fat balance. Additionally, it inspires creativity in the listener, revitalizes stagnant thoughts and emotions, and facilitates birth in pregnant women. Moreover, it helps correct improper intrauterine postures of fetuses, relieves pain and spasms, enhances sensual pleasure, and promotes relaxation.¹⁰

Although studies have examined the effects of music therapy on pain, no studies have examined the pain and OS of patients undergoing oocyte pick-up, with a focus on Catalase (CAT), Glutathione Peroxidase (GPX), Malondialdehyde (MDA), and Nitric oxide (NO). The present study aimed to investigate the effects of music on pain and OS in oocyte pick-up patients.

Methods

This study was approved by the Kahramanmaraş Sutcu Imam University Faculty of Medicine's Institutional Review Board (2017/12-14, Dated: July 19, 2017), and written informed consent was obtained from all subjects participating in the trial. The trial was registered prior to patient enrollment at clinicaltrials.gov (NCT03346031, principal investigator: YOrak, date of registration: 11/07/2017). This prospective, randomized controlled study was performed between November 15, 2017 and June 1, 2018. A total of 93 women aged 18–40 years were included in this study. All patients were considered American Society of Anesthesiologists Classification (ASA) I, and none of the patients had hearing problems. Patients who did not volunteer to participate, those with comprehension or hearing problems, those outside the 18–40 age range, and those with melophobia were excluded. The study patients were randomly divided into the following three parallel groups: Group NM (Non Music), which comprised control patients ($n=31$); Group PM, which comprised patients who listened to Turkish classical music before the operation ($n=31$); and Group CM, which comprised patients who listened to Turkish classical music both before and during the operation ($n=31$) (Fig. 1). The patients were handed sealed opaque envelopes with their group assignment in the examination room at least 1 hour before they entered the operating room and were randomized in the groups with a 1:1:1 ratio. Then, with respect to the random allocation sequence, participants will be allocated to their groups. The study procedure was shared with all patients. The patients in Group NM were taken to a relaxation room, where they remained for 1 hour and then blood samples were collected, and the values of OS parameters, including the CAT (u.mL^{-1}), GPX (u.mL^{-1}), MDA (nmoL.mL^{-1}), NO ($\mu\text{mol.L}^{-1}$) levels, were measured. The patients were then taken to the operating room. The patients in Group PM were taken to the relaxation room, where they listened to Turkish classical music with headphones for 1 hour. After listening to music, blood samples were collected, and the OS parameters were measured before they were taken to the operating room. The patients in Group CM were taken to the relaxation room, where they listened to Turkish classical music with headphones for 1 hour. After listening to music, blood samples were collected, and the OS parameters were measured. They were then taken to the operating room, where they listened to Turkish classical music with headphones for the duration of the operation.

For anesthesia induction, remifentanyl $0.5 \mu\text{g.kg}^{-1}$ and propofol 1 mg.kg^{-1} were administered intravenously in a single dose. During the operation, the Systolic Blood Pressure (SBP, mmHg), Diastolic Blood Pressure (DBP, mmHg), Heart Rate (HR), Mean Arterial Pressure (MAP, mmHg), Oxygen Saturation (SpO_2), and body movement were recorded at 1, 3, 5, 7, 10, and 15 minutes in the monitor (Dräger/Infinity Vista XL, USA). Moreover, additional analgesic and anesthetic requirements throughout the operation were recorded. Additional doses of remifentanyl and propofol were administered intravenously as single doses in response to the body movements. Upon completion of the operation, follicular fluid was collected in the operating room. The patients were taken to the relaxation room after the operation. Blood

samples were taken from all patients in the groups to measure OS parameters within 3–5 minutes. The SBP, DBP, HR, MAP, SpO_2 and pain data were recorded at 1, 5, 15, 30 and 60 minutes in the relaxation room. The Visual Analog Scale (VAS) was used to assess pain postoperatively. Patients with VAS scores of ≥ 5 and those requiring analgesic agents were administered a nonsteroidal anti-inflammatory drug (diclofenac sodium 75 mg, intramuscular), and this information was recorded. The patients were discharged when their levels of consciousness, speech and motor activity matched those at the time of admission and their vital signs were stable.

Oxidative stress measurement

The Beutler method was used for the GSH-Px activity measurement. GSH-Px catalyzes the oxidation of reduced glutathione (GSH) to oxidized glutathione (GSSG) by interacting with H_2O_2 . In the presence of H_2O_2 and t-butyl hydroperoxide, GSSG composed of GSH-Px is reduced to GSH by interacting with glutathione reductase and NADPH. GSH-Px activity is detected spectrophotometrically by measuring the difference in absorbance at a wavelength of 340 nm during the oxidation of NADPH to NADP.¹¹ The results were reported as units per milliliter (u.mL^{-1}).

CAT activity was measured as the degradation rate of H_2O_2 using the Beutler method. The rate of disappearance of H_2O_2 was assessed spectrophotometrically at a wavelength of 230 nm. The test involved $50 \mu\text{L}$ of 1 M Tris HCl buffer (pH 8), $930 \mu\text{L}$ of 10 mM H_2O_2 , $930 \mu\text{L}$ of deionized water, and $20 \mu\text{L}$ of a serum sample. CAT activity was detected as the amount of enzyme causing approximately 90% destruction of the substrate in 1 minute in a volume of 1 mL.¹² The results were reported as units per milliliter (u.mL^{-1}).

The concentration of tissue lipid peroxidation (total MDA) was measured as reported by Ohkawa. The reaction mixture included 0.1 mL of a supernatant, 1.5 mL of 20% acetic acid, 0.2 mL of 8.1% sodium dodecyl sulfate and 1.5 mL of a 0.8% aqueous solution of Thiobarbituric Acid (TBA). The pH of the mixture was regulated to 3.5, and the volume was increased to 4.0 mL with the addition of distilled water. Then, 5.0 mL of a mixture of n-butanol and pyridine (15:1, v/v) were added. After centrifugation at 4000 rpm for 10 minutes, the absorbance of the organic layer was moderated at 532 nm.¹³ The results were reported as nanomoles per milliliter (nmoL.mL^{-1}).

The serum NO levels were measured with the use of the Griess reagent (sulfanilamide and N-1-naphthylethylenediamine dihydrochloride). Five microliters of reconstituted nitrate reductase and $10 \mu\text{L}$ of 2 mmol.L^{-1} NADH were added to the samples, which were incubated at room temperature for 20 minutes to convert all the nitrate to nitrite. The samples were deproteinized, and $100 \mu\text{L}$ of Griess reagent was added. After color advancing was performed at room temperature, the absorbance values were measured at a wavelength of 540 nm. The samples were adjusted in pairs. The amount of nitrite in the serum was estimated by a standard curve obtained from the enzymatic conversion of potassium nitrate to nitrite.¹⁴ The results were reported as micromoles per liter ($\mu\text{mol.L}^{-1}$).

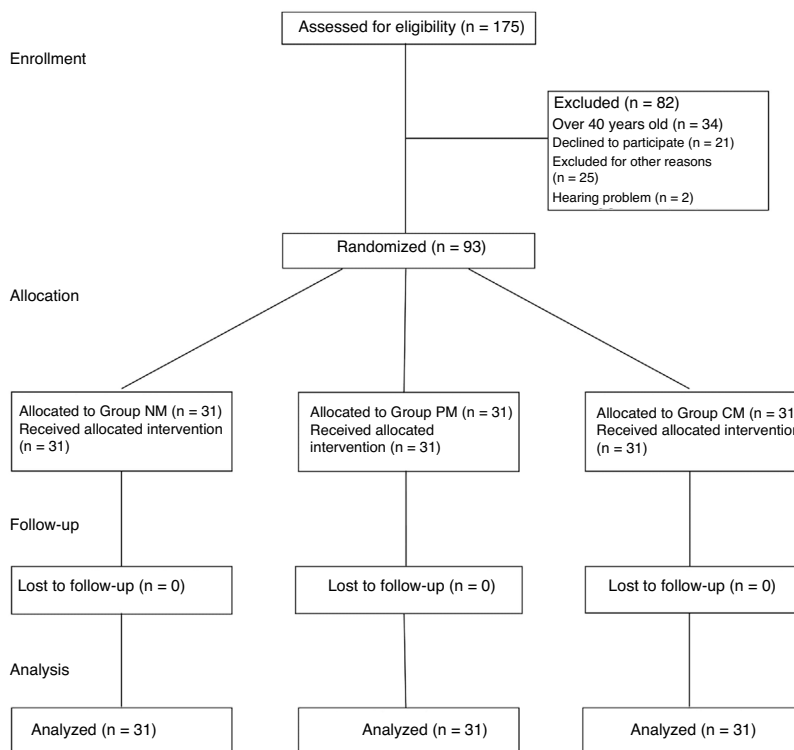


Figure 1 The consolidated standards of reporting trials (CONSORT) flow diagram. Group NM, Non-Music; Group PM, Preoperative Music; Group CM, Continuous Music.

The visual analog scale (VAS)

The VAS is commonly used for measuring pain severity. It is shown as a 10 cm horizontal line on which the patient's pain intensity and severity is represented by a point between the following limits: "no pain at all" and the "worst pain conceivable". The VAS is simple, reliable, and valid for assessing pain severity or intensity.¹⁵

Statistical analysis

In our study, the statistical parameters in the reference study¹⁶ were taken into account in determining the sample size. Our study consist of three groups, VAS and oxidative stress parameters were primary outcome measures. Hemodynamic parameters were secondary outcome measures. The postoperative pain score in the reference study was based on. Group M 33.8 ± 13.6 and Group C 45.1 ± 16.2 values were taken into consideration in the reference study. A total of 93 patients, with a test power of $\alpha = 0.05$ first type and $\beta = 0.20$ second type error level, 0.80 test power for each group, were planned.

The conformity of the variables to a normal distribution was analyzed using the Shapiro-Wilk test. Repeated measures ANOVA was applied to repeated measurements to examine the differences between the measurements for normally distributed variables. One-way ANOVA was used for comparisons between three or more groups. Post hoc multiple comparisons were conducted using Tukey's HSD test, Tamhane's T2 test, and Dunnett's test. Pre- and postoperative comparisons were examined using the Wilcoxon signed

rank test for variables that did not show a normal distribution. Comparisons between three or more groups were conducted using the Kruskal-Wallis test. Post hoc multiple comparisons were conducted using the Dunn-Sidak test. The Chi-Squared test and Fisher's exact test were used to evaluate the relationships among the frequency distributions of categorical variables. The statistical parameters of the normally distributed variables are expressed as the mean \pm SD, whereas the statistical parameters of the variables that were not distributed normally are expressed as the median (min-max). Statistical analyses were conducted using the IBM SPSS 22 package. A p -value < 0.05 was considered statistically significant.

Results

A total of 93 patients were included in the study (Fig. 1). No differences were noted between the patients' age, and Body Mass Index (BMI) (Table 1). All patients were ASA status I.

The number of patients requiring additional analgesic and/or anesthetic drugs according to their body movements was significantly lower in Groups PM and CM than in Group NM ($p = 0.013$) (Table 2).

The duration of the operation was the longest in Group PM. There was a significant difference between Group PM and Group CM in terms of the operation time ($p = 0.023$). The operation time was shorter in Group CM. The amount of additional remifentanyl required during the operation was lower in Group CM than in Groups PM and NM, and the latter difference was found to be statistically significant ($p = 0.001$

Table 1 Demographic characteristics by each group.

	Control (n = 31)	Preoperative music (n = 31)	Preoperative + perioperative music (n = 31)	<i>p</i>
BMI ^a (Mean ± SD)	26.50 ± 4.41	28.03 ± 4.36	26.46 ± 4.14	0.267
Age ^a (Mean ± SD)	31.10 ± 5.62	31.00 ± 5.96	31.55 ± 4.19	0.910

^a One Way Anova; $\alpha = 0.05$.
BMI, Body Mass Index.

and $p = 0.001$, respectively). The amount of additional propofol required was significantly higher in Group PM than in Groups NM and CM ($p = 0.003$) (Table 3).

The postoperative pain (VAS) scores at the 1st, 5th, and 60th minute were significantly lower in Groups PM and CM than in Group NM ($p = 0.001$, $p = 0.045$, and $p = 0.007$, respectively) (Table 4). The postoperative additional analgesic (diclofenac sodium 75 mg) requirements were significantly lower in Groups PM and CM than in Group NM ($p = 0.045$).

Regarding the hemodynamic parameters, the SBP values at the 1st and 10th minute ($p = 0.002$ and $p = 0.049$, respectively), the DBP value at the 1st minute ($p = 0.007$), the MAP value at the 1st minute ($p = 0.002$), and the HR values at the 1st, 3rd, 5th, and 7th minutes ($p < 0.001$, $p = 0.006$, $p = 0.008$, and $p = 0.032$, respectively) were found to be significantly higher in Group PM than in Group NM (Table 5). No statistically significant differences in SpO₂ were noted between the groups ($p = 0.138$).

The postoperative blood GPX values were significantly higher in Groups PM and CM than in Group NM ($p = 0.001$) (Table 6). The differences between the pre- and postoperative GPX values in Groups NM and CM were significant, and compared with the preoperative value, the postoperative value was higher in Group CM and lower in Group NM.

The postoperative CAT values were significantly higher in Groups PM and CM than in Group NM ($p = 0.008$ and $p < 0.001$, respectively). The difference between the pre- and postoperative CAT values in Group CM was significant, and the postoperative value was lower than the preoperative value in this group ($p = 0.006$) (Table 6).

The preoperative MDA values were significantly lower in Groups PM and CM than in Group NM (both $p < 0.001$). The difference between the pre- and postoperative MDA values in Group PM was significant, and the postoperative value was lower than the preoperative value in this group ($p = 0.006$) (Table 6).

The preoperative NO values were higher in Groups PM and CM than in Group NM ($p < 0.001$), whereas the postoperative NO values were lower in Groups PM and CM than in Group NM ($p < 0.001$). The differences between the pre- and postoperative NO values in Groups NM and PM were significant, and compared with the preoperative values, the postoperative values were lower in Group PM and higher in Group NM ($p = 0.006$ and $p = 0.001$, respectively) (Table 6).

Regarding the follicular fluid, detected no statistically significant difference in any of the groups in terms of the CAT, GPX, MDA, and NO values.

Discussion

In this study, we investigated the effects of the Acemasiran mode of Turkish classical music on pain and OS in oocyte pick-up patients. There were fewer body movements in the patients in Groups PM and CM, who were the patients who listened to music, than in the patients in Group NM; therefore, the patients in Groups PM and CM needed less additional analgesic and/or anesthetic drugs, and the differences were significant. The amount of additional remifentanyl required was significantly lower in Group CM than in Group NM. The amount of additional propofol required was significantly higher in Group PM than in Groups NM and CM. Additionally, the patient pain (VAS) scores at the 1st, 5th, and 60th postoperative minutes were significantly lower in Groups PM and CM than in Group NM. Moreover, the amount of additional analgesic used postoperatively was significantly lower in Groups PM and CM than in Group NM.

In one study, music significantly lowered not only the doses of the sedative and analgesic drugs required by patients undergoing colonoscopy but also the anxiety and pain scores of patients, while it increased the satisfaction scores and comfort of patients.¹⁷ Music therapy is a non-pharmacological, cheap, and non-invasive technique that can significantly increase patient satisfaction and decrease the pain and perioperative stress.¹⁶ In a study conducted in cesarean section patients who listened to music for 1 hour prior to surgery (consistent with the approach in the present study), postoperative tramadol consumption, total tramadol consumption, additional analgesic use, and all VAS scores were significantly reduced with music therapy.¹⁸ In a previous study, listening to music in the perioperative period reduced the need for midazolam in patients undergoing spinal anesthesia.¹⁹ Similarly, in a study conducted in burn patients, pain and anxiety were significantly lower and relaxation was higher in the music, massage, and music-plus-massage groups than in the control group, although there were no significant differences among the three study groups.²⁰

In our study, the Turkish classical music had effects on the SBP, DBP, MAP, and HR. During the operation, the SBP at the 1st and 10th minutes, DBP at the 1st minute, MAP at the 1st minute, and HR at the 1st, 3rd, 5th, and 7th minutes were significantly higher in Group PM than in Group NM. Music therapy had no effect on oxygen saturation. According to other studies, listening to Turkish classical music alone is beneficial for reducing SBP and DBP in hypertensive elderly

Table 2 Distributions of patients requiring additional operative analgesics and anesthetics based on their body movements by study group.

	Additional analgesics and anesthetics required				Total		<i>p</i>
	No		Yes		n	%	
	n	%	n	%			
<i>Control</i>							0.273
No movement	1	4.5	0	0.0	1	2.8	
Upper extremity movement	7	31.8	1	7.1	8	22.2	
Lower movement knee joint	1	4.5	1	7.1	2	5.6	
Hip movement	2	9.1	0	0.0	2	5.6	
Upper extremity + lower movement knee joint	3	13.6	5	35.7	8	22.2	
Upper extremity + hip movement	1	4.5	0	0.0	1	2.8	
Lower movement knee joint + hip movement	1	4.5	0	0.0	1	2.8	
Upper extremity + lower movement knee joint + hip movement	6	27.3	7	50.0	13	36.1	
<i>Preoperative music</i>							0.088
No movement	3	10.0	0	0.0	3	8.1	
Upper extremity movement	13	43.3	1	14.3	14	37.8	
Lower movement knee joint	2	6.7	0	0.0	2	5.4	
Hip movement	0	0.0	1	14.3	1	2.7	
Upper extremity + lower movement knee joint	5	16.7	4	57.1	9	24.3	
Upper extremity + hip movement	5	16.7	1	14.3	6	16.2	
Lower movement knee joint + hip movement	2	6.7	0	0.0	2	5.4	
<i>Preoperative music + perioperative music</i>							0.173
No movement	2	6.1	0	0.0	2	5.4	
Upper extremity movement	7	21.2	1	25.0	8	21.6	
Lower movement knee joint	3	9.1	2	50.0	5	13.5	
Hip movement	1	3.0	1	25.0	2	5.4	
Upper extremity + lower movement knee joint	9	27.3	0	0.0	9	24.3	
Upper extremity + hip movement	5	15.2	0	0.0	5	13.5	
Lower movement knee joint + hip movement	2	6.1	0	0.0	2	5.4	
Upper extremity + lower movement knee joint + hip movement	4	12.1	0	0.0	4	10.8	
<i>Total</i>							0.085
No movement	6	7.1	0	0.0	6	5.5	
Upper extremity movement	27	31.8	3	12.0	30	27.3	
Lower movement knee joint	6	7.1	3	12.0	9	8.2	
Hip movement	3	3.5	2	8.0	5	4.5	
Upper extremity + lower movement knee joint	17	20.0	9	36.0	26	23.6	
Upper extremity + hip movement	11	12.9	1	4.0	12	10.9	
Lower movement knee joint + hip movement	3	3.5	0	0.0	3	2.7	
Upper extremity + lower movement knee joint + hip movement	12	14.1	7	28.0	19	17.3	
Total	85	100.0	25	100.0	110	100.0	
<i>Control</i>	22	25.8	14	56.0	36	32.8	0.013 ^a
<i>Preoperative music</i>	30	35.2	7	28.0	37	33.6	
<i>Preoperative music + perioperative music</i>	33	39.0	4	16.0	37	33.6	

Chi-Squared test; Fisher's exact test; $\alpha = 0.05$.^a Distribution of frequencies between groups is statistically significant.

Table 3 Comparisons of the operative measurements among the study groups.

	Control (n = 31)	Preoperative music (n = 31)	Preoperative + perioperative music (n = 31)	p
	Mean ± SD	Mean ± SD	Mean ± SD	
Duration of operation	10.31 ± 3.72	12.03 ± 4.46 ^c	9.68 ± 2.87 ^b	0.023 ^d
Remifentanyl	35.06 ± 7.47	35.81 ± 6.92	34.46 ± 5.98	0.695
Propofol	68.47 ± 16.12	71.62 ± 13.23	68.92 ± 11.49	0.569
Number of follicles	9.67 ± 5.36	10.84 ± 8.07	10.08 ± 5.68	0.737
Number of oocytes	7.97 ± 5.87	9.38 ± 7.13	8.41 ± 5.74	0.619
Additional propofol dose	61.25 ± 35.22 ^b	86.49 ± 60.52 ^{a,c}	52.97 ± 22.93 ^b	0.003 ^d
Additional remifentanyl dose	55.00 ± 50.31 ^c	37.03 ± 25.48	24.32 ± 15.64 ^a	0.001 ^d

One-way Anova; post hoc: Tukey’s HSD test; Dunnett’s test; α = 0.05.

^a Difference with the control group is statistically significant.

^b Difference with the preoperative music group is statistically significant.

^c Difference with the preoperative + perioperative music group is statistically significant.

^d Difference is statistically significant.

Table 4 Comparisons of the postoperative visual analog scale (vas) scores among the study groups.

	Control (n = 31)	Preoperative music (n = 31)	Preoperative + perioperative music (n = 31)	p
	Mean ± SD	Mean ± SD	Mean ± SD	
1st min	3.69 ± 2.57 ^{b,c}	0.78 ± 0.65 ^a	1.65 ± 1.06 ^a	0.001 ^{d,f}
5th min	3.78 ± 2.52 ^c	2.78 ± 1.59	2.41 ± 1.02 ^a	0.045 ^{d,f}
15th min	4.11 ± 2.73	3.24 ± 1.69	2.92 ± 1.13	0.121 ^d
30th min	3.44 ± 2.37	3.27 ± 2.33	2.65 ± 1.69	0.254 ^d
60th min	3.31 ± 2.21 ^{b, c}	2.11 ± 0.95 ^a	1.94 ± 1.62 ^a	0.007 ^{d,f}
p	0.687 ^e	0.001 ^{e,g}	0.033 ^{e,g}	

^a Difference with the control group is statistically significant.

^b Difference with the preoperative music group is statistically significant.

^c Difference with the preoperative + perioperative music group is statistically significant.

^d One-Way Anova.

^e Repeated measures Anova; α = 0.05.

^f Intergroup difference is statistically significant.

^g Difference between the repeated measurements is statistically significant; post hoc: Tukey’s HSD test; Tamhane’s T2 test; Dunnett’s test.

Table 5 Comparisons of the perioperative heart rate measurements among the study groups.

	Control (n = 31)	Preoperative music (n = 31)	Preoperative + perioperative music (n = 31)	p
	Mean ± SD	Mean ± SD	Mean ± SD	
1st min	81.33 ± 13.18 ^b	96.32 ± 16.95 ^{a, c}	82.92 ± 12.72 ^b	<0.001 ^{d,f}
3rd min	75.42 ± 12.60 ^b	83.05 ± 14.91 ^{a, c}	73.73 ± 11.10 ^b	0.006 ^{d,f}
5th min	70.61 ± 13.15 ^b	78.59 ± 11.52 ^{a, c}	71.67 ± 9.91 ^b	0.008 ^{d,f}
7th min	71.00 ± 12.24	76.43 ± 12.08 ^c	69.50 ± 9.62 ^b	0.032 ^{d,f}
10th min	69.65 ± 12.25	73.43 ± 13.03	66.81 ± 8.56	0.168 ^d
15th min	79.50 ± 7.19	77.20 ± 9.38	68.67 ± 6.66	0.254 ^d
p	0.002 ^{e,g}	<0.001 ^{e,g}	<0.001 ^{e,g}	

^a Difference with the control group is statistically significant.

^b Difference with the preoperative music group is statistically significant.

^c Difference with the preoperative + perioperative music group is statistically significant.

^d One-Way Anova.

^e Repeated measures Anova; α = 0.05.

^f Intergroup difference is statistically significant.

^g Difference between the repeated measurements is statistically significant; post hoc: Tukey’s HSD test; Tamhane’s T2 test; Dunnett’s test.

Table 6 Comparisons of the pre- and postoperative oxidative stress parameters among the study groups.

	Control (n = 31)	Preoperative music (n = 31)	Preoperative music + perioperative music (n = 31)	p
	Median (min–max)	Median (min–max)	Median (min–max)	
GPX				
Pre	0.036 (0.006–0.061)	0.039 (0.000–0.066)	0.037 (0.011–0.071)	0.365 ^d
Post	0.030 (0.013–0.049) ^{b,c}	0.039 (0.016–0.059) ^a	0.043 (0.010–0.061) ^a	0.001 ^{d,f}
p	0.041 ^{e,g}	0.952 ^e	0.049 ^{e,g}	
CAT				
Pre	1.514 (0.352–12.038) ^{b,c}	4.576 (0.493–19.642) ^{a,c}	3.098 (0.704–70.400) ^{a,b}	0.008 ^{d,f}
Post	1.126 (0.000–12.883) ^{b,c}	2.957 (0.563–21.120) ^{a,c}	1.971 (0.422–9.856) ^{a,b}	<0.001 ^{d,f}
p	0.983 ^e	0.665 ^e	0.006 ^{e,g}	
MDA				
Pre	5.050 (0.790–12.960) ^{b,c}	3.745 (1.780–5.970) ^a	4.150 (0.000–6.210) ^a	<0.001 ^{d,f}
Post	3.885 (1.470–36.650) ^b	3.150 (0.320–10.620) ^a	3.430 (2.500–36.160)	<0.001 ^{d,f}
p	0.076 ^e	0.006 ^{e,g}	0.544 ^e	
NO				
Pre	0.432 (0.034–3.936) ^b	1.104 (0.192–3.600) ^{a,c}	0.456 (0.192–2.208) ^b	<0.001 ^{d,f}
Post	0.720 (0.384–2.016) ^c	0.672 (0.240–2.256) ^c	0.432 (0.240–1.008) ^{a,b}	<0.001 ^{d,f}
p	0.006 ^{e,g}	0.001 ^{e,g}	0.980 ^e	

GPX, Glutathione Peroxidase (u.mL⁻¹); CAT, Catalase (u.mL⁻¹); MDA, Malondialdehyde (nmol.mL⁻¹); NO, Nitric Oxide (μmol.L⁻¹).

^a Difference with the control group is statistically significant.

^b Difference with the preoperative music group is statistically significant.

^c Difference with the preoperative music + perioperative music group is statistically significant.

^d Kruskal–Wallis H test; post hoc: Dunn's test.

^e Wilcoxon sign test; α = 0.05.

^f Difference is statistically significant.

^g Pre-post difference is statistically significant.

patients.²¹ In a study conducted in preterm infants, lullabies significantly reduced the HR and respiration rate; however, there was no effect on oxygen saturation.²²

The Acemasiran mode of Turkish classical music used in this study is a genre that is believed to foster creativity and inspiration, revitalize stagnant thoughts and emotions, facilitate birth in pregnant women, help correct improper postures in intrauterine fetuses, relieve pain and spasms, add zest to life, and promote relaxation.¹⁰ We evaluated the changes in hemodynamic parameters that were related to the Acemasiran mode's ability to foster creativity and inspiration and revitalize stagnant thoughts and emotions.

The postoperative blood GPX values were higher in Groups PM and CM than in Group NM. In addition, in Group CM, the postoperative GPX value was higher than the preoperative value, whereas in Group NM, the postoperative value was lower than the preoperative value. Thus, music therapy can increase the antioxidant enzyme GPX, which inhibits the onset and development of lipid peroxidation.²³ The postoperative CAT values were higher in Groups PM and CM than in Group NM. In addition, in Group CM, the postoperative CAT value was lower than the preoperative value. The postoperative CAT values changed in both groups that listened to music. The preoperative MDA values were lower in Groups PM and CM than in Group NM. In Group PM, the postoperative MDA value was lower than the preoperative value. MDA is a biochemical marker used as an indicator of lipid damage in tissues.²⁴ Thus, music therapy decrea-

sed both preoperative and postoperative lipid peroxidation. The preoperative NO values were higher in Groups PM and CM than in Group NM. The postoperative NO values were lower in Groups PM and CM than in Group NM. Thus, music therapy can increase the preoperative NO values and decrease the postoperative values. A previous study showed that increased levels of peritoneal NO may be associated with endometriosis, its related infertility, and the pathogenesis of idiopathic infertility.²⁵

In our study, music not only reduced the need for operative and postoperative analgesics in oocyte pick-up patients but also lowered the postoperative pain scores. Furthermore, it increased the postoperative values of the antioxidant enzymes GPX and CAT and decreased the MDA and NO values.

Although many studies in the literature involve music therapy, no studies have assessed the effects of music therapy on OS. Our study is important because it is the first to investigate the effects of music therapy on OS.

Our study was a single center study. Music can have different effects in different cultures. These are limiting factors in our study.

In conclusion, Turkish classical music therapy (Acemasiran mode) has beneficial effects on pain and OS in oocyte pick-up patients. We believe that our results are valuable for the development of new studies on the use of local and cultural music in oocyte pick-up patients and in other clinical populations.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgements

The authors thank ENAGO (assignment number: ORAKT-3, filename: Yavuz.Orak_20 December 2018_19_36_37_English Music Therapy_ORAKT-3.docx) for providing English language editing for this study.

The authors thank AJE (Certificate verification code 6D73-E6DE-F217-9476-3412) for providing English language editing for this study.

We would like to thank the staff of the Department of Obstetrics and Gynecology and Department of Anesthesia and Reanimation at Kahramanmaraş Sutcu Imam Faculty of Medicine.

GETAT 2019 Traditional and Complementary Congress. 24-27 April 2019, Istanbul (Presented as verbal presentation).

References

- Sharma A, Borle A, Trikha A. Anesthesiafor in vitrofertilization. *J Obstet Anaesth Crit Care*. 2015;5:62–72.
- Kwan I, Bhattacharya S, Knox F, et al. Conscious sedation and analgesia for oocyte retrieval during IVF procedures: a Cochrane review. *Hum Reprod*. 2006;21:1672–9.
- Stener VE, Waldenström U, Nilsson L, et al. A prospective randomized study of electro-acupunctu reversus alfentanil as anaesthesia during oocyte aspiration in in-vitro fertilization. *Hum Reprod*. 1999;14:2480–4.
- Marrocco I, Altieri F, Peluso I. Measurement and clinical significance of biomarkers of oxidative stress in humans. *Oxid Med Cell Longev*. 2017:6501046.
- Agarwal A, Gupta S, Sharma RK. Role of oxidative stress in female reproduction. *Reprod Biol Endocrinol*. 2005;3:28.
- Gupta S, Ghulmiyyah J, Sharma R, et al. Power of proteomics in linking oxidative stres and female infertility. *Biomed Res Int*. 2014;2014:916212.
- Andrada JMLC, Vidal AA, Tablada TCA, et al. Anxiety during the performance of colonoscopies: modification using music therapy. *Eur J Gastroenterol Hepatol*. 2004;16:1381–6.
- Good M, Lee Picot B, Salem SG, et al. Cultural differences in music chosen for pain relief. *J Holist Nurs*. 2000;18:245–60.
- Mc Caffrey R. Music listening its effects in creating a healing environment. *J Psychosoc Nurs Ment Health Serv*. 2008;46:39–44.
- Güvenç RO. Türklerde ve Dünyada Müzikle Ruhi Tedavinin Tarihçesi ve Günümüzdeki Durumu. Doktora Tezi. 1985, s.9.
- Beutler E. Red cell metabolism. 2nd ed. New York: Grune and Stratton Company; 1975. p. 67–9.
- Beutler E. Red cell metabolism. 2nd ed. New York: Grune and Stratton Company; 1975. p. 261–5.
- Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. *Anal Biochem*. 1979;95:351–8.
- Cortas NK, Wakid NW. Determination of inorganic nitrate in serum and urine by a kinetic cadmium-reduction method. *Clin Chem*. 1990;36:1440–3.
- Katz J, Melzack R. Measurement of pain. *Surg Clin North Am*. 1999;79:231–52.
- Kahloul M, Mhamdi S, Nakhli MS, et al. Effects of music therapy under general anesthesia in patients undergoing abdominal surgery. *Libyan J Med*. 2017;12.
- Ovayolu N, Ucan O, Pehlivan S, et al. Listening to Turkish classical music decreases patients' anxiety, pain, dissatisfaction and the dose of sedative and analgesic drugs during colonoscopy: a prospective randomized controlled trial. *World J Gastroenterol*. 2006;12:7532–6.
- Şen H, Sızlan A, Yanarateş Ö, et al. The effect of musical therapy on postoperative pain after caesarean section. *TAF Prev Med Bull*. 2009;8:107–12.
- Lepage C, Drolet P, Girard M, et al. Music decreases sedative requirements during spinal anesthesia. *Anesth Analg*. 2001;93:912–6.
- Ghezjeljeha N, Ardebilib FM, Rafii F. The effects of massage and music on pain, anxiety and relaxation in burn patients: randomized controlled clinical trial. *Burns*. 2017;43:1034–43.
- Bekiroğlu T, Ovayolu N, Ergün Y, et al. Effect of Turkish classical music on blood pressure: a randomized controlled trial in hypertensive elderly patients. *Complement Ther Med*. 2013;21:147–54.
- Rafiei AE, Zarei P, Gohari K, et al. Effect of lullaby and classical music on physiologic stability of hospitalized preterm infants: a randomized trial. *J Neonatal Perinatal Med*. 2013;6:295–301.
- Hunt JV, Smith CC, Wolff SP. Autoxidative glycosylation and possible involvement of peroxides and free radicals in LDL modification by glucose. *Diabetes*. 1990;39:1420–4.
- Özcan O, Erdal H, Çakırca G, et al. Oxidative stress and its impacts on intracellular lipids, proteins and DNA. *J Clin Exp Invest*. 2015:331–6.
- Dong M, Shi Y, Cheng Q, et al. Increased nitric oxide in peritoneal fluid from women with idiopathic infertility and endometriosis. *J Reprod Med*. 2001;46:887–91.