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Original Article

Music combined with dexmedetomidine relieves preoperative anxiety and promotes postoperative recovery in patients undergoing gynecologic laparoscopic surgery: a randomized clinical trial

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Abstract: Objectives: To investigate the effects of music combined with dexmedetomidine on perioperative anxiety and postoperative recovery in gynecologic laparoscopic patients. Methods: A total of 82 female patients were enrolled in this study. Patients were randomized to the patient-preferred Music+Dexmedetomidine group (M+DEX group, n=41) and the Dexmedetomidine group (DEX group, n=41). Prior to the induction of anesthesia, dexmedetomidine was pumped intravenously at 0.5 μg/kg for 10 minutes in both groups and then maintained at 0.2 μg/kg/hour until 30 minutes before the end of surgery. In contrast to the patients in the DEX group, the patients in the M+DEX group listened to 5 minutes of their favorite music during dexmedetomidine infusion. The primary outcome was the patient's preoperative State Anxiety Inventory (SAI) score. The secondary outcomes included visual analog scale (VAS) pain scores and QoR-15 scores at 24 hours postoperatively. Results: The clinical data of a total of 82 patients were analyzed. After the music intervention, we found that the preoperative SAI scores were lower in the M+DEX group than in the DEX group (37.9±5.6 vs. 41.5±6.9; P=0.01). The M+DEX group had lower VAS scores at 24 hours postoperatively than the DEX group (1 (1.0, 2.0) vs. 2 (2.0, 3.0), P < 0.01), and the M+DEX group had higher QoR-15 scores at 24 hours after the surgery than the DEX group (127.7±10.0 vs. 122.3±11.2; P=0.03). Conclusion: Patients undergoing gynecologic laparoscopic surgery who listened to their favorite music before the induction of anesthesia had less preoperative anxiety and recovered better 24 hours postoperatively than those who only received dexmedetomidine.

Keywords: Music, dexmedetomidine, anxiety, gynecological laparoscopic surgery, postoperative recovery

Introduction

With the development of minimally invasive techniques, laparoscopic surgery has replaced traditional open surgery as the preferred surgical procedure for gynecological patients. Compared to male patients, female patients are more likely to experience perioperative anxiety [1, 2]. Carr et al. [3] reported a 67% incidence of perioperative anxiety in patients undergoing gynecologic laparoscopy. Perioperative anxiety is associated with higher postoperative pain, greater opioid use, and an increased risk of adverse postoperative outcomes, which is detrimental to patients' postoperative recovery [4, 5]. Therefore, methods to reduce perioperative anxiety and facilitate patients' postoperative recovery are receiving increasing attention.

Pharmacological interventions can alleviate perioperative anxiety. Dexmedetomidine (DEX) is a novel α2-adrenergic agonist commonly used in surgery that has sedative, analgesic, and anxiolytic effects [6]. Previous studies [7, 8] have shown that DEX can relieve anxiety and reduce postoperative pain in patients undergoing surgery. However, the loading dose infusion of DEX can cause side effects of hypertension, bradycardia and hypotension [9].

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Music is a nonpharmacological intervention that has been shown to be a safe and effective method of reducing anxiety [10, 11]. Listening to music relieves patients' anxiety, has no side effects, is inexpensive and has therefore become the focus of attention.

It is well known that intense stress activates the locus coeruleus-sympathetic-adrenomedullary system and the hypothalamic-pituitary-adrenal axis, producing adverse effects (including anxiety). Music can act on the cerebral cortex to reduce sympathetic tension and relieve anxiety [12, 13]. Dexmedetomidine acts on the hypothalamus by agonizing α2 adrenergic receptors in the nucleus accumbens to produce a sedative effect and alleviate stress-induced anxiety [14]. Therefore, music and dexmedetomidine may act synergistically on the sympathetic nervous system to better reduce patients' anxiety levels.

In previous studies, patients listened to music chosen by the music therapist or clinician. Thus, the effects of listening to patients' favorite music on their level of perioperative anxiety have rarely been reported.

Therefore, we designed this clinical trial to evaluate the effect of listening to preferred music during dexmedetomidine administration preoperatively on the perioperative anxiety level of women undergoing laparoscopic surgery.

We hypothesized that patients who listen to their favorite music prior to anesthesia induction before undergoing gynecologic laparoscopic surgery would have less preoperative anxiety and better recovery at 24 hours postoperatively than those who do not listen to their preferred music and receive DEX only.

Materials and methods

Research and design

This single-center, prospective, randomized, single-blinded (assessor-blinded) controlled clinical trial was approved by the Ethics Committee of the Fuyang Hospital affiliated with Anhui Medical University (approval number: KY2021022, date of approval: 23/11/2021) and registered at the Chinese Clinical Trial Registry (registration number: ChiCTR2100053734, date of registration: 28/11/2021).

Inclusion and exclusion criteria

Female patients who underwent elective laparoscopic surgery at our hospital from January 2022 to December 2022 were enrolled in this study. The inclusion criteria were an American Society of Anesthesiologists (ASA) classification I-II, aged 18-60 years, and a body mass index (BMI) 18-30 kg/m^2. The exclusion criteria included the inability to understand the materials of this study, hearing impairment, psychiatric and psychological disorders, history of chronic analgesic drug intake, sleep disorders, patients with anxiety, contraindications to dexmedetomidine, including sinus bradycardia, 2nd degree or greater atrioventricular block, or an allergy to the test drug.

Preoperative patient visits

The investigator visited the patients one day before the operation, selected the eligible patients and invited them to participate in this study. If patients expressed an interest in participating, they were given an information sheet to read through before signing the consent form. The State Trait Anxiety Inventory (STAI) was used to assess the patients' perioperative anxiety levels [15]. It is a self-administered questionnaire containing 40 items, with scores for each item ranging from 1 to 4. Items 1 to 20 are the State Anxiety Inventory (SAI), which is used to assess people's anxiety levels in specific situations. Items 21-40 are the Trait Anxiety Inventory (TAI), which is used to assess people's predispositions to become anxious in stressful situations. The questionnaire provides a simple, visual representation of the patient's anxiety and distinguishes their current state from their consistent anxiety symptoms. The Chinese version of the STAI was used in this study. The Quality of Recovery-15 scale (QoR-15) was chosen to assess the quality of perioperative recovery for the patients [16]. This questionnaire is a validated instrument with 15 items, each with a score of 0-10 and a sum of scores ranging from 0 to 150. Higher scores indicate a better quality of recovery.

Music intervention and anesthesia

Patients received routine preoperative preparation, and no preoperative medication was administered. At the surgical waiting area, patients were randomly divided into a patient-

preferred Music+Dexmedetomidine group (M+DEX group) and a Dexmedetomidine group (DEX group). The researcher responsible for playing the music had a brief conversation with the patient to determine the patient's preferred music type before enrolling them in the M+DEX group. After entering the operating room, electrocardiogram (ECG), heart rate (HR), pulse oximetry (SPO_2), noninvasive mean arterial pressure (MAP) and electroencephalographic bifrequency index (BIS) were monitored. Prior to the induction of anesthesia, dexmedetomidine was pumped intravenously at 0.5 μg/kg for 10 minutes in both groups and then maintained at 0.2 μg/kg/hour until 30 minutes before the end of surgery. Unlike the DEX group, the M+DEX group listened to 5 minutes of the patient's favorite music during the dexmedetomidine infusion. Wang et al. [17] reported that in lower limb orthopedic surgery, the loading dose is 0.25 ug/kg dexmedetomidine for more than 10 minutes, then maintain a dose of 0.3 ug/kg/h until the end of surgery can provide good hemodynamic status and sedation. Tobias et al. [18] reported that low-dose dexmedetomidine (0.25 ug/kg/h) also showed the sedative effect in infants and children. In our preexperiment, we observed that dexmedetomidine pumped for 5 min (0.25 ug/kg) also had a sedative effect and improved patient anxiety. Thus, five minutes after the administration of dexmedetomidine, i.e., at the completion of the music intervention, the anxiety levels of both groups were assessed with the STAI. General anesthesia was induced with intravenous midazolam (0.05 mg/kg), sufentanil (0.4 μg/kg), propofol (2 mg/kg), and cisatracurium (0.15 mg/kg). After the muscle relaxants took effect, tracheal intubation was performed. Anesthesia was maintained with propofol (4-6 mg/kg/h) and remifentanil (0.1-1.0 μg/kg/min), and the pump rate was adjusted in a timely manner to maintain the BIS between 40 and 60. In addition, cisatracurium was given intermittently to maintain adequate muscle relaxation. Half an hour before the end of the surgery, each group of patients received an injection of 50 mg of flurbiprofen axetil. At the end of the procedure, patients were transferred to the postanesthesia care unit (PACU), and the tracheal catheter was withdrawn after a satisfactory recovery. No analgesia pump was used in either group.

Outcomes

The patients' anxiety levels on the day before surgery (baseline), 5 minutes after administration of dexmedetomidine when the music intervention was completed (preoperation) and 24 hours after surgery (postoperation) were assessed in detail.

The primary outcome was the patient's preoperative SAI score.

The secondary outcomes included the visual analog scale (VAS) pain scores, QoR-15 scores at 24 hours postoperatively, MAP and HR of the patients at the following six time points: T1, entry to the operating room; T2, tracheal intubation; T3, 1 hour after the start of surgery; T4, end of surgery; T5, extubation; and T6, transfer from the PACU.

In addition, we also focused on the patients' baseline data, including age, BMI, ASA class, anesthesia and operative time, and baseline QoR-15 score.

Statistics

Based on our pilot trial, the preoperative SAI score (mean ± standard deviation, mean ± SD) was 36.93±7.56 in the M+DEX group and 42.5±9.52 in the DEX group; thus, 37 patients were needed for each group with an alpha level of 0.05 and a power of 80%. Finally, we aimed to recruit 82 patients to allow for a 10% dropout rate. Categorical data are presented as numbers (percentages) and were analyzed by the chi-square test. Independent t tests, repeated-measures ANOVA or Mann-Whitney U tests were applied to analyze continuous variables, and data are presented as the mean ± SD or median (interquartile range). A P value < 0.05 was considered a statistically significant difference. SPSS 22.0 software was used for data analysis.

Results

Before the start of the study, 2 patients refused to consent, and 5 patients were excluded because they did not meet the inclusion criteria, so we recruited a total of 82 patients between January 2022 and December 2022. In total, 82 patients finished the study and were evaluated for all study outcomes: 41 in the

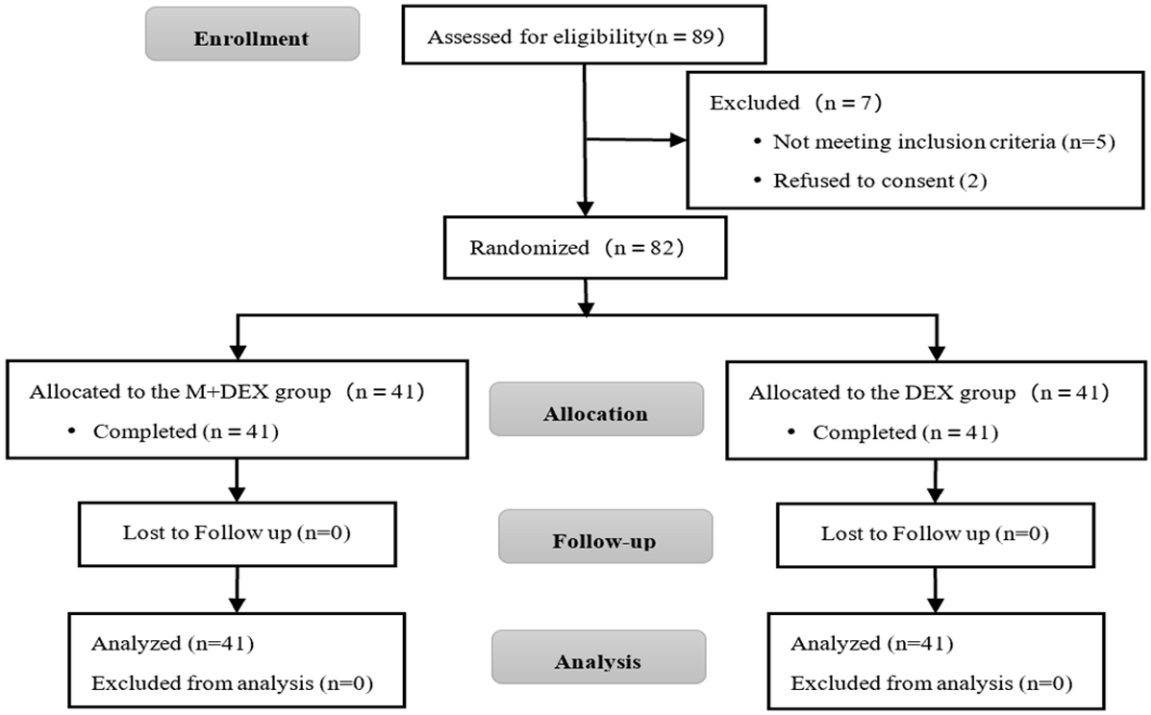

Figure 1. CONSORT flow diagram for this study.

Table 1. Basic characteristic and perioperative variables of the two groups of patients

Characteristic	M+DEX group (n=41)	DEX group (n=41)	*p*-Value
Age (years)	37.8±10.5	37.8+11.9	0.99
ASA, n			0.70
I	22 (54%)	17 (41%)	
II	19 (46%)	24 (59%)	
BMI (kg/m^2)	22.9±2.7	23.8±2.7	0.12
Surgery type, n			0.28
Endometriosis	14 (34%)	11 (27%)	
Hysterectomy	7 (17%)	10 (24%)	
Myomectomy	5 (12%)	3 (8%)	
Benign ovarian Tumor Stripping	9 (22%)	12 (29%)	
Other surgery	6 (15%)	5 (12%)	
Anesthesia time, min	144.0±31.3	139.8±30.6	0.55
Operation time, min	115.6±34.1	114.1±30.0	0.83
Blood loss	81.07±28.82	74.22±27.25	0.27

The data are expressed as numbers (percentages) or the mean ± standard deviation. ASA, American Society of Anesthesiologists. BMI, Body Mass Index. The *p* values were calculated by independent t tests or the chi-square test.

M+DEX group and 41 in the DEX group, as detailed in **Figure 1**.

No significant differences were found between the two groups in terms of age (years), ASA class, BMI (kg/m^2), surgery type, anesthesia time, operation time, or blood loss (**Table 1**). At the same time point, the MAP and HR of the patients in the M+DEX group were not significantly different from those of the DEX group patients (**Figure 2**).

The baseline anxiety levels were not significantly different between the two groups, in terms of TAI (t=0.03; P=0.97). A repeated-measures ANOVA was performed to compare the effect of music on perioperative SAI scores. The data of each group fell withing a normal distribution by Shapiro-Wilk test (P > 0.05). Sphericity test result showed that Mauchly's W=0.88, P=0.01, which did not conform to the sphericity test. Therefore, a correction was made using the "Greenhouse-Geisser" method. Repeated measures ANOVA showed that there was a statistically significant interaction effect between time point and group (F=3.47, P=0.04). Thus, a

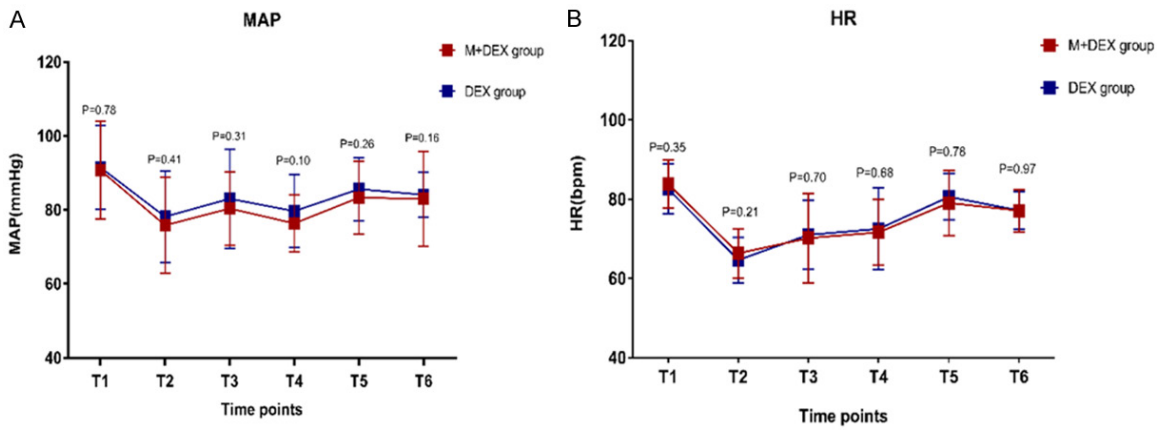

Figure 2. The MAP (A) and HR (B) between the two groups during the operation. The data are expressed as the mean ± standard deviation. T1, entered the operating room; T2, tracheal intubation; T3, 1 hour after the start of surgery; T4, end of surgery; T5, extubation; T6, transfer from the postanesthesia care unit (PACU). MAP, mean arterial pressure. HR, heart rate. The *p* values were calculated by Independent t tests.

Table 2. The perioperative anxiety of the two groups of patients

	n	SAI[a]			F	p	TAI[b]	t	p
		Bsaeline	Preoperation	Postoperation			Bsaeline		
M+DEX	41	41.2±8.9	37.9±5.6	39.5±8.1			40.2±7.1	0.03	0.97
DEX	41	41.9±8.1	41.5±6.9	40.5±8.5			40.1±6.2		
Group					1.29	0.26			
Time					4.75	0.01			
Group*time					3.47	0.04			

The data are expressed as the mean ± standard deviation. SAI, state anxiety inventory. TAI, trait anxiety inventory. a, the *p* values were calculated by repeated measures ANOVA. b, the *p* values were calculated by the independent t tests.

further separate effects analysis was performed to assess the difference in SAI scores between the two groups at different times. The post hoc Bonferroni test showed that there was no significant difference between the baseline anxiety levels of the two groups in terms of SAI (P=0.72); after the music intervention, the preoperative SAI scores of the patients in the M+DEX group were lower than those in the DEX group (P=0.01); and there was no significant difference in the SAI scores of the patients in the two groups at 24 hours postoperatively (P=0.59) (**Table 2**).

Patients in the M+DEX group had lower pain scores than control patients at 24 hours after the surgery (1 (1.0, 2.0) vs. 2 (2.0, 3.0), P < 0.01). There was no significant difference in the baseline Qor-15 score between the two groups (137.5±4.6 vs. 137.0±5.2; P=0.66), and the M+DEX group had higher Qor-15 scores than the DEX group at 24 hours postoperatively (127.7±10.0 vs. 122.3±11.2; P=0.03) (**Table 3**). The types of music selected by the patients in the M+DEX group are shown in **Table 4**.

Discussion

The operating room is an unfamiliar environment, and combined with concerns and fears about surgery and anesthesia, patients are often in a state of anxiety. Women undergoing surgery may be more sensitive and emotional than male patients and experience higher levels of anxiety in the perioperative period [2]. Therefore, gynecologic patients would benefit more from management strategies aimed at reducing the adverse effects of preoperative anxiety.

Music that is familiar to the patient can distract the patient and provide a pleasant and comfortable ambience, thus alleviating negative emotions, such as tension, anxiety and fear,

Table 3. The postoperative pain and perioperative QoR-15 score of the two groups

Variable	M+DEX group (n=41)	DEX group (n=41)	*p*-Value
VAS	1 (1.0, 2.0)	2 (2.0, 3.0)	< 0.01
QoR-15 score			
Baseline	137.5±4.6	137.0±5.2	0.66
Postoperation	127.7±10.0	122.3±11.2	0.03

The data are expressed as medians (interquartile range) or the mean ± standard deviation. QoR, quality of recovery. VAS, visual analog scale/score. The *p* values were calculated by the Mann-Whitney U test or the independent t test.

Table 4. The types of music chosen by the M+DEX group patient

No.	Name of the music
1	Bandari - Snow dreams
2	Bandari - The First Snowflakes
3	Bandari - Annie's Wonderland
4	Bandari - The Foggy Dew
5	Bandari - Childhood Memory
6	Bandari - Irish Lullaby
7	Bandari - Down By the Salley Garden
8	Bandari - One Day In Spring
9	Bandari - Moonlight Bay
10	Bandari - Melody Of Love

The M+DEX group patients chose their favorites from these 10 pieces of music.

and having a positive impact on the patient's psychology [10, 19].

Previous studies [20-22] have proven that perioperative music interventions effectively reduce preoperative anxiety in patients undergoing various types of surgery. In addition, music therapy can reduce preoperative anxiety in women undergoing laparoscopic hysterectomy [23]. Consistent with the above studies, we found that patients who received musical intervention exhibited lower levels of preoperative anxiety than the DEX group.

The mechanism of music intervention responsible for relieving patients' preoperative anxiety is related to the reduction of sympathetic nervous system activity; however, in contrast to the adverse consequences of anxiety caused by activation of the sympathetic nervous system, music activates the parasympathetic branch of the autonomic nervous system, thereby inhibiting the sympathetic nervous system and promoting relaxation [13, 24]. However, our study found that there was no significant difference in the 24-hour postoperative anxiety levels between the two groups. Casarin et al. [23] also reported no significant difference in patient anxiety scores between the early and late postoperative periods in women undergoing laparoscopic total hysterectomy after undergoing a preoperative music intervention.

Preoperative anxiety is closely related to postoperative pain, and in turn, increased postoperative pain can stimulate anxiety responses [25]. Music interventions can help reduce pain in patients undergoing different types of surgery [11], and the pain reduction associated with music exposure was greater when patients actively selected their preferred music than when passively agreeing to listen to the selected music [26]. Consistent with the results of these studies, we found that patients in the M+DEX group experienced lower levels of pain 24 hours postoperatively than those in the DEX group.

In addition, we found that patients in the M+DEX group had higher QoR-15 scores at 24 hours postoperatively than those in the DEX group, demonstrating a better recovery at 24 hours after surgery in this group. Hole et al. and Matsota et al. reported that music intervention can alleviate patients' anxiety and discomfort, reduce their neuroendocrine responses to surgery and postoperative pain, which is beneficial to their postoperative recovery [25, 27]. Sun et al. [28] reported that QoR-15 reflects the quality of recovery, including emotional state, physical comfort, psychological support, physical independence, and pain, in which pain has a significant impact on QoR-15 scores. In this study, compared with patients who received dexmedetomidine alone, patients in the music combined dexmedetomidine group had lower postoperative pain scores. Therefore, patients in the M+DEX group achieved better QoR-15 scores through pain relief. When patients listen to music before surgery, their anxiety levels decrease, and their blood pressure and heart rate improve. However, Wang et al. [29] have reported no significant difference in hemodynamics between the two groups of patients after music intervention. Hanser SB [30] indicated the lack of correlation between psycho-

logical and physiological indicators of anxiety may be explained by trait-related individual responsiveness of the sympathetic system. Thus, our **Figure 2** did not show any differences in hemodynamic fluctuation between the two groups of patients.

Preoperative music interventions have not been widely used in clinical work in China, probably for the following reasons: first, in most studies, preoperative music interventions lasted for more than 15 minutes, and the operating room is relatively busy; thus, there is insufficient time to implement a long music intervention. In addition, it requires the involvement of a professional music therapist, which is not available in most hospitals in China.

Giordano et al. [31] reported that a 5-minute musical intervention before surgery was effective in decreasing anxiety in general anesthesia patients undergoing oral surgery; therefore, a 5-minute preoperative music intervention was chosen for this study. Like many other hospitals in China, we do not have a professional music therapist, so the music intervention is implemented by an assigned researcher.

We identified several limitations of the present study. First, we observed patients' anxiety, pain and postoperative recovery levels 24 hours postoperatively, and the long-term effects of a music intervention during a dexmedetomidine infusion need to be further investigated. Second, we investigated the clinical data of female patients of selected ages, and further studies are needed to clarify the effects of music therapy combined with a dexmedetomidine infusion in other populations.

In summary, the results of this study suggest that female patients undergoing laparoscopic surgery who listened to their favorite music before surgery experienced lower levels of preoperative anxiety than those who only received a dexmedetomidine infusion. In addition, these patients had lower levels of pain and better recovery at 24 hours postoperatively. Therefore, we recommend the use of patient-preferred music combined with dexmedetomidine administration in the perioperative period of surgical patients.

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Disclosure of conflict of interest

None.

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