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Original Article

Stress reduction and analgesia in patients exposed to calming music postoperatively: a randomized controlled trial

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Summary

Background and objectives: This randomized controlled trial was designed to evaluate, first, whether intra- or postoperative music therapy could influence stress and immune response during and after general anaesthesia and second, if there was a different response between patients exposed to music intra- or postoperatively.

Method: Seventy-five patients undergoing open hernia repair as day care surgery were randomly allocated to three groups: intraoperative music, postoperative music and silence (control group). Anaesthesia and postoperative analgesia were standardized and the same surgeon performed all the operations. Stress response was assessed during and after surgery by determining the plasma cortisol and blood glucose levels. Immune function was evaluated by studying immunoglobulin A (IgA) levels. Patients' postoperative pain, anxiety, blood pressure (BP), heart rate (HR) and oxygen saturation were also studied as stress markers.

Results: There was a significantly greater decrease in the level of cortisol in the postoperative music group vs. the control group (206 and 72 mmol L^{-1} decreases, respectively) after 2 h in the post anaesthesia care unit. The postoperative music group had less anxiety and pain and required less morphine after 1 h compared with the control group. In the postoperative music group the total requirement of morphine was significantly lower than in the control group. The intraoperative music group reported less pain after 1 h in the post anaesthesia care unit. There was no difference in IgA, blood glucose, BP, HR and oxygen saturation between the groups.

Conclusion: This study suggests that intraoperative music may decrease postoperative pain, and that postoperative music therapy may reduce anxiety, pain and morphine consumption.

Keywords: MUSIC THERAPY, intraoperative, postoperative; HORMONES, cortisol; BLOOD GLUCOSE; IMMUNOGLOBULIN A; PAIN, measurement, postoperative; ANXIETY.

Surgical trauma and postoperative pain lead to an endocrine response characterized by a series of inflammatory, hormonal and metabolic changes that constitute the stress response [1,2]. This response depends on a variety of factors such as preoperative anxiety [3], severity and duration of surgical trauma, patient's age, anaesthetic methods and surgical technique [4,5]. The most important indicator of activity of stress is the hormone cortisol [2,6] and excessive cortisol levels can inhibit the immune system such as decreased immunoglobulin A (IgA) levels [5].

Music therapy during general anaesthesia can reduce postoperative pain after hysterectomy [7], hernia repair or varicose vein surgery [8]. Postoperative pain can also be reduced with postoperative music therapy after different types of elective surgery [9], gynaecological surgery [10] and hernia repair or

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varicose vein surgery [8,11]. Music as a therapeutic modality for treatment of preoperative stress can reduce cortisol [12] and glucose levels [13]. It has also been reported that music therapy administered to healthy participants can enhance the immune response as measured by IgA levels [14,15]. However, information on the impact of music intra- and postoperatively on stress and immune response has not been found.

The aim of this study was to explore whether music intra- or postoperatively could influence the stress and immune response during and after general anaesthesia and also to study if there was a different response between patients exposed to music intra- or postoperatively.

Methods

Study population and setting

This study was carried out over a 4 months period and conducted in 75 American Society of Anesthesiologists (ASA) Grade I–II consecutive patients scheduled for day care surgery between 08.00 and 11.30a.m., of open Lichtenstein inguinal hernia repair surgery under general anaesthesia. The same surgeon performed all the operations. None of the patients had any hearing impairment or diabetes mellitus. No patient was being treated with corticosteroids. Patients were randomly allocated to one of three groups. A computer generated the randomization list. A block randomization was used to keep the numbers of subjects in the different groups closely balanced at all times; block size was 25. The local Ethics Committee approved the study and all patients gave their informed consent.

Patients were not offered a premedication. Propofol 1–2 mg kg^{-1} and fentanyl 1–2 μg kg^{-1} was used to induce anaesthesia which was subsequently maintained with 70% nitrous oxide in oxygen and at least 1.2 minimum alveolar concentration (MAC) end-tidal sevoflurane after insertion of a laryngeal mask. Patients received a local infiltration with bupivacaine 0.5% 10 mL in the surgical wound at the end of the operation, according to our hospital routine. Postoperatively patients received 100 mg of diclofenac as a suppository and, on request, titrated doses of intravenous (i.v.) morphine 1–3 mg until analgesia was adequate (using a numeric rating scale where a score of $\leqslant 3$ represented adequate analgesia). All patients received nasal oxygen, 2 L min^{-1} upon arrival in the postanaesthesia care unit (PACU) and for 2 h.

Intervention

Using a computer generated randomization list, the patients were allocated to one of three groups: two intervention groups and one control group. The first author (U.N.) conducted all the interventions (music and silence) and outcome assessments but did not participate in the care of the patients. Patients in the intraoperative music group were exposed to music intraoperatively and to a sham compact disk (CD) player (CD, Discman, Model No D-181; Sony Corp., Tokyo, Japan) postoperatively. Patients in the postoperative music group were exposed to a sham CD player intraoperatively and music postoperatively. Patients in the control group had a sham CD player both intra- and postoperatively. Intraoperatively, the CD player was set on an auto-reverse mode and played continuously from the end of anaesthesia induction (when the laryngeal mask was inserted) to the end of surgery after wound dressing. Postoperatively, the CD was played from the time of arrival in the PACU and for 1 h thereafter.

Patients listened to music via headphones. Intraoperatively, the headphones covered both ears, such that no sounds from the operation room could leak in or out. Postoperatively, the patients had headphones allowing conversation between the patient and the medical staff.

The music, new-age synthesizer, was soft and relaxing and included seven different melodies, with a total of 43 minutes' playing time [16]. The sham CD showed numbers in the window as with regular CDs, despite there not being any sound. Sham and regular music CDs were thus indistinguishable, thereby preserving the blinding of the study. The anaesthesiologist, nurse anaesthetists, surgeon, physicians and nurses in the operating theatre and the PACU were blinded to the CD selection. All CD-players were set to the same audio settings and were not audible to anyone in the immediate area.

Outcome assessment

An i.v. cannula was inserted into the patient's right arm 30 min before anaesthesia and blood was drawn for measurement of serum cortisol, blood glucose and plasma IgA. Baseline samples were obtained between 08.00 and 11.00a.m. Five minutes after intubation with a laryngeal mask, a second cannula was inserted into the other arm, from which blood was drawn for cortisol, glucose and IgA at the end of surgery after wound dressing, and 1, 2 and 3 h after arrival in the PACU. The cannula was kept patent with saline. The blood was centrifuged and serum samples were stored at −20°C before analysis. Samples for glucose and IgA were taken between 8.00 and 14.30 h and analysed on the same day. The concentration of cortisol was determined by a radioimmunoassay method (Coat-a-Count® Cortisol from DPC, Los Angeles, CA, USA) and carried out according to the manufacturer's instructions. Glucose determinations

were carried out with a HemoCue Blood Glucose Analyzer (HemoCue, Ängelholm, Sweden) according to the manufacture's instructions. IgA concentrations were measured by turbidometry on a Hitachi 911 Autoanalyzer (Roche Diagnostics, Bromma, Sweden) using antibodies and calibrator (Human Serum Protein Calibrator Cat. No. X908) from DAKO A/S, Glostrup, Denmark.

Anxiety, pain, blood pressure (BP) heart rate (HR) and SpO_2 were assessed 30 min before anaesthesia and 1 h after admission to the PACU. Patients rated their anxiety and pain perception on numeric rating scales ranging from 0 = complete relaxation to 10 = worst feeling of anxiety possible, and from 0 = no pain to 10 = maximal possible pain. The scale for anxiety has been validated and tested for reliability [17] while that for pain has been tested for reliability and validity in a Swedish population [18]. HR and BP were measured with a digital BP monitor (Omron, HEM-705C; Omron Healtcare, Hoofddorp, Germany). SpO_2 was measured by pulse oximetry (Ohmeda 3800; Datex Ohmeda AB, Bromma, Sweden). The total amount of morphine used in the PACU was recorded.

Statistics

Calculation of sample size was based on the following assumptions concerning a one-way analysis (three groups) for serum cortisol. Significance level 5%, power 80%, common standard deviation (SD) 373 mmol L^{-1} and a difference in mean characterized by a variance of means of 4401. These assumptions suggested a sample size of 12 in each of the three groups. Because of the hypothesis that music intra- and postoperatively could influence stress and immune response during and after general anaesthesia, we appreciated that the power analysis may have overestimated the effect of music and therefore the size of the groups were doubled.

Data are presented as arithmetic mean and SD, although the data from the numeric rating scales are referred to as an ordinal scale. MANOVA for repeated measurement was used to analyse the levels of cortisol, glucose and IgA over time within and between the three groups. ANOVA followed by *post hoc* test with Bonferroni correction was used in the analysis of the differences in reduction of cortisol levels between the groups at the end of surgery vs. after 1, 2 and 3 h in the PACU. ANOVA was also used to analyse differences between the groups with regard to BP, HR and SpO_2. Kruskal–Wallis ANOVA by ranks followed by *U*-test with Bonferroni correction was used to analyse differences between the groups with regard to morphine requirements, anxiety and pain score. A P-value <0.05 was considered statistically significant. The computer program SPSS for Windows was used for all statistical analysis.

Results

There were no significant differences between the three study groups with regard to baseline patient characteristics, preoperative, anaesthetic and surgical factors (Table 1). The stress markers, cortisol (Fig. 1) and glucose (Fig. 2) and the immune marker IgA (Fig. 3) changed over time; there were significant

Table 1. Patient characteristic, preoperative status, anaesthetic and surgical factors.

Parameter	Intraoperative music (n = 25)	Postoperative music (n = 25)	Control (n = 25)
Age (yr)	55 (14.7)	56 (16.8)	57 (11.6)
Gender (M/F)	24/1	24/1	24/1
ASA (I/II)	21/4	20/5	19/6
Type of surgery (bard mesh/mesh plug)	7/18	7/18	9/16
Preoperative status			
Systolic BP (mmHg)	158 (26.5)	152 (20.6)	146 (23.0)
Diastolic BP (mmHg)	91 (10.8)	89 (10.5)	89 (10.5)
HR (bpm)	75 (13.2)	75 (10.8)	74 (11.1)
Anxiety (NRS 0–10)	2.4 (2.5)	1.9 (2.1)	2.2 (2.0)
Serum cortisol (mmol L^{-1})	548 (213)	459 (175)	480 (134)
Blood glucose (mmol L^{-1})	4.5 (1.0)	4.4 (1.1)	4.3 (0.5)
Plasma IgA (g L^{-1})	2.5 (1.0)	2.4 (1.1)	2.7 (1.2)
Anaesthetic and surgical factors			
Duration of anaesthesia (min)	45 (9.5)	43 (5.3)	46 (5.1)
Duration of surgery (min)	23 (8.8)	20 (3.8)	23 (4.9)
Duration of intraoperative intervention (min)	40 (9.5)	38 (5.4)	40 (5.0)
Intraoperative fentanyl (μg)	104 (28)	93 (37)	103 (25)

NRS: numerical rating scale. Data are numbers of patients or mean (SD). No statistical differences were found between the groups.

variations during the five time periods compared with baseline levels in all three groups ($P < 0.001$).

There were no differences in cortisol levels at any time between the groups. The mean levels of cortisol ranged from 281 to 548 mmol L^{-1} among the three groups and from 64 to 972 mmol L^{-1} among the individuals. However, in the first 2 h postoperatively, the decrease in cortisol was greater in the postoperative music group (45%, corresponding to 206.4 mmol L^{-1}), compared with the control patients (16%, corresponding to 72.0 mmol L^{-1}), $P < 0.05$.

There were no differences in blood glucose levels at any time between the groups. The mean levels of glucose ranged from 4.3 to 7.1 mmol L^{-1} among the three groups.

The average levels of plasma IgA ranged from 2.1 to 2.7 g L^{-1} among the three groups. During the observation period, the differences in IgA levels at any time were not significant between the groups.

After 1 h in the PACU, the patients in the postoperative music group had a significantly lower anxiety score compared with the control group, $P < 0.05$ (Table 2). At the same time, the patients in both the post- and intraoperative music groups had a significantly lower pain score compared with the control group, $P < 0.01$ (Table 2). After 1 h in the PACU, the requirement of morphine was significantly less in the postoperative music group compared with the control group (Table 2). The total requirement of morphine in the PACU was 1.2 mg in the postoperative music group and was 3.6 mg in the control group ($P < 0.05$). The total dose of morphine in the intraoperative music group was 2.3 mg ($P > 0.05$, compared with the control group). There were no significant differences between the three groups with regard to BP, HR and SpO_2 (Table 2).

Discussion

Under the conditions of this study, we found that patients who were listening to soft and relaxing music for 1 h in the immediate postoperative period after general anaesthesia had some beneficial effect on stress response as seen by a significantly greater reduction of serum cortisol levels compared with the control group. The decrease of cortisol started after 1 h in all the three groups. After 2 h, the decrease was significantly more marked in the postoperative music group (45%) compared with the control group (16%).

The number of previous studies that have examined the effect of perioperative music on stress response is very limited. Miluk-Kolsa and colleagues measured

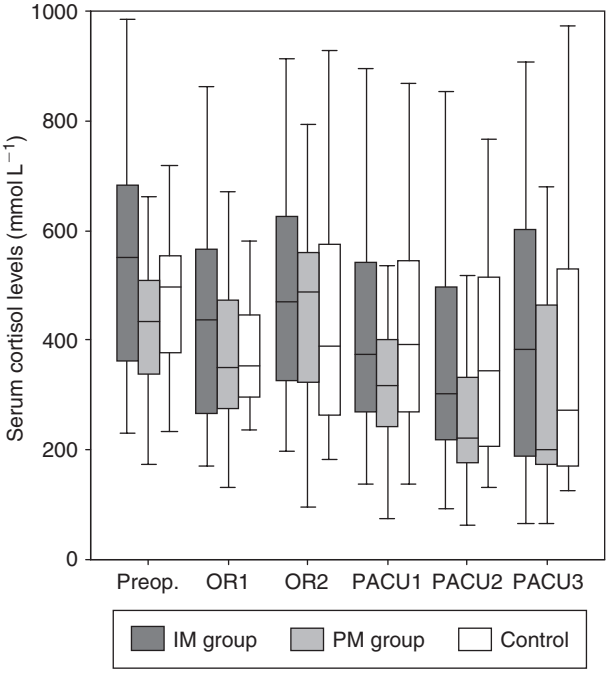

Figure 1.
Box and whisker plots of serum cortisol levels preoperatively (Preop.), at the end of surgery (OR1), after wound dressing (OR2) and 1, 2 and 3 h after arrival in the PACU in patients exposed to music intraoperatively (IM group), postoperatively (PM group) or control (sham CD player). $P < 0.001$ *in variation over time within groups compared with baseline level i.e. preoperative value.*

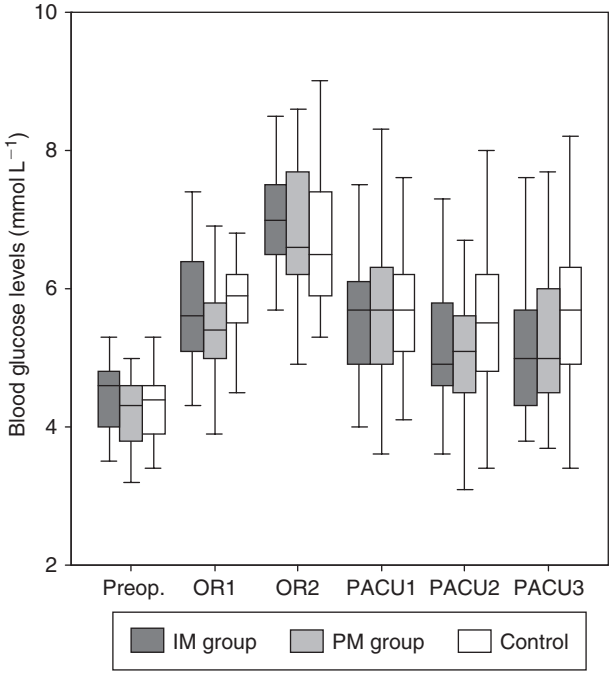

Figure 2.
Box and whisker plots of blood glucose levels preoperatively (Preop.), at the end of surgery (OR1), after wound dressing (OR2) and 1, 2 and 3 h after arrival in the PACU in patients exposed to music intraoperatively (IM group), postoperatively (PM group) or control (sham CD player). $P < 0.001$ *in variation over time within groups compared with baseline level i.e. preoperative value.*

cortisol levels in patients in conjunction with informing them that they would have to undergo surgery the following day [12]. One group received music immediately after this information, whereas the other group received no music. These investigators found that the information about the impending surgery triggered a smaller increase of cortisol in patients who listened to music. However, a recent study found no difference in cortisol levels between patients who had listened to preoperative music and those who had not [19]. The influence of music therapy on blood glucose has been reported earlier [13]. It has been shown that glucose concentration increases significantly in the postoperative period in patients undergoing hernia repair surgery [6].

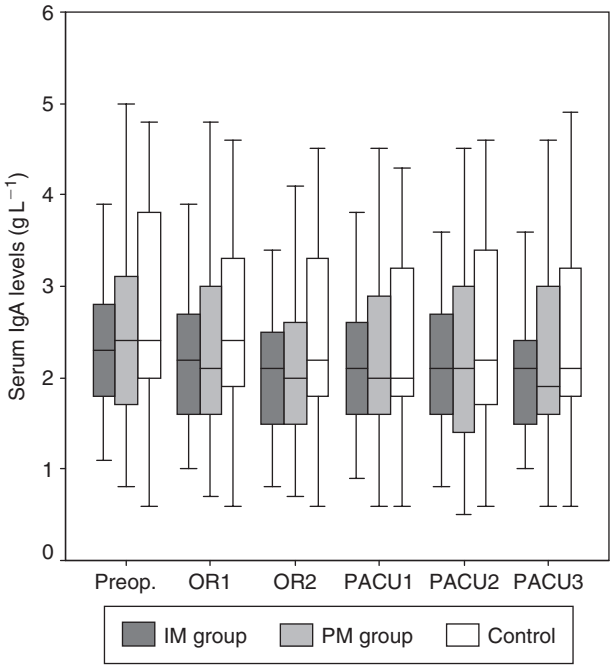

Figure 3.
Box and whisker plots of serum IgA levels preoperatively (Preop.), at the end of surgery (OR1), after wound dressing (OR2) and 1, 2 and 3 h after arrival in the PACU in patients exposed to music intraoperatively (IM group), postoperatively (PM group) or control (sham CD player). $P < 0.001$ *in variation over time within groups compared with baseline level i.e. preoperative value.*

The mechanism mediating the immune response of music is unknown [15]. In the present study, IgA levels were not influenced by the music therapy. An earlier study that investigated whether music could influence parameters involved in immune function, showed increased IgA levels [20]. More recent studies [15,21] have replicated these results. However, in these studies the music was administrated to healthy participants [15] or to cancer patients [21].

Perhaps it would have been better to avoid the local anaesthetic infiltration in order to study the effect on pain and stress response to surgery. However, this idea was abandoned because at our institution (and in most other hospitals in Sweden) subcutaneous local anaesthetic infiltration at the end of surgery is part of a well-established multimodal postoperative pain treatment. It was considered unethical to remove this analgesic technique in order to better study the effect of music therapy on pain and stress response. In a study by Pavlin and colleagues, maximum pain and duration of postoperative pain therapy were greater after hernia repair performed under general anaesthesia as compared with breast surgery, knee arthroscopy, and vaginal uterine surgery under general anaesthesia [22]. This was in spite of 96% of the hernia patients also having received a local anaesthesia infiltration in comparison with 56% of patients undergoing the other types of surgery. So pain can be a problem after hernia surgery in spite of local anaesthetic infiltration at the end of surgery. In the present study, postoperative music therapy had a pain reducing effect as seen by increased pain relief and reduced morphine consumption. A pain reducing effect of postoperative music has also been reported in earlier studies [8–11] and this analgesic effect may be due to distraction through

Table 2. BP, HR, oxygen saturation, anxiety, pain and morphine requirements after 1 h in the PACU.

Parameter	Intraoperative music group ($n = 25$)	Postoperative music group ($n = 25$)	Control ($n = 25$)	*P*-value
Systolic BP (mmHg)	123 (32.6)	132 (18.5)	127.6 (21.5)	>0.05
Diastolic BP (mmHg)	82 (17.5)	79 (9.4)	82 (14.3)	>0.05
HR (bpm)	64 (11.7)	59 (10.1)	61 (8.8)	>0.05
Oxygen saturation (%)	98.4 (1.1)	98.4 (1.4)	96.8 (3.7)	>0.05
Anxiety (NRS 0–10)	0.3 (0.9)	0.2 (0.6)	1.1 (2.0)	<0.05[a]
Pain (NRS 0–10)	2.4 (1.8)	2.1 (1.5)	3.8 (1.9)	<0.01[b]
Morphine (mg)	1.8 (2.4)	1.0 (1.8)	2.9 (3.1)	<0.01[a]

NRS: numerical rating scale. Data are mean (SD).
[a]Postoperative music vs. control $P < 0.05$.
[b]Intraoperative music vs. control $P < 0.05$ and postoperative music vs. control $P < 0.01$.

cognitive coping strategies by competing stimuli that reduce pain perception [23]. The mechanism of the pain reducing effect of music therapy during the intraoperative period, as opposed to postoperative period, is less clear. We did not use monitoring techniques such as bispectral index or midlatency auditory evoked potentials to measure the depth of anaesthesia in this study. However, anaesthesia was maintained with at least 1.2 MAC end-tidal sevoflurane. Tsuchiya and colleagues proposed that the concept of music or sound as modulators of human response to surgical stress under regional anaesthesia might also be valid in unconscious patients under general anaesthesia, but this effect is somewhat limited in the middle of a general anaesthetic, as compared with regional anaesthesia [24].

The efficacy of music therapy on preoperative anxiety has been reported [19]. In the present study, the postoperative anxiety score in the postoperative music group was significantly lower than the score in the control group. So it seems that music therapy can lead to reduced anxiety. However, there was almost no anxiety. It has been proposed that cancer patients have higher preoperative anxiety than non-cancer patients [3]. In the present study, there were no cancer surgery cases, which may explain the low pre- and postoperative anxiety scores.

Reduction in BP and HR during emergence from anaesthesia has been reported after listening to natural sounds (sounds of a ripple, a small stream, a soft wind or a twitter) intraoperatively under general anaesthesia [24] and reduction in HR after postoperative music [25]. Our results did not show any differences in BP and HR between the groups that might have reflected the level of stress. However, cardiovascular parameters may be influenced by other intra- and postoperative factors resulting from central neutral blockade and the use of vasopressor agents [3].

Subjects in the postoperative music group could not be blinded to the group assignment due to the type of intervention studied. We believe, however, that the study was well controlled. Patients were advised that they should not inform anyone about the group they were assigned to. Throughout the study, none of the nurses and physicians indicated in any way that they were aware about the study group. The physicians and nurses had agreed not to ask about randomization and there was no indication that they asked the patients. Thus, we believe they could not influence the outcome of the study.

There remains a need for more complete information through further studies on the impact of perioperative music on stress hormones and immune response. Recently, a strong need for objective outcome data was emphasized in order to establish the therapeutic efficacy of music [26].

In conclusion, our results suggest that intraoperative music may decrease postoperative pain, and that music therapy in the postoperative period may reduce pain, morphine consumption and stress response to surgery. During surgery and postoperative recovery, music can become an integral part of a multimodal analgesic regimen. This intervention is simple, inexpensive and non-invasive, and can easily be applied during intra- and postoperative care. Further randomized studies should be conducted to verify our results.

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