Music versus midazolam during preoperative nerve block placements: a prospective randomized controlled study

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ABSTRACT

Background and objectives Music medicine is a non-pharmacologic intervention that is virtually harm-free, relatively inexpensive and has been shown to significantly decrease preoperative anxiety. In this study we aim to compare the use of music to midazolam as a preoperative anxiolytic prior to the administration of an ultrasound-guided single-injection peripheral nerve block.

Methods In this randomized controlled study we compared the anxiolytic effects of intravenous midazolam (1–2 mg) with noise-canceling headphone-delivered music medicine. All patients received a preoperative ultrasound-guided single-injection peripheral nerve block indicated for a primary regional anesthetic or postoperative analgesia.

Results The change in the State Trait Anxiety Inventory-6 (STAI-6) anxiety scores from after to before the procedure were similar in both groups (music group −1.6 (SD 10.7); midazolam group −4.2 (SD 11); p=0.14; mean difference between groups −2.5 (95% CI −5.9 to 0.9), p=0.1). Patient satisfaction scores with their procedure experience were higher in the midazolam group (p=0.01); however, there were no differences in physician satisfaction scores of their procedure experience between groups (p=0.07). Both patient and physician perceptions on difficulties in communication were higher in the music group than in the midazolam group (p=0.005 and p=0.0007, respectively).

Conclusions Music medicine may be offered as an alternative to midazolam administration prior to peripheral regional anesthesia. However, further studies are warranted to evaluate whether or not the type of music, as well as how it is delivered, offers advantages over midazolam that outweigh the increase in communication barriers.

Clinical trial registry Clinicaltrials.gov #NCT03069677

INTRODUCTION

Background

Preoperative anxiety is common and can adversely affect a patient's perioperative course by elevating stress markers, promoting fluctuations in hemodynamics and negatively impacting on postoperative recovery.[1 2] Preoperative anxiety is routinely treated with pharmacologic agents such as short-acting benzodiazepines. Benzodiazepines are known to have undesirable side effects such as respiratory depression and hemodynamic perturbations and paradoxical effects such as hostility, aggression and psychomotor agitation.[3 4] The use of these medications for conscious sedation also requires continuous vital sign monitoring of patients by either anesthesia or nursing personnel. More importantly, a recent Cochrane review showed low quality of evidence that midazolam reduces pre-procedural anxiety compared with placebo.[5]

Music medicine is a non-pharmacologic intervention that has been shown to significantly decrease preoperative anxiety.[6] Music is a modality that is virtually harm-free and inexpensive. This intervention can be used as an adjunct or replacement for pharmacologic agents to help with preoperative anxiety.[6–8]

This study primarily aims to compare music with midazolam as a preoperative anxiolytic prior to the administration of an ultrasound-guided single-injection peripheral nerve block.

METHODS

The Institutional Review Board (IRB) at the University of Pennsylvania has approved this randomized controlled study conducted at a university-based ambulatory surgical center. The study was registered on clinicaltrials.gov #NCT03069677.

Patients were randomized by the research assistant in a one-to-one fashion using a computer-generated algorithm into two groups. The group designation was notified to the anesthesiologist before the start of the planned peripheral nerve block. The two groups were as follows: (1) Music group: patients listened to research-selected music (Marconi Union's 'Weightless' series) via noise-canceling headphones; (2) Midazolam group: patients received intravenous midazolam, minimum of 1 mg to 2 mg maximum, at the clinician's discretion. Marconi Union's 'Weightless' series was chosen for this research study as this track is considered to be one of the 'world's most relaxing songs'.[9] Research selected relaxing music is typically known to have characteristics such as a beats per minute range around 60 and no presence of lyrics or dramatic fluctuations in percussion.[10] The music group Marconi Union collaborated with sound therapists to produce this series of tracks with the primary goal of reducing anxiety, blood pressure and heart rate. Research was done specifically on this track by a research laboratory based in the UK, which resulted in a 65% reduction in anxiety and 35% reduction in vital signs at rest.[9]

Inclusion criteria

Patients who were 18 years of age or older who were competent to give informed consent to receive

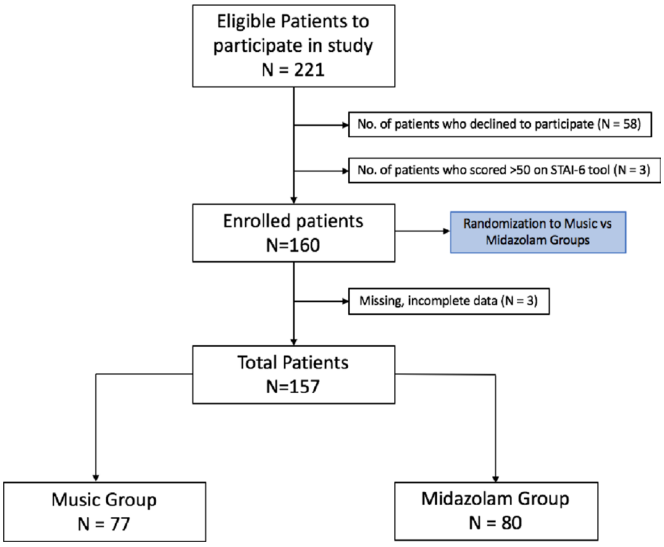


Figure 1 Consort flow diagram.

a peripheral nerve block in the preoperative bay as indicated for their primary anesthetic and/or postoperative analgesia were included in this study.

Exclusion criteria

The following were our exclusion criteria: significant psychiatric disorder such as generalized anxiety disorder, panic disorder, depression, psychosis, bipolar disorder; individuals who were incompetent to give informed consent; pregnant and/or breast feeding patients; any underlying coagulopathy, infection or other factors which would be a contraindication to receiving a peripheral nerve block; hypersensitivity to midazolam; and history of renal impairment. Patients who were extremely anxious (scores ≥50 on the State Trait Anxiety Inventory-6 (STAI-6) tool) were also excluded from the study as these patients typically require pharmacologic therapy to help reduce their anxiety and may confound the results of our study.[11 12]

Patients were approached for participation in the study on arrival at the preoperative receiving area on their day of surgery. After giving informed consent to participate, the research assistant administered the STAI-6 tool. If they were still eligible to participate in the study, patients were randomized to one of the two study groups. Prior to administration of the peripheral nerve block, study patients were placed on standard American Society of Anesthesiologists monitors and a procedure time out was performed per institution protocol. At this point, patients received either intravenous midazolam or started listening to music, based on their group assignment. We allowed 3 min to pass before needle placement and starting the peripheral nerve block.

Table 1 Patients' demographics, block type and block time

	Music	Midazolam	P value
N	77	80	
Women, n (%)	52 (67%)	36 (45%)	0.1
Age in years, mean (SD)	45 (15.6)	46 (16)	0.7
Race, n (%)			0.08
White	52 (68%)	50 (63%)	
Black	21 (27%)	23 (29%)	
Asian	4 (5%)	5 (6%)	
Other	0	2 (2%)	
General block type, n (%)			0.8
Upper extremity	59 (77%)	63 (79%)	
► Type of block	► 29 Interscalene (49%) ► 20 Supraclavicular (34%) ► 7 Infraclavicular (12%) ► 2 Axillary (3%) ► 1 Ulnar (2%)	► 41 Interscalene (65%) ► 12 Supraclavicular (19%) ► 8 Infraclavicular (13%) ► 1 Axillary (2%) ► 1 Ulnar (2%)	
Lower extremity	18 (23%)	17 (21%)	
► Type of block	► 12 Femoral (67%) ► 2 Adductor canal (11%) ► 3 Popliteal (17%) ► 1 Missing (5%)	► 14 Femoral (82%) ► 3 Popliteal (18%)	
Block time, min, mean (SD)	6.7 (4.2)	7 (4.2)	0.5

Data are presented as frequency and ratios. Block time and patients' age are presented as mean (SD). P is significant if p<0.05; t-test was used to compare age and block time. χ^2 test was used to compare gender, race and block types.

Primary outcomes

Our primary outcome was to compare the change in STAI-6 anxiety scores between study groups from after to before placement of the block.

Secondary outcomes

Secondary outcomes were to evaluate differences in patient satisfaction scores of their experience during the procedure, physician satisfaction scores of their experience while conducting the procedure, communication difficulties from provider to patient, communication difficulties from patient to provider, vital signs including mean arterial pressure and heart rate and any complications.

Description of measures used in study

State Trait Anxiety Inventory-6 (STAI-6)

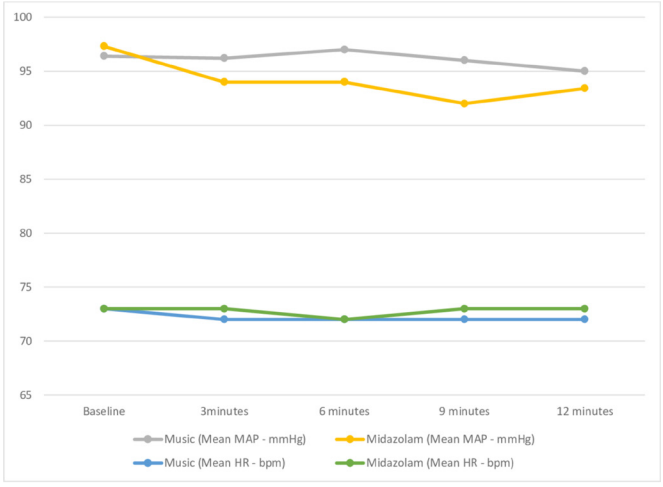
Anxiety scores were determined by the Speilberger's validated tool, the STAI-6.[11] The traditional STAI tool has a state and trait portion, each with 20 questions. For this study we used the shortened validated STAI-6 tool.[11] In the traditional STAI tool scores range from 20 to 80, with higher scores indicating higher anxiety. Although it is difficult to represent severity of anxiety with a numerical cut-off, a score of 50 or higher has been shown to be associated with a higher level of anxiety.[12] An average score that has been reported in prior music studies that have used the STAI tool to assess for anxiety in clinical settings is around 33–35.[7] The STAI-6 scores range from 6 to 24; therefore, to create scores compatible with the STAI tool, the STAI-6 scores were divided by six and multiplied by 20 to give a comparable range from 20 to 80.[11] We applied this conversion since the 20–80 scale has more clinical relevance as evidenced throughout literature and, from a statistical inference perspective, using this conversion would not change the results as both the mean and SD are shifted by a factor.[11 13–15]

Satisfaction scores of the experience during the procedure

The patient and provider satisfaction scores were recorded using a 10-point visual analog scale with 0 being the worst experience possible and 10 being the best experience possible.

Communication difficulties

Evaluation of communication difficulties between provider and patient were done by the response to the following statement on a



P is significant(*) if P<0.05; t-test was used to compare mean arterial blood pressure (MAP) and mean heart rate (HR)

Figure 2 Mean arterial pressure (MAP) and heart rate (HR) trend throughout nerve block administration between music and midazolam groups.

5-point Likert scale: "I found it difficult to communicate with the patient/provider while doing the preoperative nerve block" with a score of 1 being strongly disagree and 5 being strongly agree.

Statistical analysis

Baseline characteristics were compared between the groups using standard descriptive statistics. Categorical data are represented as frequency and percentage of the total. A χ^2 test was used to compare gender, race and block types. Block time and patients' age are presented as mean and SD. A t-test was used to compare age, block times, mean arterial blood pressure and mean heart rate. Continuous data are represented as median (IQR). The significance value was set at $p<0.05$.

Sample size for the primary outcome was calculated using a mean (SD) STAI anxiety score of 34 (8).[6 7] A clinically meaningful decrease as determined by the Cochrane review group was half of one SD (4 points on the anxiety tool).[6] Therefore, we needed to enroll 64 patients per group (alpha=0.05, power=80%) to detect a 4-point difference in the anxiety score in either direction. We increased the sample size by 25% to account for any missing data or any withdrawal from the study; therefore, our estimated sample size was 80 patients per group.

After confirming a normal distribution, the change in STAI-6 scores from after to before are presented as mean (SD). A paired two-sample t-test was used to compare the change from after to before in STAI-6 scores. The Wilcoxon rank sum test was used to compare pre STAI-6 scores, post STAI-6 scores, patient and physician satisfaction scores and the patient and physician perception of communication difficulty scores. As there is much debate regarding the best statistical analysis methods for Likert scales, we chose to analyze the results from the Likert scales in a continuous fashion as the intervals between each item (eg, 'strongly disagree' vs 'disagree') cannot be presumed equal.[16] Statistical significance is considered when $p<0.05$.

Statistical analyses were performed using STATA 13 statistical software (Dallas, Texas, USA).

RESULTS

The study period was between May 1, 2017 and June 30, 2018. A total of 221 patients were scheduled to receive a peripheral nerve block at our ambulatory surgical center and were approached to participate in the study. Fifty-eight individuals declined to participate in the study and three were excluded from the study prior to randomization due to their pre STAI-6 scores being greater than a score of 50. A total of 160 individuals were randomized to the music group or the midazolam group. Three individuals had incomplete data and were not included in the final dataset. Therefore, 157 subjects were included in the analysis with 77 individuals in the music group and 80 individuals in the midazolam group (figure 1). Patient demographics were similar between the two groups (table 1).

The change in STAI-6 scores from after to before the procedure was similar in both groups (mean change in music group −1.6 (SD 10.7); mean change in midazolam group −4.2 (SD 11); p=0.14; mean difference between the two groups in the change of STAI-6 scores −2.5 (95% CI −5.9 to 0.9), p=0.1). Pre-block STAI-6 scores were also similar between both groups (p=0.65). However, the post-block STAI-6 scores were lower in the midazolam group than in the music group (p=0.01) (table 2).

Patient satisfaction was higher in the midazolam group (p=0.01); however, physician satisfaction was similar in the two study groups. Both patients and physicians perceived communication to be more difficult in the music group than in the midazolam group (p=0.005 and p=0.0007, respectively). Mean arterial

Table 2 Patients' anxiety scores (before and after block and difference between the post-block and pre-block scores), patient and physician satisfaction scores and their perceptions of difficulty in communication

	Music	Midazolam	P value
Pre STAI-6 scores	33.3 (23.3–41.7)	30 (20–40)	0.65
Post STAI-6 scores	30 (20–40)	23.3 (20–33.3)	0.01*
Change in STAI-6 scores, mean (SD)	–1.6 (10.7)	–4.2 (11)	0.14
Patient satisfaction	8 (5–9)	9 (7–10)	0.01*
Patient perspective on communication difficulties	1 (1–2)	1 (1–1)	0.005*
Physician satisfaction	9 (8–10)	10 (8–10)	0.07
Physician perspective on communication difficulties	1 (1–2)	1 (1–1)	0.0007*

Data are presented as median (IQR), except for the change in STAI-6 scores which is normally distributed and is presented as mean (SD). Patient and physician satisfaction scores are reported on a scale from 0 to 10. Perception of communication difficulty is presented on a Likert scale (from 0 to 5).
Wilcoxon rank sum test was used to compare the two groups in all data points except for the change in STAI-6 scores in which a paired t-test was used for this comparison.
*Statistical significance is considered when p<0.05.
STAI-6, State Trait Anxiety Inventory-6.

pressure and heart rate trends were similar between the two groups throughout the nerve block administration. There were no statistically significant differences between the two groups at all time points (figure 2).

DISCUSSION

Several studies in the last few decades have shown the benefits of music medicine perioperatively by reducing preoperative anxiety, reducing sedation while under regional anesthetics and keeping patients calm in the postoperative recovery period.[6–8] Prior research has focused primarily on oral anxiolytics, which are not routinely used in the preoperative setting.[6 7] Our study is the first to compare music medicine with an intravenous pharmacologic agent, midazolam, in reducing anxiety scores for patients undergoing a single-injection peripheral nerve block. We identified better anxiolysis with midazolam compared with music, with the effect of the primary outcome of the change in STAI-6 anxiety scores being insignificant. Our findings are supported by the findings of a comparable study by Nikolajsen *et al*. This study evaluated audiovisual stimulation with music and nature compared with placebo during femoral nerve single-injection blocks and found no statistically significant differences in the change in STAI-6 scores among the groups.[17]

Secondary outcomes demonstrated better patient satisfaction with their overall experience and less difficulty in communication between patient and provider in the midazolam group; however, we question whether this is clinically meaningful. These differences may be attributed to the following reasons: (1) Patients were not given a choice to select their own music preference; although patient selection of music could have changed these results, studies demonstrate that research-selected music is effective.[8 10] (2) Patients listened to music via noise-canceling headphones rather than non-noise-canceling headphones, which could have contributed to the communication difficulties.[8 10] (3) We did not standardize the volume level for each patient which also could have affected communication between the provider and the patient. (4) There was better anxiolysis with midazolam than with music.

There are several limitations to this study: (1) Despite calculating the sample size to detect a clinically meaningful difference in the anxiety scores based on the Cochrane review by Bradt *et al*,[6] it is possible that the current study was still underpowered as evidenced by the wide confidence intervals around the change in the STAI-6 scores from after to before the intervention between both groups. (2) We allowed only 3 min to lapse after the procedure time out was performed and before the block was started. It is recommended that music be played for at least 20 min to reap the benefits of anxiolysis,[6] which was not possible in this setting due to adherence to operating room efficiency and timely patient readiness. We instead waited 3 min before starting the nerve block to simulate the length of time it takes for intravenous midazolam to reach peak effect.[18 19] (3) We used noise-canceling headphones instead of non-noise-canceling headphones. (4) We did not give various music selection options for the patients and only played one track. The use of noise-canceling headphones and limiting the selection of music may have contributed to the perceived difficulty in communication and lower satisfaction rates of the overall experience during the block, respectively. (5) The 10-point visual analog scale used for patient and physician satisfaction was not a validated instrument.

CONCLUSIONS

Music medicine offers an alternative to intravenous midazolam prior to single-injection peripheral nerve block procedures. The results of the current study have to be cautiously interpreted within the context of the multiple limitations. Further studies should be conducted to evaluate whether or not music genre and techniques of music delivery can offset the trend of improved anxiolysis and fewer communication barriers using midazolam.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The Institutional Review Board (IRB) at the University of Pennsylvania has approved this randomized controlled study conducted at a university-based ambulatory surgical center

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

REFERENCES

1 Kain ZN, Sevarino F, Alexander GM, *et al*. Preoperative anxiety and postoperative pain in women undergoing hysterectomy. A repeated-measures design. *J Psychosom Res* 2000;49:417–22.
2 Maranets I, Kain ZN. Preoperative anxiety and intraoperative anesthetic requirements. *Anesth Analg* 1999;89:1346–51.
3 White P, Eng MR. Intravenous anesthetics. In: Barash P, Cullen BF, Stoelting RK, *et al*, eds. *Clinical anesthesia*. 6th edn. Lippincott, 2009.
4 Badner NH, Nielson WR, Munk S, *et al*. Preoperative anxiety: detection and contributing factors. *Can J Anaesth* 1990;37:444–7.
5 Conway A, Rolley J, Sutherland JR. Midazolam for sedation before procedures. *Cochrane Database Syst Rev* 2016;(5):Cd009491.
6 Bradt J, Dileo C, Shim M. Music interventions for preoperative anxiety. *Cochrane Database Syst Rev* 2013;(6):Cd006908.
7 Bringman H, Giesecke K, Thörne A, *et al*. Relaxing music as pre-medication before surgery: a randomised controlled trial. *Acta Anaesthesiol Scand* 2009;53:759–64.
8 Hole J, Hirsch M, Ball E, *et al*. Music as an aid for postoperative recovery in adults: a systematic review and meta-analysis. *Lancet* 2015;386:1659–71.
9 The world's most relaxing song. Available: https://www.forbes.com/sites/jordanpassman/2016/11/23/the-worlds-most-relaxing-song/ - 2a5141e32053 [Accessed 15 May 2019].
10 Gooding L, Swezey S, Zwischenberger JB. Using music interventions in perioperative care. *South Med J* 2012;105:486–90.
11 Marteau TM, Bekker H. The development of a six-item short-form of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI). *Br J Clin Psychol* 1992;31 (Pt 3):301–6.
12 Julian LJ. Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale-Anxiety (HADS-A). *Arthritis Care Res* 2011;63:S467–S472.
13 Alam M, Roongpisuthipong W, Kim NA, *et al*. Utility of recorded guided imagery and relaxing music in reducing patient pain and anxiety, and surgeon anxiety, during cutaneous surgical procedures: a single-blinded randomized controlled trial. *J Am Acad Dermatol* 2016;75:585–9.
14 McDermott MS, Marteau TM, Hollands GJ, *et al*. Change in anxiety following successful and unsuccessful attempts at smoking cessation: cohort study. *Br J Psychiatry* 2013;202:62–7.
15 Powell H, McCaffery K, Murphy VE, *et al*. Psychosocial outcomes are related to asthma control and quality of life in pregnant women with asthma. *J Asthma* 2011;48:1032–40.
16 Jamieson S. Likert scales: how to (ab)use them. *Med Educ* 2004;38:1217–8.
17 Nikolajsen L, Lyndgaard K, Schriver NB, *et al*. Does audiovisual stimulation with music and nature sights (MuViCure) reduce pain and discomfort during placement of a femoral nerve block? *J Perianesth Nurs* 2009;24:14–18.
18 Clausen TG, Wolff J, Hansen PB, *et al*. Pharmacokinetics of midazolam and alpha-hydroxy-midazolam following rectal and intravenous administration. *Br J Clin Pharmacol* 1988;25:457–63.
19 Chau SW, Chen CD, Yip WH, *et al*. [Intravenous midazolam for sedation in epidural anesthesia]. *Ma Zui Xue Za Zhi* 1993;31:157–64.