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Effect of slow tempo music on markers of anxiety during cataract surgery: Randomized control trial

Azlan Musa[1]*, Qi Xiong Ng[2], Yong Zheng Wai[2], Tajunisah Iqbal[3]

Abstract:

PURPOSE: This study aims to objectively measure the effect of slow tempo music on various markers for anxiety.

MATERIALS AND METHODS: This is a repeated measure randomized control trial of patients with age-related cataracts undergoing cataract extraction through phacoemulsification under local anesthesia. Patients were randomized into two groups: music group where a standardized piano music was played and control group. Salivary alpha-amylase (sAA) levels were measured at the beginning and at the end of surgery. Blood pressure and heart rate were also measured at 5 min before surgery and at four other standardized points during and after surgery. Visual Analog Scale for anxiety was also gauged: preoperatively, perioperatively, and 15 min postoperatively.

RESULTS: Ninety-two patients were randomized equally to the music group and control group. Paired sample *t*-test showed a reduction in the level of sAA during surgery in the music group ($P = 0.019$). The odds ratio for a drop in sAA with music was 4.407 ($P = 0.001$). Lower systolic blood pressure was observed in the music group: at delivery of local anesthesia ($P = 0.047$), at first incision ($P = 0.023$), and during sculpting ($P = 0.15$). Similarly, diastolic blood pressure was lower at first incision ($P = 0.019$) in the music group. The visual analog scale for anxiety during surgery was found to be lower in the music group ($P = 0.046$).

CONCLUSION: A slow tempo music during cataract surgery was shown to significantly reduce several indicators for anxiety at various points during cataract surgery.

Keywords:

Cataract, lens, music, phacoemulsification, salivary alpha-amylase, stress

[1]Department of Ophthalmology, Universiti Teknologi MARA, Shah Alam, [2]Department of Ophthalmology, Queen Elizabeth Hospital, Kota Kinabalu, Sabah, [3]Department of Ophthalmology, University of Malaya, Kuala Lumpur, Malaysia

***Address for correspondence:**
Dr. Azlan Musa, Level 6, Surgical Office, Academic Block, UiTM Sungai Buloh Campus, Jalan Hospital 47000, Sungai Buloh, Selangor, Malaysia.
E-mail: azlanazha@yahoo.co.uk

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Introduction

Cataract is the leading cause of treatable blindness in the elderly population worldwide.[1] More than 10 million cataracts are operated in a year worldwide and these numbers are on the increase with each passing year.[2-6] Cataract surgery is one of the most frequent surgical procedures done by an ophthalmologist and commonly done under local anesthesia[7] which can lead to anxiety and unfavorable surgical outcome.[8-10]

Anxiety is a form of psychological stress that originates centrally stimulating the sympathetic autonomic nervous system.[11] Secretion of salivary alpha-amylase (sAA) is involved in this same autonomic nervous regulation.[12-14] As such, there have been many studies that linked an increase in sAA with an increase in anxiety.[15,16] Music, on the other hand, has been shown to affect ones' mood and aid with relaxation.[17,18] It is also reported that music significantly reduces blood pressure, heart rate, and anxiety in patients undergoing various ophthalmic and surgical procedures.[19-21]

To the best of our knowledge, only one study conducted by Arai *et al*. that focuses

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on the effect of sounds on sAA.[22] This study is the closest to our study and although the study size was small, they achieved the study power of >80% to conclude that natural sounds before surgery reduce sAA. Though, the authors could not conclude the similar effect on other parameters such as heart rate and blood pressure.

Our study was designed to answer whether music influences anxiety, particularly on sAA where we believe it is a reliable, objective marker for stress and anxiety. We also intend to improve previous studies by playing only one music with a constant tempo, volume, and relaxing beat throughout the duration of surgery.

Having the data on the effect of music on stress and anxiety could potentially lessen the use of sedative agents before cataract surgery. This would also aid to better postoperative outcomes and reduce cancellation cases.

Materials and Methods

This study adhered to the principles governed by the World Medical Association Declaration of Helsinki and conducted after the Medical Ethics Board of University of Malaya committee approval (MECID. NO: 2015111886).

This study was a parallel trial design with an allocation ratio of 1:1. It was carried out in the Day-care Surgery University of Malaya Medical Centre.

Patients admitted to the day-care surgery with age-related cataract were identified. Informed consent was taken, and patients were carefully examined for fulfillment of the inclusion and exclusion criteria. All data are anonymous, and patients were given a subject number according to the time of signed consent.

Inclusion criteria include:
1. Ability to give informed consent
2. Malaysian over the age of 40 years
3. Diagnosis of age-related cataracts which qualifies for phacoemulsification
4. Surgery done by a competent surgeon.

Exclusion criteria include:
1. Patients with an alternative diagnosis other than age-related cataracts
2. Patients with hearing impairment
3. Patients who have had or were given any sedative medications
4. Complications during cataract surgery such as posterior capsule rupture
5. Prolonged surgical time of more than 90 min
6. Patient who has any salivary gland or facial surgery which may alter saliva production.

The G * Power Version 3.1.9.2 software was used to calculate the sample size required. Findings by Arai *et al*. were selected for sample calculation.[22] The paired means and standard deviations at wound closure in control group (61 ± 54 kU/L) and sounds group (27 ± 16 kU/L) obtained from this study were entered to the software. The sample size estimate is calculated with a precision of 5% and a study power of 95%. The estimated total sample size was 74.

Patients were randomized into two arms in the morning of surgery. Blocking randomization size of 1:1 ratio was used with an aim of 37 patients per arm. The random sequence generator from the website www.random.org was used for this purpose. A random series of numbers based on the total number of cases on the day of surgery were generated and divided into two columns: music group and control group. These numbers generated represent the order by which patients will undergo surgery. The randomization, recruitment, and assignment of each participant are done by one of the authors.

Demographic data including age, gender, race, comorbid, occupation, education level, and socioeconomic income were collected. Patients were then randomized to the music group or control group. Before entering the operating theater (OT), a patient's anxiety level was gauged using the Visual Analog Scale for Anxiety score (VAS-A).

Once inside the OT, baseline sample of sAA (sAAbefore), blood pressure (BP0), and heart rate (HR0) were taken. sAA was measured using the Cocorometer (Nipro inc, Japan). A test strip is placed under the tongue filled with saliva for 30 s before it is placed into the Cocorometer machine.

The test strip reagent contains 2-chloro-4-nitrophenyl-galactopyranosylmaltoside (Gal-G2-CNP) which will be hydrolyzed by sAA into its components which will turn the strip reagent color from white to yellow. This enzymatic reaction is calculated using dry chemistry system, based on the reflectance spectrophotometry.[23] sAA activity is quantified in kU/L. One unit of alpha-amylase activity (U) is defined as the enzymatic reaction at 37°C to produce 1 μmol of maltose/min (is also known as μmol/min).[23]

In the music group, a piano musical recording (Andromeda by Gabriel Tosi) was played repeatedly as soon as surgery starts. This music had a soothing rhythm of <70 beats/min and was calibrated to a maximum volume of 60 dB as to not disturb the surgeon. No other music was played elsewhere apart from inside the OT and was only played when surgery starts to ensure standardization.

Since there were a maximum of eight patients operated on any given day, their order during surgery was classified as; early (patient order 1–3), middle (patient order 4–5), and late (patient order 6–8) to facilitate statistical analysis.

Measurements of blood pressure and heart rate were taken at four various stages: during administering local anesthesia (BP1/HR1), at first incision (BP2/HR2), during sculpting, or at first phacoemulsification power used in cases of phaco-chop (BP3/HR3), during wound hydration (BP4/HR4). Soon after drapes were removed, the sAA was measured again (sAAafter). In the recovery hall, patients were asked to self-report their anxiety level during surgery (VAS-A 1–4) and after surgery (VAS-A 5).

Statistical Package for the Social Sciences (SPSS for Windows Version 23.0, SPSS Inc., Chicago, USA) was used for all statistical analysis.

All variables that required a *t*-test were tested for normal distribution based on histograms and Kolmogorov–Smirnov test. Data were compared between the two study groups with the Independent *t*-test for normally distributed continuous data or Mann–Whitney test for nonparametric data and the Pearson Chi-square test for categorical or dichotomous data. If the data show >20% of cells have expected count of <5, then for analysis, either categorical data were combined to fulfill Pearson Chi-square test assumptions, or the test was done using Fisher's Exact test. Data with repeated measures were tested with Paired sample *t*-test. The estimated effect size is represented by Cohen's d coefficient.

Results

A total of 100 patients were recruited in the study, eight were excluded due to posterior capsule rupture during surgery[Figure 1] where the recruitment period was from January 18 2016 to December 16, 2016. Forty-six patients were randomized per arm. Baseline data were largely normally distributed [Table 1] and there were no statistical differences in baseline data between groups [Table 2].

The mean preoperative sAA (sAAbefore) did not show a statistically significant difference between the music group versus control group (P = 0.614). Postoperative sAA (sAAafter) likewise did not yield a statistically significant difference between the two groups (P = 0.456).

A statistically significant lower systolic blood pressure (SBP) was observed in the music group at three different points during surgery: delivery of local anesthesia (SBP1) (153.52±22.05 kU/L vs. 162.83±22.25 kU/L P = 0.047), first incision (SBP2) (146.46 ± 20.79 kU/L vs. 156.72 ± 21.83 kU/L P = 0.023), and during sculpting (SBP3) (141.63 ± 15.96 kU/L vs. 151.30 ± 21.07 kU/L P = 0.015).

Table 1: Kolmogorov-Smirnov normality test for continuous variables

Characteristics	MG (*P*)	CG (*P*)
Number of patients (*n*)	46	46
Age	0.14	0.20
Surgical time	0.003*	0.001*
sAA		
Before	0.20	0.021*
After	0.002*	0.064
SBP		
0	0.20	0.20
1	0.054	0.20
2	0.068	0.192
3	0.20	0.20
4	0.040*	0.20
DBP		
0	0.20	0.20
1	0.20	0.20
2	0.20	0.20
3	0.176	0.20
4	0.20	0.044*
HR		
0	0.20	0.20
1	0.20	0.20
2	0.20	0.20
3	0.20	0.20
4	0.20	0.20

*P<0.05 suggests that data do not follow a normal distribution. sAA=Salivary alpha-amylase, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, HR=Heart rate, MG=Music group, CG=Control group

Similarly, diastolic blood pressure (DBP) was observed to be significantly lower at first incision (DBP2) (73.80 ± 12.48 kU/L vs. 80.22 ± 13.17 kU/L P = 0.019). The patient's heart rate did not show any significant difference between the two groups at any point: before or during surgery.

The visual analog scale (VAS) for anxiety during surgery (VAS-A 1–4) showed a significantly higher proportion of patients with no anxiety in the music group compared to the control group (56.6% vs. 28.3% P = 0.046). All data of comparisons are represented in Table 3.

The overall data were split between the two groups and the paired sample *t*-test was conducted to evaluate the statistical significance between repeated values [Table 4]. It was noted that there was a statistically significant drop in sAA comparing sAAafter and sAAbefore in the music group (−13.174 ± 36.825 kU/L, P = 0.019). In contrast, there was a nonsignificant increase in sAA in the control group (+0.154 ± 39.351 kU/L, P = 0.979).

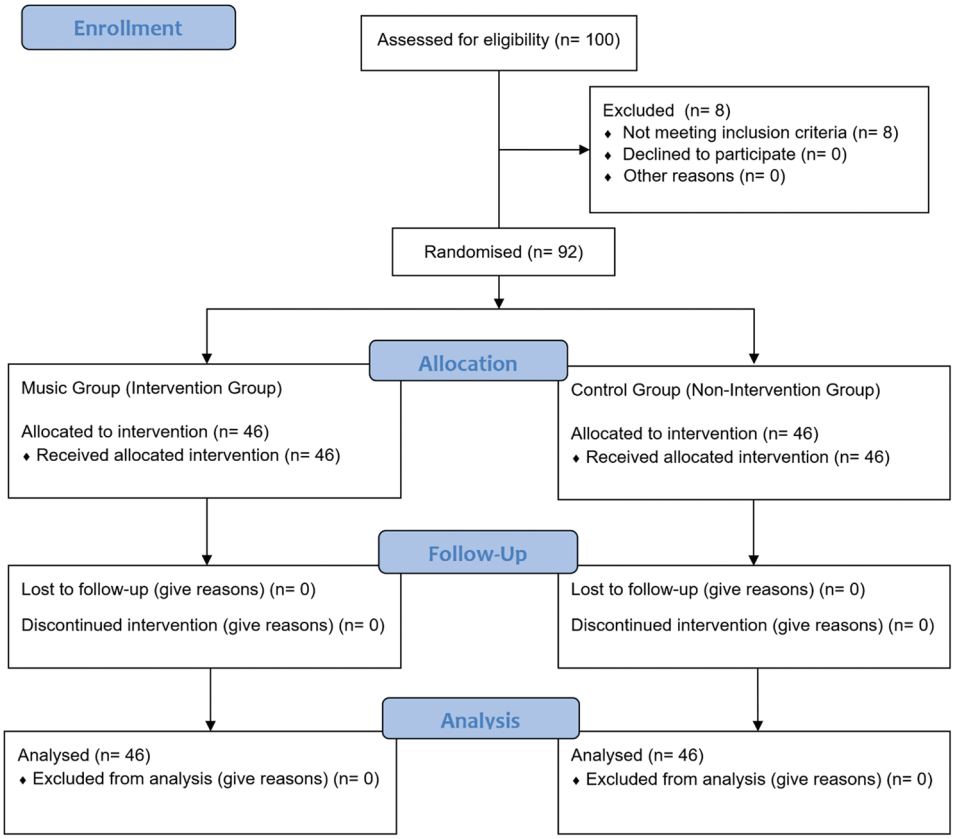

Figure 1: Study flow diagram (adapted from CONSORT 2010)

The difference between sAA after surgery and before surgery was calculated (sAAafter– sAAbefore). A drop in sAA is defined as a negative value obtained. Value of zero was not regarded as a drop. The risk estimate was analyzed, and the cross tabulation is represented in Table 5. Risk estimate calculation was conducted, and the odds ratio was 4.407 (95% confidence interval 1.819–10.682; $P = 0.001$). This suggests that it is 4.407 times more likely to have a drop in sAA with music compared to standard care.

Discussion

In our study, we demonstrated a significant drop in sAA with music played during cataract surgery and it managed to achieve the sample size needed to make this conclusion. We also demonstrated higher decline in blood pressures and heart rates at various standardized points during cataract surgery while listening to music.

This study is a nonblinded trial as surgeons can listen to the music played; this may pose as potential bias. Improvement can be made using in-ear headphones on patients to mask the surgeons and investigators.

Additional limitation of this study is the use of subtenon injection in more than 80% of patients. This can potentially lead to the initial spike in blood pressure and heart rate during administering anesthesia due to pain. It may also increase comfort during surgery leading to a potentially lower blood pressure, heart rate, anxiety level, and pain level. We are unable to reliably subanalyze these two groups of different anesthesia as the numbers are wildly disproportionate.

Nijkamp *et al*. reported that most patients experience some degree of anxiety prior to cataract surgery. The peak of anxiety is often just before surgery and declines immediately after.[24] To further support this, Nigussie *et al*. did an analysis of 239 preoperative patients and found that 70.3% of them had significant anxiety measured using the State-Trait Anxiety Inventory Scale before surgery. It was also noted that being anxious can lead to intraoperative complications and a longer period of recovery.[25] In our study, it was crucial to time the collection of saliva at a point of highest anxiety. It was clear by the above-mentioned studies that immediately before surgery is most likely where anxiety peaks.

Controlling patient's anxiety level is paramount to a successful cataract surgery done under local anesthesia. Wiwatwongwana *et al*. concluded that music statistically decreases anxiety level and reduces SBP.[26] However,

Table 2: Comparison of baseline characteristics between music group and control group

Characteristics (units)	MG (%)	CG (%)	*P*
Number of patients (*n*)	46	46	
Age (years), mean±SD	69.04±8.086	67.70±7.760	0.417
Gender			
Male	54.3	43.5	0.297
Female	45.7	56.5	
Race			
Malay	43.5	34.8	0.375
Chinese	21.7	34.8	
Indian	34.8	30.4	
Hypertension			
Yes	71.7	82.6	0.214
No	28.3	17.4	
Diabetes			
Yes	47.8	52.2	0.677
No	52.2	47.8	
IHD			
Yes	4.3	6.5	1.000[a]
No	95.7	93.5	
Occupation			
Working	10.9	8.7	1.000[a]
Not working	89.1	90.2	
Education			
Primary	28.3	28.3	0.877
Secondary	47.8	43.5	
Tertiary	23.9	28.3	
Income			
Low	76.0	67.4	0.697[a]
Middle	19.6	28.3	
High	4.3	4.3	
Laterality			
Right eye	45.7	52.2	0.532
Left eye	54.3	47.8	
Number of surgery			
First	63.0	52.2	0.291
Second	37.0	47.8	
Order of surgery			
Early	54.3	47.8	0.786
Middle	30.4	37.0	
Late	15.2	15.2	
Anesthesia			
Subtenon	91.3	82.6	0.216
Topical/intracameral	8.7	17.4	
Surgical time (min), mean±SD	37.67±11.203	39.72±15.159	0.801[b]

Comparison for continuous data was made using independent *t*-test, Comparison for categorical data was made using Pearson Chi-square test unless noted. [a]Comparison was made using Fisher exact test, [b]Comparison was made using Mann–Whitney U test. MG=Music group, CG=Control group, SD=Standard deviation, IHD=Ischemic heart disease

studies done on the effect of music on the anxiety that paid emphasis on cataract surgery were rather limited. Camara *et al*. were some that did such study. However, they used different songs during their study. Some of these songs have sudden loud (*forte*) tunes that may be quite disturbing. Since it is also played live on a piano, there was no standardization on its volume, style of play, and tempo. Furthermore, the authors did not assess the level of anxiety during surgery. We believe that music is feasible to modulate anxiety in the OT.

Camara *et al*. showed that live piano music reduced blood pressure, heart rate, and respiratory rate immediately before various ophthalmic surgeries ($P < 0.002$). The authors concluded that piano music reduces blood pressure and heart rate in patients undergoing various ophthalmic surgery.[27] However, the music was not played during surgery and hence, the authors are unable to conclude that music reduces the fore mentioned parameters intraoperatively. Our study was designed as an extension of this study where music was played throughout the surgery.

A similar study conducted by Ko *et al*. that included 138 patients concluded that the music by Kevin Kern significantly reduces level of anxiety (measured with the State-Trait Anxiety Inventory) in patients undergoing colonoscopy.[28] On further assessment of the music used, we noticed that they were mainly slow tempo instrumental music. Lorch *et al*. and Cardoso *et al*. have also proven that music with sedative and soothing tone is linked to reduction in stress and reduces the parameters associated with it in premature infants.[29,30]

Thus, based on the above studies, we selected Andromeda by Gabriele Tosi as our study music based on these studies. Mr. Tosi has kindly agreed for the music to be royalty and copyright free for this study. The music was also set to a maximum volume of 60 dB to match the volume of an average conversation based on the findings of Chasin.[31]

Arai *et al*. recruited patients undergoing inguinal hernia repair and compared the sAA activity at wound closure with and without natural sounds. Even though this paper used natures' sounds and the surgery was different to cataract surgery, the methodology of research was comparable to our study design. To the best of our knowledge, this was the only study to use the Cocoro Meter in a similar fashion. This paper also had enough statistical study power to form a conclusion despite having a small number of recruits. Hence, we decided to use their findings to calculate our required sample size.

sAA was initially thought to be directly linked to the sympathoadrenal medullary axis, which is also responsible for the secretion of adrenaline and noradrenaline.[32] However, there have not been any statistically significant correlations of its increase to a reproducible upsurge in sympathetic output such as blood pressure, cardiac output, cortisol levels, heart rate, and its variability.[33] A further study was conducted

Table 3: Comparison of characteristics between music group and control group

Characteristics (units)	MG (%)	CG (%)	*P*	Cohen's
Number of patients (*n*)	46	46		
VAS-A (0)				
Not anxious (0-1)	47.8	37.0	0.381[a]	
Mild (2-4)	32.6	37.0		
Moderate (5-7)	13.0	23.9		
Severe (8-10)	6.5	2.2		
VAS-A (1-4)				
Not anxious (0-1)	56.5	28.3	0.046[a,*]	
Mild (2-4)	19.6	39.1		
Moderate (5-7)	17.4	23.9		
Severe (8-10)	6.5	8.7		
VAS-A (5)				
Not anxious (0-1)	95.7	95.7	1.000[a]	
Mild (2-4)	4.3	4.3		
Moderate (5-7)	0	0		
Severe (8-10)	0	0		
sAA (kU/L), mean±SD				
Before	74.46±45.225	68.91±58.872	0.614, 0.264[b]	0.106
After	61.28±51.487	69.07±48.099	0.456, 0.323[b]	0.156
SBP (mmHg), mean±SD				
0	145.22±19.628	150.17±19.106	0.223	0.085
1	153.52±22.046	162.83±22.247	0.047*	0.420
2	146.46±20.789	156.72±21.832	0.023*	0.481
3	141.63±15.963	151.30±21.068	0.015*	0.517
4	139.41±16.180	145.72±19.343	0.094, 0.138[b]	0.354
DBP (mmHg), mean±SD				
0	74.15±10.758	76.87±10.813	0.230	0.252
1	78.35±14.518	81.09±13.219	0.347	0.197
2	73.80±12.479	80.22±13.165	0.019*	0.501
3	73.93±11.008	77.83±13.027	0.125	0.323
4	72.89±11.146	76.57±12.612	0.142, 0.201[b]	0.309
HR (beats/min), mean±SD				
0	76.39±14.747	77.63±14.435	0.685	0.085
1	76.13±14.026	77.26±13.447	0.694	0.082
2	73.48±13.075	74.15±13.187	0.806	0.051
3	72.00±12.730	72.00±12.300	1.000	0
4	70.96±12.367	71.48±12.757	0.843	0.041

*$P<0.05$, [a]Comparison was made using Fisher exact test, [b]Comparison was made using Mann-Whitney U test. Comparison for continuous data was made using independent *t*-test, Comparison for categorical data was made using Pearson's Chi-square test unless noted. sAA=Salivary alpha-amylase, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, HR=Heart rate, MG=Music group, CG=Control group, SD=Standard deviation, VAS-A=Visual Analog Scale for anxiety score

Table 4: Comparison of the mean difference of characteristics contrasted between the music group and control group

Characteristics (units)	MG	*P*	CG	*P*
sAA (kU/L)				
After - before	−13.174 (36.825)	0.019*	+0.154 (39.351)	0.979

*$P<0.05$. Comparison for continuous data was made using paired sample *t*-test. sAA=Salivary alpha-amylase, MG=Music group, CG=Control group

by Ehlert *et al*. reported that sAA is related to the central release of noradrenaline as appose to peripheral release (which is largely responsible for the rise of the aforementioned parameters).[34] To further prove this, Meyerbroeker *et al*. induced central noradrenaline by administering yohimbine hydrochloride which among others also significantly increases the sAA in those human subjects.[35] Since the central autonomic nervous system modulates the secretion of sAA, psychological anxiety also influences its secretion.[36,37]

We noted that blood pressure readings were highest during local anesthesia and this was apparent with or without the use of music. Since most of our patients received subtenon anesthesia (87%), we believe this may contribute to the sudden surge in blood pressure due to pain. There is a possibility that topical and intracameral anesthesia could minimize this effect. However, we are unable to reliably confirm this as the number of cases done under topical and/or intracameral anesthesia was too small (13%).

Table 5: Cross tabulation of drop in salivary alpha-amylase

	Drop in sAA		Total
	Yes	No	
MG	34	12	46
CG	18	28	46
Total	52	40	92

sAA=Salivary alpha-amylase, MG=Music group, CG=Control group

Conclusion

Our study showed that music played during cataract surgery significantly reduces several indicators for anxiety at various points during surgery. This study can be generalized to standardized cataract surgery by means of phacoemulsification under local anesthesia. We also recommend the use of slow tempo music as an adjunct to sedative agents in anxious patients undergoing cataract surgery.

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Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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