



The Therapeutic Effect of Music on Oxidative Stress Markers and Anxiety in Hypertension

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Objective : Cardiovascular disease is amenable to mortality and morbidity in India and worldwide. The asymptomatic nature of hypertension made it a silent killer. Evidence suggests the role of oxidative stress and anxiety in the pathogenesis of hypertension. Lifestyle modification can control hypertension and, thus, can prevent complications. Music therapy is a non-invasive, non-pharmacological, and economic practice used for the management of hypertension, anxiety, and oxidative stress. The present study aims to evaluate the therapeutic effect of Raga Ananda Bhairavi on oxidative stress and anxiety in hypertensive patients.

Materials and Methods: This randomized control study comprises of a total of 120 participants of age between 30-60years. All the study participants were divided into an experimental and control group. The instrumental music of Raga Ananda Bhairavi was provided to the experimental group for three months. The anthropometric measurements, blood pressure assessment, and estimation of oxidative stress parameters were done in all subjects before and after three months of intervention.

Results: The systolic blood pressure, diastolic blood pressure, anxiety levels, and oxidative stress marker malondialdehyde significantly reduced after music therapy, and the superoxide dismutase level significantly improved after the intervention.

Conclusion: Music can be used as an adjunct therapy for the management of hypertension.

Keywords: Anxiety; hypertension; music; oxidative stress.

1. INTRODUCTION

Hypertension has no warning signs and symptoms until blood pressure levels reach a hostile life stage [1,2]. Nearly 970 million people are estimated to have high blood pressure and approximately, 1.56 billion adults are expected to live with hypertension by 2025 [3] The reports from the Global Burden of Disease (GBD) study of 2016 revealed 1.63 million hypertension steered deaths in India [4] There are virtually 43 people out of 100 people who have hypertension in South India. In Kerala, the hypertension prevalence was 43% [5] The average incidence between men and women is indistinguishable but fluctuates with age. More than 90% of people with high blood pressure are estimated to have essential hypertension [6] Lifestyle modifications and medications can control essential or primary hypertension [2,6,7]

According to updated guidelines on hypertension by Eighth Joint National Committee (JNC-8), Systolic BP ≥ 140 mm Hg and Diastolic BP ≥ 90 mm Hg in people less than 60 years should start with antihypertensive medications [8] Hypertension develops when there was the influence of genetic factors, various environmental threats, cigarettes, sedentary lifestyle, overweight, increased salt intake, anxiety, depression as well as in older adults [9]. In comparison with healthy individuals, people with persistently elevated hypertension have an advanced level of trait anxiety and hard-driving behavior [10]. Humans with hypertension have decreased antioxidant levels and elevated amounts of reactive oxygen species. The imbalance between antioxidants and reactive oxygen species resulted in oxidative stress [11]. Studies revealed that oxidative stress is associated with hypertension [12]. The non-specific markers of oxidative stress like superoxide and hydrogen peroxide was increased in hypertension [13].

Lifestyle modifications are recommended for all patients with hypertension [14]. Relaxing music seems to be effective in decreasing blood pressure and heart rates in hospitalized pre-hypertensive pregnant women [15]. The positive effect of music in prehypertension and hypertension was due to its influence on autonomic nervous system [16]. In patients undergoing hemodialysis, music therapy reduces anxiety and blood pressure [17].

Engagement with creative activities has the potential to contribute toward reducing stress and depression and can serve as a vehicle for alleviating the burden of chronic disease. Music is the most accessible and most researched medium of art and healing, and there has been a principal emphasis on the soothing capacity of music and its ability to offset overly technological approaches to care. A review article on 'stress reduction through Indian classical music' by Balaji Deekshitulu PV mentioned various ragas and its effect on the human body and also pointed out the effect of Raga Ananda Bhairavi in the suppression of stomach pain, kidney problems and controlling blood pressure [18,19] Studies are showing the beneficial effect of Raga Ananda Bhairavi in reducing pre-procedural anxiety and post-operative pain management.[19-21]. Anxiety and hypertension are meticulously related and the effect of Indian classical music on anxiety and blood pressure is evident from different studies [20,22-23] Hence, the present study was conducted to assess the effect of music on oxidative stress markers and anxiety in hypertensive patients.

1.1 Aim

The present study aims to evaluate the therapeutic influence of Raga Ananda Bhairavi on oxidative stress and anxiety in hypertension.

1.2 Objectives

- To assess the blood pressure, anxiety level, and the parameters of oxidative stress in hypertensive patients before and after music intervention in the experimental group and to compare with the control group.
- To correlate the changes in oxidative stress parameters with alterations in blood pressure and anxiety levels with music intervention.

2. MATERIALS AND METHODS

The present study was an open-label randomized control study. The present study registered in the ISRCTN clinical trial registry (ID: ISRCTN13863348). The study was conducted from November 2018 to November 2019.

The study was conducted in employees of Little Flower Hospital and Research Centre,

Angamaly. A total of 120 subjects participated in the study between 30-60 years of age and sex-matched people. Patients who are already diagnosed to have stage 1 hypertension by a registered medical practitioner within three years and taking any of the first-line antihypertensive medications like calcium channel blocker or beta-blocker were included for the present study. The study participants were randomly divided into an experimental and control group, with 60 participants in each group by block randomization. The participants with severe coronary artery disease, stroke, hepatic disorders, renal disorder, hearing problems, ear implants, ear surgeries, and ear infections were excluded from the study.

Anthropometric measurements like height, weight, waist circumference, and hip circumference were estimated. Waist circumference and hip circumference were measured by the WHO STEPS protocol [24]. Body mass index (BMI) and waist-hip ratio (WHR) were calculated. A mercury sphygmomanometer (Elko mercurial sphygmomanometer 300 manufactured by Anita Industries New Delhi) was used to measure blood pressure [25]. The estimation of blood pressure was performed after 10 minutes of rest by the participants.

The markers of oxidative stress estimated were superoxide dismutase (SOD) and malondialdehyde (MDA). The blood samples were collected, cooled, and centrifuged for 10 minutes at 4000rpm. The serum separated was kept at -20°C . The serum concentration of SOD and MDA was determined by the spectrophotometric method. SOD was estimated by Marklund and Marklund method [26]. MDA was analyzed by Beuge and Aust Method [27].

The Malayalam adaptation of the Spielberger State-Trait Anxiety Inventory (STAI) by Vinod Kumar and Das M used to assess the anxiety level of the participants [28]. All the participants were able to read and write Malayalam. The questionnaire comprises two systems to measure state anxiety and trait anxiety. Each scale consists of 18 statements and rated on a 4-point scale (not at all, somewhat, moderately so, very much so). The STAI scores range from a minimum of 18 to a maximum score of 72 on both subscales.

The prerecorded instrumental music of Raga Ananda Bhairavi was provided to the

experimental group. They were instructed to assemble in a hall every day. A soundproof room was selected as a setting to avoid unnecessary external noises. The participants of the experimental group allowed to relax and listened to music from an audio speaker. The intervention was provided to the experimental group between 7 am and 10 am with 15 minutes duration per day for three months. Meanwhile, the participants in the control group were allowed to sit and relax for 15 minutes. The participants were advised to take the medication as usual and were advised to report any change or addition of medication, unfamiliar health outcomes, or any difficulties during the study period. Blood pressure, oxidative stress, and anxiety level assessment were carried out in all subjects before and after music therapy.

2.1 Pilot Study

A pilot study was conducted for a period of three months from August 2018 to October 2018 at Little Flower Hospital and Research Centre, Angamaly. Twenty hypertensive participants were selected and randomly divided into an experimental and control group with ten participants in each group. Individual written informed consent was obtained before the onset of the study. Baseline parameters were collected from the participants. The participants in the experimental group gathered to a hall, permitted to sit and relax. They allowed listening instrumental music of Raga Ananda Bhairavi 15 minutes/day for three months from an audio speaker. All the data reassessed after 3 months. The conclusion drawn from the pilot study was musical auditory stimulation was feasible, simple, and admissible for the participants. There was an attrition rate of 5%. The duration and the method of administration of intervention were found to be effective. There were no side effects found for the intervention.

2.2 Statistical Analysis

The analysis of the data performed by using Statistical Package for Social Science (SPSS) Version 20.0. Baseline characteristics were expressed using descriptive statistics. The quantitative data expressed by mean \pm SD. The intragroup comparison was done by paired t-test and Wilcoxon signed rank test. The correlation of reduction in oxidative stress parameters with variations in blood pressure and anxiety was done by Spearman's rank correlation. A p-value <0.05 was considered as statistically significant.

3. RESULTS

The study consisted of 120 subjects aged 30-60 years with stage 1 hypertension. Of these, 57 were males, and 63 were females. Table 1 shows the clinical characteristics of the participants of the present study.

Values expressed in mean ± SD. Gender, food habits, family history of hypertension, physical activity of the participants are expressed in frequency and percentage. BMI- Body mass index, WHR- Waist hip ratio.

3.1 Comparison of Parameters within the Experimental And Control Group of the Study Participants

The data in Table 2 shows blood pressure, oxidative stress markers, and anxiety levels of the study participants. There is a significant decrease in systolic blood pressure, diastolic blood pressure, malondialdehyde, state anxiety, and trait anxiety in the experimental group after intervention. There is a significant increase in the superoxide dismutase activity in the experimental group after intervention.

Table 1. Clinical characteristics of the study participants

Characteristics	Music therapy Group (n=60)	Control Group (n=60)
Age (years)	48.90±7.76	49.24±8.11
Gender		
Male	31(51.7%)	26(43.3%)
Female	29(48.3%)	34(56.7%)
BMI (kg/m ²)	25.77±4.12	26.71±3.89
WHR	0.97±0.06	0.97±0.02
Duration of disease (months)	17.33±5.46	18.01±4.87
Food Habits		
Vegetarian	3.3%	6.7%
Non-vegetarian	0	0
Mixed Diet	96.7%	93.3%
Family History of hypertension		
Yes	50%	58.3%
No	50%	41.7%
Physical Activity		
Heavy Worker	13.3%	13.3%
Moderate Worker	76.7%	78.3%
Sedentary Worker	10.0%	8.3%

Table 2. Comparison of parameters in hypertensive patients before and after music therapy

Variables	Experimental Group			Control group		
	Pretest	Post-test	p	Pretest	Post-test	p
SBP(mm Hg) ^a	150.1±4.9	146.2±4.8	<.05*	150.03±4.89	152.27±4.81	<.05*
DBP(mm Hg) ^b	97.45±2.4	95.2±2.53	<.05*	97.58±2.49	97.97±2.67	<.05*
SOD(U/ml) ^a	9.53±1.85	10.7±1.93	<.05*	9.68±1.77	8.71±1.70	<.05*
MDA(nmol/ml) ^a	3.71±0.4	3.23±0.39	<.05*	3.84±0.34	4.38±0.43	<.05*
State Anxiety ^a	48.75±4.10	39.22±2.51	<.05*	48.57±3.50	49.23±3.42	<.05*
Trait Anxiety ^a	49.58±3.71	39.15±3.15	<.05*	49.20±3.83	49.93±3.89	<.05*

*a-Paired sample t-test, b- Wilcoxon signed rank test. Values expressed as mean ± SD. SBP- systolic blood pressure, DBP- diastolic blood pressure, MDA - malondialdehyde, SOD - superoxide dismutase, *-p<0.05 statistically significant*

3.2 The Correlation of Change in Oxidative Stress Parameters with Changes in Blood Pressure and Anxiety in Study Participants

Table 3 shows the correlation of change in oxidative stress parameters with change in blood pressure and anxiety levels. The analysis was performed in the pooled data of experimental and control group. From the table, it is clear that change in MDA has a significant positive correlation with changes in systolic BP, diastolic BP, state anxiety, and trait anxiety. The change in superoxide dismutase has a significant negative correlation with changes in blood pressure and anxiety levels.

4. DISCUSSION

Music has a comprehensive application with each stage of the development of human life. Music therapy is a novel approach for the management and control of anxiety and hypertension. The different ragas in Indian classical music elicit distinct emotions and health benefits [29] However, the scientific studies of Indian music as an intervention are meagre.

Raga Ananda Bhairavi is an auspicious raga in the Indian tradition of classical music and its relaxing effect was well appreciated by hypertensive patients during pilot study in comparison with any other genre of music. Hence, the present study used the relaxing technique of Raga Ananda Bhairavi as an intervention for three months in hypertensive patients. The relaxing music exerts its effect on the cardio vascular system by the activation of the parasympathetic division of the autonomic nervous system. The parasympathetic stimulation results in a decrease in blood pressure and heart rate. A number of reports revealed the modulation of the cardiac autonomic nervous system with classical music.[16,30,31]

The recorded relaxing music had reduced the state anxiety in patients with myocardial

infarction [30]. Kumar TS *et al.* reported a reduction in postoperative analgesic requirements with Raga Ananda Bhairavi [19]. Varghese J and Joshi M revealed that there is a significant change in blood pressure and anxiety level after the administration of Kalavati Raga as music therapy [17]. Studies also reported the effect of Raga Ananda Bhairavi in reducing pre-procedural anxiety and also in dental anxiety [20,21]. Our results were consistent with the above studies and showed a significant reduction in state anxiety, trait anxiety, and blood pressure in hypertensive subjects after music intervention.

The anxiolytic action of music is due to the modulation of autonomic nervous system as well as due to the diminished activity of the hypothalamo pituitary adrenal axis [32]. Raga Ananda Bhairavi is a beautiful raga and has a soothing effect on one's mind. Hence, this traditional raga ensures the psychological comfort of an individual.

A meta-analysis of music therapy's influence on systolic blood pressure, diastolic blood pressure, and heart rate showed a significant reduction in systolic BP, diastolic BP, and heart rate [33]. A randomized control trial using instrumental music of Indian classical music in hypertensive patients was also observed a significant decrease in blood pressure [34]. The passive listening to Indian classical music especially by Raga Bhimpalas with lifestyle modifications found to be effective in normalizing blood pressure, and enhancing parasympathetic activity in prehypertensive and hypertensive patients [16]. Various studies were also concomitant with the above results.[23,33,35] The present interventional study with Raga Ananda Bhairavi in hypertensive subjects had shown the same result after three months. Jomon *et al.* demonstrated the equivalent effect of choice music and Raga Ananda Bhairavi [20]. The antihypertensive effect of music-based interventions is due to the enhancement of parasympathetic activity [16,30,31].

Table 3. The correlation of change in oxidative stress parameters and change in blood pressure and anxiety levels

Variables	Correlation Coefficient (MDA)	Correlation Coefficient (SOD)
SBP	.801***	-.784***
DBP	.764***	-.770***
State Anxiety	.723***	-.772***
Trait Anxiety	.796***	-.737***

*Spearman's rank correlation, p<0.05-statistically significant, ***- p<0.001, SBP-systolic blood pressure, DBP- diastolic blood pressure, MDA - malondialdehyde, SOD - superoxide dismutase*

The discrepancy between reactive oxygen species (ROS) production and the antioxidant defence systems results in oxidative stress [11]. MDA is the best mutagenic product of lipid peroxidation by the ROS [36] MDA has a simplistic reaction with thiobarbituric acid (TBA) and has been broadly used as a suitable biomarker for lipid peroxidation [37] The high reactivity of MDA made it as a famous and trustworthy marker that define oxidative stress in clinical situations and the biomedical research community [38]

The human antioxidant protection is multifaceted and essentially reduces the ROS level. SOD is an antioxidant enzyme within the cell that catalyzes superoxide radical's dismutation into hydrogen peroxide and oxygen and has a defending role in atherosclerosis. SOD modifies elevated BP by vasodilation, vasoconstriction, blood vessel alteration, and cardiac hypertrophy [39] The superoxide is the primary ROS generated from different sources. Its dismutation by SOD is crucial for each cell [40] Ahamed A et al. reported that MDA levels were considerably increased in hypertensive people, whereas antioxidant enzyme SOD was significantly reduced in both prehypertension and hypertension [13] The significance of SOD and MDA in hypertension made it as a significant markers of oxidative stress than any others.

A study in monocytes of hypertensive patients had shown a significant association between trait anxiety and reactive oxygen species production [41] The malondialdehyde, which is a marker of reactive oxygen species, was elevated in hypertensive patients. After three months of music sessions, the MDA level has declined. The anxiety levels and MDA were significantly reduced in the experimental group after intervention. This result strongly confirms the correlation between anxiety and oxidative stress. Our results were consistent with the reports by Ahmad et al. [13], and the SOD levels significantly improved with modification in blood pressure.

The results of the present study are in good agreement with a randomized control trial by Orak et al., and they demonstrated a favourable result on oxidative stress with Turkish classical music in individuals undergoing oocyte pick-up [42] 489 An animal study used a combination of Mozart classical music and cocoa powder and found out a significant improvement in the antioxidant activity [43] 490 Music moderated the

oxidative stress in hypertensive patients as marked by the results of the present study and the above observation may be due to the overall improvement in the anxiety level and blood pressure with music intervention. Hence, these parameters can influence the body's antioxidant status and oxidative stress. However, advanced research regarding the pathophysiological mechanism is not well flourished.

The limitations of the study were the complications associated with hypertension were not considered as well as the study limited to stage 1 hypertensive patients who were taking any of the first line antihypertensive medications. The present study included only two significant parameters of oxidative stress and future study can be directed by including all other parameters.

5. CONCLUSION

Hypertension exists as a significant public health problem. The control and management of hypertension are inevitable in the present scenario. The evidence of the therapeutic impact of music existed from centuries back. The results of the present study revealed that the systolic blood pressure, diastolic blood pressure, anxiety levels, and oxidative stress marker malondialdehyde significantly reduced after music therapy, and the superoxide dismutase level significantly improved after the intervention. The music intervention is an inexpensive, non pharmacological, non-invasive and valid physiological approach with no side effects. Hence, it can be incorporated as a complementary health care practice in hypertensive patients to maintain and control blood pressure and its associated ailments.

CONSENT AND ETHICAL APPROVAL

Institutional ethics committee approval (IEC/LFMRC/2018/1) obtained and informed consent provided by all the participants before the commencement of the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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