Original Article

Music therapy improves pregnancy-induced hypertension treatment efficacy

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Abstract: Pregnancy-induced hypertension (PIH), also known as pre-eclampsia, is an increasingly common complication of pregnancy characterized by elevated blood pressure, albuminuria, and edema. Conventional treatment for PIH, typically consisting of bed rest and early delivery of the fetus, is costly and can lead to complications. Therefore, alternative treatments are of interest to the medical community. Here, we describe the effects of music therapy on patients being treated for PIH. Sixty patients with PIH were randomly divided into two groups of 30 subjects each; one group received music therapy in addition to conventional treatment and the other group received only conventional treatment. Systolic blood pressure (SBP), diastolic blood pressure (DBP), Hamilton anxiety scale (HAM-A) scores, Hamilton depression scale (HAM-D) scores, and serum angiotensin II (Ang II) levels were assessed before and after treatment. At the end of treatment, short-form health survey (sF-36) scores were compared between groups. SBP, DBP, HAM-A scores, and HAM-D scores were all significantly lower following treatment in the patients that received music therapy compared to those in the control group. Additionally, quality of life scores were higher in patients that received music therapy, and their serum Ang II levels were significantly lower than those of the control group. These results suggest that music therapy is an effective supplement in the treatment of PIH, as it lowered blood pressure, reduced serum Ang II, alleviated negative emotions, and improved quality of life.

Keywords: Music therapy, pregnancy induced hypertension, pre-eclampsia, angiotensin II, anxiety state, depression state, quality of life

Introduction

Pregnancy-induced hypertension (PIH) is a common pregnancy complication, affecting approximately 2% of pregnant women worldwide, and is one of the primary causes of death for pregnant mothers [1]. The onset of PIH typically occurs at 20 weeks gestation and is marked by elevated blood pressure, albuminuria, and edema [2]. Multiple organs dysfunction can occur, endangering the life of the mother and fetus [3]. The etiology of PIH is not well understood. Recent studies support the involvement of hereditary and immune factors, as well as abnormal placental function and inflammatory reactions [4, 5]. A drop in trophoblast invasiveness is thought to lead to insufficient spiral artery recasting and superficial implantation of the placenta, resulting in decreased blood supply to placental tissues [2]. The resulting placental anoxia induces trophoblast secretion and cytokine release, vascular endothelial injuries, and activation of inflammation immunity, which can expand to other organs and lead to systemic damage [6]. Because even moderate PIH can pose a severe threat to the safety of the mother and fetus, early recognition and diagnosis of PIH is critical to providing effective therapeutic measures [7].

PIH can have serious adverse effects on pregnancy outcome. Perinatal infant mortality, asphyxia neonatorum, fetal distress, placental abruption, postpartum hemorrhage, and C-section rates increase in every form of PIH [2]. The incidence of fetal distress, placental abruption, premature birth, C-section, and postpartum hemorrhage related to PIH is increasing at a progressively higher rate, posing increasing concern for perinatal infants [8, 9]. PIH also

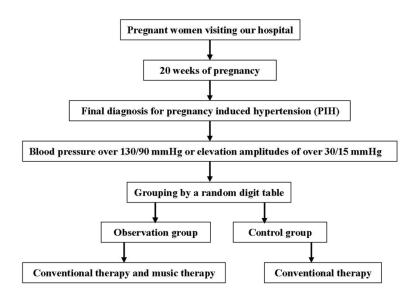


Figure 1. A flow chart for patient enrollment and treatment.

causes patients to experience negative emotions. Studies have found that anxiety and depression increases significantly in women with this disorder, and that patient anxiety can influence other family members [10]. Recent clinical studies involving interventional measures, such as nursing intervention, have attempted to relieve PIH-induced negative emotions in an effort to protect women and newborns from adverse outcomes [11, 12]. Additionally, a decrease in quality of life is a common manifestation of PIH. Studies indicate that somatization, depression, anxiety, hostile behaviors, obsessive-compulsiveness, fear, interpersonal sensitivity, and anxiety symptoms such as worrying are significantly more likely in PIH women than in healthy pregnant women while physical function, vitality, emotional health, mental health, and general health are significantly impaired compared to healthy pregnant women [13].

Excessive activation of the renin-angiotensin-aldosterone system is thought to be the primary mechanism of hypertension onset and abnormalities of the renin-angiotensin-aldosterone system are associated with cardiovascular disease, hypertension, left ventricular hypertrophy, and myocardial infarction [14]. Ang II is the primary active peptide in the renin-angiotensin-aldosterone system and acts on two receptors, AT1R and AT2R, both of which are widely expressed in human tissues [15]. Abnormal Ang II levels play an important role in

the development of PIH [16]. Rate-limiting enzyme angiotensin converting enzyme (ACE) has been found to be highly associated with PIH susceptibility [17]. As PIH conditions progress, serum ACE activity gradually increases, correlated with edema and urine protein [18]. A recent study found that, among Chinese, the risk of PIH onset among individuals with a deletion of the polymorphism D allele in the ACE gene is significantly increased [19]. In addition, elevation of Ang II levels leads to a significant increase in 24-hour mean SBP and is positively correlated with HAM-D scores [20],

supporting a link between the renin-angiotensin-aldosterone system, blood pressure, and negative emotions.

Music therapy has slowly gained popularity in Western countries as a means to improve physical and mental states [21]. Music therapy has been shown to be effective in manipulating stress reactions, anxiety, pain, and muscular tension [22], as well as in surgery- or traumarelated pain and anxiety [23], post-chemotherapeutic reactions [24], and fears related to dentistry [25]. Music therapy has shown to significantly lower anxiety and depression in elderly patients with hypertension, improve quality of life, lower postoperative blood pressure fluctuation, decrease the probability of re-bleeding and mean hospitalization length of hypertensive patients with cerebral bleeding, and provide patients with a positive prognosis after hypertensive cerebral bleeding surgery [26]. The combined application of music therapy and conventional drugs not only delivers anti-hypertensive results but also lowers resting heart rates and sympathetic nerve activity. The application of music therapy in PIH patients who have undergone a C-section can also lower angiotensin II levels [27].

Since medical treatment is likely to produce toxic side effects like xerostomia, elevated liver enzymes, hepatitis, hepatic necrosis and others [28], the potential harm from these treatments should be carefully considered, and

Table 1. General information of the participants

Indexes		Observation group (n=30)	Control group (n=30)	x²/t	P values
Ages (years)		29.9±4.6	28.8±3.8	1.010	>0.05
Times of delivery		1.5±0.6	1.4±0.6	0.645	>0.05
Gestational weeks (weeks)		25.8±2.1	26.5±2.4	1.202	>0.05
Fertility	Primiparous	25	24	0.111	>0.05
	Multiparous	5	6		
Pregnancy status	Singleton	28	29	0.351	>0.05
	Multiple	2	1		
Body mass (kg)		65.8±5.6	64.7±5.9	0.741	>0.05

alternative methods, such as music therapy, should be explored [29]. Effective prenatal treatment can improve prenatal and postnatal quality of life of PIH pregnant women [30, 31]. Here, we describe the application of music therapy in conjunction with conventional treatments in patients with PIH.

Methods

Participants

Sixty patients with PIH admitted to our hospital between December 2013 and December 2014 were selected as study participants; they were enrolled as described in Figure 1. All patients had a blood pressure of over 130/90 mmHg or blood pressure elevation amplitudes of over 30/15 mmHg after 20 weeks of pregnancy. All patients included in the study had completed at least a junior/middle school level of education and provided informed consent in accordance with the hospital's policies. Women were excluded from the study if they had hypoproteinemia, functional lesions in any organs, mental illness, had undergone surgery within the last three months, or if they suffered from hearing loss or could not complete the study. The age of participants ranged from 22 to 39 years with a mean of (29.6±4.1) years. Fortynine were primipara and 11 were pluripara; 57 had monocyesis and 3 had polycyesis. Treatment lasted between 22 and 30 weeks with a mean of (26.3±2.1) weeks. A random digit table was used to assign 30 patients to an observation group and 30 to a control group, with no statistical significance between the two groups in terms of age, parity, gestational week, or body mass. Table 1 describes the basic information and clinic features for both groups.

Treatment methods

Patients in both groups were given a conventional therapeutic regimen, including spasmolysis with magnesium sulfate, lowering blood pressure with nifedipine and others. Patients in the observation group were also given music therapy in addition to conventional treatment: the people with qualifications formulated personalized music selections according to self-reported emotions from patients, primari-

ly consisting of folk music and symphonies by Beethoven, Schubert, and Tchaikovsky, as well as the patient's favorite slow and deliberate songs. Treatments began two hours after breakfast and two hours after dinner and lasted 30 to 60 minutes every day for each patient, and the volume was kept between 50 to 60 decibels. In addition, each patient was issued a small MP3 player with an earpiece and the music was saved in the MP3 player so that the patient could listen at any time. All patients received continuous treatment for four weeks.

Blood pressure measurement

Patient systolic and diastolic blood pressures (SBP and DBP) were measured with electronic sphygmomanometer (OMRON 7301-IT) before and after each treatment session.

Mental health assessment

The Hamilton Anxiety Scale (HAM-A) was used to assess patients' anxiety levels before and after each treatment session. If the HAM-A score was greater than 29 points, patients were considered to have severe anxiety. If a patient scored 21 points or more, it was considered obvious anxiety, if a patient scored 14 points or more, they were considered to have anxiety, and patients who scored less than 7 points were considered to be free of anxiety. Additionally, the Hamilton Depression Rating Scale (HAM-D) was used to assess depression status. A HAM-D score over 35 points indicated severe depression. A score between 20-34 points was considered to be typical depression, while a score less than 8 points was considered to be depression-free. The short-form health survey (sF-36 scale) was also used to assess quality of life in both groups after treatment was complete.

Music therapy of PIH

Table 2. The systolic blood pressures in patients with PIH

Crauna	Case	SBP (r	nmHg)	DBP (mmHg)		
Groups	Numbers	Before treatment	After treatment	Before treatment	After treatment	
Control group	30	155.42±12.15	148.32±12.18 ^b	95.51±12.23	92.64±12.20b	
Observation group	30	155.38±12.14	131.50±12.16a,b	95.37±12.15	81.60±11.41 ^{a,b}	

Note: ^aP<0.05, vs control group; ^bP<0.05, vs before treatment.

Table 3. The HAM-A and HAM-D scores in patients with PIH

Crauna	Case	HAMA s	scores	HAMD scores		
Groups	Numbers	Before treatment	After treatment	Before treatment	After treatment	
Control group	30	20.30±3.68	20.30±3.62	17.28±3.59	17.24±3.58	
Observation group	30	20.40±3.64	15.40±3.59 ^{a,b}	17.31±3.63	14.34±3.65 ^{a,b}	

Note: ^aP<0.05, vs control group; ^bP<0.05, vs before treatment.

Table 4. Quality of life after treatment

	sF-36 scale score							
	Physiological	Physiological	Physical	Overall	\/i+ali+	Social	Emotional	Mental
	Function	Functioning	Pain	Health	Vitality	Functions	Functioning	Health
Observation (N=30)	84.5±10.6°	82.6±10.1°	74.5±10.4ª	84.2±11.2ª	88.4±10.3°	74.9±9.1ª	73.3±9.4ª	81.5±8.3°
Control (N=30)	71.2±10.4	72.3±9.8	62.6±9.6	70.5±11.9	74.2±10.7	62.9±8.3	60.5±9.8	72.6±8.4

Note: ^aP<0.05, vs control group.

Circulating angiotensin II

Peripheral venous blood was collected from all patients before and after each treatment. Enzyme-linked immunoabsorbent assay (ELISA) was used to measure the serum Ang II levels with reagents provided by Wuhan Boster Biology Technology Company, which was conducted according to manufacturer protocols.

Statistical analysis

SPSS 13.0 (IBM, Armonk, NY) was used to perform statistical analysis. Data were expressed as (mean \pm standard deviation). An independent sample t-test was used to compare results from the two groups, while a paired t-test was used to make comparisons within groups before and after treatment. A p-value less than 0.05 indicated a statistically significant difference.

Results

Music therapy enhances the blood pressure reducing effects of conventional therapies

There were no significant differences in blood pressure between the two groups prior to starting treatment. After treatment, however, SBP and DBP levels of patients in both groups decreased significantly (P<0.05), and the SBP and DBP levels of the patients in the music therapy group were significantly lower than those in the control group after treatment (P<0.05). The distribution of SBP and DBP levels are shown in **Table 2**.

Anxiety/depression is reduced with music therapy

There were no significant differences in HAM-A or HAM-D scores between the two groups prior to beginning treatment, but after treatment, the HAM-A and HAM-D scores of patients in the observation group dropped significantly compared to pre-treatment scores (P<0.05), while patients in the control group showed no significant changes after treatment. Notably, the HAM-A and HAM-D scores of the patients in the observation group were significantly lower than those in the control group after treatment (P<0.05). The distribution of HAM-A and HAM-D scores is shown in **Table 3**.

Patient quality of life improves with music therapy

SF-36 scores of patients in the music therapy group were significantly higher than those in

Table 5. The serum levels of Angiotensin II in patients with PIH

Groups	Case	Before	After	
Groups	numbers	treatment	treatment	
Control group	30	32.84±2.87	27.21±2.78 ^{a,b}	
Observation group	30	32.77±2.75	32.54±3.08	

Note: ^aP<0.05, vs control group; ^bP<0.05, vs before treatment.

the control group following treatment (P<0.05) (**Table 4**).

Serum angiotensin II is decreased with music therapy

While there were no significant differences in serum Ang II levels prior to the start of treatment, serum Ang II levels of the patients in the observation group, but not in the control group, dropped significantly after treatment compared to starting levels (*P*<0.05). Additionally, Ang II levels in the observation group were significantly lower after treatment than those in the control group after treatment (*P*<0.05). The distribution of Ang II levels is shown in **Table 5**.

Discussion

Our study revealed that music therapy had a profound influence on the success of conventional treatment for PIH patients. Both the SBP and DBP levels of patients who received conventional and music therapy treatment were significantly lower than those who only received conventional treatment (P<0.05). In addition, the HAM-A and HAM-D scores of patients who received music therapy were significantly improved compared to patients who did not receive music therapy (P<0.05). Ang II levels were significantly lower in patients who received music therapy compared to those who did not receive music therapy (P<0.05).

Our results support the application of music therapy in the treatment of PIH, based on its ability to significantly control patients' blood pressure and serum Ang II, relieve negative emotions, anxiety, and depression, while improving pregnancy outcomes for women and infants. Music therapy may, in fact, prove to be useful in improving the quality of life of any patient suffering from hypertension.

Disclosure of conflict of interest

None.

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References

- [1] Pennings JL, Kuc S, Rodenburg W, Koster MP, Schielen PC, de Vries A. Integrative data mining to identify novel candidate serum biomarkers for pre-eclampsia screening. Prenat Diagn 2011; 31: 1153-1159.
- [2] Kintiraki E, Papakatsika S, Kotronis G, Goulis DG, Kotsis V. Pregnancy-Induced hypertension. Hormones (Athens) 2015; 14: 211-223.
- [3] Rubattu S, Pagliaro B, Pierelli G, Santolamazza C, Castro SD, Mennuni S, Volpe M. Pathogenesis of target organ damage in hypertension: role of mitochondrial oxidative stress. Int J Mol Sci 2015; 16: 823-839.
- [4] Deveer R, Engin-ustun Y, Akbaba E, Halisdemir B, Cakar E, Danisman N, Mollamahmutoglu L, Yesilyurt A, Candemir Z. Association between pre-eclampsia and inherited thrombophilias. Fetal Pediatr Pathol 2013; 32: 213-217.
- [5] Ayuk PT, Matijevic R. Placental ischaemia is a consequence rather than a cause of pre-eclampsia. Med Hypotheses 2006; 67: 792-795.
- [6] Champion H, Innes BA, Robson SC, Lash GE, Bulmer JN. Effects of interleukin-6 on extravillous trophoblast invasion in early human pregnancy. Mol Hum Reprod 2012; 18: 391-400.
- [7] Knerr I, Weigel C, Linnemann K, Dötsch J, Meissner U, Fusch C, Rascher W. Transcriptional effects of hypoxia on fusiogenic syncytin and its receptor ASCT2 in human cytotrophoblast BeWo cells and in ex vivo perfused placental cotyledons. Am J Obstet Gynecol 2003; 189: 583-588.
- [8] Nahar L, Nahar K, Hossain MI, Yasmin H, Annur BM. Placental changes in pregnancy-induced hypertension and its impacts on fetal outcome. Mymensingh Med J 2015; 24: 9-17.
- [9] Veerbeek JH, Wietske H, Breimer AY, van Rijn BB, Koenen S. Cardiovascular disease risk factors after early-onset preeclampsia, lateonset preeclampsia, and pregnancy-induced hypertension. Hypertension 2015; 65: 600-606
- [10] Dekker GA. Management of preeclampsia. Pregnancy Hypertens 2014; 4: 246-247.
- [11] Osman O, Bakare AO, Elamin S. The prevalence of proteinuria among pregnant women as detected by a semi-quantitative method:

- a single center experience. Arab J Nephrol Transplant 2011; 4: 77-82.
- [12] Xie RH, Guo Y, Krewski D, Mattison D, Walker MC, Nerenberg K, Wen SW. Association between labetalol use for hypertension in pregnancy and adverse infant outcomes. Eur J Obstet Gynecol Reprod Biol 2014; 175: 124-128.
- [13] Stern C, Trapp EM, Mautner E, Deutsch M, Lang U, Cervar-Zivkovic M. The impact of servere preeclampsia on maternal quality of life. Qual Life Res 2014; 23: 1019-1026.
- [14] Koopmans CM, Bijlenga D, Aarnoudse JG, Beek EV, Bekedam DJ. Induction of labour versus expectant monitoring in women with pregnancy induced hypertension or mild preeclampsia at term: the HYPITAT trial. BMC Pregnancy Childbirth 2007; 7: 14.
- [15] Abdel-Fattah MM, Salama AA, Shehata BA, Ismaiel IE. The potential effect of the angiotensin II receptor blocker telmisartan in regulating OVA-induced airway remodeling in experimental rats. Pharmacol Rep 2015; 67: 943-951.
- [16] Li Y, Zhu M, Hu R, Yan W. The effects of gene polymorphisms in angiotensin II receptors on pregnancy-induced hypertension and preeclampsia: a systematic review and meta-analysis. Hypertens Pregnancy 2015; 34: 241-260.
- [17] Serrano NC, Díaz LA, Páez MC, Mesa CM, Cifuentes R, Monterrosa A, González A, Smeeth L, Hingorani AD, Casas JP. Angiotensin-converting enzyme I/D polymorphism and preeclampsia risk: evidence of small-study bias. PLoS Med 2006; 3: e520.
- [18] Ma YZ, Kong LF, Nan K, Qi SY, Ru LS, Ding C, Wang DM. Apolipoprotein-J prevents angiotensin Il-induced apoptosis in neonatal rat ventricular cells. Lipids Health Dis 2015; 14: 114.
- [19] Hou S, Lu Y, Huang D, Luo X, Yue D, Zhang J. Association of atrial fibrillation with gene polymorphisms of connexin 40 and angiotensin II receptor type 1 in Chongming adults of Shanghai. J Clin Exp Med 2015; 8: 11803-11810.
- [20] Hashikata T, Yamaoka-Tojo M, Namba S, Kitasato L, Kameda R, Murakami M, Niwano H, Shimohama T, Tojo T, Ako J. Rivaroxaban Inhibits Angiotensin II-Induced Activation in Cultured Mouse Cardiac Fibroblasts Through the Modulation of NF-κB Pathway. Int Heart J 2015; 56: 544-550.

- [21] Liu Y, Petrini MA. Effects of music therapy on pain, anxiety, and vital signs in patients after thoracic surgery. Complement Ther Med 2015; 23: 714-718.
- [22] Liao H, Jiang G, Wang X. Music therapy as a non-pharmacological treatment for epilepsy. Expert Rev Neurother 2015; 15: 993-1003.
- [23] Solli HP. Battling illness with wellness: a qualitative case study of a young rapper's experiences with music therapy. Nord J Music Ther 2015: 24: 204-231.
- [24] Solli HP, Rolvsjord R. "The Opposite of Treatment": A qualitative study of how patients diagnosed with psychosis experience music therapy. Nord J Music Ther 2015; 24: 67-92.
- [25] Rolvsjord R, Stige B. Concepts of context in music therapy. Nord J Music Ther 2015; 24: 44-66.
- [26] Yu JY, Huang DF, Li Y, Zhang YT. Implementation of MP3 player for music therapy on hypertension. Conf Proc IEEE Eng Med Biol Soc 2009; 2009; 6444-6447.
- [27] Geretsegger M, Holck U, Carpente JA, Elefant C, Kim J, Gold C. Common Characteristics of Improvisational Approaches in Music Therapy for Children with Autism Spectrum Disorder: Developing Treatment Guidelines. J Music Ther 2015; 52: 258-281.
- [28] Mustafa R, Ahmed S, Gupta A, Venuto RC. A comprehensive review of hypertension in pregnancy. J Pregnancy 2012; 2012: 105918.
- [29] Patterson S, Duhig M, Darbyshire C, Counsel R, Higgins N, Williams I. Implementing music therapy on an adolescent inpatient unit: a mixed-methods evaluation of acceptability, experience of participation, and perceived impact. Australas Psychiatry 2015; 23: 556-560.
- [30] Kazemian E, Sotoudeh G, Dorosty-Motlagh AR, Eshraghian MR, Bagheri M. Maternal obesity and energy intake as risk factors of pregnancyinduced hypertension among Iranian women. J Health Popul Nutr 2014; 32: 486-493.
- [31] Watanabe K, Kimura C, Iwasaki A, Mori T, Matsushita H, Shinohara K, Wakatsuki A, Gosho M, Miyano I. Pregnancy-induced hypertension is associated with an increase in the prevalence of cardiovascular disease risk factors in Japanese women. Menopause 2015; 22: 656-659.