Research Square

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The Effects of Personalized Music Intervention on Mechanically Ventilated Preterm Infants

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Abstract

Background: Music-based interventions may promote the growth and development of preterm infants, and appropriate sound intervention in the neonatal intensive care unit (NICU) can stabilize their physiological state.

Purpose: This study aimed to systematically evaluate the effects of a personalized music intervention on mechanically ventilated preterm infants in the NICU.

Methods: 60 mechanically ventilated preterm infants were randomized to an intervention group (n=30) or a control group (n=30). The control group received routine care, while the intervention group received an additional personalized music intervention (maternal voice, maternal heartbeat, and prenatal music). The intervention was administered by two trained nurses three times daily for 30 minutes each session, 30 minutes after artificial feeding. Written informed consent was obtained from parents or legal guardians before enrollment. Growth indicators (weight, length, head circumference, upper arm circumference), blood gas parameters (PaO_2, $PaCO_2$) and Oxygen Saturation (SPO_2) were assessed.

Results: The study results showed that there were no statistically significant differences between the two groups in all outcome measures prior to intervention ($p > 0.05$). After 3 weeks of intervention, weight, SpO_2, and appeared to be affected by personalized music intervention($p<0.05$). There were no statistically significant differences in body length, head circumference, upper arm circumference, PaO_2, and $PaCO_2$ ($p > 0.05$).

Conclusion: This study provides evidence that a personalized music intervention may have beneficial effects on weight gainand oxygen saturation in mechanically ventilated preterm infants. It represents a safe and effective adjunctive intervention in the NICU, but it should not be regarded as proof of hypoxia relief. Further studies with larger samples, longer follow-up, and collection of maternal comorbidities, ventilation duration, and preterm complications are needed.

1 Introduction

Preterm infants, born before 37 weeks of gestation, have immature organ systems and are susceptible to multi-organ injury, growth retardation, and brain damage [1]. Mechanical ventilation is a crucial respiratory support technique but can induce significant physiological and behavioral stress due to noise and invasive procedures [2, 3].

Prolonged ventilation may impair growth, prolong hospitalization, and increase risks of bronchopulmonary dysplasia and retinopathy. Although analgesic and sedative medications may reduce pain, agitation, and stress, they should be used cautiously in preterm infants because of safety concerns, limited evidence of efficacy, and potential long-term neurodevelopmental effects [4]. Therefore, non-pharmacological interventions are needed.

Personalized music interventions, using acoustic stimuli such as maternal voice or soothing sounds, have been suggested to regulate autonomic function, reduce stress hormones, and stabilize heart rate and breathing [5]. However, a Cochrane review found no evidence that musical or vocal interventions increase oxygen saturation during the intervention, with high-certainty evidence for this outcome [6]. The rhythm, melody, and sound wave vibrations of specific types of music may regulate autonomic nervous system function, reduce stress hormone levels (such as cortisol), and create a soothing acoustic environment similar to the uterine environment [7]. Numerous studies have demonstrated that appropriate sound interventions for NICU preterm infants can stabilize their physiological state, alleviate adverse stimuli caused by procedural pain, accelerate feeding progress, and benefit neural growth and development as well as long-term outcomes [8, 9]. A recent Cochrane systematic review concluded that musical and vocal interventions may improve short-term physiological stability and parental bonding, although evidence for long-term neurodevelopment is still emerging [10].Furthermore, a randomized clinical trial reported that music therapy did not significantly improve neurodevelopmental outcomes at 24 months, highlighting the need for further high-quality research [11]. However, previous studies primarily focused on non-ventilated infants or short-term physiological outcomes.

In this study, we conducted a randomized controlled trial to comprehensively evaluate the effects of a personalized music intervention on physiological parameters and blood gas metabolism in mechanically ventilated preterm infants, aiming to provide high-quality evidence to optimize non-pharmacological intervention protocols.

2 Materials and Methods

2.1 Study Design

The study was designed as a prospective, randomized controlled clinical trial. Preterm infants were randomly assigned to either the intervention group or the control group. There were no differences between the groups in medical care. The study was approved by the Ethics Committee of ***(***). Written informed consent was obtained from all parents or legal guardians before enrollment.

2.2 Participants

60 preterm infants were recruited in the NICU at the *** Hospital. Inclusion criteria were: (1) gestational age 28–36 weeks; (2) admission to the NICU for respiratory distress/failure requiring mechanical ventilation for respiratory support (e.g., respiratory distress syndrome, transient tachypnea of the newborn, apnea of prematurity, or pneumonia); (3) NICU stay ≥ 48 h; and (4) passed bilateral hearing screening. Exclusion criteria were: (1) severe cranial brain disease, defined as grade III or IV intraventricular hemorrhage or periventricular leukomalacia confirmed by cranial ultrasound; (2) genetic metabolic disorders confirmed by genetic testing or newborn screening; (3) heart disease requiring medical or surgical intervention (e.g., critical congenital heart disease); (4) other severe conditions including necrotizing enterocolitis (stage ≥ 2) or septic shock; and (5) use of sedatives or muscle relaxants within 48 hours prior to enrollment.

2.3 Randomization

Randomization was performed using a computer-generated list created before study initiation. Allocation ratio was 1:1. Allocation concealment and random sequence minimized selection bias. Sealed, opaque, numbered envelopes were opened only after the envelope had been irreversibly assigned to the participant. Preterm infants randomized to the control group received standard care including maintaining appropriate indoor temperature and humidity, feeding according to medical orders, centralized administration of various treatments and care, strict adherence to disinfection and isolation protocols, and proper hand hygiene. Preterm infants allocated to the intervention group received a personalized music intervention additionally to the standard care as explained below. The intervention was delivered by trained nurses, not by a certified music therapist.

2.4 Intervention

(1)Sound Collection:Maternal Voice Recording: Primarily captures the mother's communication with the baby during pregnancy, continuing until the mother ceases speaking.Maternal Heartbeat Recording: Utilizes a Doppler fetal heart monitor to collect the mother's heartbeat, recorded once her emotions and heart rate stabilize.Pregnancy Music Collection: In a quiet room, the researcher interviewed the mother regarding the type and frequency of music she had played for the fetus during pregnancy. Data on prenatal music exposure (e.g., genres, frequency per week, and whether singing was involved) were recorded. Based on the mother's vocal characteristics from fetal communication or singing recordings, a professional music producer created a 3-minute track that incorporated the mother's singing voice, combined with her speech and heartbeat recordings.

(2) Intervention Measures: In addition to routine care, the intervention group received personalized recorded music via low-electromagnetic-interference speakers placed inside the incubator (10 cm from the infant's head). The speakers were disinfected with 75% alcohol wipes before each use and covered with a single-use sterile protective sleeve to prevent contamination. Music was delivered three times daily for 30 minutes per session, starting 30 minutes after artificial feeding, for a total of 3 weeks. Volume was controlled at 40–50 dB. During sessions, procedures were avoided, lights were dimmed, covering incubators with small blankets, adding sound-absorbing materials inside incubators and ambient noise was kept below 50 dB. These measures were applied to both groups.

The produced track was individualized for each infant according to maternal voice, heartbeat, and prenatal music exposure; therefore, musical content differed across infants, and between-infant comparisons of different music genres were not possible.

2.5 Data collection and instruments

Physiological indicators include weight, head circumference, and upper arm circumference; and anothor indicators such as: arterial partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide ($PaCO_2$) and oxygen saturation (SpO_2).

Anthropometric measurements were performed by two trained NICU nurses using calibrated electronic scales and non-stretch tape measures. Infants were weighed naked. Each measurement was repeated twice, and the mean was recorded. Measurements were performed at the same time of day under standardized conditions. The arterial partial pressure of oxygen (PaO_2) and partial pressure of carbon dioxide ($PaCO_2$) were based on the blood and qi test results. SpO_2 was measured by continuous pulse oximetry. The reported values were single measurements / mean values over a specified period / values obtained during or after music sessions.

2.6 Statistical analysis

Sample size was calculated using G*Power software (version 3.1). Based on a previous study on music therapy in preterm infants, we assumed a moderate effect size (Cohen's d = 0.65) for the primary outcome (weight gain), with a two-sided significance level of α = 0.05 and statistical power of 80%. The required sample size was estimated as 26 per group. Considering a 15% dropout rate, we aimed to recruit 30 preterm infants per group, for a total of 60 participants.

Statistical analysis was performed using SPSS 26.0 software. Count data were described using case numbers and percentages (%), while measurement data were described using means and standard deviations ($\bar{X} \pm s$). Comparisons between means of the two groups were performed using the independent samples t-test. $P < 0.05$ were considered statistically significant. Exact p-values are reported where possible; $p < 0.001$ is used for very small values.

3 Results

3.1 Population

Seventy-two preterm infants were recruited (January 2025-May 2025). Twelve preterm infants were excluded due to transfer to another hospital and parental withdrawal. A CONSORT flow diagram is provided as Fig. 1. Ultimately, data were obtained from 30 preterm infants in the intervention group and 30 preterm infants in the control group.

Among them, there were 12 males and 18 females in the control group. Gestational age ranged from 27 to 33 weeks, (mean (SD) gestational age 29.87 (± 1.78) at birth); 26 cases were cesarean sections and 4 cases were vaginal deliveries. In the intervention group, gestational age ranged from 27 to 33 weeks, (mean (SD) gestational age 29.90 (± 1.32) at birth); 27 cases were cesarean sections and 3 cases were vaginal deliveries. There were no statistically significant differences in general characteristics between the two groups ($p > 0.05$). Baseline characteristics, including gestational age, birth weight, sex, postnatal age at randomization, baseline respiratory support, and FiO_2, are presented in Table 1.

Table 1
Baseline characteristics for the Participants

Items		**n (%)**
Age (weeks)		30.33 ± 1.45
Sex	Male	28 (46.7)
	Female	32 (53.3)
Delivery Method		
	Vaginal Delivery	7 (11.7)
	Cesarean Section	53 (88.3)
Birth weight (g)		1357.00 ± 305.48
Head Circumference		28.10 ± 1.23
Body Length		37.75 ± 1.95
Upper arm circumference		8.88 ± 0.71
Nutrition		
	Breast milk	13 (21.7)
	Formula for premature infants	32 (53.3)
	Infant formula	15 (25.0)
Baseline respiratory support mode		
	CPAP	35 (58.3)
	NHFOV	2 (3.3)
	NIPPV)	8 (13.3)
	SIMV	15 (25.0)

3.2 Physiological indicators

Before intervention, there were no statistically significant differences between the intervention group and the control group in terms of head circumference, body length, upper arm circumference, and weight ($p > 0.05$). After intervention, the weight of preterm infants in the intervention group was higher than that in the control group, with a statistically significant difference ($p < 0.05$), as shown in Table 2.

Table 2
Physiological indicators of the preterm infants in the intervention and control group

Group	Head circumference		Body length		Upper arm circumference		Weight	
	Before	After	Before	After	Before	After	Before	After
Control group	28.12 ± 1.39	28.82 ± 1.20	37.79 ± 2.20	38.82 ± 1.90	8.89 ± 0.62	9.19 ± 0.70	1368.67 ± 351.10	1473.67 ± 330.00
Intervention group	28.08 ± 1.07	28.98 ± 1.17	37.70 ± 1.69	39.05 ± 1.84	8.87 ± 0.75	9.27 ± 0.76	1345.33 ± 257.50	1742.67 ± 260.00
t	-0.15	0.52	-0.18	0.50	-0.21	0.63	-0.42	3.01
p	0.88	0.61	0.86	0.62	0.83	0.53	0.68	0.004*
*$p<0.05$								

3.3 Blood gas parameters

Before intervention, there were no statistically significant differences in arterial oxygen saturation(PO_2), arterial oxygen partial pressure(PCO_2), and carbon dioxide partial pressure(SPO_2) between the intervention group and the control group ($p > 0.05$). After the intervention, the arterial oxygen saturation levels of preterm infants in the intervention group were higher than those in the control group, with statistically significant differences ($p < 0.05$), as shown in Table 3.

Table 3
Blood gas parameters and spo2 of the preterm infants in the intervention and control group

Group	SPO_2(%)		PO_2(mmHg)		PCO_2(mmHg)	
	Before	After	Before	After	Before	After
Control group	94.07 ± 1.01	95.07 ± 0.98	56.57 ± 1.91	59.57 ± 1.95	45.90 ± 1.18	43.90 ± 1.15
Intervention group	94.17 ± 0.95	97.23 ± 0.90	56.73 ± 1.74	59.73 ± 1.80	45.83 ± 1.05	43.83 ± 1.10
t	0.39	12.50	0.28	0.25	-0.20	-0.18
p	0.70	< 0.001*	0.78	0.80	0.84	0.86
*$p<0.05$						

Before intervention, there were no statistically significant differences in arterial partial pressure of oxygen (PaO_2), arterial partial pressure of carbon dioxide ($PaCO_2$), and oxygen saturation (SpO_2) between the intervention group and the control group ($p > 0.05$). After the intervention, the SpO_2 levels of preterm

infants in the intervention group were higher than those in the control group, with statistically significant differences ($p < 0.05$), as shown in Table 3.

4 Discussion

Mechanically ventilated preterm infants, due to their underdeveloped respiratory systems, are prone to issues such as apnea, cyanosis, and tachycardia. Additionally, various invasive procedures can cause severe stress reactions, which can have a serious impact on their growth and development [12]. Delayed growth and development can lead to low birth weight and underdeveloped organs, increasing the risk of complications such as infections and retinal lesions [13]. Growth and development indicators are important assessment tools for evaluating neonatal health status and the effectiveness of clinical interventions. The results of this study showed that the weight of preterm infants in the intervention group was higher than that of the control group before and after intervention, indicating that the personalized music intervention used in this study had a certain impact on the growth and development of mechanically ventilated preterm infants. The possible reason is that benign auditory stimulation helps maintain the stability of the patient's physiological state, regulates their multi-system functions, including digestion, nervous, and circulatory systems, increases milk intake, reduces stress responses, and decreases energy consumption and catabolic metabolism caused by pain and anxiety, thereby increasing weight and promoting growth and development [14, 15]; Additionally, the intervention group had small blankets covering the incubators, and sound-absorbing materials were added inside the incubators to reduce echo noise, thereby weakening the noise stimulus source, improving the infants' adaptability to their current growth environment, reducing heat and oxygen loss, and benefiting their growth and development.

By collecting blood gas indicators from mechanically ventilated preterm infants, healthcare providers can promptly understand their respiratory and hypoxic status and monitor disease progression. Previous studies have shown that music therapy can effectively improve newborn physiological stability and reduce the incidence of complications such as bronchopulmonary dysplasia and retinopathy [16, 17]. The results of this study showed that the SpO_2 of preterm infants in the intervention group was higher than that of the control group before and after intervention. However, this finding should not be interpreted as proof that the intervention alleviates hypoxia. A Cochrane review found no evidence that musical or vocal interventions increase oxygen saturation during the intervention, with high-certainty evidence [18]. The observed difference may be influenced by ventilation status, respiratory support, and other clinical factors. This may be because music can regulate autonomic nervous system balance (e.g., by reducing sympathetic nervous system activity and enhancing parasympathetic nervous system activity), making breathing patterns more stable and regular[19], thereby reducing oxygen consumption caused by apnea or increased respiratory effort, and indirectly improving oxygenation; simultaneously, it promotes the secretion of β-endorphins in the newborn's brain, improving their mental state, and thereby regulating their physiological functions such as breathing and circulation [20–22]; Furthermore, music has a calming and soothing effect on mechanically ventilated preterm infants, and the mild improvement

in respiratory rate and heart rate can reduce oxygen consumption to some extent, thereby increasing blood oxygen saturation [23, 24].

The intervention tested here was a personalized music intervention, not interactive music therapy delivered by a certified music therapist[25]. It combined maternal voice, maternal heartbeat, prenatal music, and a professionally produced track. Therefore, we cannot isolate which component(s) produced the observed effects, and the individualized tracks differed across infants, preventing comparisons of specific music genres. Future studies should use factorial or component-isolation designs and clearly define whether the intervention is music therapy or music medicine.

Maternal comorbidities (e.g., pregestational or gestational diabetes and hypertensive disorders of pregnancy) and IUGR/SGA were not systematically collected; residual confounding by these factors cannot be excluded. Duration of mechanical ventilation, extubation time, respiratory support mode, and preterm complications such as BPD, ROP, IVH, NEC, and sepsis were not included in the original analysis. These factors may influence growth and blood gas parameters, this should be collected and adjusted for in future studies.

5 Conclusion

Personalized music intervention shows beneficial effects on weight gain and SpO_2in mechanically ventilated preterm infants, suggesting it may improve short-term physiological stability. However, causal conclusions regarding hypoxia relief are not supported by this study or by prior high-certainty Cochrane evidence. The intervention appears safe and suitable for clinical application as an adjunctive therapy. Future studies should include larger samples, longer intervention and follow-up periods, collect maternal comorbidities, IUGR/SGA, mechanical ventilation duration, and preterm complications, assess different music types and timing, and evaluate long-term neurodevelopmental outcomes.

Declarations

Ethical Approval:

In accordance with the Declaration of Helsinki, ethical approval was provided by the Ethics Committee of Qingdao University Affiliated Hospital in advance of implementation. (QYFYEC2024-08)

Author Contribution

Yafei Zhao: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Visualization, Writing - original draft. Yang Zhao: Conceptualization, Validation, Writing - review & editing. Yuan Wu: Conceptualization, Supervision, Validation. Shanshan Yu:Conceptualization, Data curation, InvestigationXiaoman Yu:Conceptualization, Data curation, Writing -

review & editing.Wen Bi:Conceptualization, InvestigationQianqian Li: Supervision, Validation. Rong Yu: Writing - review & editing.Lili Wei: Visualization, Supervision. Qian Wu: Formal analysis, Methodology, Resources, Software, Visualization, Writing - review & editing.

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Data availability statement

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Figures

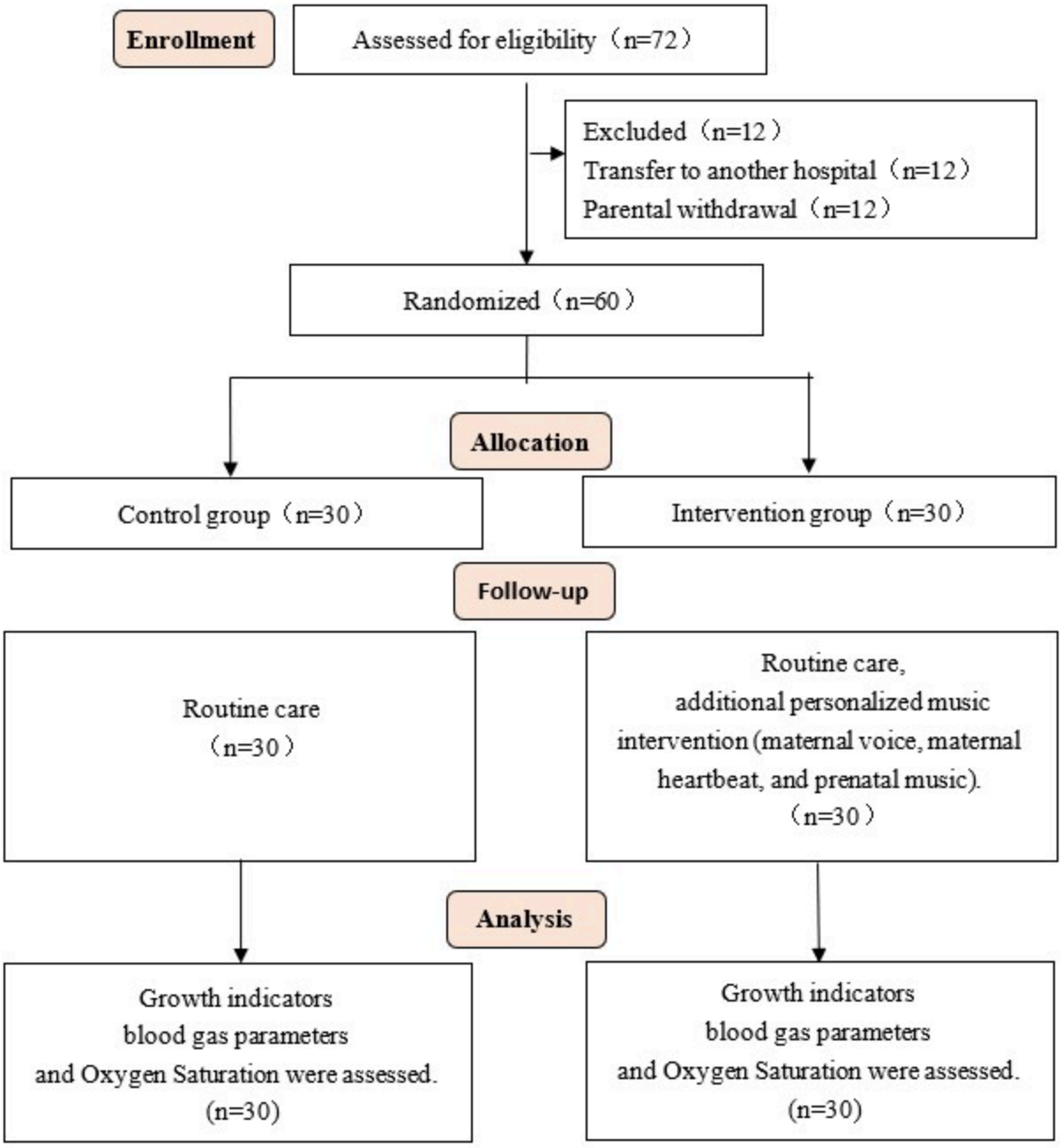

Figure 1

CONSORT Flow Diagram