European Journal of Integrative Medicine 19 (2018) 105–109

Contents lists available at ScienceDirect

European Journal of Integrative Medicine

journal homepage: www.elsevier.com/locate/eujim

Clinical Trial

Effect of music intervention on pain responses in premature infants undergoing placement procedures of peripherally inserted central venous catheter: A randomized controlled trial

Lei Tang[a], Huanhuan Wang[a], Qiaohong Liu[a], Fei Wang[a], Miao Wang[a], Jia Sun[a], Lin Zhao[b,c,*]

[a] Zhengzhou Children's Hospital, Zhengzhou, Henan Province, 450053, China
[b] Institute of Food and Agriculture Standardization, China National Institute of Standardization, Beijing, 100191, China
[c] School of Basic Medical Sciences, Peking University Health Science Center, Beijing, 100191, China

ARTICLE INFO

Keywords:
Premature infant
Music intervention
PICC
PIPP
Cortisol
Randomized controlled trial

ABSTRACT

Introduction: Premature infants are highly sensitive to pain because of their immature and vulnerable nervous systems, which lead to peripherally inserted central venous catheter (PICC) difficulty. The objective of this study was to investigate the application of a music intervention (MI) during PICC placement procedures in premature infants.

Methods: A randomized controlled trial was conducted on sixty premature infants (gestational age of 28 weeks to 36 weeks). Infants hospitalized to receive PICC puncture and meeting the study entry criteria were randomly assigned to an MI group (n = 30) or a control group (n = 30). The effects of MI were assessed by determination of heart rate, blood oxygen saturation, pain rating, cortisol concentration and operating time during PICC placement procedures in both groups. Furthermore, pain level was identified using premature infant pain profile.

Results: There was no statistically significant difference between the two groups in terms of heart rate, blood oxygen saturation and pain score before intervention ($P > 0.05$). During PICC placement procedures, a significant increase in term of blood oxygen saturation ($P < 0.05$) and reductions in terms of heart rate ($P < 0.05$) and cortisol accumulation were observed in the group receiving music intervention compared with the control group. Furthermore, MI led to a significant reduction in pain score (mean difference: 3.4, 95% confidence interval: [2.0, 4.8]), and remarkably decreased the time needed for PICC placement in the MI group compared to control group.

Conclusions: During PICC placement procedures for premature infants, MI significantly reduced stress hormone levels, physiological parameters and behavioral response of pain.

1. Introduction

Premature Infants are those born before 37 weeks gestational age, and whose birth weight is less than 2500 g. They are born before their body organs have fully developed, and as gastrointestinal feeding is not established rapidly, they need a long period of intravenous nutrition [1]. Peripherally inserted central catheter (PICC), due to its high safety, long indwelling time, less complications, has been widely used in premature infants [2]. Infant catheterization is a problem in clinical medicine.

Pain is an unpleasant sensory and emotional experience associated with potential tissue damage [3]. Previous research suggests that premature infants have an even stronger sensitivity towards discomfort and pain compared with older infants [4]. Being subjected to frequent painful stimuli before the neural system has developed might lead to behavioral changes, even a future susceptibility to psychosomatic problems and mental disorders in premature infants [5]. Regarding the importance of pain control, health professionals are increasingly aware that methods should be proposed to control pain in premature infants.

In recent decades, there has been a growing interest in complementary medicine. Music intervention is used for individuals of all ages and in specialties such as intensive care, palliative care, surgery, oncology and pain management [6–8]. Music entertainment (synchronization and control of a physiologic rhythm by application of music) may be vital for pain management [9]. For the premature infants, the unpredictable noise in the neonatal intensive care unit (NICU) may

Abbreviations: MI, music intervention; PICC, peripherally inserted central catheter; PIPP, premature infants pain profile; SpO_2, oxygen saturation

* Corresponding author at: Institute of Food and Agriculture Standardization, China National Institute of Standardization, Beijing, 100191, China.
E-mail address: zhaolin07@bjmu.edu.cn (L. Zhao).

https://doi.org/10.1016/j.eujim.2018.03.006
Received 3 November 2017; Received in revised form 16 March 2018; Accepted 17 March 2018

adversely affect physiologic stability. Using music intervention, nurses can change the environment to improve health and well-doing [10]. The soothing, enjoyable and active nature of music makes it particularly applicable as a treatment medium for children [11]. Several observational studies indicate that music may have a positive effect on physiological parameters of premature infants [12–16]. Systematic review and *meta*-analysis suggests there are some benefits of music therapy on premature infant respiratory rate and maternal anxiety during NICU hospitalization [17,18]. Live sound and lullabies may improve feeding behaviors and sucking patterns and sustain a quiet-alert state [19]. Music can provide an auditory stimulus that modulates pain perception and obviation, and may help to relieve pain response [20–22]. The *meta*-analysis shows that music interventions can be used as an effective complementary approach for the relief of acute, procedural and chronic pain in the medical setting [23]. Pain treatment using music intervention for routine procedures in the NICU is an acceptable form, which is economically viable and easily available. Moreover, there are scarcely any cultural and legal issues about its use [24].

The purpose of this study was to determine whether a music intervention was effective in relieving pain and discomfort for premature infants during the process of PICC placement. We compared the premature infants pain profile (PIPP) scores and cortisol concentrations between premature infants who did and did not receive music intervention.

2. Methods

2.1. Study design and subjects selection

This randomized, data-analysts-blinded, controlled trial with two parallel arms was performed from October 2016 to March 2017 at the NICU of Zhengzhou Children's Hospital. The medical treatment follows the NIDCAP model. After obtaining permission from ethics committee 1 Zhengzhou Children's Hospital (code: 172102310006) and registration of the present study on Zhengzhou Children's Hospital Registry of Clinical Trials, sampling was performed without gender discrimination in infants, who had been hospitalized and need to receive PICC puncture. Written informed consent was obtained from each legal guardian of infant before participation. During the trial period, the legal guardians of infants did not know about the group allocation.

The sample size was calculated based on information obtained from study by Shabani et al. [5]. 30 subjects per group were required to establish a significance level of more than 95%, a power of 80% and $\alpha = 0.05$ (Sample Power 2.0 [SPSS Inc, Chicago, IL]). The total sample size was 60 infants (Control n = 30 and MI n = 30). Selected participants need to meet the study's inclusion criteria listed as follow: the legal guardians of infants willing to pursue the study; gestational age of at least 28 weeks and a maximum of 36 weeks; weight lower than 2500 g. The exclusion criteria were: congenital disorder; auditory disability; significant parenchymal brain injury; disseminated intravascular coagulation and other causes of abnormal clotting time; no sedatives administered within the last 24 h.

2.2. Randomization and intervention

Subjects meeting the inclusion criteria were randomly assigned to the experimental group and control group, using computer-generated random numbers and an allocation ratio of 1:1. Infants in the experimental group underwent PICC placement with music intervention. Infants in the control group underwent PICC placement without music intervention.

"UTAH MEDICAL PRODUCTS 1.9F" catheter was selected as tools for PICC. During operation, the infants were placed on the far infrared radiation heating station, connected with the transcutaneous oxygen saturation detection instrument. All the process of PICC placement occurred in the morning. According to standard procedures, selected the vein and measured catheter length in vitro. For the experimental group, the music intervention as "music medicine" was conducted. Music was played on an MP4-player with small mobile speaker from 10 min before PICC puncture and continued until 10 min after operation completion. Carefully applied use of music was chosen for properties that induce relaxation, rest and comfort. This included lullabies and nursery rhymes, and more than 10 pieces of children's music with slower tempo were selected from "Chinese children music library" (a music collection for children) and the volume was adjusted to 50–60 dB (dB). According to this acoustic measurement, speakers were placed inside the incubator at a distance of 30 cm from the infants' ears and maintained background noise near the infant's ear < 45 dB. This volume level was implemented to meet criteria in accordance with current knowledge of infant auditory development. The environment of operation was quiet to limit noise and unnecessary personnel move. After the operation, we saw the location of the catheter by X-ray film. In the two groups, the puncture instrument, puncture product and puncture staff were consistent, and all steps and measurements, except music intervention, were the same for the control group.

2.3. Outcome measures

Primary outcomes are the infant's vital signs (facial actions, heart rate and SpO_2) and infant's level of pain. Cortisol levels as secondary outcomes were recorded. For this study, the premature infants pain profile (PIPP) is an instrument designed to assess acute pain in premature infants [25]. The scoring system includes seven items, two items describe baseline characteristics (gestational age and behavioral state), two items describe physiologic state of the neonate (heart rate and oxygen saturation), three items describe facial actions (brow bulge, eye squeeze, and nasolabial furrow), each graded from 0 to 3. These items were assessed and scored by three trained research nurses at the bedside, immediately before, during and after the procedure (flow diagram, Fig. 1). The scores of two groups (MI group and control group) were recorded according to the PIPP scale.

2.4. Cortisol concentration

Blood samples were collected from both groups immediately before, during and after the procedure of PICC placement in the morning. The cortisol concentrations (ng/ml) were measured using a highly sensitive electrochemiluminescence immunoassay (Roche Diagnostics, Mannheim, Germany) on the same three occasions (Fig. 1).

2.5. Statistical analysis

All statistical analyses were performed using SPSS Statistics for Windows Version 18 (IBM Corp., Armonk, NY, USA). The results of PIPP were compared between the two groups using the unpaired *t*-test. The data are presented as the mean ± standard deviation (SD). Differences were considered significant at $P < 0.05$.

3. Results

Subject recruitment occurred from October 2015 to March 2016. After obtaining parental consent, research was carried out from 60 subjects that met study criteria (flow diagram, Fig. 1). The following information was gathered: gestational age (weeks), birth weight (g), body length (cm) and sex (male/female). As described in Table 1, no significant differences in the demographic characteristics between the control and MI group.

These groups were homogenous in terms of many demographic parameters, the heart rate and SpO_2 of the MI group were similar to those of the control group ($P > 0.05$; Table 2) in the first analysis. And the mean PIPP scores were 7.8 ± 1.2 and 7.6 ± 1.1 base on the results of mean, no significant difference was found between the control and