**Music Therapy and Procedure-Related Pain in Preterm Neonates**

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 Previous research suggests that frequent exposure of premature infants to pain is associated with potential tissue damage, alterations in behavior, and worsening of neurodevelopmental outcomes. Additionally, premature infants’ sensitivity towards pain is thought to be even greater than that of full-term infants. These realities make decreasing premature infants’ procedure-related pain an important area of research. Music therapy is a non-invasive, inexpensive method to provoke feelings of familiarity and security in a Neonatal Intensive Care Unit (NICU) environment of generally unpredictable noise. Soft, rhythmic music deflects attention away from pain inducers. It triggers the release of endorphins, reduces adrenocorticotropic hormone levels, upregulates phenethylamine secretion, and prompts the autonomic nervous system to release tension in the body. Music therapy is already widely used in branches of medicine such as palliative care and oncology.

 To perform a thorough review of the literature on music therapy and premature neonates, I searched PubMed, Web of Science, and EMBASE databases (please see key words, MeSH terms, and Emtree terms at bottom). My searches yielded a total of 181 unique articles, 93 of which were most relevant to the topic. I then narrowed the scope to music therapy and pain responses in premature neonates; 14 of the 93 articles focused specifically on pain as an outcome. From there, I selected 4 articles based on abstract quality, variety of study types, and diversity of approach. My PICO question was: “Is music therapy associated with decreased procedural pain scores in premature neonates?”

 Tang *et al.* (2018) was a randomized, data-analysts-blinded, controlled trial focusing on the effect of music on pain scores, physiological measurements, and cortisol levels in premature infants undergoing placement of peripherally inserted central venous catheters (PICCs). The authors assessed acute pain using the Premature Infant Pain Profile (PIPP) scoring system and found a statistically significant improvement in pain scores with music during and after PICC placement (p-values 0.015 and 0.028, respectively). The study passed the appraisal for validity and applicability and appeared to have clinical, in addition to statistical, relevance. Limitations included study activity in a single hospital, only morning placement of PICC lines, utilization of a pain scale that has since been revised, and presentation of mean data (therefore sensitive to outliers). Overall, I would recommend significant change to clinical practice based on the results of this study.

 Kurdahi Badr *et al.* (2017) was a double-blind randomized cross-over study centered on the effect of mother’s music and recorded lullabies on pain scores and physiological measurements during heel sticks. The authors assessed acute pain using the Neonatal Pain, Agitation and Sedation Scale (N-PASS) and found a statistically significant improvement in pain scores with mother’s music vs. no music during the procedures (p-value 0.009). The study passed the appraisal for validity and applicability and appeared to have clinical, in addition to statistical, relevance. Headphones were applied regardless of whether or not the infant was receiving music therapy to ensure blinding, and nurses were well-trained and well-versed in the N-PASS scoring system. In terms of limitations, study participants needed to have mothers who listened to music regularly during the third trimester of pregnancy, N-PASS scores were only measured during heel sticks (there was no post-procedure data), and authors presented mean data. Overall, I would recommend significant change to clinical practice based on the results of this study.

 van der Heijden *et al.* (2016) was a systematic review that assessed the potential benefits of music interventions on a variety of outcomes. I focused on the subset including behavioral state, relaxation, and pain. While criteria for article selection were appropriate and the validity of included studies was appraised and addressed in the review, the majority of the studies had unclear risk of bias and did not provide information on study blinding. The majority of the studies showed statistically significant improvement in behavioral state or sleep pattern with the utilization of music therapy. Regarding limitations, in addition to unclear information on bias and blinding, there was no meta-analysis performed. Overall, based on these results, I would recommend little change to clinical practice. While the differences observed are promising, some studies’ lack of attention to bias risk and blinding made the results less meaningful.

 Finally, Cardoso *et al.* (2014) was an experimental double-blinded analytical study and randomized clinical trial. It examined the effect of music intervention + 25% glucose (vs. standard of care 25% glucose alone) on pain scores and other variables during arterial puncture. The authors assessed acute pain using the PIPP scoring system and found no statistically significant differences in pain scores among the groups (p-value 0.398). Since PIPP scores were categorized into low (6 and under) and high (7 and over) as opposed to presented as means, I calculated control and experimental event rates as well as absolute risk increase and number needed to harm. The risk of having a high pain score increased by approximately 6% when music therapy was added to the standard of care 25% glucose. About 17 infants would need to be exposed to music therapy in addition to standard of care 25% glucose for one additional infant to have a high pain score. It is important to remember, however, that the differences in pain scores between the control and experimental groups were not statistically significant. The study passed the appraisal for validity and applicability and appeared to have clinical, in addition to statistical, relevance. In terms of limitations, supplemental oxygen was permitted but later determined to be a confounder, group sizes were unequal, and the PIPP scoring system has since been revised. Overall, based on these results, given that there was no statistically significant difference in pain scores between the groups in a well-designed study, I would recommend little change to clinical practice.

 In summary, music therapy is often associated with decreased pain scores. These findings appear to show no drawbacks to therapy as long as decibels are closely monitored for compliance with American Academy of Pediatrics guidelines. Based on these results, I believe we should change our practice significantly to incorporate music therapy into our care for premature infants undergoing procedures. To strengthen this argument, my recommendations for further studies would include larger sample sizes, more objective data, longer follow-up periods, and inclusion of neurodevelopmental outcomes data in follow-up analyses.

**References:**

Cardoso, M., et al. (2014). “Music and 25% glucose pain relief for the premature infant: A

Randomized Clinical Trial.” Revista Latino-Americana de Enfermagem 22(5): 810-8.

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were played the same music their mothers listened to during pregnancy." Acta Paediatr

106(3): 438-445.

Tang, L., et al. (2018). "Effect of music intervention on pain responses in premature infants

undergoing placement procedures of peripherally inserted central venous catheter: A

randomized controlled trial." European Journal of Integrative Medicine 19: 105-109.

van der Heijden, M. J., et al. (2016). "Do Hospitalized Premature Infants Benefit from Music

Interventions? A Systematic Review of Randomized Controlled Trials." PLoS One 11(9):

e0161848.

**Search Terms:**

(a) PubMed: (”Infant, Premature"[Mesh:NoExp] OR premature OR preterm) AND ("Music Therapy"[Mesh] OR "music therapy")

(b) Web of Science: (premature OR preterm) AND "music therapy"

(c) EMBASE: ('prematurity'/exp OR premature OR preterm) AND ('music therapy'/exp OR 'music therapy')