

Non-pharmacologic Measures for Pain Relief in Preterm Neonates

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It is now established that even very premature infants feel pain [1]. Apart from the ethical necessity for pain relief, there is also general consensus that painful stimuli lead to adverse consequences among infants [1,2]. Hence, avoiding painful stimuli, or when they are unavoidable, utilizing non-pharmacologic or pharmacologic measures to reduce the intensity of pain, should be part of developmentally supportive care in the neonatal intensive care unit (NICU).

There is adequate evidence that oral sucrose, skin-to-skin contact, breastfeeding and breastmilk feeding are effective in relieving pain associated with procedures such as venipuncture, heel lance prick and intramuscular injections [3-5]. Kangaroo Mother Care (KMC) has specifically been assessed for pain relief in the Indian context and shown to be effective [6]. However, pain is still a difficult problem to tackle in neonates for many reasons. Pain is subjective and must be assessed indirectly in neonates through changes in physiological or behavioral parameters [7]. Hence, it is difficult to prove that an intervention actually reduces pain instead of just reducing the physiologic disturbances or behavioral changes. There is also paucity of evidence regarding the long-term effect of these measures, particularly repeated doses of oral sucrose [3]. Most studies have addressed acute procedure-related pain, and not chronic pain. And finally, the optimal combination of non-pharmacologic or pharmacologic measures is not known.

The study by Shukla, *et al.* [8] reported in this issue of *Indian Pediatrics*, examines the effect of two pain control interventions separately and in combination using a 2x2 factorial randomized controlled trial (RCT). The investigators randomized preterm infants of 28 to 36 weeks gestational age undergoing heel-prick for glucose measurement to one of four groups to receive KMC alone, music therapy alone, KMC with music therapy, or no intervention. Notably, all participants received 2 mL of expressed breast milk orally prior to the procedure. The Premature Infant Pain Profile (PIPP) score was used to quantify pain. Although a revised version of this score

(PIPP-R) is available, the older version is more extensively validated [9]. The score was calculated based on video recording by fellows blinded to the group assignment. Mean PIPP scores were compared between the groups. For ordinal variables such as the PIPP score, comparing the medians would have been more appropriate. The investigators found that the scores were lowest in the groups receiving KMC, indicating better pain relief. The study attempts to address one of the knowledge gaps in neonatal pain by combining two non-pharmacologic measures. This is clearly an area where more research is required. The interventions studied were inexpensive and culturally acceptable. Blinding of the assessors was a commendable effort; although, blinding may not have been complete if the assessors also worked in the NICU. The results suggest that KMC combined with breastmilk feeds is a better option than breastmilk alone for reducing pain. While music therapy seems to be independently effective, the role of combining it with KMC is not clear.

This single-center study has many limitations, some of which are difficult to avoid. Sick and extremely premature infants, who are more likely to undergo multiple painful procedures, were excluded. This is understandable given the nature of the interventions, but nevertheless limits the external validity of the study. Only acute pain due to heel-prick was studied. The use of an app to measure sound level is suboptimal and may not give reproducible results [10]. The authors have conducted a per-protocol analysis rather than intention-to-treat analysis; one infant who did not receive music therapy (as randomized) was added to the control group for analysis. Also, adjustments were not made for multiple comparisons.

Non-pharmacologic measures like KMC have multiple other benefits and negligible drawbacks, making them easier to recommend for general use. With the increasing focus on developmentally supportive aspects of neonatal intensive care, we hope that more centers adopt neonatal pain relief policies incorporating these interventions.

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