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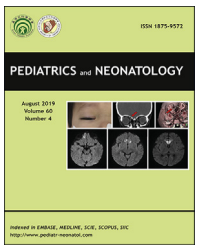

Letter to the Editor

What happened to the principle of equipoise in the planning, designing and conducting of placebo-controlled trials for neonatal procedural pain?

Dear Editor,

We refer to the recent study published by Hsieh and colleagues[1] comparing the effects of 10% glucose and expressed breast milk (EBM) on pain scores during heel lance in preterm infants. The enrolled infants underwent four heel lance procedures while receiving EBM, 10% glucose, water, or no intervention. Results demonstrated significantly lower pain scores for the EBM and 10% glucose groups than for the water and no intervention groups. However, all infants obviously experienced moderate pain (e.g., Premature Infant Pain Profile scores higher than 6) during the first 30 s after heel lance irrespective of the allocated group. Nevertheless, the authors concluded that EBM and 10% glucose were effective and safe. Unfortunately, infants included in this study for all the four heel lance procedures were not administered any evidence-based pain treatments that have been already demonstrated to be effective in reducing pain.

Extensive research conducted over the past three decades has clearly shown that sweet solutions, if sufficiently sweet, are effective in reducing pain during heel lance in newborns. A systematic review of 35 trials reported that 20%–30% glucose solution reduced pain during painful procedures.[2] However, lower concentrations, including 10% glucose, were found to be ineffective across numerous trials.[2] Analgesic effects are known to be dependent on sweet taste, which explains why higher concentrated solutions exert superior analgesic effects. Another systematic review of sweet solutions used for neonatal pain, published in Chinese databases, included 31 trials confirming the same results, i.e., small volumes of sweet solutions, as long as they are sufficiently sweet, reduce pain in infants.[3] Finally, a systematic review of 168 studies showed that a state of equipoise has not existed in the analgesic effects of sweet tasting solutions for almost 20 years.[4]

On the other hand, results of systematic reviews have consistently demonstrated limited efficacy of EBM for infant procedural pain relief.[5] Breast milk contains 7% lactose, which is the least sweet tasting substance and may explain its poor analgesic effects when offered alone.

Exposing infants to placebo, no intervention, or interventions already shown to be ineffective, including low concentrations of sweet solutions and EBM, in pain studies can be considered as unethical. Researchers must use the best evidence available to design their studies, and research ethics committees should not approve studies on infant procedural pain where best evidence is not the standard of care.

What about parents? Parental consent is required for newborns to participate in research. However, are parents truly informed? Do they know that there is already strong evidence to support sweet solutions that are being tested in these studies? Furthermore, are they informed that there is strong evidence to support breastfeeding and skin–skin care, and that they could be advocating for these strategies for their newborns during painful procedures?

Ongoing research should be informed by the best evidence available, including a state of uncertainty. Nevertheless, these principles of equipoise appear not to have been fully considered while conceptualizing and implementing the study of Hsieh and colleagues.[1] Research should focus on implementing the best evidence available

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into clinical practice while continuing to explore improved methods to consistently reduce newborn pain.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pedneo.2019.05.003.

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