Journal of Tropical Pediatrics, 2015, 61, 135–138
doi: 10.1093/tropej/fmu073
Advance Access Publication Date: 25 December 2014
Brief Report

BRIEF REPORT

Efficacy of Expressed Breast Milk in Reducing Pain During ROP Screening—a Randomized Controlled Trial

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SUMMARY

Objective: To assess the effectiveness of expressed breast milk (EBM) on neonatal pain during screening for retinopathy of prematurity (ROP).

Methods: Neonates who were on oral feeds undergoing ROP screening were included. Babies were randomized into intervention group (EBM + Standard practice) and control group. The standard practice is proparacaine, nesting and swaddling. Pain was assessed by PIPP scale, during and at 1 and 5 min after the procedure by the principal investigator who was blinded.

Results: The groups were similar in baseline characteristics. The group receiving EBM had significantly lower PIPP scores during the procedure 12.7 ± 1.69 compared to the control group 15.5 ± 1.78 ($p < 0.05$). The beneficial effect persisted at 1 min and 5 min after the procedure 6.20 ± 1.9 vs. 12.4 ± 2.54 ($p \leq 0.05$) at 1 min; 3.2 ± 1.5 and 6.85 ± 2.4 ($p < 0.05$) at 5 min.

Conclusion: Oral EBM significantly reduces pain during and after ROP screening.

KEYWORDS: retinopathy of prematurity, screening, expressed breast milk, premature infant pain profile scale: PIPP.

INTRODUCTION

Neonates admitted to the neonatal intensive care unit (NICU) are exposed to numerous painful procedures. Repeated painful events in preterm babies may cause changes in the pain thresholds, perception and tolerance of pain during subsequent painful events and may have a negative impact on neurodevelopmental outcomes [1]. Retinopathy of prematurity (ROP) is a preventable cause of blindness and therefore screening for it is essential. This screening is painful and requires repeated examinations until the entire retina is completely vascularized. The recent recommendations for analgesia during ROP screening are to use non-pharmacological techniques, oral sucrose and local

anesthetics [2, 3]. However, studies show that in spite of these measures, babies still feel moderate pain [4]. Breast milk has been tried for other painful procedures and has been found to be a good analgesic [5].

Hence, our objective was to study the efficacy of expressed breast milk (EBM) on pain during ROP screening.

METHODS

This double-blinded randomized controlled trial was conducted in the NICU of a tertiary care hospital from June to October 2012 after obtaining permission from the institutional ethical review board.

Babies with a gestational age of less than 35 weeks (as assessed by New Ballard Score), birth weight less than 2000 g, requiring an ROP screening and who were on at least partial oral feeds were included in the study after informed parental consent. Newborns on opioid analgesics, sedatives, anticonvulsants or on mechanical ventilation were excluded from the study.

The eligible babies were randomly allocated to the intervention and control groups using computer-generated random numbers. Allocation concealment was done by using sequentially numbered opaque sealed envelopes containing the codes for intervention. Babies in the control group were nested, swaddled and received topical proparacaine which is the standard practice in the unit. Infants in the intervention group were given 2 ml of EBM orally by paladai, (a small cup used to feed neonates) 2 min prior to the procedure along with standard practice.

Demographic details and baseline characteristics were recorded on a pre-designed proforma. Pain was assessed by the Premature Infant Pain Profile (PIPP) score. This score incorporates maximum heart rate, minimum saturations, gestational age and three facial reactions—presence of nasolabial furrow, brow bulge and eye squeeze. It is graded as mild (<6), moderate (6–12) and severe (>12) [6]. The score was assessed at baseline (before starting the procedure), during the procedure and at 1 and 5 min after the procedure. The principal investigator videotaped the face of the baby, while another nurse observed the maximum heart rate and minimum saturations on a pulse oximeter. Both these observers were blinded. Each video was replayed thrice to assess each of the facial reactions. To avoid inter-observer variation; video recording and analysis of pain were done by the same observer. A co-investigator validated 10% of the videos. The same ophthalmologist did the screening procedure for all babies. Adverse effects like vomiting, apnea and feed intolerance were noted.

Based on a previous study [7] on analgesia during ROP screening which had used oral sucrose and distilled water as a placebo, a sample size of 12 in each arm was required. This would detect a three point difference in PIPP scores with a power of 80% and a 5% level of significance. Therefore, 20 babies were included in each group.

The data were analysed using the Mann–Whitney U test to detect a difference between the two groups. A p value of 0.05 was considered significant.

RESULTS

In all, 40 neonates were included in the study, with 20 babies in each group.

Table 1 shows the baseline characteristics, which were similar in both groups. There was no difference

Table 1. Baseline characteristics

Characteristics	Interventional group (EBM + standard practice) mean ± SD	Control group (standard practice) mean ± SD
Birth weight (grams)	1426 .7 ± 366.7	1285.2 ± 245.6
Gestational age (weeks)	31.5 ± 2.4	30.3 ± 1.89
Post-natal age (days)	23.4 ± 11.4	27.8 ± 19.8
Time since last feed (minutes)	26.7 ± 10.4	30 ± 11.23
Sex (M)	7	10
Required resuscitation	12	8

$p > 0.05$ for all baseline parameters.

Table 2. PIPP scores

Timing of PIPP scores	Interventional group (EBM + standard practice) mean ± SD	Control group (standard practice) mean ± SD	*p* value
Baseline	3.85 ± 1.9	5.25 ± 2.3	0.054
During procedure	12.7 ± 1.7	15.3 ± 1.78	<0.05
At 1 min after procedure	6.2 ± 1.98	12.4 ± 2.54	<0.05
At 5 min after procedure	3.2 ± 1.58	6.85 ± 2.41	<0.05

in the mean gestational age, birth weight, age at screening or time since last feed.

The PIPP scores were significantly less in the group that received EBM during the procedure and this difference persisted even at 5 min after the procedure. (Table 2)

At baseline, there was no statistical difference between the two groups as expected. During the procedure, babies in both groups perceived severe pain which was significantly more in the control group. At 1 min, the babies in the control group continued to feel severe pain, while it had subsided to moderate pain in the intervention group. At 5 min after the procedure, the control group felt moderate pain while the intervention group perceived only mild pain.

DISCUSSION

This present study demonstrates that EBM decreases pain in newborns during screening for ROP, as assessed by the PIPP score. It not only decreased pain during the actual procedure but also for 5 min after the procedure. The analgesic effect of EBM, which contains a disaccharide – lactose—is probably based on the link between the oro-gustatory effects of sweet solution given orally and the endogenous opioid pathway. In all probability, this is due to the sweet taste perception, a sense well developed even in premature infants at birth [8]. Breast milk also contains tryptophan which could lead to higher levels of beta endorphins, thereby decreasing pain [9, 10]. Breast milk is natural, easily available and safe and therefore we decided to use it in our study to decrease pain. Similar analgesic effects of EBM were observed in studies on heel lance and venepuncture in the recent Cochrane meta-analysis. However, these procedures cause mild pain. (PIPP scores 6–12) [5]. We did notice that the PIPP score at baseline was lower in the intervention group, although the *p* value is border line. A possible reason may be that the PIPP scores at baseline were taken after the EBM was given, hence it may have already had a calming effect on the baby, leading a lower score.

The current recommendation for pain relief during ROP screening is to use proparacaine, in addition to non-pharmacological measures like swaddling and non-nutritive sucking [2, 3].

In spite of these recommendations, there are conflicting reports on the efficacy of proparacaine by other authors. Saunders *et al.* found no decrease in pain when proparacaine was used [11], while Cogen found a decrease that did not reach statistical significance [12]. Two studies have reported a beneficial effect; Mehta [13] and Marsh [14] both showed a decrease in PIPP scores at the time of speculum insertion and at 1 min respectively, however, there was no difference at 5 min in either study and hence the benefit was not sustained. In a previous study done at our institution, we found that the pain in ROP is a severe type of pain (PIPP ~ 14) and is due to insertion of the speculum, sclera depression, manipulation of the globe during visualization, bright light and physical restraints, all of which cause deep pain, not relieved by proparacaine [15, 16]. Thus, proparacaine, a local anaesthetic, might not alleviate this deeper pain.

Other methods of pain relief include use of dextrose or sucrose. In our previous study, we had tried 25% dextrose orally, but found it did not decrease pain scores [15], which was similar to other studies [17]. Therefore, we decided to use EBM.

Non-pharmacological measures like swaddling and nesting are known to reduce pain but may not be enough for ROP screening which is a severe type of pain [18] (PIPP scores >12 during the

procedure). This is the standard practice for all babies in our NICU.

No adverse effects of vomiting or apnea were noted with the use of EBM.

The main strengths of the study were the use of PIPP scale, which is a very objective, validated and reliable tool for assessment of pain response in preterm neonates, and blinding of the investigators.

CONCLUSIONS

The severe pain of ROP screening is significantly reduced by the use of EBM. This analgesic effect lasts even at 5 min after the procedure.

ACKNOWLEDGEMENTS

The authors would sincerely like to acknowledge Sr. Gracy for her help with ensuring blinding and monitoring of the babies.

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