

# Which is Better for Pain Reduction before Venipuncture: Glucose, Lidocaine or Expressed Breast Milk?

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## Abstract

**Aim:** The aim of this study was to compare effects of 2 cc oral glucose (50%), topical application of lidocaine, 2 cc of expressed breast milk (EBM), and nothing per oral for reducing of pain before painful procedures. **Patients and methods:** In this case-control study, 121 term neonates were included. There were 3 groups of cases and one control group. Inclusion criteria were: term neonates (38-42 weeks); stable condition; per oral feeding; five minutes APGAR>7; and no history of narcotic usage. Neonates were randomly divided in 4 groups. Two milliliter of glucose solution (50%), topical application of lidocaine, and 2 cc of expressed breast milk via syringe were used for group I, II, and III respectively. Group IV is the control group. For control group, no additional measure was done. Data analysis was performed using SPSS ver 11.0 (SPSS Inc, Chicago, IL, USA). Chi-square, t-test, and ANOVA were used for analysis.  $P<0.05$  was considered significant. **Results:** Score of Douleur Aiguë Nouveau-né was significantly lower in group III compared to other group ( $P<0.05$ , Tukey). Crying time in group III was significantly lower than group IV. Respiratory rate in group II was significantly lower than group IV ( $P=0.018$ ). Pulse rate was significantly lower in group III compared to other group. **Conclusion:** Expressed breast milk is the safe and natural agents for reducing pain of neonates. Another clinical trial study with more samples is recommended.

## Key words

Expressed breast milk; Glucose; Lidocaine; Neonate; Pain

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## Introduction and Aim

Newborn infants routinely undergo painful invasive procedures, even in uncomplicated situation. There is evidence that shows neonates do feel pain and even have increased sensation to pain with longer duration compared to older children.<sup>1</sup> Also, evidence showed even premature newborns may experience pain that could unfavourably affect clinical and behavioural parameters of their present and future.<sup>2</sup> Some research showed sucrose as the most effective while other showed breastfeeding.<sup>3,4</sup> In the Skogsdal et al study, they found 1 ml of glucose 30% had significant effect to reduce mild pain compared to breast milk.<sup>5</sup> In the study from Turkey, repeated doses of hindmilk administration was an effective analgesic intervention.<sup>6</sup> But in another study from Turkey, neither hindmilk nor foremilk is superior in relieving pain compared to placebo.<sup>7</sup>

Although there are studies on pharmacologic<sup>8,9</sup> and non pharmacologic agents which may reduce neonatal pain, more research are needed to find the most effective, and

least expensive method for decreasing pain in neonates. This pharmacologic (Sucrose) or non pharmacologic agents (pacifier) may interfere with correct breastfeeding.<sup>10</sup> So, it may be interesting, especially in developing country; to use safest, less expensive and most available method such as breast milk for analgesia. The aim of this study was to compare effects of 50% glucose 2 cc topical lidocaine, breast milk 2 cc and control for reducing pain following painful procedures.

## Patients and Methods

In this case-control study, 121 term newborns ( $6.21 \pm 6.49$  day, range:1-30 day) were included. In our study sample size was calculated according to research conducted by Mathai et al<sup>11</sup> and Yilmaz and Arikan studies.<sup>12</sup> Newborns were randomly placed in 4 groups: 3 groups of cases and one control group. Inclusion criteria were: term neonates (38-42 weeks); without evidence of poor feeding; stable condition; per oral feeding; five minute APGAR>7; and no history of narcotic usage. Exclusion criteria were difficult venipuncture. We included cases with 1st time venipuncture on the hand. In our cases, venipuncture was done for blood sampling. Neonates were randomly divided in 4 groups. For group I (glucose), 2 cc glucose 50% was administered

orally, 2 minutes before procedure. Thirteen minutes before venipuncture, 1 gr of Lidocaine gel (2%) was administered topically in group II.<sup>13,14</sup> For group III (breast milk), 2 cc breast milk was administered orally via syringe at 2 minutes before venipuncture. For control group, routine venipuncture was performed without adding anything. Venipunctures were done in the quiet room. After 1st step, an experienced nurse who is blind to group allocation of patients came for evaluation. During venipuncture, an experienced nurse measured crying times in the 1st 3 minutes after procedure. Validated Score of DAN (Douleur Aiguë Nouveau-né) scale (primary outcome measure)<sup>15,16</sup> was used for pain assessment (Table 1). Facial expression, limb movements, and vocal expression were evaluated by DAN scale. A score from 0 (no pain) to 10 (highest pain) was attributed to each neonates, according to intensity of pain.<sup>15,17</sup> Data analysis was performed using SPSS ver 11.0 (SPSS Inc, Chicago, IL, USA). Two-sample t-test, ANOVA, Spearman, and Tukey tests were used for analysis.

## Results

Of 121 cases, 83 (68.6%) were male and 38 (31.4%) were female (Chi<sup>2</sup>=33.47, P<0.0001). Male ratios in glucose, lidocaine, EBM, and control were 63.33%, 60%,

**Table 1** Douleur Aiguë Nouveau-né behavioural scale for rating acute pain in neonates

Measure	Score
<b>Facial expressions</b>	
Calm	0
Snivels and alternates gentle eye opening and closing	1
Intensity of eye squeeze, brow bulge, nasolabial furrow:	
Mild, intermittent with return to calm	2
Moderate	3
Very pronounced, continuous	4
<b>Limb movements</b>	
Calm or gentle movements	0
Intensity of pedaling, toes spread, legs tensed and pulled up, agitation of arms, withdrawal reaction:	
Mild, intermittent with return to calm	1
Moderate	2
Very pronounced, continuous	3
<b>Vocal expression</b>	
No complaints	0
Moans briefly: for intubated child, looks anxious or uneasy	1
Intermittent crying (for intubated child, gesticulations of intermittent crying)	2
Long lasting crying, continuous howl (for intubated child, gesticulations of continuous crying)	3

73.33%, and 77.41% respectively. There were no significant difference between groups regarding sex ratio ( $P=0.41$ ). Mean $\pm$ SE of age was  $6.21\pm 6.49$  day. Crying time was significantly less in group III ( $P=0.0001$ , ANOVA). DAN score was significantly lower in group III ( $P<0.05$ , ANOVA). Respiratory rate was significantly lower in group I ( $P=0.018$ , ANOVA). Among the four groups, the lowest pulse rate was seen in group III ( $P=0.000$ , ANOVA). By using Tukey-test, there was significant difference between mean crying time of group III ( $21.600\pm 3.138$ ) and group IV ( $55.96\pm 6.85$ ). Mean of DAN score was significantly lower in group III compared to group I, II and IV ( $P<0.05$ , Tukey). There were no significant differences between other groups using Tukey-test. Respiratory rate in control subjects was significantly higher than EBM cases. Pulse rate was significantly lower in group III compared to other group using Tukey-test. Pulse rate was significantly higher in group IV compared to other groups ( $P<0.05$ ).

## Discussion

In our study, crying time was significantly lesser in group III compared to control group. In the study by Olsson and

Eriksson, there was no significant difference between case and controls.<sup>18</sup> Their study was conducted on pre-term neonates while we studied term neonates. In the study by Miazzo et al on the infants 30-36 weeks of gestation, using 24% sucrose solution, significant reduction in crying subscale of the Neonatal Infant Pain scale was found.<sup>19</sup> They didn't include breast milk in their study but we included 50% glucose, lidocaine, and EBM in our study. In our study, in term neonates, we showed that EBM is more effective than higher sucrose concentration even 50%.

In our study mean of DAN score was significantly lower in group III (EBM) compared to group I, II, and IV. In the study by Upadhyay et al, the modified Neonatal Facial Coding Scores (NFCS) was significantly lower in the EBM group compared to placebo.<sup>20</sup> The results of two studies were similar regarding effect of EBM on reducing pain. In their study, distilled water was used as a placebo. We compared EBM with 50% glucose, lidocaine, and nothing per oral in this study.

In the study by Ors et al, 25% sucrose was superior to expressed breast milk in pain relief, especially in crying time and behavioural variable.<sup>21</sup>

In the study by Askarpour et al, authors concluded that oral glucose is the safe analgesic agent. In their study,

**Table 2** Crying time, score of Douleur Aiguë Nouveau-né (DAN), respiratory rate, and pulse rate in four groups of study

	Group	Mean $\pm$ SE	95% CI for mean	
Crying time	I	46.083 $\pm$ 8.923	27.833	64.334
	II	40.400 $\pm$ 8.377	23.266	57.534
	III	21.600 $\pm$ 3.138*	15.182	28.018
	IV	55.968 $\pm$ 6.855	41.967	69.969
Score of DAN	I	4.833 $\pm$ 0.625	3.5545	6.1112
	II	5.033 $\pm$ 0.584	3.8384	6.2282
	III	2.900 $\pm$ 0.231*	2.4261	3.3739
	IV	6.064 $\pm$ 0.310	5.4297	6.6994
Respiratory rate	I	43.383 $\pm$ 1.259	40.8067	45.9600
	II	50.466 $\pm$ 2.31	45.7302	55.2031
	III	49.483 $\pm$ 2.35	44.6692	54.2975
	IV	51.612 $\pm$ 1.71	48.1024	55.1234
Pulse rate	I	134.350 $\pm$ 1.34	131.5907	137.1093
	II	136.950 $\pm$ 1.47	133.9278	139.9722
	III	127.050 $\pm$ 1.32*	124.3474	129.7526
	IV	146.193 $\pm$ 2.51	141.0652	151.3219

Group I: Glucose; Group II: Lidocaine gel; Group III: Expressed Breast Milk (EBM); Group 4: Control

\*( $P<0.05$ , Tukey)

comparison between different solutions of glucose and distilled water was performed.<sup>22</sup> In the study by Eriksson et al, the choice of blood sampling has no impact on the pain symptom if blood glucose was given prior to sampling.<sup>23</sup>

In our study we showed that breast milk significantly reduced crying time and DAN score. In the study by Bueno et al on 113 newborns to compare EBM versus 25% glucose, they found that 25% glucose was more effective than EBM in reducing pain and crying.<sup>24</sup> But in their study, groups were similar regarding demographics and clinical characteristics, except for birth weight at data collection day. In both studies, groups were not completely similar, and this may affect final measurement. In the study by Jatana et al, on 125 full term newborn (5 groups of 25 each), they found 10%; 25%; 50% of glucose solutions and EBM were found to reduce physiological and behavioural response in neonates undergoing painful procedures. EBM and 10% glucose solution have similar effect but less than 25% and 50% glucose solution.<sup>25</sup>

Pulse rate was significantly lower in group III case compared to other especially versus controls. In another study on the effect of expressed breast milk, changes in heart rate was significantly lower in expressed breast milk group compared to distilled water as a placebo.<sup>20</sup> The results of the two studies were similar regarding effect of EBM on the heart rate.

In the Simonse et al study on 71 preterm neonates, they found no significant difference in Premature Infant Pain Profile in neonates receiving glucose and those receiving breast milk (either breast fed or bottle fed).<sup>26</sup>

Several studies showed superiority of glucose/sucrose for reducing pain compared to breast feeding/breast milk.<sup>24</sup> Shah et al in a systematic review concluded, breastfeeding or breast milk should be used to alleviate pain in neonates undergoing painful procedure. Administration of sucrose/glucose had similar effect.<sup>27</sup> In another study by Codipietro et al, on 101 term neonates undergoing heel lance using an automated device, median of Premature Infant Pain Profile was significantly lower in breast fed neonates.<sup>28</sup>

Previous studies by Skogsdal et al,<sup>5</sup> and Ors et al,<sup>21</sup> showed a trend toward reduction in pain with use of 1-2 ml of expressed breast milk, but their results were not statistically significant. Upadachay et al showed significant effect of 5-ml of expressed breast milk compared to placebo.<sup>20</sup> In the current study, we showed significant effect of 2-ml of EBM compared to 50% glucose, topical lidocaine, and nothing per oral. All studies on the effect of EBM had different

ages and weights of the cases. There is also differences between dose of EBM used in studies.

Dose related response may be important in the evaluation of effect of EBM. EBM has a 7% lactose which was lower than the same volume of glucose. Duration of venipuncture may be important. Age of the cases varied between 1-15 days in Ors et al,<sup>21</sup> 8-9 days in Upadhyay,<sup>20</sup> to 40-46 days in Mathai et al<sup>11</sup> study. More studies are needed in this matter.<sup>29</sup>

In this study, there was no significant difference between effect of local anesthetic and nothing per oral group. This may be due to inappropriate anesthetic agent, and shorter duration of use. However, we assessed lidocaine gel as the most available drug in our province. Most of studies used Eutectic Mixture of Local Anesthetics with a duration more than 1 hour.<sup>30</sup>

## Conclusion

Our results supported expressed breast milk as the safest, more effective, and inexpensive method for analgesia in neonates. Another prospective study with more sample and measurement of beta endorphin and lactose level is recommended when compared to glucose/sucrose.

## Limitation

In this study, however we selected cases randomly but age of the cases had significantly different, age of the cases in the EBM group was higher than other group.

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## Conflict of Interest

There is no conflict of interest.

## References

- Anand KJ. Clinical importance of pain and stress in preterm neonates. *Biol Neonate* 1998;73:1-9.
- Franck LS, Greenberg CS, Stevens B. Pain assessment in infants and children. *Pediatr Clin North Am* 2000;47:487-512.
- Uga E, Candriella M, Perino A, et al. Heel lance in newborn during breastfeeding: an evaluation of analgesic effect of this procedure. *Ital J Pediatr* 2008;34:3.
- Iturriaga GS, Unceta-Barrenechea AA, Zarate KS, Olaechea IZ, Nunez AR, Rivero MM. [Analgesic effect of breastfeeding when taking blood by heel-prick in newborns]. *An Pediatr (Barc)* 2009; 71:310-3.
- Skogsdal Y, Eriksson M, Schollin J. Analgesia in newborns given oral glucose. *Acta Paediatr* 1997;86:217-20.
- Altun-Koroglu O, Ozek E, Bilgen H, Cebeci D. Hindmilk for procedural pain in term neonates. *Turk J Pediatr* 2010;52:623-9.
- Uyan ZS, Ozek E, Bilgen H, Cebeci D, Akman I. Effect of foremilk and hindmilk on simple procedural pain in newborns. *Pediatr Int* 2005;47:252-7.
- Taddio A, Ohlsson A, Einarson TR, Stevens B, Koren G. A systematic review of lidocaine-prilocaine cream (EMLA) in the treatment of acute pain in neonates. *Pediatrics* 1998;101:E1.
- Shah V, Taddio A, Ohlsson A. Randomised controlled trial of paracetamol for heel prick pain in neonates. *Arch Dis Child Fetal Neonatal Ed* 1998;79:F209-11.
- Howard CR, Howard FM, Lanphear B, et al. Randomized clinical trial of pacifier use and bottle-feeding or cupfeeding and their effect on breastfeeding. *Pediatrics* 2003;111:511-8.
- Mathai S, Natrajan N, Rajalakshmi NR. A comparative study of nonpharmacological methods to reduce pain in neonates. *Indian Pediatr* 2006;43:1070-5.
- Yilmaz F, Arikan D. The effects of various interventions to newborns on pain and duration of crying. *J Clin Nurs* 2011;20: 1008-17.
- Lehr VT, Taddio A. Topical Anesthesia in Neonates: Clinical Practices and Practical Considerations. *Semin Perinatol* 2007; 31:323-9.
- Friedman PM, Mafong EA, Friedman ES, Geronemus RG. Topical Anesthetics Update: EMLA and Beyond. *Dermatol Surg* 2001;27:1019-26.
- Carbajal R, Veerapen S, Couderc S, Jugie M, Ville Y. Analgesic effect of breast feeding in term neonates: randomised controlled trial. *BMJ* 2003;326:13.
- Carbajal R, Paupe A, Hoenn E, Lenclen R, Olivier-Martin M. [APN: evaluation behavioral scale of acute pain in newborn infants]. *Arch Pediatr* 1997;4:623-8.
- Guideline statement: management of procedure-related pain in neonates. *J Paediatr Child Health* 2006;42 Suppl 1:S31-9.
- Olsson E, Eriksson M. Oral glucose for pain relief during eye examinations for retinopathy of prematurity. *J Clin Nurs* 2011; 20:1054-9.
- Milazzo W, Fielder J, Bittel A, et al. Oral sucrose to decrease pain associated with arterial puncture in infants 30 to 36 weeks' gestation: a randomized clinical trial. *Adv Neonatal Care* 2011; 11:406-11.
- Upadhyay A, Aggarwal R, Narayan S, Joshi M, Paul VK, Deorari AK. Analgesic effect of expressed breast milk in procedural pain in term neonates: a randomized, placebo-controlled, double-blind trial. *Acta Paediatr* 2004;93:518-22.
- Ors R, Ozek E, Baysoy G, et al. Comparison of sucrose and human milk on pain response in newborns. *Eur J Pediatr* 1999; 158:63-6.
- Askarpour S, Dehdashtian M, Marashi S. Effect of oral glucose and the response to pain in the term neonate. *Pak J Med Sci* 2007;23:733-5.
- Eriksson M, Gradin M, Schollin J. Oral glucose and venepuncture reduce blood sampling pain in newborns. *Early Hum Dev* 1999; 55:211-8.
- Bueno M, Stevens B, de Camargo PP, Toma E, Krebs VL, Kimura AF. Breast milk and glucose for pain relief in preterm infants: a noninferiority randomized controlled trial. *Pediatrics* 2012;129: 664-70.
- Jatana SK, Dalal SS, Wilson CG. Analgesic effect of oral glucose in neonates. *Med J Armed Forces India* 2003;59:100-4.
- Simonse E, Mulder PG, van Beek RH. Analgesic effect of breast milk versus sucrose for analgesia during heel lance in late preterm infants. *Pediatrics* 2012;129:657-63.
- Shah PS, Aliwalas L, Shah V. Breastfeeding or breastmilk to alleviate procedural pain in neonates: a systematic review. *Breastfeed Med* 2007;2:74-82.
- Codipietro L, Ceccarelli M, Ponzzone A. Breastfeeding or oral sucrose solution in term neonates receiving heel lance: A randomized, controlled trial. *Pediatrics* 2008;122:e716-e21.
- Schollin J. Analgesic effect of expressed breast milk in procedural pain in neonates. *Acta Paediatr* 2004;93:453-5.
- Rushforth JA, Griffiths G, Thorpe H, Levene MI. Can topical lignocaine reduce behavioural response to heel prick? *Arch Dis Child Fetal Neonatal Ed* 1995;72:F49-51.