Feeding and oral glucose—additive effects on pain reduction in newborns

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Abstract

Aims: The aims of this study were to compare the pain reducing effect of oral glucose with that of being breast-fed shortly before venipuncture in newborns, and also the pain score and crying time with parents’ assessment. Design: Randomised, controlled trial. Subjects: 120 full term newborns undergoing venipuncture randomly assigned to one of four groups: I, Breast-fed and 1-ml placebo; II, Breast-fed and 1-ml 30% glucose; III, Fasting and 1-ml placebo; and IV, Fasting and 1-ml 30% glucose. Outcome measures: Pain during venipuncture was measured with the Premature Infant Pain Profile (PIPP). Crying time was recorded. The parents assessed their babies’ pain on a Visual Analogue Scale (VAS). Results: The PIPP score was significantly lower in the infants receiving glucose, than in those not given glucose ($p=0.004$). There was no significant difference in PIPP score between the infants who were fed and the fasting infants. The PIPP score was lower in group II (median 7) than in group I (md 10). There was a similar difference between group IV (md 9) and group III (md 11). The median crying times during the first 3 min in groups I, II, III, and IV were 63, 18, 142 and 93 s, respectively. There was low agreement between the parents’ assessment of pain and the PIPP score and crying time. Conclusion: Breast-feeding shortly before venipuncture has no major impact on the pain score but on crying time. The combination of oral glucose and breast-feeding shows the lowest pain score and significantly shorter duration of crying.

Keywords: Neonate; Pain; Glucose; Breast-feeding

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1. Introduction

Newborns routinely experience pain from invasive procedures such as blood sampling. The sick infant may experience repetitive pain from many diagnostic or therapeutic procedures. Apart from short-term effects, pain also has long-term effects, which may later affect the newborns neurological development, including reaction to pain [1–3].

Various methods are used to reduce procedural pain in the newborn. One of the most frequently studied is oral administration of sugar solutions [4]. The pain-reducing effect of oral sugar solutions is believed to be mediated by two mechanisms: an orotactile stimulation by the intraoral fluid gives an initial effect and an orogustatory stimulation prolongs the effect through release of endogenous opioids [5–7]. In a series of studies, oral sucrose or glucose has been used to alleviate pain reactions during blood sampling, by heel stick [8–11] or venipuncture [9,12–15]. Other interventions such as non-nutritive sucking [12,16], skin-to-skin contact [17] and swaddling [18] have also been proposed as means of reducing pain during blood sampling in newborns.

Throughout history, feeding has been used to calm and comfort infants. Today, many care professionals encourage breast-feeding before a painful procedure to keep the neonate satisfied and not showing so much pain. Questions have been raised whether breast-feeding could be effective to reduce pain and used instead of oral sweet solutions. There are few scientific studies in this field. Gray and colleagues found that among infants undergoing blood sampling, those who were breast-fed during the procedure showed less crying and grimacing than control infants [19]. Bilgen et al. [20] reported that breast-feeding during blood sampling was less effective than oral sucrose, on the basis of the crying time and behavioural variables, and Carbajal et al. [21] found breast-feeding superior to water or holding but noted no difference between the effects of breast-feeding during blood sampling and orally given glucose. Time since feeding is often stated among background characteristics in studies about neonatal pain, indicating this to be important for the response to a painful procedure. Whether the time since feeding correlates with pain response is rarely studied. In a study on pain response at 4- or 6-month vaccination, Taddio et al. [3] found that time of last feeding did not correlate significantly with pain response. Studies looking at pain response in newborns recently fed versus not fed has so far not been performed.

As pain is a multidimensional phenomenon, a multidimensional measure of pain, combining behavioural and physiological factors with contextual factors such as gestational age and behavioural state, has been found to be superior to other measures [22]. The Premature Infant Pain Profile (PIPP) fulfils this requirement and is easy to use [22,23].

For research about effectiveness of pain-relieving methods, and in clinical practice, it would also be easier if the parents could assess the infants’ pain by themselves. There are few studies on parental assessment of neonatal pain. Xavier Balda et al. [24] found that parents were able to correctly indicate a newborn with pain, when looking at pictures of different facial expressions. A comparison of symptoms used by mothers and nurses to identify an infant with colic pain showed some similarities [25].
The aims of this study were:

– to compare the pain-reducing effect of recently being breast-fed with that of oral glucose prior to venipuncture in newborns;

– to compare the parents’ assessment of their infant’s pain with measurements made with the PIPP score and crying time during the procedure.

2. Materials and methods

2.1. Participants

The study was undertaken at the maternity ward at Örebro University Hospital between March 2001 and September 2002. It was approved by the Local Ethics Committee and informed consent was obtained from each parent. One hundred and twenty healthy, term breast-fed infants undergoing the metabolic screening blood test at the age of 3–5 days were studied. Babies with feeding problems or with suspicion of any illness were not included.

The infants were randomly assigned to one of four study groups using a system of sealed envelopes: Group I, breast-fed and placebo (sterile water); group II, breast-fed and 30% glucose (Kabi Pharmacia, Stockholm, Sweden); group III, fasting and placebo; and group IV, fasting and 30% glucose.

In the breast-fed groups the infants were breast-fed ad libitum within 45 min prior to blood sampling. The amount of breast milk being consumed was not noted. In the fasting groups the blood sampling was performed at least 2 h after the last feed. The median length of time since feeding was 5 min (range 0–25) in group I, 5 min (0–40) in group II, 135 min (120–240) in group III and 130 min (120–295) in group IV. Other characteristics of the studied infants are presented in Table 1.

On the basis of a previous study [9], we calculated that a sample size of 30 infants per group would be required to achieve a statistically reliable difference in pain score with a power of 80% and a $p$ value of $<0.05$. We hypothesized a difference of 1.7, a standard

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of study groups</th>
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<tbody>
<tr>
<td></td>
<td>I Breast-fed $(n=27)$</td>
</tr>
<tr>
<td>Number of females</td>
<td>12</td>
</tr>
<tr>
<td>Mean birth weight, g</td>
<td>3638 (2325–4425)</td>
</tr>
<tr>
<td>Median Apgar at 5 min</td>
<td>10 (9–10)</td>
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<tr>
<td>Vaginal delivery, number</td>
<td>18</td>
</tr>
<tr>
<td>Median time since breast-feeding, min</td>
<td>5 (0–25)</td>
</tr>
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deviation (S.D.) of ~ 3.0, and added 10% to the sample size to ensure for the use of non-parametric statistics.

2.2. Procedure

The procedure was conducted in a quiet observation room. The babies were placed on a preheated nursing table and connected to a pulsoximeter (Datex Ohmeda 3800, Helsinki, Finland). Any parent wishing to be present during the blood sampling was allowed to do so, but was asked not to talk to or comfort the baby. The infant’s face and the pulsoximeter were filmed during the study period with two cameras (Panasonic Digital Video Camera NV-DS15, Panasonic Svenska, Stockholm, Sweden) and mixed into one tape using a mixer (Panasonic Digital AV Mixer WJ-AVE 55, Panasonic Svenska). An experienced nurse, trained in this particular project, performed the blood sampling. The nurse identified an appropriate vein on the dorsal aspect of the hand, and the baseline heart rate, oxygen saturation and behavioural state were then recorded during a period of 15 s. One millilitre of 30% glucose (Kabi Pharmacia) or sterile water was given by a syringe into the infant’s mouth by the nurse who did not know the content of the syringes. One minute afterwards, the nurse cleaned the skin with a local disinfectant and performed the venipuncture, using a 21-gauge needle (Terumo, Leuven, Belgium). When the blood collection was completed, an adhesive bandage was applied and the infant was left undisturbed for a 3-min recovery phase.

After the procedure, the parents marked their opinion of their infant’s pain during the skin puncture on a Visual Analogue Scale (VAS) scoring from 0 to 100 (0 = no pain, 100 = severe pain) [26].

2.3. Outcome measures

One observer not aware of the assignments to the study groups scored all videotapes. Pain response was measured with use of the PIPP during the first 30 s after the skin puncture. PIPP is a seven-indicator composite scale assigning points for three behavioural (facial actions: brow bulge, eye squeeze and nasolabial furrow) two physiological (heart rate and oxygen saturation) and two contextual (gestational age, behavioural state) indicators of pain [23]. The infants in this study could reach a maximum PIPP score of 18. Crying was measured continuously as the presence of audible distressed vocalization.

The observer’s intercoder reliability for PIPP was 0.847.

The parental assessment of pain was divided into three groups: no or minimal pain (VAS<33), minor–moderate pain (VAS 34–67), and moderate–severe pain (VAS>67), and was compared with the PIPP score, which was divided into no or minimal pain (PIPP<6), minor pain (PIPP 7–12), moderate or severe pain (PIPP>12) [23] and crying time divided into crying <15, 15–60 and >60 s.

In some instances, data were missing because of equipment failure, such as losing the signal for heart rate or losing the recording of sound. If data were missing, the infant was excluded from that particular analysis, but was included in other analyses that did not involve the missing variable. For this reason, the numbers of subjects for each analysis differed.
In comparison of differences between groups, Kruskal–Wallis one-way ANOVA was used for PIPP and for crying within the first 3 min. Significance in comparisons between two groups was assessed by the Mann–Whitney U test with Bonferroni–Holm adjustment [27]. Agreement between parental assessment and PIPP score and crying time, respectively, was measured by weighted kappa. The statistical analysis was carried out with the SPSS for Windows software program. A p value < 0.05 was considered significant.

3. Results

The four groups were comparable in background characteristics. Nine infants were excluded after randomisation; three because the mothers did not want to proceed and six because of technical problems with the video recordings.

The PIPP score was significantly lower in the infants receiving glucose (groups II + IV; median 7) than in those not given glucose (groups I + III; median 11) (p = 0.004).

There was no significant difference in PIPP score between the infants who were fed (groups I + II; median 9) and the fasting infants (groups III + IV; median 9).

Fig. 1 shows the PIPP scores obtained in the four groups. The PIPP score was lower in group II (breast-feeding and glucose; median 7) than in group I (breast-feeding and placebo; median 10). There was a similar difference between the fasting group receiving glucose (group IV; median 9) and that without glucose (group III; median 11). Analysis of variance showed that the median PIPP scores were significantly different (p = 0.037).

Fig. 1. Bubble plot showing Premature Infant Pain Profile scores for the infants in the four groups undergoing venipuncture. Horizontal lines indicate median values. Size of the bubble represents number of individuals.
Pairwise comparisons of median PIPP scores did not reach statistical significance with use of Bonferroni–Holm correction.

The infants not receiving glucose (groups I + III) were more likely to show pain (PIPP > 6) than those receiving glucose (groups II + IV) (relative risk [RR] 1.6; 95% confidence interval [CI] 1.2–2.0). For the infants that were fasting (groups III + IV) compared to the infants being fed (groups I + II), the corresponding relative risk was 1.1 (95% CI 0.9–1.5).

The median crying times during the first 3 min in groups I, II, III, and IV were 63, 18, 142, and 93 s, respectively (p < 0.0001) (Fig. 2). Statistical significance was achieved for group I (breast-feeding and placebo) versus (group II (breast-feeding and glucose) (p = 0.008) and versus group III (fasting and placebo) (p = 0.005), and for group III (fasting and placebo) versus group IV (fasting and glucose) (p = 0.009).

There was also a significant difference in this respect between the breast-feeding and glucose group (group II) and the fasting and placebo group (group III) (p = < 0.001) and the fasting and glucose group (group IV) (p = 0.022).

There was no difference between the groups regarding experience of previous invasive procedures, or the duration of the blood collection procedure. In groups I, II, III, and IV, there were 27, 28, 25, and 28 infants having less than five earlier procedures, and mean duration was 94, 83, 84 and 81 s, respectively.

There was low agreement between the parents’ assessment of pain and the PIPP score and crying time during the procedure, with weighted kappa 0.25 (95% CI 0.1–0.4) and 0.44 (95% CI 0.29–0.59), respectively.

![Fig. 2. Bubble plot showing the crying times during the first 3 min for the infants in the four groups. Crying time by different groups. Horizontal lines indicate median values. Size of the bubble represents number of individuals.](image-url)
4. Discussion

Oral sugar solutions with or without non-nutritive sucking have been shown to be effective for treatment of procedural pain in newborns [4,9,12,15,28]. Very few studies addressed the question of pain-reducing effects of breast-feeding before a painful procedure. In some recently published studies, breast-feeding the infant during the painful procedure has been found to have an effect of the pain reaction [19,21]. In Sweden, as in many other countries, most hospitals work with a “Baby Friendly Hospital Initiative” [29], which implies not interrupting feeding, making painful procedures as blood sampling during breast-feeding improper.

It is not clear whether feeding of an infant before a painful procedure is of benefit or not. The objective of this study was therefore to investigate the effect on pain in newborns being breast-fed shortly before a procedure and to compare this effect with that of orally administered glucose. Our study suggests that if oral glucose is given prior to the venipuncture, the question of recently being fed or being fasting has no major impact on the pain score but on crying time. A combination of breast-feeding and oral glucose yielded the lowest pain score and was associated with a significantly shorter duration of crying, indicating a combined effect on discomfort due to pain and perhaps hunger.

In our study, we have been looking on the effect of being breast-fed. Whether feeding with bottle or feeding tube and use of formula instead of breast milk will gain a similar result or not, we do not know.

Crying is not specific for pain, and neonates cry to express several basic needs. Despite this fact, crying has been used in many studies as a measure of pain, especially after a painful procedure [22,30,31]. The somewhat divergent results in our study between the pain score and the crying time might be explained by the fact that some babies were fasting and cried because of hunger.

Oral glucose given prior to a painful procedure is effective and has as known no side effects when used in term infants. In a recently published study, it was found that preterm infants (<31 weeks) receiving sucrose during the first week of life prior to all procedures that were assumed to cause pain were at risk for poorer neurobehavioral and physiological outcomes compared to controls. The authors concluded that routine use of sucrose for every painful event cannot therefore be recommended for preterm infants [32]. This needs to be confirmed by further studies.

Unfortunately some infants had to be excluded from the analysis of the PIPP score because of missing data in some part of the analysis, especially in the breast-fed and water group (group I) and also in the fasting and water group (group III). These missing data might have affected the result. To check for this possibility, we used a model that substituted the group median for the missing values (heart rate and oxygen saturation). Similar results were obtained with use of this model on the PIPP score, indicating that the missing data probably had no or only minor impact on the results.

Recent knowledge [22] favours the use of composite scales including both physiological and behavioural measures for evaluating pain in newborns. One of the most frequently applied methods is PIPP. This scale was developed to assess acute pain in preterm and full term newborns [23]. It has been submitted to extensive reliability and validity testing under controlled research conditions, and has also been found to have good validity and
reliability for use in clinical settings [33]. The authors of the PIPP scale state a difference of 2 in PIPP score to be of clinical importance (Personal communication with Celeste Johnston). In clinical practice it would be useful if parental assessment of their infant’s pain could be used instead of scores, such as PIPP. However, in this study the parents’ assessment of their infant’s pain during venipuncture was not in accordance with the PIPP score or crying time. The results of the parental assessment showed a wide range, and other factors such as their own experiences of painful procedures, fear, culture and experience of newborns might have influenced their assessment. Parental assessment of their infant’s pain cannot, in our opinion, replace measurement by pain scores.

5. Conclusion

Oral glucose reduces the signs of pain from venipuncture in the healthy, term newborn. When combining oral glucose and breast-feeding shortly before the procedure, the reduction is even greater. We recommend that in full-term neonates, in clinical practice, oral glucose should be given at venipuncture and, if possible, the infant should be breast-fed before. If, for any reason, the infant cannot be fed before the procedure, oral glucose should always be used.

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References