Analgesia with breastfeeding in addition to skin-to-skin contact during heel prick

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ABSTRACT

Objective To investigate the analgesic effect (measured with Neonatal Infant Pain Scale (NIPS)) of breastfeeding (BF) in addition to skin-to-skin contact (SSC) versus other methods of non-pharmacological analgesia during blood sampling through heel lance in healthy term neonates.

Design Randomised controlled trial.

Setting Tertiary level maternity ward.

Patients One hundred thirty-six healthy term newborns. Inclusion criteria: healthy term neonates, wish to breastfeed and absence of feeding during the previous 60 min.

Intervention Neonates were randomly assigned to four groups: Group breastfed with SSC (BF+SSC Group) (n=35); Group sucrose with SSC (Sucrose+SSC Group) (n=35); SSC Group (n=33); or Sucrose Group (n=33). Babies were recorded with a video camera.

Outcome measures Three observers watched the videos and measured NIPS score at three time points (t_0: 2 min before heel prick; t_1: During heel prick; and t_2: 2 min after the heel prick). The influences of non-pharmacological methods on crying time, percentage of crying while sampling, heart rate, number of attempts and duration of sampling were also studied.

Results BF+SSC Group achieved a significant lower median NIPS score (value=1) compared with other groups (value=2, 4 and 4, respectively). The percentage of neonates with moderate-to-severe pain was also lower in the BF+SSC Group. Both groups BF+SSC and Sucrose+SSC achieved a significant lower percentage of crying compared with SSC Group.

Conclusions This study suggests that BF in addition to SSC provides superior analgesia to other kinds of non-pharmacological analgesia in healthy term neonates during heel prick.

Trial registration number (ClinicalTrials.gov): NCT01576432

What is already known on this topic

Breastfeeding, skin-to-skin contact and oral sucrose have shown analgesic properties in neonates for minor painful procedures.

What this study adds

Breastfeeding in addition to skin-to-skin contact provides superior analgesia compared to other types of non-pharmacological analgesia in healthy term neonates during heel prick.

INTRODUCTION

Heel lance for neonatal screening is the most frequent standardised painful procedure performed in healthy term newborns. Regardless of the available evidence, appropriate systematic analgesia in common painful procedures in neonates is far from adequate.[1 2]

Painful stimuli in neonates may have short-term physiologic (increase in intracranial pressure, increase in heart rate (HR) or decrease in oxygen saturation) and behavioural consequences (cry, eye squeeze)[3–5]; as well as long-term consequences (altered pain response in later infancy).[6] Different non-pharmacological methods of analgesia, such as sucrose,[7 8] skin-to-skin contact (SSC),[9 10] breastfeeding (BF),[11 12] sensorial saturation[13] or music,[14] have been used to reduce pain in neonates undergoing venipuncture or heel lancing, and different physiologic pathways to explain the underlying mechanism have been proposed; but studies about the analgesic effects of BF plus SSC are scarce.

A variety of valid and reliable pain assessment instruments have been developed over the past decades. The Neonatal Infant Pain Scale (NIPS)[15] and the Premature Infant Pain Profile (PIPP)[16] were selected by an international consensus neonatal pain group for acute procedural pain in neonates.[17]

Our main objective was to investigate the analgesic effect (measured with NIPS) of BF in addition to SSC versus other methods of non-pharmacological analgesia (namely, sucrose+SSC, SSC alone and sucrose) during blood sampling through heel lance in healthy term neonates. Furthermore, the influences of non-pharmacological methods on crying time, percentage of crying while sampling, HR, number of attempts and time of sampling were studied.

METHODS

Protocol

This randomised controlled trial was performed on 136 healthy term newborns in the maternity ward of a tertiary hospital. The inclusion criteria were as follows: healthy term neonates (37–41 weeks[6] of gestation) confirmed through a routine physical examination during the first 24 h of life, wish to breastfeed and absence of feeding during the previous 60 min. Exclusion criteria were as follows:

maternal use of opioids, birth under general anaesthesia, artificial feeding, previous capillar or venous sampling and previous admission to the neonatal unit.

Written informed consent was asked of parents during consultation. Study protocol and informed consent forms were approved by the local ethics committee.

Intervention

Participating neonates were randomly assigned to four groups: BF+SSC Group (n=35); Sucrose+SSC Group (n=35); SSC Group (n=33); or Sucrose Group (n=33). Randomisation was by closed envelopes and nurses and parents were masked to the randomisation group but not blinded to the treatment assignment. 268 opaque envelopes with the group assignment were made at the beginning of the study and mixed. Parents selected one envelope. In the BF+SSC Group, neonates dressed with a diaper were held in prone, in SSC with the mother; BF was started at least 5 min before heel lance and maintained during sampling. In the Sucrose+SSC Group, neonates were held in prone between the mothers' breast at least 5 min before sampling and 2 mL 24% sucrose was given with a sterile syringe in the mouth 2 min before heel lance. In the SSC Group, neonates were held between the mother's breast as in Sucrose+SSC Group, but no sucrose was given. In the Sucrose Group, 2 ml 24% sucrose was administered through a sterile syringe in the mouth 2 min before heel lance to neonates laid supine on a cot; the procedure was done in the presence of the mother. Mothers were allowed to speak or touch their babies in all the groups. The standardised procedure of heel prick in our hospital is such as described in the Sucrose Group.

Throughout the duration of the test, babies were continuously recorded with a video camera at least 2 min before sampling and 2 min after the procedure. The heel was warmed up by a glove with lukewarm water at least 2 min before the sample. Heel lance was made with an automated piercing device for routine neonatal screening for congenital disorders at 48 h of life. HR was monitored continuously by a pulse oximeter (Radical MasimoSet Datascope, Masimo Corporation, Irvine, California, USA) set on the infant's hand or foot. Special attention was given to three time points: t_0 (2 min before sampling); t_1 (the highest value of the first 10 s after heel prick); and t_2 (2 min after the procedure).

Blood sampling was performed through a standardised procedure by five experienced nurses, who obtained five dried spots of blood collected on a filter paper card. If the sample was not enough to complete all of the dried spots on the filter card, a new heel lance was practiced in few seconds. In this case, neonates were assessed for NIPS measure only after the first heel lance; secondary outcomes were evaluated during the whole sampling. Crying time was defined as the duration of crying while sampling. Percentage of crying was defined as the ratio between crying time while sampling and time of the procedure.

Pain scale

The NIPS scale is a validated six-indicator scale for the assessment of acute pain in neonates.[15 17] It measures movement of arms and legs, breathing patterns, cry, facial expression and state of arousal. Score ranges from 0 (no pain) to 7 (severe pain). NIPS score <4 means no pain to mild pain. NIPS score ≥4 means moderate-to-severe pain. NIPS score was measured continuously at three time points taking the highest value: $NIPS_0$ (between 110–120 s before sampling); $NIPS_1$ (between 0–10 s after heel prick); and $NIPS_2$ (between 120–130 s after sampling). $NIPS_2$ was not recorded if sampling had not finished at this time point. This took place in one newborn (2.8%) of the BF+SSC group, five (14.2%), six (18.1%) and five (15.1%) of the Sucrose+SSC, SSC and Sucrose groups, respectively. NIPS was measured by three researchers who watched the videos: one expert neonatologist (Observer 1) and two young paediatricians (Observers 2 and 3). Intraclass Correlation Coefficient (CCI) was >0.60 between observers (see online supplementary additional tables S1 and S2). Given the good correlation between observers, only data of the expert neonatologist is shown.

Statistical analysis

A sample size of 67 infants in each group was calculated to achieve a power of 80% with an α of 0.05 to detect a 0.5-point difference in the NIPS score (assuming SD=1). We decided to make a midpoint analysis when half of the neonates were recruited in order to detect if any of the analgesic methods was better than the standard procedure.

Results were expressed as mean (SD) or median (range). Box plots show the median, quartiles and extreme values for the variable. Categorical variables were analysed with the χ^2 test and the Fisher test. We compared mean between groups with the t test, the Analysis of Variance test and Bonferroni test. We used Mann–Whitney U test, non-parametric ANOVA and Kruskal–Wallis to compare median between groups. ICC is a measurement of agreement for continuous variables. The SPSS V.14.0 software package was used to perform all statistical analysis (SPSS Inc, Illinois, USA). A p-value of 0.05 was considered a statistically significant level of difference. The analysis of the main objective was conducted on an intention-to-treat. Secondary objectives were analysed according to protocol.

RESULTS

One hundred thirty-six neonates were included in the study and randomised as follows: 35 neonates each in BF+SSC and Sucrose+SSC Groups, and 33 neonates in the SSC and the Sucrose Groups (figure 1). The demographic features of the groups are shown in table 1. There were no significant differences between the groups in terms of maternal age, gestational age, birth weight, sex, mode of delivery or Apgar score.

The median NIPS score for each group, as well as crying time, percentage of crying while sampling, HR, number of attempts and duration of sampling is shown in table 2. For the primary end point, the BF+SSC group of infants achieved a significantly lower NIPS score compared with other groups. The percentage of neonates with moderate-to-severe pain was also lower in the BF+SSC group (11.4%) than in other groups (31.4% in Sucrose +SSC group; 51.5% in SSC group; 51.5% in Sucrose group).

Figure 2 shows NIPS score for each of the three study phases by infant group. During baseline, infants in the BF+SSC group had significantly lower NIPS score than those in the Sucrose +SSC group (p=0.002) and Sucrose group (p=0.04). During heel prick, NIPS score was also significantly lower in the BF +SSC group than in other groups (p≤0.01). Two minutes after the procedure, NIPS score in the Sucrose+SSC group was lower than the Sucrose group (p=0.02).

For the secondary end point (percentage of crying during blood sampling) both BF+SSC and Sucrose+SSC groups achieved significant lower percentages compared with SSC group.

There were no differences in HR during heel prick (correct hear rate measure was obtained at heel prick in 78.5% in BF +SSC group; 91.4% in Sucrose+SSC group; 60.6% in SSC group and 87.8% in Sucrose group), attempts of heel lances and sampling duration. No adverse effects were noted in any infant.

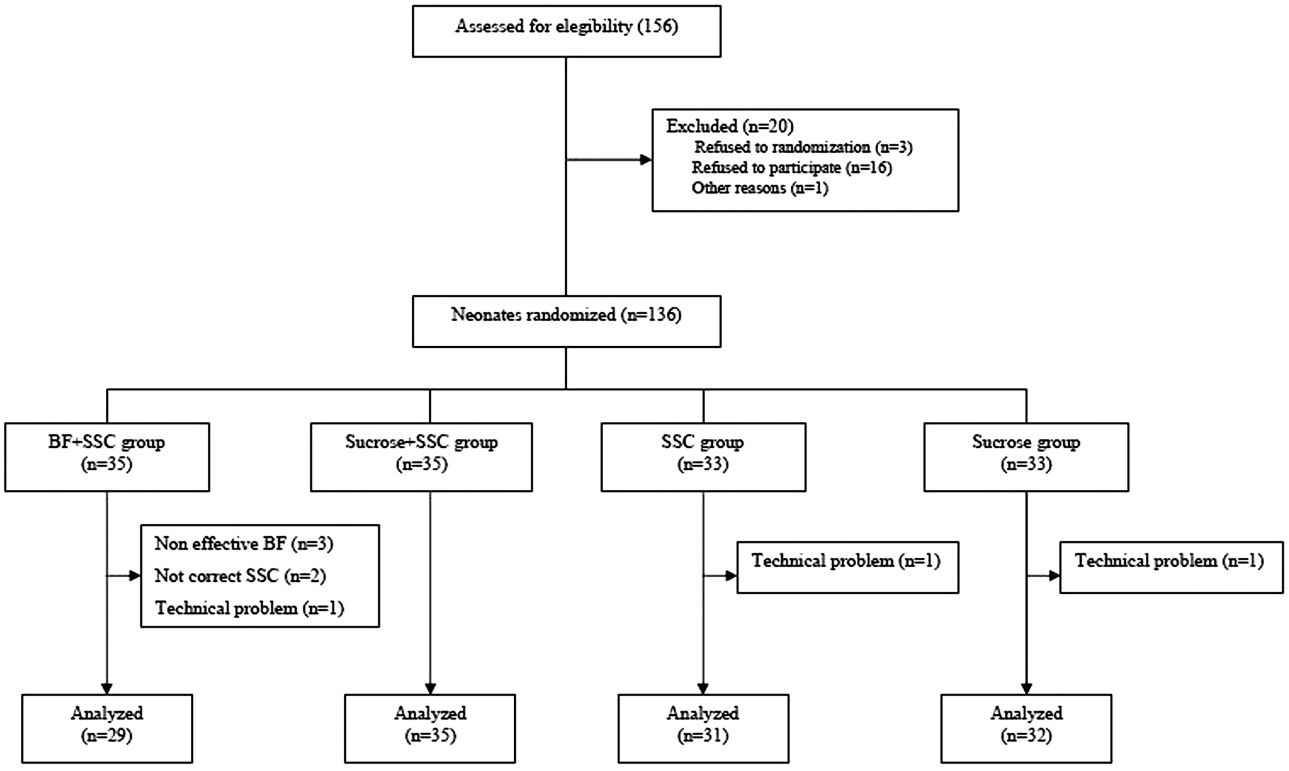


Figure 1 Neonates flow. BF, breastfeeding; SSC, skin-to-skin contact.

The study was finalised at midpoint analysis because the data showed that NIPS score was higher for our standardised method of sampling; therefore, it was considered unethical to continue the study.

DISCUSSION

This study suggests that BF in addition to SSC provides superior analgesia than other kinds of non-pharmacological analgesia in healthy term neonates during heel prick. We detected at least a 1.3-point difference in terms of NIPS mean score. The median NIPS score of one point in the BF+SSC group should be considered a minimal pain response. Moreover, the proportion of patients who experienced moderate-to-severe pain was also lower in the BF+SSC group. The outcomes regarding crying behaviour were better in the two groups where two non-pharmacological methods were associated. This result is clinically relevant as it shows that in otherwise healthy term neonates, analgesia for minor invasive procedures can be provided by a natural, worldwide available method, that is, BF in addition to SSC.

The main weakness of our study is that observers obviously recognised the four groups when they were evaluating the recordings. Mean NIPS score and HR were lower in the BF+SSC group prior to heel prick and may involve a lower state of arousal. However, in our opinion, this is insufficient to explain all differences observed in pain scores among groups. Another weakness of the study is related to the use of anaesthesia during labour. We have not controlled the amount of fentanyl used in the mother, and perhaps, it may have impacted on neonatal pain response. Our inability to detect statistically significant group differences in HR during heel prick may have been due to missing data. Another weakness of the study is related to scale use. Although the NIPS has been validated and used by many researchers, pain is a subjective experience, and its evaluation is only a first step to assess the effectiveness of analgesic interventions. Missing data in our study was greater in the BF+SSC group than in other groups. However, the proportion was less than 20%. Furthermore, analysis for the primary objective was conducted on an intention-to-treat, so differences obtained in pain scores may be true. The study was finalised at midpoint analysis and results may vary if the whole sample size was included.

Sucrose has been extensively evaluated for its effectiveness in the relief of procedural pain.[18–20] Several studies support a

Table 1 Maternal and neonatal baseline characteristics

	BF+SSC group	Sucrose+SSC group	SSC group	Sucrose group	p Value
Maternal age	32 (19–41)	33 (20–42)	32 (19–41)	33 (23–42)	0.65
Gestational age	40 (37–42)	40 (37–41)	39 (37–41)	39 (37–41)	0.35
Eutocic delivery	69.7%	77.1%	59.4%	63.6%	0.64
Apgar score 1 m	9 (6–9)	9 (5–10)	9 (7–10)	9 (7–10)	0.69
Apgar score 5 m	10 (8–10)	10 (8–10)	10 (9–10)	10 (9–10)	0.15
Birth weight, g	3289 (2266–4338)	3349 (2340–4108)	3359 (2832–3900)	3215 (1945–4176)	0.46
Male	68.6%	48.6%	66.7%	66.7%	0.26

Results expressed as median (range) for all the variables except for birth weight, expressed as mean (range); p value is a result of ANOVA test and χ^2 test.
BF, breastfeeding; SSC, skin-to-skin contact.

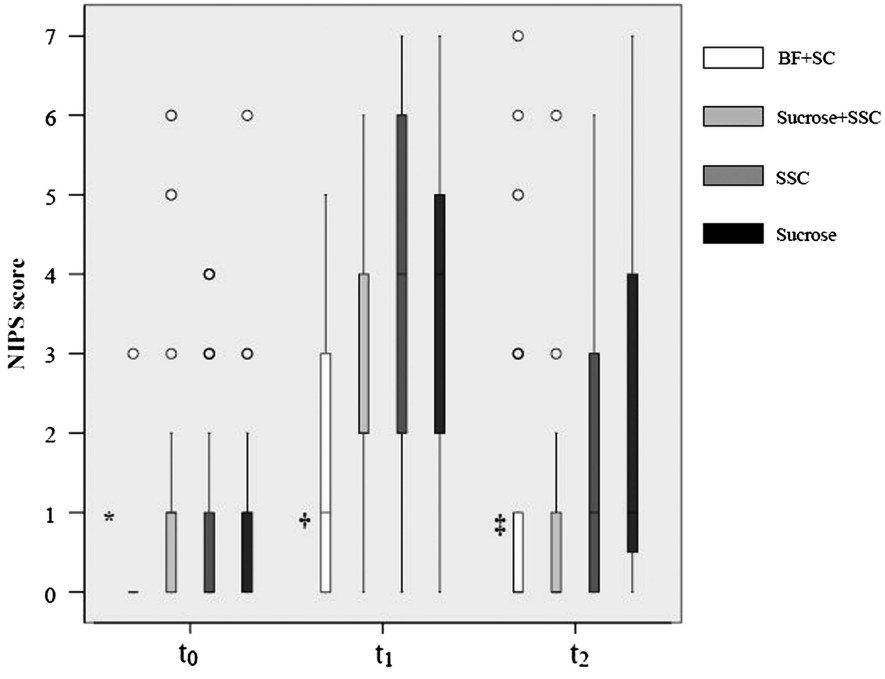
Table 2 Measures of NIPS score and other outcomes

	BF+SSC group	Sucrose+SSC group	SSC group	Sucrose group
$NIPS_0$	0 (0–0)[a,b]	1 (0–1)[a]	0 (0–1)	1 (0–1)[b]
HR-t_0	124 (17.2)[c,d]	141 (16.3)[c]	130 (18.5)	143 (16.8)[d]
$NIPS_1$	1 (0–3)[e]	2 (2–4)	4 (2–6)	4 (2–5)
HR-t_1	130 (15.2)	141 (19.4)	136 (23.5)	138 (15)
$NIPS_2$	0 (0–1)	0 (0–1)[f]	1 (0–3)	1 (0–4)[f]
HR-t_2	129 (21.4)	140 (30.5)	135 (23.4)	143 (19.9)
Crying time, s[g]	2 (0–25)	5 (0–26)	26 (1–62)	13 (2–74)
% of crying in blood sampling	3 (0–52.5)[h]	5 (0–41)[i]	52 (3–94)[h,i]	23 (1–91)
No. of heel lances, %				
1	93.1%	97.1%	81.3%	96.8%
2	6.9%	2.9%	18.7%	3.2%
Sampling duration, s	80 (50.1)	66 (34.2)	80 (50.1)	74 (40.4)

Results expressed as median and IQR for NIPS score, Crying time and % of crying in blood sampling. Results expressed as mean (SD) for Hear Rate and Sampling duration.
[a]p=0.002 between BF+SSC Group and Sucrose+SSC Group.
[b]p=0.04 between BF+SSC Group and Sucrose Group.
[c]p=0.007 between BF+SSC Group and Sucrose+SSC Group.
[d]p=0.001 between BF+SSC Group and Sucrose Group.
[e]p≤0.01 between BF+SSC Group and other groups.
[f]p=0.02 between Sucrose+SSC Group and Sucrose Group.
[g]p=0.01 between groups.
[h]p=0.02 between BF+SSC Group and SSC Group.
[i]p=0.03 between Sucrose+SSC Group and SSC Group.
BF, breastfeeding; NIPS, Neonatal Infant Pain Scale; SSC, skin-to-skin contact.

mechanism of action where sucrose mediates release of endogenous opioids,[21] although this has recently been challenged.[22] Although sucrose administration is the most studied non-pharmacological intervention for procedural pain relief, a recent review suggests that neither the exact dose nor the safety of sucrose has yet been established.[23]

In the same way, several studies have assessed the efficacy of breast milk or BF in reducing pain for minor procedures. In a recent research[24] it was observed that BF especially reduced crying and grimacing during heel-prick in contrast with infants swaddled in a bassinet. Codiprieto *et al*[25] conducted a randomised controlled trial with 101 term neonates allocated to BF (it took place without SSC and no specification was made about constant BF while sampling) or sucrose. They observed lower pain scores in the BF group. Carbajal *et al*[26] randomised 180 term neonates to be either breastfed, held by their mothers but not fed, given water placebo or given 30% glucose followed by a pacifier. Pain scores were significantly reduced for the breastfed group compared to all the other groups except for the glucose/pacifier group. It should also be noted that blood sampling was performed through



*p=0.002 between BF+SSC group and Sucrose+SSC group and p=0.04 between BF+SSC group and Sucrose group
†p≤0.01 between BF+SSC group and other groups
‡p=0.02 between Sucrose+SSC group and Sucrose group

Figure 2 Neonatal Infant Pain Scale score for each of the three study phases by infant group. t_0: 2 min before heel prick; t_1: During heel prick; t_2: 2 min after the heel prick. The '○' symbol means more than 1.5 times the IQR.

venipuncture and breastfeeding was continued throughout the sampling. In a randomised study, Upadhyay *et al*[27] assessed the effectiveness of expressed breast milk in reducing pain in term neonates. In this study, blood sampling was made through venipuncture, mean postnatal age was older than 7 days and control group received distilled water as placebo.

Similarly, SSC has been evaluated for potential procedural pain reduction. Castral *et al*[28] studied 59 preterm infants held in kangaroo care for 15 min before heel lance or lying in a lateral decubitus in an incubator. Neonatal facial coding system scores were significantly reduced in the SSC group. Johnston *et al*[29] randomised 74 preterm infants held in SSC 30 min before sampling or lying in a prone position in an incubator. PIPP scores were significantly lower in the kangaroo group. In a study of 30 healthy term newborn infants, Gray *et al*[30] randomised to either SSC or no contact as a control and found a reduction in the occurrence and duration of crying and grimacing in the SSC group.

Very few studies in the literature have investigated the antinociceptive effects of BF in addition to SSC during common pain procedures. Okan *et al*[31] randomised 107 neonates to three groups: being breastfed with SSC, being held in their mother's arms with SSC but not breastfed or lying on the table. They found that HR, oxygen saturation changes and length of crying were significantly reduced in the first and the second group, but no difference was found between the SSC group and the BF +SSC group. Our study revealed that BF in addition to SSC was superior not only to the SSC group but also to other groups in relation to the NIPS score. Moreover, percentage of crying while sampling was lower in the BF+SSC group and the Sucrose+SSC group than in the SSC group.

Physical proximity to the infant during SSC enables the mother to provide her baby containment, warmth, maternal heart beat sound, maternal odour and prone position.[32] There is evidence that touch-based interventions may be regulated by opiods and cholecystokinin, with other neuropeptides, playing an important role in infant stress and emotion regulation development.[33] Similarly, milk and fat have a postgastric antinociceptive effect that is mediated through the release of the cholecystokinin.[34] Moreover, suckling reduces energy expenditure through reduced crying, HR, and gross motor activity as well as decreased reactivity to noxious stimulation.[35] Thus, the association of BF and SSC may improve the analgesic effect by adding different pathways of pain reduction.

In conclusion, this study suggests that BF in addition to SSC provides superior analgesia than other kinds of non-pharmacological analgesia. This method could be regarded as a non-invasive, worldwide and natural way of reducing pain in healthy term neonates.

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Competing interests None.

Ethics approval Local Ethics Committee in Hospital Universitario Puerta de Hierro-Majadahonda.

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