

ORIGINAL ARTICLE

Venepuncture is preferable to heel lance for blood sampling in term neonates

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Background: The analgesic effect of oral sucrose in newborn infants undergoing painful procedures is generally accepted. For blood sampling, some studies have shown that venepuncture (VP) is less painful than heel lance (HL).

Objective: To determine the least painful and most effective method among blood sampling by VP or HL with or without sucrose.

Design: Randomised, double blind, placebo controlled trial.

Subjects: A total of 100 healthy, full term newborn infants being screened for inborn errors of metabolism were randomly allocated to one of four experimental groups (25 infants in each).

Intervention and outcome measure: Seven specially trained nurses took turns to carry out blood sampling two minutes after administration of oral sucrose or water. Neonatal pain was assessed by the neonatal facial coding system (NFCS), as well as by crying.

Results: Without sucrose, the NFCS score was higher in the HL group than the VP group during blood sampling (median 58 v 23, $p < 0.001$). Oral sucrose significantly reduced the score of the HL group (58 v 47, $p < 0.01$) and also tended to reduce the score of the VP group (23 v 2, $p < 0.1$). However, the HL with sucrose group still had a higher score than the VP without sucrose group (47 v 23, $p < 0.01$). Crying and the total procedure time showed the same trends as the NFCS score.

Conclusions: VP is less painful and more effective than HL for blood sampling in newborn infants. Although oral sucrose may have an additive analgesic effect, it is not necessarily required if VP is used for blood sampling.

It was long believed that newborn infants, especially premature infants, did not find painful stimuli unpleasant and could not remember painful experiences. However, recent studies have clearly proved that newborn infants possess sufficiently developed anatomical, physiological, and chemical systems to allow the perception of pain.¹ In fact, newborn infants may actually be more sensitive to pain than older children and adults.² Furthermore, painful experiences in the newborn period may have long term adverse effects later in life and even influence brain development and subsequent behaviour.³⁻⁶ On the basis of these findings, the following recommendations have been made for the prevention and management of pain in newborn infants: healthcare professionals should use appropriate interventions and should develop protocols to prevent, reduce, or eliminate neonatal pain.^{7,8}

The analgesic effect of oral sucrose has been studied for a decade and has generally been confirmed when administered before blood sampling or circumcision in neonates.⁹⁻¹⁸ Other studies have verified that venepuncture (VP) is less painful than the use of a heel lance (HL) for blood sampling in term neonates.¹⁹⁻²³ To confirm the assumption that VP after oral sucrose administration is the least painful method, and HL without sucrose is the most painful, we performed a randomised, four group comparison of VP or HL with or without prior administration of oral sucrose in term neonates. A similar study using oral glucose instead of sucrose showed that HL was more painful than VP without oral glucose pretreatment, whereas both methods were equally painful after oral glucose.²¹ However, in our study we used a placebo controlled, double blind design, unlike the trial of oral glucose. In addition, to avoid the possible bias originating from a single operator that was present in

previous studies that compared VP and HL, both sampling methods were performed randomly by several trained operators. To our knowledge, this is the first study to compare HL or VP combined with sucrose analgesia for blood sampling in neonates.

Because a lack of crying does not necessarily mean a lack of pain, we assessed pain responses by the neonatal facial coding system (NFCS), which is one of the standardised pain assessment scores,^{8,24} in addition to estimating the crying response.

MATERIALS AND METHODS

The study protocol was approved by the ethics committee of our hospital, and investigations were only performed after written informed consent had been obtained from a parent of each subject. The study was performed at the neonatal intensive care unit of Osaka Medical College Hospital between November 1999 and March 2000. Healthy, full term infants (gestational age ≥ 37 weeks) were consecutively enrolled in the study at the time of screening for inborn errors of metabolism. This was usually performed on day 5 of life, and at least 0.3 ml blood was needed to screen for six diseases simultaneously—phenylketonuria, maple syrup urine disease, homocystinuria, galactosaemia, congenital hypothyroidism, and congenital adrenal hyperplasia.

Practice for the sampling procedure

Seven experienced nurses were trained to perform HL and VP for about three months before the study. Each nurse practiced both manoeuvres repeatedly about 10 times each until sufficient blood was usually obtained by a single puncture.

Abbreviations: VP, venepuncture; HL, heel lance; NFCS, neonatal facial coding system

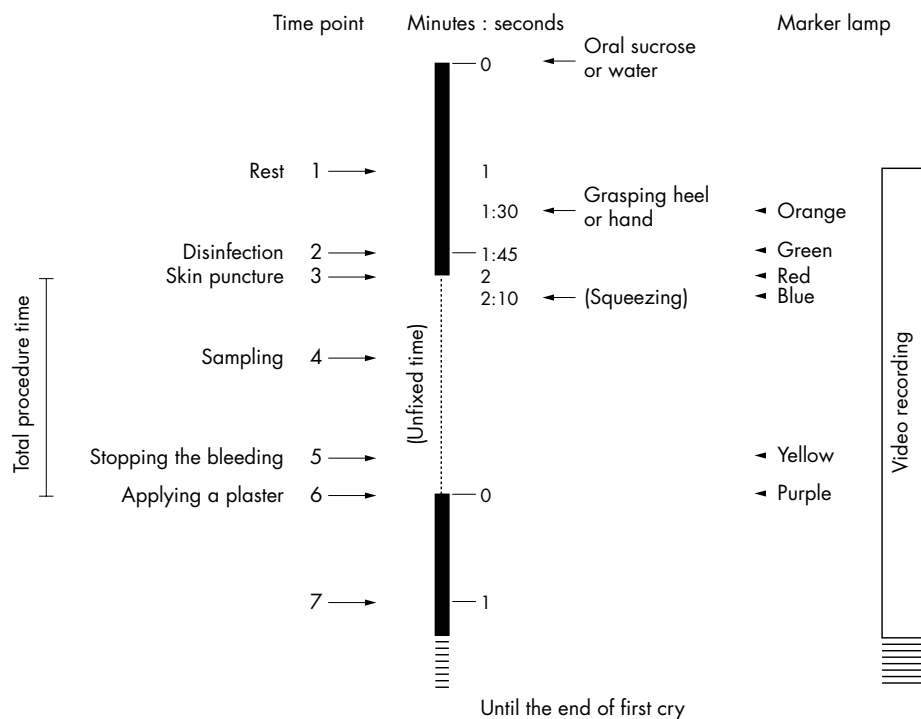


Figure 1 Experimental schedule. Point 4 was set five seconds before the middle of the interval between skin puncture (point 3) and the start of compression to stop bleeding (point 5). From 10 seconds after the skin puncture, squeezing to expel blood was permitted, if necessary. Audio-video recording was performed from one minute after oral administration (point 1) to one minute after application of the adhesive plaster (point 7). If an infant was still crying, recording was continued until the first cry ceased. Marker lamps were consecutively illuminated to indicate the time points to the nurse taking the blood sample as well as the video analyser. Total procedure time was defined as the duration between skin puncture (point 3) and application of the adhesive plaster (point 6).

Randomisation procedure

The infants were randomly allocated to one of four experimental groups of 25 infants each (HL or VP with or without oral sucrose) using 100 sealed envelopes. Each set of sequential procedures, including randomisation, sampling, and video recording, was carried out by a team of three nurses: nurse 1 performed the randomisation, the instructing of the other nurses about the oral medication and sampling method, and the video recording; nurse 2 performed the oral administration; nurse 3 performed the blood sampling. Seven nurses took turns in these roles. Sham procedures were not performed.

Sampling procedure

Figure 1 outlines the schedule for blood sampling. Just before blood sampling, the infants were resting quietly while awake or sleeping lightly two hours after their previous feed. Each infant was then placed on a flat table in the supine position and left alone for three minutes. Then nurse 2 blindly accepted a sterile syringe containing 50% sucrose or sterile water from nurse 1, instilled 1 ml liquid on to the tip of the infant's tongue within 30 seconds, and left the place of sampling. Two minutes after the oral administration, nurse 3 carried out blood sampling according to instructions from nurse 1. To estimate the response to the skin puncture per se, no effort to accelerate blood removal was made during the initial 10 seconds after the puncture by either sampling method. Figure 2 illustrates the method of immobilising the foot (HL) or hand (VP). Fifteen seconds after the skin had been wiped with alcohol soaked cotton wool, the skin puncture was performed using a standard lancet (HL) with a sharp triangular edge that was 2.5 mm long and 1 mm wide (Feather Safety Razor Co, Ltd, Osaka, Japan) or a 23 gauge needle. The heel was gently squeezed to expel blood

after 10 seconds of an undisturbed phase with the HL method, whereas squeezing was generally not carried out with the VP method if blood flow remained constant. With both methods, if blood flow ceased despite repeated squeezing, a further puncture was attempted by the same method. After sufficient blood had been obtained, the puncture site was gently compressed with an alcohol soaked cotton wool swab until bleeding ceased, and an adhesive plaster was applied.

Recording procedure

Nurse 1 recorded the facial expression and crying continuously with an audio-video camera (Sony PCR-PC3) mounted on a tripod, from one minute after the oral administration (point 1) to one minute after application of the adhesive plaster (point 7). If an infant was still crying, recording was continued until the crying ceased. Small coloured lamps were successively illuminated by nurse 1 to indicate the respective time points of the serial sampling procedure to nurse 3, and these were also recorded to mark the assessment time points for the video investigator (an orange lamp for grasping the heel or hand, a green lamp for disinfection, a red lamp for skin puncture, a blue lamp for permission to squeeze, a yellow lamp for stopping the bleeding, and a purple lamp for application of the adhesive plaster; fig 1).

Assessment of pain

A single investigator (SO), who was blinded to the sampling method as well as the use of oral sucrose, analysed all video recordings to assess neonatal pain. Ten facial actions were estimated according to the NFCS, including brow bulge, eye squeezing, nasolabial furrow, open lips, lip pause, vertical mouth stretch, horizontal mouth stretch, taut tongue, tongue protrusion, and chin quiver. From the seven time points

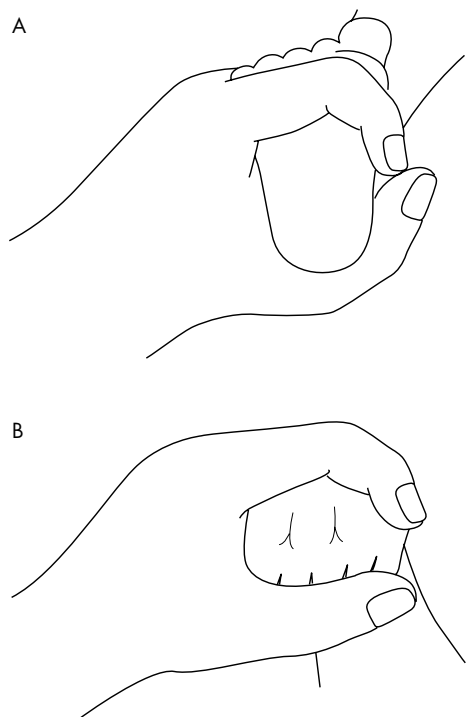


Figure 2 Method of immobilising the foot or hand. (A) In the groups in which heel lancing was performed, the nurse grasped the Achilles tendon with a thumb and the sole with the other fingers to grip the ankle tightly. Next, the heel was wiped with alcohol soaked cotton wool and then a standard lancet was inserted into the lateral border of the heel. (B) In the groups in which venepuncture was performed, the nurse grasped the fingers with a thumb and held the forearm with the other fingers to visualise the veins on the dorsum of the hand, then cleaned the skin with alcohol soaked cotton wool, and punctured an appropriate vein with a 23 gauge needle.

shown in fig 1, each facial action was scored as 1 point (present) or 0 points (absent) every second, and the score was accumulated for the following 10 seconds. Therefore the total score for each assessment point ranged from 0 to 100. Point 4 was set at five seconds before the middle of the time between skin puncture (point 3) and the start of stopping the bleeding (point 5). The duration of the first cry, which was defined as the duration of continuous, high pitched vocalisation before a quiet interval of five seconds, was also analysed.

Adverse effects

Any adverse effects of the procedure itself and those occurring after completion, including local bruising or haematoma, were recorded by nurse 1.

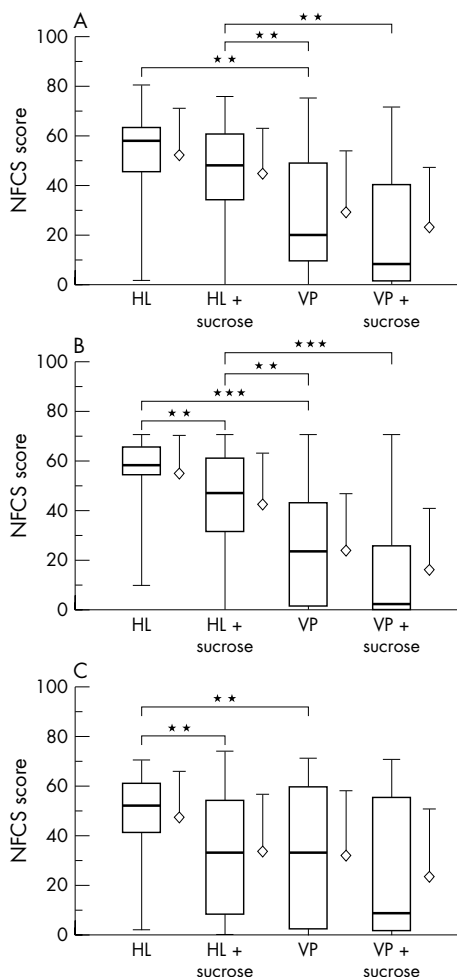


Figure 3 Box and whisker plot showing the median and interquartile range of the neonatal facial coding system (NFCS) score at the time of skin puncture (A), during blood sampling (B), and at the time when bleeding was being stopped (C). The mean and SD are also represented as the diamonds with bars. Intergroup differences were assessed by the Kruskal-Wallis test followed by the Mann Whitney U test: **p<0.01, ***p<0.001. HL, Heel lance; VP, venepuncture.

Statistical analysis

Differences between the groups were assessed by the Kruskal-Wallis test followed by the Mann Whitney U test for continuous variables or by the χ^2 test for categorical data. p<0.05 was considered significant. Data were analysed using SPSS statistical software (SPSS Inc, Chicago, Illinois, USA).

Table 1 Clinical characteristics of neonates investigated

	HL (n=25)	HL with sucrose (n=25)	VP (n=25)	VP with sucrose (n=25)
Gestational age (weeks)	40 (38–42)	39 (37–41)	39 (37–41)	39 (37–41)
Birth weight (g)	3030 (2530–3550)	2995 (2380–3590)	3274 (2295–3715)	3050 (2052–3425)
Apgar score				
at 1 min	10 (7–10)	9 (7–10)	9 (8–10)	10 (8–10)
at 5 min	10 (6–10)	10 (8–10)	10 (7–10)	10 (9–10)
Caesarean section (n)	1/25	5/25	3/25	4/25
Male (n)	12/25	14/25	12/25	14/25

Where applicable, values are median (range). Differences between the four groups were assessed by the Kruskal-Wallis test followed by the Mann-Whitney U test for continuous variables or by the χ^2 test for categorical data. There were no significant differences in any variables between the four groups. HL, Heel lance; VP, venepuncture.

RESULTS

Table 1 summarises the clinical characteristics of the infants studied. There were no significant differences between the groups with respect to any basic data. The distribution of the seven nurses among the groups was also approximately equal (data not shown).

NFCS score

There were no significant differences in the NFCS score during the 10 second assessment periods after resting (point 1), disinfection (point 2), application of the plaster (point 6), and one minute after application of the plaster (point 7).

As shown in fig 3, in the 10 second periods after the first skin puncture (point 3), during blood sampling (point 4), and during compression to stop bleeding (point 5), the VP with sucrose group had the lowest scores, whereas the HL without sucrose group had the highest scores. Without sucrose administration, the scores of the HL group were significantly higher than those of the VP group at all of these time points (median (interquartile range): 58 (46–63) v 20 (10–48) after skin puncture, 58 (54–65) v 23 (1–41) during blood sampling, and 52 (41–61) v 32 (2–59) while the bleeding was being stopped. Oral sucrose significantly reduced the scores of the HL group during blood sampling (58 (54–65) v 47 (31–60)) and while the bleeding was being stopped (52 (41–61) v 32 (8–54)). Although the difference was not significant, sucrose also tended to reduce the score of the VP group during blood sampling (23 (1–41) v 2 (0–25), $p < 0.1$). However, the scores of the HL with sucrose group were still significantly higher than those of the VP without sucrose group after skin puncture (47 (35–60) v 20 (10–48)) and during blood sampling (47 (31–60) v 23 (1–41)). In addition, even with oral sucrose, the differences between the HL and VP groups at either time were still significant (47 (35–60) v 9 (5–40) after skin puncture and 47 (31–60) v 2 (0–25) during blood sampling).

Crying

With respect to the duration of the first cry, the percentage of the first crying time relative to the total procedure time, and the number of crying babies, the rank of order was HL without sucrose, HL with sucrose, VP without sucrose, and VP with sucrose (table 2). In other words, the VP with sucrose group had the shortest duration of crying and the lowest frequency, whereas the reverse was true for the HL without sucrose group. Irrespective of sucrose administration, the difference in these variables between the HL and VP groups was significant. In addition, the differences were also significant between the HL with sucrose and VP without sucrose groups. Indeed, almost all of the infants in the HL group did cry, whereas half of the infants in the VP group did not cry. However, oral sucrose neither shortened the duration of the first cry nor reduced its incidence in the HL and VP groups.

Total duration and number of procedure

The total procedure time from skin puncture (point 3) to application of plaster (point 6) showed the same trend as the crying variables (table 2)—that is, the duration was shortest in the VP with sucrose group and longest in the HL without sucrose group. In contrast with the NFCS scores or crying features, the total procedure time for the HL with sucrose group was not significantly different from that for the VP without sucrose group. However, sucrose shortened the total procedure time in both the HL and VP groups.

No infant needed a second skin puncture.

Adverse effects

No apparent adverse effects were observed in any of the infants.

DISCUSSION

In this study, we reconfirmed the superiority of VP over HL with respect to pain control and efficient blood sampling in newborn infants. Our results agreed well with those of previous studies.^{19–23} An additive analgesic effect of oral sucrose was also observed for most of the variables tested in the HL and VP groups, although statistical analysis only revealed a significant improvement of the NFCS scores in the HL group and total procedure time in both the HL and VP groups.

Most previous studies on the prevention and management of pain in newborn infants targeted HL as a painful procedure, and these studies generally detected an analgesic effect of oral sucrose. Our data for the HL group confirmed these earlier findings. Only a few studies have been conducted on other painful procedures such as VP or circumcision. We found three studies on the effect of sucrose on VP, and all of them detected a pain relieving effect of oral sucrose.^{15 25 26} Perhaps because of the wide variation in NFCS scores in the VP group, our study would have required a sample size of 100 infants per group to achieve 80% power at a 5% level of significance for detecting a difference in the scores between VP with and without sucrose. Therefore we acknowledge that our study was underpowered for detecting a beneficial effect of oral sucrose on pain during VP.

Only one other study has examined the combined effect of a sweet oral solution on HL or VP.²¹ Glucose was used in that study instead of sucrose, and the pain score (premature infant pain profile) was estimated by an observer who was not blinded to the sampling method. The authors concluded that the pain caused by HL and VP was comparable after oral glucose administration, in contrast with our finding that VP was less painful than HL irrespective of sucrose pretreatment.

The most distinctive feature of our study is that seven specially trained nurses performed both HL and VP in turn, unlike previous studies in which VP was carried out by a single investigator. The difference between our findings and

Table 2 Crying variables and total procedure time

	HL	HL with sucrose	VP	VP with sucrose
Duration of first cry (s)	121 (0–344)††† 156 (108)	102 (0–460)†††,‡‡‡ 135 (128)	8 (0–349) 44 (77)	0 (0–224) 30 (58)
Total procedure time (s)	180 (61–397)*,††† 174 (93)	111 (53–358) 128 (71)	93 (29–321)‡‡ 109 (67)	68 (22–273) 86 (69)
First crying time/total procedure time (%)	106 (0–395)†† 113 (89)	108 (0–318)††,‡‡‡ 114 (85)	8 (0–271) 48 (73)	0 (0–470) 61 (133)
Crying;no crying	24:1††	24:1††,‡‡	13:12	10:15

Values are median (range) and mean (SD).

Intergroup comparisons were performed by the Kruskal-Wallis test followed by the Mann-Whitney U test for continuous variables or by the χ^2 test for categorical data: * $p < 0.05$ v HL with sucrose; †† $p < 0.01$, ††† $p < 0.001$ v VP without sucrose; ‡‡ $p < 0.01$, ‡‡‡ $p < 0.001$ v VP with sucrose.

The duration of the first cry was defined as the duration of continuous, high pitched vocalisation before a quiet interval of five seconds. Total procedure time was defined as the period from skin puncture to application of a plaster. HL, Heel lance; VP, venepuncture.

What is already known on this topic

- The analgesic effect of oral sucrose is generally accepted in newborn infants undergoing painful procedures
- For blood sampling, some studies have shown that venepuncture is less painful than heel lance

What this study adds

- The superiority of venepuncture over heel lance with respect to pain control and efficient blood sampling in newborn infants is confirmed
- With regard to pain control, oral sucrose is not necessarily required when venepuncture is chosen as the method of blood sampling, although oral sucrose may have an additive analgesic effect

earlier results may be partly explained by this study design. Although interprocedural variation is certainly reduced when a single person carries out all the procedures, there is a risk of an unexpected bias peculiar to the individual. Moreover, assessment of the effect of multiple personnel provides a study design that is closer to the actual clinical setting.²³

The diversity of the methods used to assess neonatal pain further complicates any attempt to make comparisons between studies. The NFCS score is a well validated pain assessment system, although it depends entirely on behavioural responses and does not take any physiological indicators into account. Behavioural changes associated with pain (such as crying and various facial expressions) may also accompany non-painful procedures and may even appear spontaneously. Moreover, neonatal pain is not necessarily accompanied by behavioural reactions. Therefore it is theoretically preferable to assess pain using a multidimensional composite score that includes both behavioural and physiological indicators.^{7, 8} However, the significance of physiological variables such as heart rate and breathing pattern as indicators of neonatal pain has not yet been clearly confirmed.²¹ Therefore we decided to use the NFCS score for this study, although this could also be seen as the main disadvantage of our methodology. Further studies using several validated pain scores are needed to confirm the most suitable method of blood sampling in neonates.

In conclusion, VP is less painful and more effective than HL for blood sampling in newborn infants. With regard to pain control, oral sucrose is not necessarily required when VP is chosen as the method of blood sampling, although it may have an additive analgesic effect. It is generally thought that VP is more difficult to perform and takes longer to learn than HL, but we found that only about 10 practice procedures were needed to become proficient at VP. Therefore we recommend VP over HL for neonatal blood sampling.

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Competing interests: none declared

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