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

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Keywords
Venepuncture, Heel lance, Sucrose, Pain, Analgesia
Abstract

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

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

**Design:** Randomized, double-blind placebo-controlled trial.

**Subjects:** One hundred healthy full-term newborn infants who underwent screening for inborn errors metabolism were randomly allocated to one of four experimental groups (25 infants each).

**Intervention and outcome measure:** Seven specially trained nurses performed blood sampling in turn at 2 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 vs. 23, \(p<0.001\)). Oral sucrose significantly reduced the score of the HL group (58 vs. 47, \(p<0.01\)) and also tended to reduce the score of the VP group (23 vs. 2, \(p<0.1\)). However, the HL with sucrose group still had a higher score than the VP without sucrose group (47 vs. 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.

**Abbreviations**

VP, venepuncture

HL, heel lance

NFCS, Neonatal Facial Coding System
Introduction

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. In fact, newborn infants may actually be more sensitive to pain than older children and adults. Furthermore, painful experiences in the newborn period may show long-term adverse effects later in life and even have an influence on brain development and subsequent behaviour. On the basis of these findings, recommendations have been devised for the prevention and management of pain in newborn infants, which state that health care professionals should use appropriate interventions and should develop protocols to prevent, reduce, or eliminate neonatal pain.

The analgesic effect of oral sucrose has been studied for a decade and has generally been confirmed when administered prior to blood sampling or circumcision in neonates. Other studies have verified that venepuncture (VP) is less painful than use of a heel lance (HL) for blood sampling in term neonates. In order to confirm the assumption that VP following oral sucrose administration is the least painful method, while HL without sucrose is the most painful, we performed a randomized four-group comparison of VP or HL with or without prior administration of oral sucrose in term neonates. Using oral glucose instead of sucrose, a similar study previously showed that HL was more painful than VP without oral glucose pretreatment, whereas both methods were equally painful after oral glucose. However, the present study employed a placebo-controlled, double-blind design, unlike the trial of oral glucose. In addition, to avoid possible bias originating from a single operator in previous studies comparing VP and HL, both sampling methods were done randomly by several pretrained 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 standardized pain assessment scores, 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 of blood was needed to screen for 6 diseases simultaneously (i.e., phenylketonuria, maple syrup urine disease, homocystinuria, galactosemia, congenital hypothyroidism, and congenital adrenal hyperplasia).

Practice for the sampling procedure
Seven experienced nurses were trained to perform HL and VP for about 3 months prior to the study. Each nurse practiced both maneuvers repeatedly about 10 times each until sufficient blood was usually obtained by a single puncture.

Randomization 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 envelops. Each set of sequential procedures, including randomization, sampling, and videorecording, was carried out by a team of 3 nurses, one performed randomization, instructions of the oral medication and sampling method to the other nurses, as well as videorecording (nurse 1), one performed oral administration (nurse 2), and third performed blood sampling (nurse 3). The seven nurses took turns in these roles. Sham procedures were not done.

Sampling procedure
The schedule for blood sampling is outlined in fig 1. Just prior to blood sampling, the infants were resting quietly while awake or sleeping lightly at 2 hours after their previous feed. Each infant was then placed on a flat table in the supine position and left alone for 3 min. Then a nurse (nurse 2) blindly accepted a sterile syringe containing 50% sucrose or sterile water from nurse 1, instilled 1 ml of liquid onto the tip of the infant’s tongue within 30 sec, and left the sampling place. Two minutes after oral administration, nurse 3 carried out blood sampling according to the instructions of nurse 1. To estimate the response to skin puncture per se, no effort to accelerate blood removal was made during the initial 10 sec after puncture by either sampling method. The method of immobilizing the foot (HL) or hand (VP) is illustrated in fig 2. Fifteen
seconds after wiping the skin with alcohol-soaked cotton wool, skin puncture was done 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 sec of undisturbed phase with the HL method, whereas squeezing was generally not done for the VP method if blood flow remained constant. With both methods, if blood flow ceased despite repeated squeezing, 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 1 min after oral administration (point 1) to 1 min after application of the adhesive plaster (point 7). If an infant was still crying, recording was continued until the crying ceased. Small colored 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, analyzed all video-recordings to assess neonatal pain. Ten facial actions were estimated according to the NFCS, including brow bulge, eye squeezing, naso-labial furrow, open lips, lip pause, vertical mouth stretch, horizontal mouth stretch, taut tongue, tongue protrusion, and chin quiver. From the 7 time points shown in fig 1 (point 1: rest, 2: disinfection, 3: skin puncture, 4: sampling, 5: stopping the bleeding, 6: plastering, and 7: 1 min after plaster application), each facial action was scored as 1 point (present) or 0 points (absent) every second and the score was cumulated for following 10 seconds. Therefore, the total score for each assessment point ranged from 0 to 100. Point 4 was set at 5 sec before the middle of the time between skin puncture (point 3) and the start of arresting the bleeding (point 5). The duration of first cry, which was defined as the duration of continuous high-pitched vocalization before a quiet interval of 5 seconds, was also analyzed.

**Adverse effects**

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

**Statistics**

Differences between the groups were assessed by Kruskal-Wallis test followed by Mann-Whitney U test for continuous variables or by chi-square test for categorical data. A p value < 0.05 was considered significant. Data were analyzed using SPSS statistical software (SPSS Inc, Chicago, IL, USA).

**Results**

Table 1 summarizes the clinical characteristics of the infants studied. There were no significant differences between the groups with respect to any demographic data. The distribution of the 7 nurses among the groups was also approximately equal (data not shown).

**NFCS score**

There were no significant differences of the NFCS score during the 10-sec assessment periods after resting (point 1), disinfection (point 2), plastering (point 6), and 1 min after plastering (point 7). As shown in fig 3, in the 10-sec 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] vs. 20 [10-48] after skin puncture, 58 [54-65] vs. 23 [1-41] during blood sampling, and 52 [41-61] vs. 32 [2-59] while stopping the bleeding). Oral sucrose significantly reduced the scores of the HL group during blood sampling (58 [54-65] vs. 47 [31-60]) and while stopping the bleeding (52 [41-61] vs. 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] vs. 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] vs. 20 [10-48]) and during blood sampling (47 [31-60] vs. 23 [1-41]). In addition, even with oral sucrose, the differences between the HL and VP groups at either time were still statistically significant (47 [35-60] vs. 9 [5-40] after skin puncture and 47 [31-60] vs. 2 [0-25] during blood sampling).
Crying
With respect to the duration of 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 of these variables between the HL and VP groups was statistically 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 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 plastering (point 6) showed the same trend as the crying variables (table 2). That is, the duration was the shortest in the VP with sucrose group and it was the longest in the HL without sucrose group. In contrast to 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 the present 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][20][21][22][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 of the previous studies on the prevention and management of pain in newborn infants were performed targeting HL as a painful procedure and these studies generally detected an analgesic effect of oral sucrose. Our data for the HL group did not contradict these earlier findings. Only a few previous studies have been conducted on other painful
procedures such as VP or circumcision. We found three studies about the effect of sucrose on VP, and all of them detected a pain-relieving effect of oral sucrose.[15][25][26] Perhaps due to wide variation of the NFCS scores in the VP group, our study would have required a sample size of 100 infants per group to achieve an 80% power of test at a 5% level of significance for detecting a difference in the scores between VP with and without sucrose. Therefore, it is undeniable that our study was underpowered to detect a beneficial effect of oral sucrose on pain during VP.

There has only been one other study that 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 to our finding that VP was less painful than HL irrespective of sucrose pretreatment.

The most distinctive feature of our study was that 7 specially trained nurses performed both HL and VP in turn, unlike previous studies in which VP done by a single investigator. The difference between our findings and earlier results may be partly explained by this study design. Although inter-procedural 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, though 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 like the heart rate and breathing pattern as indicators of neonatal pain has not yet been clearly confirmed.[21] Therefore, we decide to use the NFCS score for the present 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 oral sucrose 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 enough to become proficient at VP. Therefore, we recommend VP over HL for neonatal blood sampling.

Acknowledgments
The authors thank the doctors and nursing staff of the neonatal intensive care unit for their kind assistance and advice.

Competing Interests
No competing interests are existed.

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Figure Legends

Figure 1
Experimental schedule. Point 4 was set 5 sec before the middle of the interval between skin puncture (point 3) and the start of compression to stop bleeding (point 5). From 10 sec after skin puncture, squeezing to expel blood was permitted, if necessary. Audio-video recording was performed from 1 min after oral administration (point 1) to 1 min 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 analyzer. Total procedure time was defined as the duration between skin puncture (point 3) and application of the adhesive plaster (point 6).

Figure 2
Method of immobilizing the foot or hand. A). In the HL groups, 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 VP groups, the nurse grasped the fingers with a thumb and held the forearm with the other fingers to visualize the veins on the dorsum of the hand, cleaned the skin with an alcohol-soaked cotton wool, and punctured an appropriate vein with a 23-gauge needle. HL: heel lance, VP: venepuncture.

Figure 3
Box and whisker plot showing the median and inter-quartile range of the NFCS score at the time of skin puncture (A), during blood sampling (B), and at the time of stopping the bleeding (C). The mean and SD are also represented as the diamonds with bars. Inter-group differences were assessed by Kruskal-Wallis test followed by Mann-Whitney U test. HL: heel lance, VP: venepuncture.
** p < 0.01, and *** p < 0.001
References


Table 1  Clinical characteristics

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

Values are the median (range). Differences between the four groups were assessed by Kruskal-Wallis test followed by Mann-Whitney U test for continuous variables or by chi-square test for categorical data. There were no significant differences of any variables between the four groups.

HL, heel lance; VP, venepuncture
Table 2  Crying variables and total procedure time

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

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

Inter-group comparisons were performed by Kruskal-Wallis test followed by Mann-Whitney U test for continuous variables or by chi-square test for categorical data. The duration of first cry was defined as the duration of continuous high-pitched vocalization before a quiet interval of 5 seconds. Total procedure time was defined as the period from skin puncture to application of a plaster. *p<0.05 vs. HL with sucrose, ††p<0.01, †††p<0.001 vs. VP without sucrose, ‡‡p<0.01, ‡‡‡p<0.001 vs. VP with sucrose.

HL, heel lance; VP, venepuncture.
Time point | min:sec | Oral sucrose or water | Marker lamp
---|---|---|---
rest | 1 | | orange
disinfection | 2 | | green
skin puncture | 3 | | red
sampling | 4 | | blue
stopping the bleeding | 5 | | yellow
applying a plaster | 6 | | purple
until the end of first cry | 7 | |