

Effect of oral glucose administration on pain in neonates undergoing peripheral blood collection

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Abstract

Background Peripheral blood sampling with heel sticks in neonates could represent minor invasive procedure which generates pain. The oral glucose administration can reduce the pain in neonates during this procedure.

Objective To compare the pain sense after oral glucose administration or placebo during peripheral blood sampling with heel sticks in neonates.

Methods A double blind randomized clinical trial study was conducted from January to March 2004 in three teaching hospitals in Medan. The population of this study was divided into two groups (glucose and placebo) and each group consisted of 32 neonates. The intervention group got 1 ml of 40% glucose and the placebo group got 1 ml of sterile water. Blood sample was taken with sterile hemolet with heel sticks from healthy aterm neonates. The pain was measured using NIPS score and measured in first 30 seconds after heel sticking. The heart and respiratory rate measurement was done before and during the intervention and we also counted crying time. Data were analyzed with student t-test.

Results The significant mean difference of NIPS score in glucose group was 2.22 (SD 0.83) vs 4.72 (SD 0.96) in placebo group ($P \leq 0.0001$). There was significant mean difference of crying time, i.e. 0.16 (SD 0.37) in glucose group vs 2.05 (SD 0.77) in placebo group ($P \leq 0.0001$). There was significant differences of heart rate before and during heel sticking in both groups.

Conclusion There were some differences of pain sense in neonates who received 40% glucose compared to those who received sterile water during peripheral blood sampling. [Paediatr Indones 2007;47:185-188].

Keywords: pain, glucose, neonates, blood sample.

Blood sampling done with heel sticks, or with vein puncture, represents minor invasive procedure which often could generate pain.^{1,2} According to Shah *et al*³, heel sticks could produce more pain, but it is far easier and more modest compared to vein puncture.

The analgesic procedures in neonates is often neglected for it is assumed that their sensoric nerve have not well developed enough as in adults. This problem has been debated whether neonates require analgesic or not. It also have been figured out that the nerve growth of neonates have already started even in preterm babies. It is understood that invasive procedure in neonates without analgesic could also produce pain.⁴

Some studies have shown that the administration of oral glucose could lessen the pain in neonates during the minor invasive procedure. This effect was proven by the release of endorphin (which represents

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an endogenous opiate hormone that produced by our body and has the same characteristic as morphine) and by the mechanism of preabsorption related to the sweet tasting.^{1,5} Gradin *et al*¹ have shown that oral glucose could lessen pain, and it was proven to lower the pain score about 20% in oral glucose group compared to EMLA group (Eutectic Mixture Local Anesthetics), which is about 40%.

The aim of this study was to compare the pain in neonates after the administration of oral 40% glucose or placebo during the peripheral blood sampling with heel sticks.

Methods

A double blinded randomized clinical trial was done in Perinatology Ward in H. Adam Malik Hospital, Dr. Pringadi Hospital and Tembakau Deli Hospital (three of them were teaching hospitals in Medan, North Sumatera). Subjects of this study were healthy term neonates delivered at those three hospitals from January to March 2004. Sample size of 32 neonates for each group was attempted. The inclusion criteria were neonates with ≥ 37 weeks gestation period and birth weight ≥ 2500 grams. We excluded neonates with neurological problems, those with oxygen therapy, and all neonates who accepted sedatives in the previous 24 hours.

The babies were lied down on the bed. In a quite situation, we measured the neonates heart and respiratory rate by using LitmanTM stethoscope. Two minutes before heel sticks procedure, 1 ml of 40% glucose or 1 ml placebo (sterile aqua) was put into babies mouth with a syringe for about 15 seconds. Blood

sample was taken with sterile hemolet by sticking the medial peripheral or lateral foot heel which had already been disinfected with 70% alcohol, within deepness 2.5 mm in dorsiflexion position.⁶ Afterwards, the pain response was immediately measured with NIPS score, heart rate and respiratory rate were recounted during heel sticking and the crying time was measured using a stopwatch.

The pain response was measured with Neonatal Infant Pain Scale (NIPS) score in first 30 seconds after heel sticking. This scale consisted of 0 to 7 score. Each pain response use three scales point with 0 = no pain, 1 = little pain, 2 = very painful.³ The evaluated items were: face expression while crying, breathing pattern, foot and hand position, and also the alert situation (wake up or sleeping) during heel sticking.⁴ (Appendix)

Data were analyzed with SPSS version 10.0. The independence t-test was used to check the difference of mean pain score, crying time, heart and respiratory rate. The paired t-test was used to define the mean difference of heart and respiratory rate before or during the heel pricks. The level of significance was $P < 0.05$.

Results

There were no significant difference between the glucose and placebo groups baseline characteristics (Table 1). Table 2 shows that there was a significant difference between glucose and placebo group in NIPS score following the procedure. Significant difference was also noted between the glucose and placebo groups in terms of crying time (Table 3) and heart rate (Table 4).

Table 1. Neonates characteristics

| Characteristics | Glucose group | | | Placebo group | | | P |
|--------------------------|---------------|---------|--------|---------------|---------|--------|-------|
| | n | Mean | SD | n | Mean | SD | |
| Gender | | | | | | | |
| - Boys | 21 | | | 16 | | | 0.200 |
| - Girls | 11 | | | 16 | | | |
| Maternity Type | | | | | | | |
| - Spontaneous | 11 | | | 12 | | | 0.786 |
| - <i>Sectio caesarea</i> | 20 | | | 18 | | | |
| - Vacuum | 1 | | | 2 | | | |
| Birth weight (gram) | 32 | 3323.56 | 394.72 | 32 | 3316.56 | 395.14 | 0.945 |
| Birth length (cm) | 32 | 48.59 | 1.19 | 32 | 48.81 | 1.89 | 0.581 |
| Last time drink (minute) | 32 | 54.38 | 33.40 | 32 | 51.88 | 31.15 | 0.758 |

Table 2. Comparison of NIPS score between glucose and placebo group

| NIPS Score | N | Mean | SD | P |
|------------|----|------|------|--------|
| Glucose | 32 | 2.22 | 0.83 | 0.0001 |
| Placebo | 32 | 4.72 | 0.96 | |

Table 3. Comparison of crying time between glucose and placebo group

| Crying time | N | Mean | SD | P |
|-------------|----|------|------|--------|
| Glucose | 32 | 0.16 | 0.37 | 0.0001 |
| Placebo | 32 | 2.05 | 0.77 | |

Discussion

This study shows the influence of oral glucose to reduce the pain while taking the neonate blood sample with heel sticks. The measurement of pain in neonates was difficult because the pain was a subjective phenomenon, various pain scales have been used to assess the pain sense. NIPS represents one of the measurement pain scale in neonates which scaled within 0 up to 7.^{3,7} The NIPS score of oral glucose group after taking the blood sample with heel stick showed lower score compared with that of the placebo group. This result was the same as that of the study done by Gradin *et al*¹. Jatana *et al*⁸ found that the administration of oral glucose could reduce the pain score. Besides the easy availability, the other advantages of oral glucose are that, it also gives quick effect and it is well tolerated by neonates.¹

Many sweet-tasted liquid such as glucose, sucrose and fructose have been used in analgesic study in neonates. The quality of each sweet-tasted liquid to stimulate taste sense is very difficult to check because human is assumed to be unable to differentiate the sense between the three of them; this condition is called monogeusia. The inability to differentiate the taste between glucose, fructose and sucrose would explain why the three of this liquid could be used for study.⁹ We used 40% glucose concentration since 40% glu-

cose concentration is widely available at home and drug store, so it is easy to be used directly.

Crying may represent a real form of pain for most neonates. This study found significant difference of crying time between the glucose and placebo groups. Studies show the significant difference of crying time among glucose group and EMLA compared with glucose and sterile water. Use of pacifier along with glucose has been done and shows synergic effect;¹⁰ the result is better in preterm than in term babies.¹¹ We did not use pacifier in our study.

The heel sticking procedure could stimulate the activation of sympathetic nerve system, and it was marked with the increase of heart rate, even though that the change was not the only way to determine the effect of that intervention and it is also difficult to interpret as a consequence of no-pain action.¹ A study in Germany found that the administration of oral glucose could degrade the pain expression and crying time in neonates. But in the reality, oral glucose could not prevent the increase of heart rate.¹²

The effect of glucose as an analgesic have been studied on the correlation of endorphin-activated mechanism and the mechanism of sweet flavor preabsorption sense.^{1,5,10} Endorphin was one of the neurotransmitter which role was in part of pain suppressor. How glucose stimulates the release of endorphin was still unknown yet.⁸ The endorphin was produced by fetus during delivery and had role during distress period of neonates.⁷ The plasma endorphin concentration in neonates increases with the administration of oral glucose, but in this study, we were not able to measure the endorphin concentration after the administration of oral glucose, due to facility limitation in our hospitals.

We conclude that there is a significant difference of pain between neonates who were given oral glucose compared with those given the placebo during the peripheral blood sampling with heel sticks.

Table 4. Neonates heart and respiratory rate before and during heel sticking in both groups

| Variables | Group | \bar{x} | \bar{x} | Paired t-test | Increased \bar{x} | P |
|------------------|---------|-------------------|-------------------|---------------|---------------------|--------|
| | | Before heel stick | During heel stick | | | |
| Heart rate | Glucose | 128.56 | 133.06 | 0.0001 | 4.5±3.2 | 0.0001 |
| | Placebo | 128.72 | 138.75 | 0.0001 | 10.0±5.1 | |
| Respiratory rate | Glucose | 41.81 | 43.38 | 0.032 | 1.56±3.93 | 0.310 |
| | Placebo | 42.31 | 45.56 | 0.038 | 3.25±8.47 | |

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