

## ORAL HYPERTONIC GLUCOSE, FOR ANALGESIA IN THE PREMATURE NEWBORNS

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**Background:** A number of studies have shown that orally administered sweet tasting solutions reduce signs of pain during painful procedures in the term newborns. The aim of the present study was to compare the pain reducing effect of orally administered glucose with that of placebo during venipuncture in preterm infants. **Methods:** A Randomized, double-blind, placebo controlled trial was carried out at the neonatal intensive care unit at the Alzahra Hospital –Isfahan-Iran from June to September 2005. Thirty six preterm newborns (gestational age 28-34 weeks; postnatal age (1-14 days) undergoing venipuncture for clinical purposes, were enrolled in the study. Each infant was assessed two times receiving 1 ml 30% glucose or 1 ml sterile water by mouth, 2 minutes before venipuncture. The behavioral pain reactions were scored with the Premature Infant Pain Profile and duration of crying and heart rate were measured. **Results:** The PIPP scores were significantly lower in the glucose group compared with the placebo group ( $8.94 \pm 3.013$  VS  $11.44 \pm 3.42$  respectively,  $P < 0.001$ ). The duration of crying in the first 3 minutes was significantly lower in 30% glucose compared with placebo group ( $24.1 \pm 18.48$  VS  $39.6 \pm 26.8$  respectively,  $P = 0.002$ ). **Conclusion:** We found that 30% glucose may be a useful and safe analgesic for minor procedures in preterm newborns.

**Key words:** Pain, Preterm, Glucose, newborn

### INTRODUCTION

Newborns routinely experience pain associated with invasive procedures such as blood sampling, immunization, vitamin K injection or circumcision. The sick or preterm infant may experience repetitive or prolonged pain resulting from many diagnostic, surgical or therapeutic procedures.<sup>1,2</sup>

Although the exact gestational age of nociceptive capacity to feel pain has not readily been determined, the fetus is likely to have the nociceptive capability to feel pain from around 20-24 weeks of gestational age.<sup>3</sup> There is now a growing body of evidence that multiple painful and stressful events undergone by infants born prematurely not only induce acute changes, but that permanent structural and functional changes may also result.<sup>4</sup> Therefore a proper management analgesia in newborns who require medical procedures is mandatory.<sup>5</sup> Oral sucrose, with and without nonnutritive sucking, has been the most frequently studied nonpharmacological intervention for pain relief during minor procedures in neonates.<sup>6</sup>

Oral glucose was effective in reducing symptoms associated with pain from venipuncture in term neonates<sup>7-8</sup> but the analgesic effects of oral glucose in premature infants has not yet been reported in literature.<sup>5</sup> The aim of this study was to compare the pain reducing effect of orally administered glucose with that of sterile water during venipuncture in newborns.

### MATERIAL AND METHODS

A double blind, randomized placebo controlled trial was carried out in the neonatal intensive care unit of Alzahra Hospital-Isfahan-Iran over a four month period from June to September 2005. Written informed consent was obtained from parents of each newborn before the infant participated in the study. A total of 36 neonates were enrolled in the study. The inclusion criteria were: gestational age between 28 to 34 weeks (as assessed by new Ballard score); postnatal age of more than 1 day and less than 14 days; breathing spontaneously and clinically stable. Babies with APGAR score  $< 3$  at 5 minutes, an analgesic or sedative given within 2 days, on ventilator, or gross congenital malformation or neurological symptoms, were excluded from the study.

All blood sampling in the study was performed for clinical purposes. Each infant was assessed two times, receiving 1 ml 30% glucose or 1 ml sterile water by syringe, 2 minutes before venipuncture. The dosage was chosen with regard to previous studies.<sup>7,9</sup>

The infant was placed on a preheated nursing table, a pulse oxymeter (Novamatrix, Wallingford, CT, 06492, made in USA) was taped to the infant's foot and observe the baseline oxygenation and heart rate. The assistant nurse squeezed the infant's hand with the fingers to visualize the vein and then cleaned the skin with a local disinfectant. To access the vein, a butterfly needle was used. After the blood was collected, an adhesive bandage was applied. Pain response was

measured by the premature infant pain profile (PIPP). The PIPP assigns points for changes in 5 parameters during the first 30 seconds after a painful event: 3 for facial actions (brow bulge, eye squeeze, nasolabial furrow), 1 for heart rate, and 1 for oxygen saturation.<sup>10</sup> the data were analyzed using SPSS, version 11.5. A P value of <0.05 was taken as significant.

**RESULTS**

Ranges for gestational age, birth weight, and 5 minute APGAR score were 28-34 weeks, 950-2000 gram and 6-10 respectively. The PIPP score, duration of crying during the first 3 minutes, decrease in spo2,

and increase in heart rate between baseline and venipuncture period are shown in table 1.

The mean PIPP scores were significantly lower in the glucose group compared with the placebo group:(8.94±3.013 VS 11.44±3.42 respectively, p<0.001).The mean duration of crying in the first 3 minutes was significantly lower in 30% glucose compared with the placebo group(24.1±18.48 VS 39.6±26.8 respectively, p=0.002). The mean decrease in spo2 between baseline and venipuncture period, was significantly lower in the glucose group (2.79±3.81% VS 4.41± 3.49% respectively ; p= 0.008). There was no difference in the mean increase in heart rate between baseline and venipuncture period between the groups ( 11.4±11.06 VS 13.8± 12.4 respectively; p=0.33).

**Table-1: Mean (SD) of the PIPP score, duration of crying during the first 3 minutes, decrease in spo2, and increase in heart rate between baseline and venipuncture period**

	<b>Group1(glucose) n=36</b>	<b>Group 2 (placebo) n=36</b>	<b>P</b>
PIPP score (mean ±SD)	8.94±3.013	11.44±3.42	<0.001
Duration of crying (seconds) (mean ±SD)	24.1±18.48	39.6±26.8	0.002
Decrease in spo2% (mean ± SD)	2.79±3.81	4.41±3.49	0.008
Increase in heart rate (mean ±SD)	11.4±11.06	13.8±12.4	0.33

**DISCUSSION**

In this study, we demonstrated that 1 ml glucose 30% given orally before venipuncture reduced PIPP scores, crying time and oxygen desaturation after the acute pain.

Minor procedures are extremely common in preterm infants and effective analgesia must be used in these patients .current pharmacologic treatments are not appropriate for these newborns during acute and short- lasting procedures.<sup>5</sup>

The oral administration of small doses of 30% glucose seem to be a simple analgesia in preterm neonates.<sup>2</sup> Although this study shows a significant reduction of procedural pain in preterm infants yet we should notice that this effect is not constant. In our study,13 newborns did not show a reduction in pain score with glucose and from 23 infants that show a reduction in pain score, only 8 infants(20.4%)had a PIPP score Of =6. This data indicates that oral glucose is not yet the perfect analgesic in this setting. This study supports the previously observed effectiveness of oral glucose in reducing pain at venipuncture.<sup>5,10-12</sup>

Of patients in the glucose group, 79.6% showed a PIPP score that indicates pain, compared with more than 94.4% in the placebo group. As in our study,

other workers used duration of first cry to assess the efficacy of pain relief in full term and preterm newborns. In all of them sucrose and glucose reduced the duration of crying significantly.<sup>7,2</sup>

Duration of crying induced by a noxious stimulation, is considered a valuable measure of pain in full term newborns, and has therefore frequently used in pain studies. Extension of this tool for the assessment of pain to preterm infants is reasonable in the absence of any obvious impairment to vocalization.

The present study, unlike that of Skogsdal et al did not show any significant change in heart rate.<sup>9</sup> Our founding was similar to some other studies in respect to changes in heart rate.<sup>9,2</sup> Although heart rate changes have been used for response evaluation to pain relief, this reflex response is unpredictable, since newborn infants have a parasympathetic dominance compared with later in life.

The present study, unlike that of Laxmikant et al and Bauer et al shows a statistically significant decrease in oxygen saturation in placebo group compared with glucose group.<sup>9,2</sup>

We found that 1 ml glucose 30% significantly reduced the immediate behavioral pain response rated with the PIPP score and shortened crying after venipuncture compared with controls. A

1 ml glucose 30% solution was effective in some studies<sup>7,9</sup> but ineffective in another.<sup>13</sup>

In 3 patients in glucose group a slight and brief oxygen desaturation, during administration of 30% glucose was observed. This is similar to founding of Ricardo et al.<sup>5</sup> Although this did not reach statistical significance when compared with sterile water administration, staff should be aware of this potential transient complication in very preterm neonates, so that oral glucose is administered very slowly. Additional studies should look at this potential complication of oral sugar solutions in preterm neonates.

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