

# The Use of Oral Sucrose to Relieve Minor Procedural Pain in Neonates

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## ABSTRACT

**Objective:** To evaluate the effectiveness of oral sucrose as analgesic for minor painful procedures in neonates.

**Methods:** A case control study was conducted in the neonatal intensive care unit at King Hussein Medical Center during the period between June 1 and December 30, 2009. A total of 100 preterm and term neonates with postnatal ages ranging from one to 20 days, who underwent heel pricks for collection of blood for bilirubin estimation were randomly assigned into two groups. The treatment group received 24% sucrose solution two minutes before heel prick and the control group did not receive sucrose solution. The pain was assessed using the Premature Infant Pain Profile which is a multidimensional acute pain rating scale with scores ranging from 0 (no pain) to 21 (maximum pain). The exclusion criteria included the following: age less than 30 weeks gestational age, newborns on ventilators, newborns with major congenital or neurologic anomalies or clinical diagnosis of birth asphyxia or seizures, those on analgesics or sedatives and sick newborns with unstable vital signs. The student's t test was used to compare the relevant data. P value less than 0.05 was considered to indicate statistical significance.

**Results:** A total of 100 newborns, who were born with 30 weeks and above gestational age, were included in the study and divided into treatment and control groups in equal numbers. The mean Premature Infant Pain Profile scores were significantly lower in the treatment group, than in the control.

**Conclusion:** Our study suggests that sucrose is an effective non-pharmacological analgesic for minor painful procedures in neonates.

**Key words:** Analgesia, Newborn, Pain, Sucrose

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## Introduction

The prevention of pain should be the goal of all caregivers, because repeated painful exposures have the potential for deleterious consequences including altered pain sensitivity and permanent neuroanatomic and behavioral abnormalities.<sup>(1-4)</sup> Despite an increasing awareness regarding pain in neonates and its detrimental effect on neurobehavioral development, newborns

continue to be subjected to procedural pain without analgesia.<sup>(5)</sup> There is evidence that neonates, including preterm ones, have the neurological capacity to feel pain.<sup>(6)</sup> The neurological system necessary for the perception of pain is formed between 24<sup>th</sup> and 28<sup>th</sup> week of pregnancy (in preterm newborns the peripheral and central structures necessary to sense pain are present and functioning at birth).<sup>(6)</sup>

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**Table I:** Premature Infant Pain Profile (PIPP)

Indicator	Finding	Points
<b>Gestational age</b>	≥ 36 weeks	0
	32-35 weeks	1
	28-31 weeks	2
	< 28 days	3
<b>Behavioral state</b>	Active/awake eyes open facial movements	0
	Quite/awake eyes open no facial movements	1
	Active/sleep eyes closed facial movements	2
	Quite/sleep eyes closed no facial movements	3
<b>Heart rate maximum</b>	0-4 beats per minute increase	0
	5-14 beats per minute increase	1
	15-24 beats per minute increase	2
	≥ 25 Beats per minute increase	3
<b>Oxygen saturation maximum</b>	0-2.4 % decrease	0
	2.5-4.9 % decrease	1
	5-7.4 % decrease	2
	7.5 % decrease or more	3
<b>Brow bulge</b>	None ≤ 9 % of time	0
	Minimum 10-39 % of time	1
	Moderate 40-69 % of time	2
	Maximum ≥ 70 % of time	3
<b>Eye squeeze</b>	None ≤ 9 % of time	0
	Minimum 10-39 % of time	1
	Moderate 40-69 % of time	2
	Maximum ≥ 70 % of time	3
<b>Nasolabial furrow</b>	None ≤ 9 % of time	0
	Minimum 10-39 % of time	1
	Moderate 40-69 % of time	2
	Maximum ≥ 70 % of time	3

PIPP = sum for all 7 indicators

Interpretation: Minimum score: 0

Maximum score: 21

The higher the score the greater the pain

The use of oral sucrose to decrease pain during painful or stressful procedures is the most extensively studied pharmacologic intervention in neonates.<sup>(7)</sup> Although not fully understood, the mechanism of action of sucrose is thought to involve activation of the endogenous opioid system through taste. This is supported by presence of opioid receptors on the tongue; animal studies showed that analgesia can be reversed by opioid antagonist during noxious stimulation.<sup>(2,8,9)</sup> The data supporting the use of sucrose as an analgesic for minor painful procedures are sufficiently strong that the American Academy of Pediatrics and Canadian Pediatric Society have recommended the use of sucrose for such procedures as heel lances, injections and intravenous line insertions.<sup>(2)</sup>

The aim of our present study was to evaluate the effectiveness of oral sucrose as analgesic for minor painful procedures in neonates.

## Methods

A case-control study was conducted in a neonatal intensive care unit at King Hussein medical center during the period between June 1 and December 30, 2009. A total of 100 preterm and term neonates with postnatal ages range from 1-20 days who underwent heel prick for collection of blood for bilirubin estimation were randomly assigned into two equal groups: the treatment group received 24% sucrose solution before heel prick and the control group did not receive sucrose solution and nothing per mouth during the procedure. A trained nurse did the

**Table II:** Demographic characteristics of the study groups.

Character	Case group (with sucrose )	Control group (without sucrose)
Total numbers	50	50
Gender: Male (%)	27(54)	36(72)
Female (%)	23(46)	14(28)
Mean gestational age (weeks)	35.5	35.9
Mean birth weight (grams)	2400	2460
Mean postnatal age (days)	4.3	3.8
Mean baseline heart rate (beat per minute )	130.5	128.7
Mean baseline oxygen saturation (%)	98.3	98.4

**Table III:** Measures of PIPP scale

Variable	Case group	Control group	P value
PIPP scale, mean,( range)	3.4(0-8)	11.68(5-18)	<0.001

heel prick in a standard manner with a lancet as ensured that squeezing of blood was done not more than three times to collect the sample. Beginning two minutes before the procedure, the nurse assigned to each newborn in the first group used a sterile syringe to administer 24% sucrose to the anterior surface of the tongue over a period of 60 seconds with a dose of 0.5ml, 1ml and 2ml for infants weighing <1500 grams, 1500-2500 grams and >2500 grams respectively. About five minutes before each procedure a portable pulse oximeter was applied to the newborn's foot or hand and recorded baseline heart rate and oxygen saturation for each newborn. Throughout the procedure we observed newborn's face and recorded his or her physiologic responses (heart rate, oxygen saturation). We assessed pain using a validated composite pain measure; Premature Infant Pain profile (PIPP) with scores ranging from 0 (no pain) to 21 (maximum pain) as shown in Table I, the assessment was done by the same person. This profile includes three facial actions (brow bulge, eyes squeezed shut, nasolabial furrow), and two physiologic (heart rate, oxygen saturation) and two contextual (gestational age, behavioral state) indices of pain. We scored each facial action as present or absent in two second intervals for the first 30 seconds of the heel prick, For physiologic data, changes in heart rate and oxygen saturation from baseline were recorded over the same period. We scored the behavioral state before the potentially painful event by observing the infant for 15 seconds. We calculated total Premature Infant Pain Profile scores for each procedure by summing the scores of the seven indicators. We excluded newborns

with gestational age less than 30 weeks, newborns on ventilators, newborns with major congenital or neurologic anomalies or clinical diagnosis of birth asphyxia or seizures, those on analgesics or sedatives and sick newborns with unstable vital signs. We used the student's t test to compare relevant data and p values were calculated. P value less than 0.05 was considered to indicate statistical significance.

## Results

A total of 100 preterm and term neonates were randomly assigned into two equal case and control groups. The demographic characteristics of the two groups are shown in Table II. The measures of Premature Infant Pain Profile (PIPP) scale are shown in Table III. The mean Premature Infant Pain Profile scores were significantly lower in the treatment group than the control group who did not receive sucrose solution.

## Discussion

In recent years, administration of sucrose with or without non-nutritive sucking has been a frequently studied intervention for relief of procedural pain in neonates.<sup>(4)</sup> In our study we found a significant difference in pain response between the two studied groups with lowest mean premature infant pain profile scores among the sucrose group as shown in Table III ( mean PIPP=3.4, P <0.001 ). Many studies have addressed the role of sucrose as analgesic in minor painful procedures in preterm and term neonates. Stevenens *et al.* performed a

prospective study on 122 Very Low Birth Weight (VLBW) infants with gestational age range between 27-31 weeks using the PIPP scale to assess the pain in four randomly ordered interventions during consecutive routine heel lance procedures and found a significantly reduced PIPP scores in preterm neonates given a pacifier with sucrose ( $F=24$ ,  $p$  value  $<0.001$ ) and a pacifier with sterile water ( $F=9$ ,  $P= 0.003$ ) as compared with neonates kept in the prone position ( $F=2.4$ ,  $P=0.137$ ).<sup>(9)</sup> They also observed a tendency towards a lower PIPP scores among neonates given a pacifier with sucrose compared with a group given a pacifier with sterile water ( $F=3.62$ ,  $p <0.05$ ).<sup>(9)</sup> In another prospective study, Stevenes *et al.* enrolled 66 preterm neonates to receive standard care (positioning and swaddling), sterile water plus pacifier or 24% sucrose plus pacifier prior to all painful procedures in the neonatal intensive care unit during the first 28 days of life. A significant difference occurred between the sucrose plus pacifier group and standard care group ( $t(60)= -2.54$ ,  $p=0.01$ ) with mean PIPP scores generally higher in the standard care group.<sup>(4)</sup> Gibbins *et al.* found that a sucrose solution followed by non-nutritive sucking was the most effective intervention at reducing PIPP scores following heel lance during the first week of life for three groups of neonates with gestational ages of 27-31 weeks, 32-35 weeks and 36 to 42 weeks when compared with sucrose alone or sterile water followed by non-nutritive sucking.<sup>(11)</sup> Three studies performed by a single team of Canadian researchers employed sucrose solution in repeated doses and all of these were compared preterm neonates with a control group given sterile water.<sup>(2,12,13)</sup> In the study by Johnston *et al.* repeated doses were given three times during a single painful capillary puncture procedure, two minutes before the procedure, at the exact moment of the procedure and two minutes after the painful procedure. The neonates were randomized into three groups, who were given either, sucrose solution for the first dose and sterile water for the next two, three sucrose solution doses or three doses of sterile water. The results revealed that the groups of neonates who were given 0.05 ml of sucrose at 24%, both in single and triple doses had lower PIPP scores than the group given water.<sup>(12)</sup> In the study by

Johnston *et al.* neonates were randomized into treatment groups and given sucrose solution or a control group, given sterile water before every invasive procedure for seven days, their results revealed that 0.1ml of sucrose solution at 24% administered in repeated doses exhibited efficacy for reducing Neonatal Facial Coding System (NFCS) scores during capillary puncture, venous puncture and tracheal aspiration.<sup>(2)</sup> Boyer *et al.* set themselves the objective of evaluating the efficacy for physiological stability of administering sucrose solution for all painful procedures, the same sample and procedures as described immediately above were employed. This study found a significant negative correlation between the standard deviation for heart rate and the number of doses of sucrose, in those neonates who had received a large number of sucrose solution doses (9 doses or more within 24 hours), the higher the number of sucrose solution doses the lower the standard deviation for heart rate.<sup>(13)</sup> One study investigated the efficacy of sucrose and breast feeding in reducing the pain of full term neonates undergoing capillary puncture and found that crying time was significantly reduced among neonates given 2 ml of 25% sucrose solution two minutes before the painful procedure compared with group of neonates who were breastfed or given sterile water. The group given sucrose also exhibited a significant reduction in recovery time compared with groups given human milk via syringe or sterile water and a significant reduction in Infant Body Scoring System (IBCS) scores compared with the groups given human milk via syringe, breast feeding or sterile water.<sup>(14)</sup> Our result is supported also by a study authored by Taddio *et al.* when he included 240 newborns from diabetic and non-diabetic mothers  $\geq 36$  weeks gestation, each newborn received 2ml of 24% sucrose or placebo solution before venipuncture for screening tests and he used PIPP to assess pain. He reported that newborns who received sucrose had lower pain scores compared with those who received a placebo (newborns of nondiabetic mothers: mean difference -3.2, 95% CI -4.6 to -1.8) (Newborns of diabetic mothers: mean difference -2.4, 95% CI -3.8 to -1).<sup>(8)</sup> In contrast to our results, we found three studies reported that sucrose had lesser efficacy than other non-pharmacological interventions. The first study by

Carbajal *et al.* found that non-nutritive sucking was more effective than sucrose solution for pain relief of full term neonates.<sup>(6)</sup> In the second study Greenberg *et al.* reported greater pain relief efficacy for non-nutritive sucking together with granulated sugar than for sucrose solution with full term neonates.<sup>(6)</sup> The third of these studies done by Mathai *et al.* from India stated that rocking or giving a baby a pacifier were more effective non-pharmacological analgesics than expressed breast milk, distilled water, sucrose or massage for pain of heel pricks in neonates.<sup>(5)</sup>

## Conclusion

Sucrose solution is an effective analgesic for minor painful procedures in neonates. However further assessment of other non-pharmacological methods for pain relief in minor procedures in neonates in a prospective study is needed.

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