Be Sweet to Sick Babies: Analgesic effects and concomitant opioid analgesics of oral sucrose

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Introduction

Infants in the neonatal intensive care unit (NICU) require on average 10 painful procedures per day.[1] In addition to temporary distress, repetitive painful procedures may result in long-term neurocognitive effects on preterm infants that adversely affect normal development.[2]

Although large numbers of studies support the use of oral sucrose for reducing pain in neonates during acute minor painful procedures, evidence concerning the effectiveness of oral sucrose when used in conjunction with opioid analgesics remains inconclusive.

The purpose of this pilot study was to determine the preliminary efficacy of oral sucrose and concomitant opioids on behavioural and physiological responses of neonates during acute minor painful procedures. The secondary objective was to determine the feasibility of conducting a full-scale trial.

Methodology

Design: Two-armed pilot randomized control trial

Setting: One level III NICU

Participants: Inpatients in the NICU; requiring a heel lance or insertion of a nasogastric/orogastric tube; receiving a continuous intravenous opioid analgesic up to a maximum dose equivalent to 20mcg/kg/hour of morphine; parents or guardians fluent in French or English.

Interventions: Participants were randomized to receive either a clear oral sucrose solution or sterile water (placebo). The solutions were drawn into identical 1 mL syringes in accordance with randomization code. The solution was administered 2 minutes before and immediately before the beginning of the procedure, and every 2 minutes until the end of procedure.

Primary outcome: Premature Infant Pain Profile-Revised (PIPP-R) scores 30 and 60 seconds after the start of the procedure. The PIPP-R measures neonatal pain using a combination of physiological (changes in heart rate and blood oxygen saturation) and behavioural criteria (eye squeeze, brow bulge, and nasolabial furrow) **(Figure 1)**. Infants were videotaped during the procedure to capture vital signs and behavioural indicators.

Data analysis: Demographic and outcome data were entered into an Excel spreadsheet for analysis. Descriptive statistics are presented. No hypothesis testing was completed due to insufficient power.

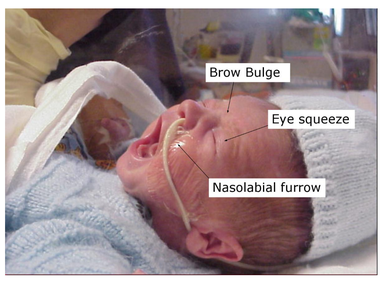


Figure 1: Facial criteria (brow bulge, eye squeeze, and nasolabial furrow) used in calculating PIPP-R scores.

Results

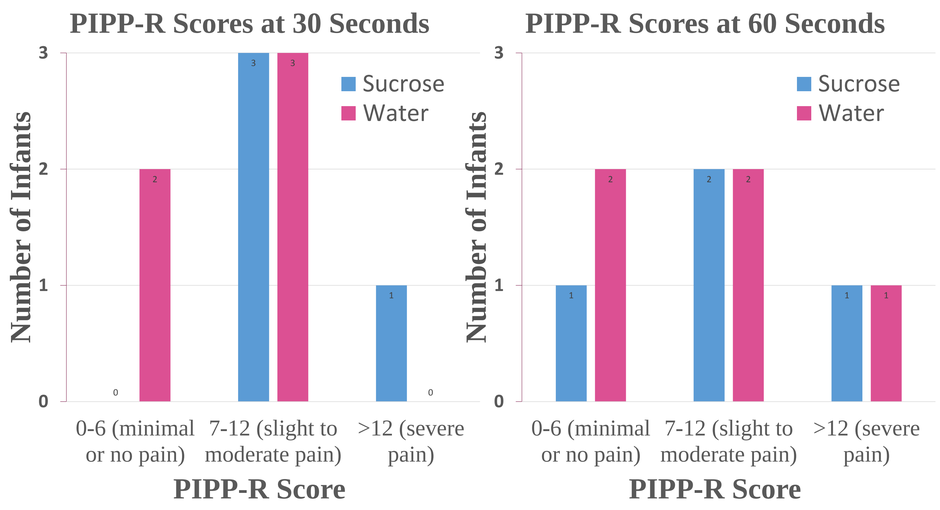
- Between June 2012 and September 2015, 9 infants undergoing heel lance or nasogastric/orogastric tube insertion were randomized (placebo=5, sucrose=4). Baseline characteristics are presented in Table 1.
- The median PIPP-R scores for the whole group, as well as the intervention and control group are presented in Table 2.
- At 30 seconds, the majority of PIPP-R scores for both the intervention and control group were between 7 and 12, signifying moderate pain (Figure 1).
- At 60 seconds, PIPP-R scores were similar between the intervention and control group (Figure 2).

Table 1: Demographic information for all infants, and by group.

	All Participants (n = 9)	Sucrose Solution (n=4)	Water (n = 5)
Age at time of data collection (days)	Median: 10 IQR: 37.5	Median: 17.5 IQR: 31	Median: 10 IQR: 61.5
Gestational age (days)	Median: 236 IQR: 90.5	Median: 261.5 IQR: 82.5	Median: 236 IQR: 88.5
Sex	Male: 4 Female: 5	Male: 1 Female: 3	Male: 3 Female: 2
Location prior to admission	Directly admitted to CHEO: 3 Transferred from another hospital: 5 Admitted from home: 1	Directly admitted to CHEO: 1 Transferred from another hospital: 2 Admitted from home: 1	Directly admitted to CHEO: 2 Transferred from another hospital: 3 Admitted from home: 0
Diagnosis	Gastrointestinal – surgical: 8 Sepsis: 1	Gastrointestinal – surgical: 4 Sepsis: 0	Gastrointestinal – surgical: 4 Sepsis: 1
Previous sucrose use	Yes: 5 No: 2 Unknown: 2	Yes: 1 No: 1 Unknown: 2	Yes: 4 No: 1 Unknown: 0
Type of procedure	Heel lance: 8 OG tube insertion: 1	Heel lance: 4 OG tube insertion: 0	Heel lance: 4 OG tube insertion: 1
Length of procedure (seconds)	Median: 299 IQR: 206	Median: 281 IQR: 207.75	Median: 380 IQR: 314
Number of attempts during procedure	1: 7 2: 2	1: 2 2: 2	1: 5 2: 0
Type of opioid	Morphine: 2 Fentanyl: 7	Morphine: 1 Fentanyl: 3	Morphine: 1 Fentanyl: 4
Dose of opioid	Morphine: 15.00 Fentanyl: 0.9143	Morphine: 10.00 Fentanyl: 1.00 (0.825)	Morphine: 20.00 Fentanyl: 0.8 (0.825)

Table 2: Median PIPP-R scores for all infants, and by group

	All participants (n=9)	Sucrose Solution (n=4)	Water (n=5)
PIPP-R Score (30 seconds)	Median: 10 IQR: 5.07	Median: 9.5 IQR: 6.25	Median: 10 IQR: 7.29
PIPP-R Score (60 seconds)	Median: 9 IQR: 8	Median: 9.5 IQR: 8	Median: 9 IQR: 9.36



Discussion

Overall, no conclusive findings can be made regarding the preliminary efficacy of oral sucrose and concomitant opioids on behavioural and physiological responses of neonates during acute minor painful procedures, due to a small and thus underpowered sample size.

The pilot study was launched with the secondary objective of determining the feasibility of a full randomized control trial. Only 9 infants were enrolled over the 3 year study period. The most probable explanation for the low enrollment is the change in practice since the study was initially designed. Today, infants receiving opioids intravenously are unlikely to require heel lances because blood tests can be performed using the existing lines in order to reduce the number of painful procedures. As a result, this pilot study would not be feasible on a larger scale without initiating a multi-site approach to maximize the number of eligible patients.

Possible next steps include using this study data in a meta-analysis to provide more conclusive evidence regarding the potential relationship between oral sucrose and pain scores in infants receiving concomitant opioids.

Conclusion

This pilot study has demonstrated a lack of feasibility of conducting a single-site trial. Further investigation is required to evaluate the effects of oral sucrose on infants being concomitantly medicated with opioid analgesics to inform best practice guidelines for clinical settings.

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