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Brief Report

A RANDOMIZED DOUBLE-BLIND TRIAL COMPARING THE EFFECT ON PAIN OF AN ORAL SUCROSE SOLUTION VS. PLACEBO IN CHILDREN 1 TO 3 MONTHS OLD UNDERGOING SIMPLE VENIPUNCTURE

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☐ **Abstract—Background: Few clinical trials evaluating the efficacy of oral sweet solutions for procedures in the emergency department (ED) have been published. Objectives: To compare the efficacy of an oral sucrose solution vs. a placebo in reducing pain in infants undergoing venipuncture without cannulation. Methods: A randomized, double-blinded clinical trial was conducted in a pediatric ED. Infants 1 to 3 months old were randomly allocated to receive 2 mL of 88% sucrose or 2 mL of placebo, 2 min prior to venipuncture. The outcome measures were the difference in pain levels as assessed by the Face, Legs, Activity, Cry and Consolability Pain Scale (FLACC) and Neonatal Infant Pain Scale (NIPS) scores, crying time, and variations in heart rate. Results: Eighty-two participants were recruited. Data were analyzed for 38 patients from each group (excluding protocol deviations). The mean difference in FLACC scores 1 min post venipuncture compared with baseline was 2.84 ± .64 (sucrose) vs. 2.71 ± .62 (placebo) (p = 0.98). For the NIPS score, it was 2.32 ± .47 (sucrose) vs. 1.63 ± .49 (placebo) (p = 0.60). The difference in the median crying time was not statistically significant between the two groups: 63.0 ± 3 (sucrose) vs. 48.5 ± 5 s (placebo) (p = 0.17). No significant difference was found in participants' heart rates 1 min post venipuncture compared with baseline: 33 ± 6 (sucrose) vs. 24 ± 5 beats per minute (placebo) (p = 0.44). Conclusions: In infants 1 to 3 months of age undergoing simple venipuncture, administration of an oral sweet solution did not statistically decrease pain scores, and participants' heart rate variations and crying time were not significantly changed.**

☐ **Keywords—pediatric; pain; sucrose solution; venipuncture; pain scales**

INTRODUCTION

In emergency departments (EDs), children undergo many painful procedures. Weisman et al. found that inadequate analgesia in young children during procedures diminished the effects of adequate analgesia during subsequent procedures (1). There is evidence nowadays on the negative effects of early life negative experiences on growth and development in infants, and there is good evidence on the effectiveness of several nonpharmacological interventions for pain relief in neonates and infants (2,3). Many studies have suggested that the prompt and accurate recognition and treatment of pain in young infants is important for their immediate comfort and for their best possible lifelong development (4).

Use of sucrose has been widely studied for procedural pain in the neonatal intensive care unit and in the newborn nursery settings, particularly for venous blood sampling, capillary blood tests, and circumcision (5–11). In these studies, infants receiving oral sucrose solutions prior to

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procedures cried less and had overall decreased behavioral pain responses when compared with those receiving a placebo. Furthermore, sucrose is considered safe, with no serious life-threatening adverse events and only few reported side effects. Although the evidence of efficacy has been established in neonates, there have been a limited number of published clinical trials in older infants for the commonly performed painful procedures in any setting. Uncertainties remain on the effectiveness beyond the newborn period (11,12).

We hypothesized that providing an oral sucrose solution prior to venipuncture would decrease pain levels in infants 1 to 3 months of age. The objective of our study was to compare the efficacy of an oral sucrose solution vs. a placebo in reducing pain in infants 1 to 3 months of age undergoing venipuncture without cannulation in the ED.

MATERIALS AND METHODS

Study Setting – Population

This study took place in the ED of a tertiary care pediatric university-affiliated hospital with an annual patient census of 80,000 visits.

Eligible infants were those from 28 days to 3 months of actual age (not corrected) requiring a venipuncture as part of their planned ED management. Infants were excluded if they were born prior to 37 weeks of gestation, had acute respiratory illness, had a chronic cardiopulmonary condition, had assisted ventilation (such as tracheostomy or oxygen dependence), were technology dependent (such as enteral feeding tube), had a developmental delay, had an oropharyngeal malformation or dysfunction (such as cleft palate or micrognathia), or had a metabolic disease. Infants were also excluded if their parents were unable to understand the study and provide informed consent due to language barriers. Finally, infants who had previously participated in this study or who underwent a painful procedure in the preceding 60 min (bladder catheterization, bladder puncture, lumbar puncture, capillary blood tests) were also excluded.

Study Design

This was a randomized, double-blinded, placebo-controlled clinical trial. From April 2011 to September 2014, a convenience sample of infants presenting to the ED and requiring venipuncture was recruited when one of the two designated research nurses was available daytime during weekdays. The painful procedure chosen for our study was simple venipuncture without cannulation for withdrawal of blood samples. Venipuncture is frequently performed in the ED with infants of this age group. For patients in whom venipuncture was not successful at the first attempt, the ED nurse or laboratory technician performed subsequent venipuncture as required by the patient's care after the study was completed (5 min post intervention). These participants were included for analysis because they also had an attempt at venipuncture while penetrating skin surface.

Outcomes Measures

The primary outcome measure was the difference in pain levels as assessed by the Face, Legs, Activity, Cry and Consolability Pain Scale (FLACC) 1 min post venipuncture vs. baseline. To date, there are no pain scales that have been validated precisely for the age group studied in our project. However, the FLACC scale is recommended by expert consensus groups to assess pain in children 2 months to 7 years, as its validity and reliability have been previously established (13,14). FLACC is an easily applicable pain scale in which the observer scores a patient for five categories, from 0 to 2 points, for a total maximal score of 10 points (Appendix 1) (14). Therefore, this pain scale was chosen as the measure of our primary outcome, in our population of infants from 1 to 3 months old.

Our secondary outcome measures included: variations in heart rate and crying time, differences in pain levels as assessed by the Neonatal Infant Pain Scale (NIPS) 1 min post venipuncture vs. baseline. The NIPS (Appendix 2) is a well-validated pain scale for newborns up to 1 month of age (15,16). The two recruiting research assistants had prestudy training with the two selected pain scales. Excellent unweighted kappa values were obtained between both of them (0.88 for FLACC and 0.91 for NIPS scales, respectively) on a sample of five potentially eligible patients prior to start of recruitment.

Side effects and adverse events were also recorded.

Interventions

The randomization process was performed by the institution's pharmacy via computer-generated blocks of four. The randomization allotment was known only by a pharmacist who was not involved in the study. All providers involved in the patient's care, research assistants, and parents were blinded to group assignment. Participants were randomly assigned to either study group: 2 mL of 88% sucrose solution (Syrup BP) or 2 mL of a placebo solution (sterile water).

Systematic reviews of the current literature have been unable to demonstrate superiority of one concentration of a sweet solution over another, but many studies suggest that higher concentrations of sweet solutions seem more effective (17–21). Therefore, we chose to study the