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Original Article

Evaluate the Mean Effect of Oral 25% Glucose Solution for Pain Relief in Term Infants, as Compared with Control Group, During Venipuncture

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ABSTRACT

Objective: To determine the efficacy of 25% oral glucose solution in providing analgesia as compared to control group in full-term neonates undergoing venipuncture.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Paediatrics, Pak-Emirates Military Hospital, Rawalpindi Pakistan, from Nov 2021 to Apr 2022.

Methodology: A total of 112 neonates born at full-term requiring venipuncture were included in our study. Neonates who required more than one prick per cannulation, those who couldn't tolerate oral feeding, or had received opiates, sedatives or NSAIDs since birth were excluded. All patients underwent venipuncture, however, patients in Group A received oral 25% glucose solution while those in Group B received breast milk. All patients were scored according to the NIP score at 1-, 5- and 10-minutes post venipuncture. Data was analyzed by SPSS 26.0.

Results: The patients in our sample had a mean age of 2.85±1.24 days, of whom males were 67(59.8%). The average time taken per venipuncture was 30.11±6.65 seconds. There was no difference between the two groups at baseline in terms of NIPS. In addition, no statistical difference between the two groups post-procedure in terms of NIPS was seen at 1-, 5- and 10-minutes post-venipuncture (p=0.201, p=0.411 and p=0.454, respectively).

Conclusion: The use of oral 25% glucose solution can be used a comparable substitute to breast milk in the provision of analgesia for neonates who have trouble with lactation, while undergoing venipuncture.

Keywords: Analgesia, Breast milk, Glucose solution, Venipuncture.

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INTRODUCTION

Approximately 140 million births occur every year, globally,[1] with 6.8% of full-term neonates requiring admission in neonatal intensive care units just after birth, a number which is even higher in pre-term ones.[1,2] Most of these neonates require prolonged stays in intensive care units ranging from a mean of 4.9 days in full-term neonates to as long as 81 days in premature ones.[3] During the course of these prolonged admissions, these neonates are required to go extensive testing and the administration of medication parenterally, which necessitates the need to endure intramuscular injections, venipunctures and heel sticks which can be painful to the newborn.[4] Human neonates are born in a state of immaturity and, as a result of persistent and recurring painful provocations, abnormal development of synaptic connections occur which not only have short-term consequences but also affect in the individual in later life where they exhibit hyperactivation and inappropriate responses to similar provocations.[5] In addition, it can result in long-term physical and psychological disabilities.[6]

Different approaches have been devised to alleviate pain in this population, especially when performing procedures such as venipuncture, some of which include oral glucose solutions, breast-feeding, the use of local anaesthetic creams/sprays and the Kangaroo-Mother Care method.[7,8] Glucose solutions are thought to provide analgesia using a number of different methods, one of which includes the increased production and release of endorphins due to the intake of a sweet solution, an action that is thought to be similar to breast milk.[9] In fact, breast milk is thought to be superior as the added effects of cradling and the feeling of direct skin-to-skin contact appears to provide greater comfort to the neonate.[9,10] The net result is a decrease in the intensity of pain felt, as well as a rise in the level of threshold for unbearable pain. However, breast milk is not always readily available in sufficient

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quantities on-demand, thus alternatives such as oral glucose solutions are being explored as alternatives.[9,10]

Best practice as to what the dosage and timing of administration of oral glucose solution should be, as well as its efficacy, is still the subject of some debate. Thus, this study was conducted to determine whether oral glucose solutions were effective in the alleviation of pain associated with venipunctures in neonates in an effort to lessen both short- and long-term morbidity in this patient population.

METHODOLOGY

We conducted this Quasi-experimental study between Oct 2021 to Apr 2022 in the Department of Paediatrics, Pak-Emirates Military Hospital, Rawalpindi Pakistan, on 112 neonates whose guardians consented to participate in the study and who were undergoing a venipuncture for cannulation. All patients were included via consecutive non-probability sampling. The WHO sample size calculator was used to calculate the sample size keeping a level of significance (α) of 1%, power of test (1–β) of 99%, population standard deviation (σ) and variance (σ2) of 3.39 and 11.4921, respectively, and test value of the population mean and anticipated population mean of 4.55 and 7.54, respectively.[11]

Inclusion Criteria: Non-low birth weight neonates of both genders, born at term, aged between 1 and 5 days who were about to receive venipuncture for the first time, on the leg were included for study.

Exclusion Criteria: Neonates who were crying before the procedure, required more than one prick per cannulation, those who couldn't tolerate oral feeding, were suffering from chronic liver or renal diseases, neurological or congenital heart disorders, or those who had received opiates, sedatives or NSAIDs since birth were excluded.

All participants were evaluated with a thorough medical history, and clinical examination. The last feed of all patients was confirmed to be at least one hour ago before starting the procedure. They were randomly divided into Groups A or B via lottery method. Group A patients received oral 25% Dextrose solution started 10 minutes before venipuncture (quantity varied from patient to patient, on intake, and was documented), while the neonate was cradled in the mother's lap, with skin-to-skin contact, while Group B received mother's expressed breast milk via a feeding bottle, which was also initiated 10 minutes before venipuncture, and continued right up to it, with cradling and skin-to-skin contact (quantity varied from patient to patient, on intake, and was documented).

Both groups subsequently underwent venipuncture: All procedures were conducted by a trained phlebotomist with minimum ten years' experience in paediatric cannulation. The neonate was cradled in the lap of the mother, and a site on the dorsum of the foot was chosen for venipuncture. A second phlebotomist acted as an immobilizer, along with the mother and used their hand as a tourniquet for the limb-to-be-venipunctured. All personnel wore sterile gloves, and the skin of puncture site was swabbed with iodopovidone solution, following which a venipuncture was carried out with a 21-gauge scalp vein needle, which was then secured with sticking plaster. The study participants were observed for 10 minutes post-procedure. Scoring for pain was done according to the NIPS scale, shown in Table-I, before the start of the procedure and at 1, 5, and 10 minutes post-procedure.

Table-I Neonatal Infant Pain Score (NIPS)

Feature	Score 0	Score 1	Score 2
Crying	No Cry	Whimper	Vigorous
Facial Expression	Relaxed	Grimace	-
Breathing Pattern	Relaxed	Change in breathing pattern	-
State of Arousal	Sleeping/Awake but Relaxed	Fussy	-
Arms and Legs (Arms/Legs Scored Separately)	Relaxed	Flexed/Extended	-

SPSS Version 26 was used for data analysis. Quantitative variables specifically age, gestational age at birth, length, weight, volume of therapeutic measure consumed, procedure time, time since last feed, NIPS pre-procedure, NIPS 1,5, and 10 minutes post-procedure were measured by mean and standard deviation. Qualitative variables specifically gender, and mode of delivery were measured as frequency and percentage. The Chi square test was used to compare qualitative variables while the independent sample t-Test was applied to compare quantitative variables between groups. A p-value ≤ 0.05 was considered significant.

RESULTS

Our study sample was composed of 112 neonates who to receive a venipuncture procedure. These patients were divided into two groups composed of 56 patients each. Th mean age of these patients was 2.85±1.24 days. Male neonates accounted for 67(59.8%) patients, out of the total sample. The mean length and weight of the neonates at birth were 47.01±5.47 cm and

3.29±0.33 kg, respectively. The mean gestational age at birth of the sample was 38.87±1.18 weeks. The majority of the patients i.e., 86(76.8%) were delivered by vaginal delivery, while the remaining 26(23.2%) neonates were delivered by caesarean section. The mean time before last feed was 101.40±24.69 mins. The pre-procedure characteristics of the patients are shown in Table-II.

Table-II: Pre-Venipuncture Patient Characteristics

Variable	Group-A	Group-B	*p*-value
Age (days)	2.68±1.21	3.02±1.26	0.148
Gender			
Male	35(62.5%)	32(57.1%)	0.563
Female	21(37.5%)	24(42.9%)	
Length (cm)	47.66±5.45	46.36±5.46	0.209
Weight (kg)	3.28±0.34	3.30±0.32	0.669
Gestational Age (weeks)	38.88±1.21	38.86±1.17	0.937
Mode of Delivery			
Vaginal Route	38(67.9%)	48(85.7%)	0.025
Caesarean Section	18(32.1%)	8(14.3%)	
Time Before Last Feed (mins)	24.27±3.24	24.77±3.31	0.113

Neonates who were assigned to the breast milk group consumed a higher volume of breast milk by volume in comparison to those who were assigned to the glucose group, (p=0.048). The average time taken per venipuncture was 30.11 ± 6.65 seconds. There was no difference between the two groups at baseline. In addition, there was no statistical difference between the two groups post-procedure in terms of NIPS at 1-, 5- and 10-minutes post-venipuncture (p=0.201, p=0.411 and p=0.454, respectively). The NIP scores are shown in Table-III along with other pertinent data.

Table-III: NIPS and Post-Procedure Results

Variable	Group-A	Group-B	*p*-value
Glucose/Milk Volume Consumed (mL)	47.66±11.25	52.34±13.47	0.048
Time Taken for Venipuncture (s)	30.41±7.02	29.80±6.29	0.631
NIPS* Pre-Procedure	0.48±0.50	0.45±0.50	0.708
NIPS at 1-Minute Post-Procedure	2.57±1.75	3.00±1.78	0.201
NIPS at 5-Minute Post-Procedure	2.14±1.34	2.36±1.41	0.411
NIPS at 10-Minute Post-Procedure	0.79±0.59	0.87±0.53	0.454

**NIPS: Neonatal Infant Pain Score*

DISCUSSION

The purpose of this study was to review the efficacy of 25% glucose in providing pain relief in neonates undergoing venipuncture and comparing it to that of expressed breast milk. Studies such as Chermount *et al.* have already demonstrated that 25% glucose has a significant analgesic effect, when compared to placebo, in this scenario, but we wanted to establish whether this was comparable to expressed breast milk, which has significant analgesic action in its own right.[12,13] The logic behind this proposition was that not all new mothers are able to express adequate amounts of breast milk, and 25% glucose may be used as an effective substitute if proved to be equivalent to expressed milk in terms of analgesia provision.[14]

In our study, the pain scores with 25% glucose and expressed breast milk were comparable at 1-, 5- and 10-minutes post-venipuncture and, despite the breast milk group consuming more milk per neonate, no statistical difference between the two modalities at any of these times, (p=0.201, p=0.411 and p=0.454, respectively). Rawal *et al* compared 25% dextrose to expressed breast milk and found that it was markedly superior to sterile water, and substantially to expressed breast milk in providing analgesia to neonates, post-venipuncture, within and at three minutes post-procedure, (p<0.001), findings that were echoed by Bueno *et al*. and Sahoo *et al*. both of whom noted that a 25% sugar solution was superior to breast milk in providing analgesia during venous sampling or cannulation procedures.[11,15,16] Conversely, Fitri *et al.* compared 24% sucrose to expressed breast milk, among other modalities and found that while sucrose did provide some analgesia, it was inferior to breast milk, (p<0.001).[17] We believe the differences across our studies can be attributed to a number of factors: a) studies varied as to whether they allowed skin-to-skin contact and cradling in the mother's lap and b) different sugar solutions were used at different strengths, and at different doses.

Different strengths of glucose solutions have been used to determine which dose was optimal in providing analgesia. Jatana *et al*. used breast milk in comparison with increasing increments of glucose solution in strengths of 10%, 25%, and 50% on neonates who were to undergo foot lancing and found that breast milk and 10% glucose were comparable to each other in terms of analgesia while 25% and 50% glucose had a much superior effect indicating that the analgesic effect may be attributable to the sugar content, calories or sweetness.[18] Furthermore, studies conducted by Shah *et al.* and Upadhyaya *et al.* reported that the degree of analgesia provided varied with the

quantity of therapeutic effect consumed i.e., smaller volumes were less effective than larger ones, in addition, the type of procedure also factors into whether a procedure will be minimally painful or not, with heel sticks being demonstrably more painful than venipuncture procedures.[19,20] The mechanism by which sweet solutions such as glucose water or breast milk produce analgesia is unclear but is thought to associated with the release of endorphins, in addition, breast milk is thought to contain precursor substances for melatonin such as tryptophan which may also have some effect, in addition, the gustatory receptors on the anterior portion of the tongue which sense sweet taste may also have a role, as the direct administration of sweet solutions into the stomach via a tube do not produce the same analgesic effect.[21,22]

STUDY LIMITATIONS

Performing a successful venipuncture on a neonate is a difficult task that is much easier to accomplish if the subject is comfortable, and in minimal pain. While our study showed that a 25% glucose solution resulted in an analgesic effect that was comparable to breast milk, there were some limitations. Firstly, there was no placebo arm for comparison, therefore, it was difficult to establish the degree of analgesia provided by both our study and control arm. Secondly, our patients were all sick neonates, and the argument could be made that these patients already had a low pain threshold, resulting in confounding of results. Lastly, the neonates each consumed a variable amount of the therapeutic measure belonging to their respective group, so an adequate or minimal dose required cannot be established based on our study.

CONCLUSION

Adequate analgesia and patient comfort are essential to performing a successful venipuncture on a neonate. The use of 25% glucose in this role is an effective measure that can be regularly employed, even as a substitute to maternal breast milk, especially when the latter is not readily expressible. Further research is required to establish the adequate time of administration pre-procedure, the quantity and concentration, as well as type of formulation of sugar that is optimal for peri-procedure analgesia.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

RUBM: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

ZA & SZ: Data acquisition, data analysis, approval of the final version to be published.

ST & AAJ: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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