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Effect of Non Pharmacological Intervention Sweet-Tasting Solution on Pain in Term Infants Who Receive Vaccination

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A B S T R A C T

Introduction: Infant immunization by intramuscular injection is a painful procedure for infants. The goal of this study was to determine the effectiveness of oral sucrose on pain severity in term newborns undergoing vaccination.

Materials & Methods: In this randomized controlled trial, 90 term newborns undergoing hepatitis B vaccine injection, which was performed in Shahid Mustafa Hospital in Ilam, were selected and randomly assigned into three groups: intervention, control, and placebo. Then 2 minutes before vaccine injection, 2 mL of 25% sucrose or water for injection was instilled into the mouths of infants in the intervention or placebo groups, respectively. The newborns of the control group didn't take anything, and pain intensity was measured by the Neonatal Infant Pain Scale (NIPS) during 1-2 min. The statistical test included ANOVA and LSD. Finally collected data were analyzed by SPSS V.18 at the significance level of less than 0.05.

Results: According to the results, there was no significant difference between groups in terms of delivery type, sex, head circumstance, weight, and height. Comparison of pain severity in two groups, mean and standard deviation of pain, group that received sucrose solution had lower intensity than sterile water group (3 ± 1.66 vs. 4.05 ± 1.23), but this difference was not significant statistically ($p = 0.78$). Comparison of pain intensity showed that the pain intensity in the control group is higher than the intervention and placebo groups ($p<0.001$).

Conclusion: A sweet solution of sucrose can be used as a simple and safe non-pharmacological method to reduce the pain following immunization in newborns.

Keywords: Sucrose, Newborn, Pain, Vaccination

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Introduction

Generally, neonates undergo painful procedures such as injections, for example, for receiving vitamin K1, phlebotomy, and vaccination. In fact, immunization is one of the most common procedures inflicting pain on children and neonates. In Iran, vaccination for hepatitis B virus (HBV) is a routine procedure during infancy care, which is a painful procedure (1, 2). Such procedures, when used without appropriate analgesics, cause considerable pain and discomfort for newborns, who generally receive no pain-reducing interventions prior to undergoing painful procedures (3, 4). Uncontrolled pain can permanently interrupt the cognitive growth and development of neonates due to the flexibility of the growing brain, interfering with responses to subsequent painful stimuli (5). Therefore, pain control is an integral part of neonatal care (6, 7), and pain management should be considered a routine part of medical and nursing care during the neonatal period (8). Pain management measures encompass pharmaceutical and non-pharmaceutical approaches. For short-term pain relief in neonates, medications are rarely used due to uncertainty about their pain-relieving effectiveness and their possible side effects (9). Numerous non-pharmaceutical pain-relieving methods have been proposed to be used for neonates. An optimal pain-reducing method should be fast-acting, effective, and without side effects. Sweet oral solutions have been proposed to reduce pain and elevate tolerance to painful stimuli, partly by increasing the levels of intrinsic endorphins (10). Sucrose is a safe and effective pain-reducing agent that can be used for neonates. This molecule is a sweet disaccharide consisting of fructose and glucose. Sucrose is assumed to exert its analgesic effects by inducing either intrinsic opioids or dopamine and acetylcholine (11, 12). Multiple studies have been conducted on the analgesic effect of different doses of sucrose in neonates undergoing blood sampling from the heels. However, the results of these studies cannot be extrapolated to more painful procedures such as intramuscular hepatitis B vaccination. A few studies have addressed the analgesic effects of sucrose during procedures such as intramuscular injections in neonates, and the results of existing studies offer contradictory findings (13, 14). Therefore, our aim was to investigate the analgesic effects of a 25% sucrose solution in neonates receiving HBV vaccination.

Materials and Methods

Study design

This double-blinded randomized clinical trial was conducted on 90 eligible neonates in the Shahid Mostafa Khomeini Hospital of Ilam City (IRCT 201304096790N3). After receiving the necessary approval from the research ethics committee, the researcher visited and initiated the study in the postpartum ward of the hospital.

Setting & Randomization & Blinding

At first, the subjects were selected by non-random convenience sampling, and then they were randomly assigned to one of the three groups: 1) sucrose 25% solution, 2) distilled water, and 3) no-intervention. In order to fully comply with ethical guidelines, the newborn's parents were completely briefed on the objectives of the research, and only after obtaining their informed consent was the baby included in this trial. For randomization, a table of random numbers was used. Blinding of the study was double-blind. The researcher and the research units were unaware of the type of intervention. Inclusion criteria were full-term birth, birth weight >2500 grams, being born by either natural delivery or caesarean section, and a 1-minute Apgar score > 7. Exclusion criteria were the diagnosis of medical problems, congenital anomalies, breastfeeding within half an hour before the procedure, and the mother's consumption of narcotics.

Measurements & Validity and Reliability

1. Demographic tool

The demographic variables included gestational age, weight, height, head circumference, gender and, deliver.

2. Neonatal Infant Pain Scale (NIPS)

This scale measures the intensity of pain based on facial expression changes, crying, respiratory patterns, positioning of the arms and legs, and the newborn's consciousness status. On this scale, a score of 0 indicates no pain, and a score of 7 shows the maximum pain intensity. The validity of its original version has been approved, and reliability was 0.84 (15). Also, the content validity of the Iranian version of this scale has been approved, reporting a Pearson correlation coefficient of $r = 0.93$ (15).

Intervention

In the first and second experimental groups, the newborns were fed with 2 mL of either 25% oral sucrose or distilled water through a syringe within 30 seconds in the same way. Two minutes afterward, the hepatitis B

vaccine was injected, followed by measuring pain intensity using the NIPS scale within 1-2 minutes. In order to determine the sample size, we utilized a specific formula and the data of similar studies, leading to the determination of n = 30 participants per group.

Ethical Considerations

Ethical concerns included acquiring an ethical code (IR.MEDILAM.REC.22/52/999/18), ensuring integrity in library collection and data reporting, getting signed informed permission from all participants in accordance with the Declaration of Helsinki, and adhering to principles of interventional human research.

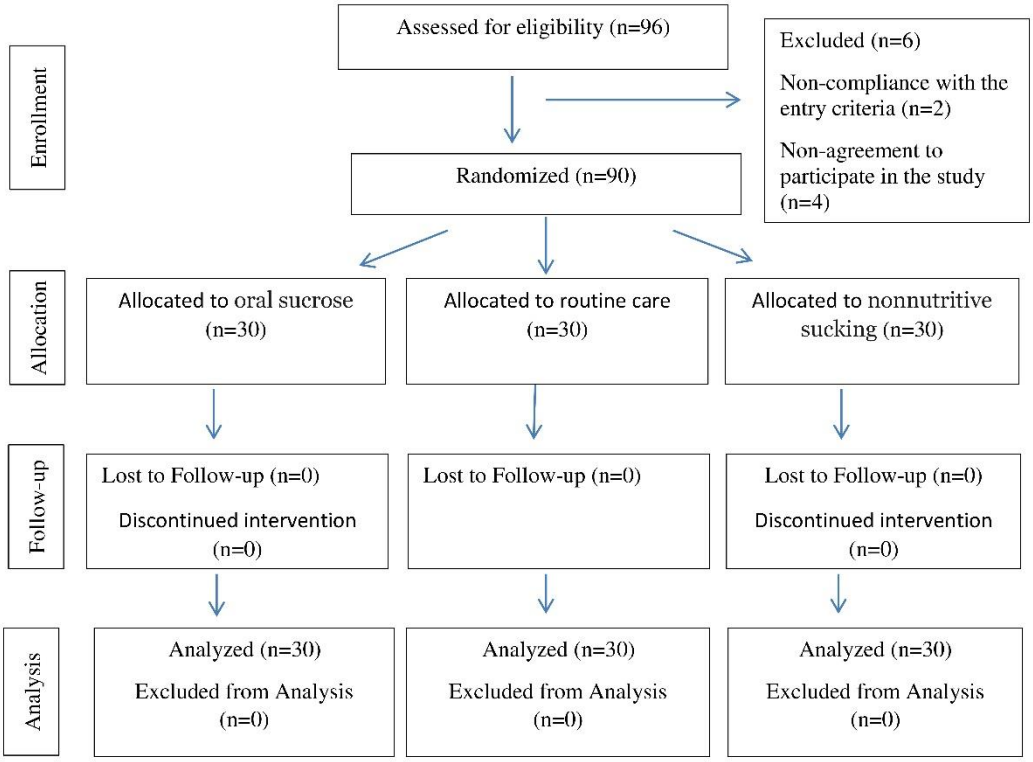


Figure 1. Consort chart of three groups in the study

Statistical and Data Analysis

For statistical analysis, SPSS software (version 18) was employed. In order to homogenize the study groups in terms of delivery route, neonate's gender, head circumference, weight, and height, as well as to compare pain intensity between the three groups at the same time, the one-way analysis of variance (ANOVA) test was performed. Also, to ascertain a significant difference between the groups in terms of the mean pain intensity score, the least significant difference (LSD) was employed for paired comparisons between the groups. A P-value of less than 0.05 was considered statistically significant.

Results

In this research, 90 newborns were randomly allocated to the three groups of 25% sucrose, distilled water, and control (no intervention). The three groups were comparable in terms of gestational age, weight, and height, head circumference, gender, and type of delivery (P > 0.05) (Table 1).

Table 1. Comparison of demographic characteristics between the study groups

Variables/groups	Sucrose			Distilled water			Control			P*
	M	SD	%	M	SD	%	M	SD	%	
Gestational age (weeks)	3305	316	-	3278	289	-	3401	311	-	0.321
Weight (g)	3238.33	285.77	-	3309.31	288.72	-	3263.33	272.89	-	0.638

Height	50.17	1.26	-	50.35	1.22	-	50.27	1.28	-	0.781
Head circumference (cm)	33.93	1.91	-	34.22	1.83	-	33.73	1.78	-	0.384
Gender (female)	-	-	53.3	-	-	48.8	-	-	50	0.533
Delivery (natural)	-	-	63.3	-	-	69.4	-	-	73.3	0.367
M: Mean SD: Standard Deviation *: ANOVA										

Regarding the main objective of the research, the results showed that the mean (SD) of the pain intensity score was 2.90±1.44 in the sucrose group, 4.05±1.23 in the distilled water group, and 5.20±1.03 in the control group. The ANOVA statistical test revealed a significant difference between the three groups in terms of pain intensity (P<0.001). According to the LSD test, there was no significant difference in the pain intensity score between the sucrose group (2.90 ± 1.44) and the distilled water group (4.05 ± 1.23) (P-value = 0.78); however, a significant difference was found comparing the control group with both the sucrose and distilled water groups (P<0.001) (Table 2).

Table 2. Comparison of the mean (SD) of the pain intensity score between the newborns receiving sucrose, distilled water, and no-intervention

Pain intensity/group	N	M	SD	95% CI		P-value
				Lower limit	Upper limit	
Sucrose	30	2.90	1.44	2.36	3.44	<0.001
Distilled water	30	4.05	1.23	3.59	4.51	
Control	30	5.20	1.03	4.81	5.58	
Total	90	3.70	1.75	3.33	4.06	
N: Number M: Mean SD: Standard Deviation CI: Confidence Interval *: ANOVA						

Discussion

Today, sucrose is widely used to alleviate the pain intensity in neonates and infants undergoing painful procedures (4, 8). Although various animal and human studies have affirmed the effectiveness of sucrose in reducing pain during painful procedures, there is still no consensus on the most effective dose and the best administration route of sucrose to relieve pain in neonates (16). In this regard, it is necessary to gather more research evidence on the analgesic effects of oral sucrose in neonates and infants up to the age of 18 months (17). Therefore, the aim of the present study was to compare the pain-reducing effects of oral sucrose at 25% during HBV vaccination in 90 newborns. The results showed that feeding with 25% oral sucrose two minutes prior to the procedure significantly reduced pain intensity compared to the control group. Several studies have investigated the analgesic effects of sucrose in infants during painful procedures, such as venous blood sampling, blood sampling from the heel, circumcision, and vaccination. In most of these studies, sucrose solution has been compared with placebo (distilled water), resulting in contradictory findings (4, 6, 10, 13, 14, 18-23). In this regard, Tadiyo *et al.* reported that the analgesic effects of sucrose were confined to intravenous injections, and no such effects were observed during intramuscular injections and lancet penetration (14). A systematic review and meta-analysis provided research evidence supporting the analgesic effects of breastfeeding, local anesthetics, and sweet solutions during vaccination among neonates and children (24). A limited number of studies have compared the pain-reducing effects of sucrose, placebo, and control (no intervention). In agreement with our study, Yarahmadi *et al*. compared the effectiveness of sucrose, distilled water, and no intervention in alleviating pain during blood sampling from the heel in term newborns, declaring statistically significant differences between the intervention and control groups in terms of pain intensity, heart rate, and arterial oxygen saturation. Furthermore, it was noted that this difference was related to the comparison between the sucrose and no-intervention groups; however, the difference between the

sucrose and placebo groups was not statistically significant (16). In a study by Ahuja *et al.*, the pain intensity was compared between the three groups of a sucrose solution, distilled water, and control (no-intervention), and the results disclosed a statistically significant difference between the sucrose and control groups, but the difference in pain intensity was not significant comparing the sucrose solution and distilled water groups (25). The fundamental analgesic mechanism recruited by sucrose is still not completely understood (26, 27). It seems that sucrose, similar to narcotics, can reduce pain perception and responsiveness by binding to opioid receptors in the central nervous system (28). The limitation of this study can be cisidered like time of intervention and number of screeing tools.

Conclusion

The results of the present study showed that sucrose 25% solution reduced pain perception in neonates following the intramuscular injection of the HBV vaccine, so it is recommended to use this pain-alleviating solution as a simple and safe non-pharmacological method to reduce the pain following immunization in newborns.

More studies are suggested to investigate the analgesic effects of sucrose solutions with different concentrations using different pain measurement tools in neonates undergoing various painful procedures.

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Conflict of interest

The authors declare no conflict of interest.

Authors' contributions

Conceptualization: ZS, Methodology, Validation, Formal Analysis, Investigation, Resources, Data Curation, writing– Original Draft Preparation, writing–Review & Editing, Visualization, Supervision, Project Administration: ZS, HT, Funding Acquisition: Ilam University of Medical Sciences.

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