EHD
Available online at: https://dergipark.org.tr/tr/pub/jnef
Doi: 10.46483/10.46483/jnef.1620940

ORIGINAL ARTICLE / ORİJİNAL MAKALE

Comparison of Different Methods for Reducing Pain during Vaccination: A Randomized Study with Placebo and Control Groups

Aşı Sırasındaki Ağrıyı Azaltmada Farklı Yöntemlerin Karşılaştırılması: Plasebo ve Kontrol Gruplu Randomize Bir Çalışma

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Received: 13.09.2022, **Accepted:** 24.12.2024

Abstract

Background: Pain can cause deterioration in physiological, behavioural, and cognitive functioning. It is important to reduce perceived pain during painful procedures such as vaccination using pharmacological and non-pharmacological methods.

Objectives: The study was carried out to compare the effectiveness of different non-pharmacological methods in pain management during vaccination.

Methods: This randomised controlled study with placebo and control groups was conducted with 175 infants, who were randomly assigned to one of the ShotBlocker® (n = 35), ShotBlocker®-placebo (n = 35), sucrose (n = 35), sucrose-placebo (n = 35) or control (n = 35) groups. Pain levels of the infants were determined by assessors (nurses, parents, and observer) using the Neonatal Infant Pain Scale (NIPS) before and during vaccination.

Results: There was no significant difference in infant age, weight, length, and gender among the five groups. There were statistically significant differences between the pain scores determined by the parents, nurses, and observer for the ShotBlocker®, sucrose, ShotBlocker®-placebo, sucrose-placebo, and control groups. The pain scores of infants in the ShotBlocker® and sucrose groups were statistically lower than those in the placebo and control groups ($p < .001$).

Conclusion: It was concluded that the use of ShotBlocker® and sucrose reduced pain levels during vaccination according to all observers and that there was no statistically significant difference between these two methods. In order to minimize the perceived pain in infants during vaccination it is recommended that healthcare professionals (nurses and midwives) would use these methods in clinical practice.

Keywords: Infants, Pain Management, ShotBlocker®, Sucrose, Vaccination

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Cite This Article: Cengiz Z, Zengin M, Yayan EH, Vicnelioğlu E. Comparison of Different Methods for Reducing Pain during Vaccination:A Randomized Study with Placebo and Control Groups. Journal of Nursing Effect. 2025;18(1): 111-126

Journal of Nursing Effect published by Cetus Publishing.

Öz

Giriş: Ağrı fizyolojik, davranışsal ve bilişsel işlevlerde bozulmaya neden olabilir. Aşı uygulaması gibi ağrılı işlemler sırasında farmakolojik ve non-farmakolojik yöntemler kullanarak algılanan ağrıyı azaltmak önemlidir.

Amaç: Bu araştırma aşı uygulaması sırasında farklı non-farmakolojik yöntemlerin ağrı yönetimindeki etkinliğini karşılaştırmak amacıyla yapıldı.

Yöntem: Plasebo ve kontrol gruplu randomize kontrollü çalışma, ShotBlocker® (n=35), ShotBlocker®-plasebo (n=35), sukroz (n=35), sukroz-plasebo (n = 35) ya da kontrol (n = 35) gruplarına rastgele atanan 175 bebekle yapıldı. Bebeklerin ağrı düzeyleri değerlendiriciler (hemşireler, ebeveynler ve gözlemci) tarafından aşı uygulaması öncesinde ve sırasında Neonatal Infant Pain Scale (NIPS) kullanılarak belirlendi.

Bulgular: Beş grup arasında bebeğin yaşı, kilosu, boyu ve cinsiyeti bakımından anlamlı bir fark yoktu. Ebeveynler, hemşireler ve gözlemcinin ShotBlocker®, sukroz, ShotBlocker®-plasebo, sukroz-plasebo ve kontrol grupları için belirledikleri ağrı skorları arasında istatistiksel olarak önemli farklılık vardı. ShotBlocker® ve sucrose grubundaki infantların ağrı skorları plasebo ve kontrol gruplarına göre istatistiksel olarak daha düşüktü (p<.001).

Sonuç: Tüm gözlemcilerin değerlenirmesinde ShotBlocker® ve sukroz kullanımının aşı sırasındaki ağrı düzeyini azalttığı ve bu iki yöntem arasında istatistiksel olarak anlamlı bir fark olmadığı sonucuna varıldı. Bebeklerde aşı uygulaması sırasında hissedilen ağrıyı en aza indirmek için sağlık profesyonellerinin (hemşire ve ebeler) bu yöntemleri klinik uygulamada kullanmaları önerilmektedir.

Anahtar Kelimeler: Bebek, Ağrı Yönetimi, ShotBlocker®, Sukroz, Aşı Uygulaması

INTRODUCTION

Intramuscular (IM) vaccinations are the most common and painful procedures used in children and they are administered until the child is two years old (Centers for Disease Control and Prevention, 2010). Vaccine injections are the most common reason for iatrogenic pain in childhood (Taddio et al., 2009)

Inadequate paediatric pain management can have adverse psychological consequences for children, parents, and staff (Celebioglu et al., 2010; Taddio et al., 2008). Moreover, previous studies have shown that pain can cause deterioration in physiological, behavioural, and cognitive functioning (DeMore & Cohen, 2005; Reis et al., 2002). It is reported that untreated pain can have lasting detrimental effects on the central nervous system at an early age. In addition, early painful experiences have also been associated with negative health behaviours and the avoidance of medical procedures in adulthood (DeMore & Cohen, 2005). For these reasons, the importance of pain management within the paediatric population cannot be neglected (Canbulat Sahiner et al., 2018).

Swaddling, breastfeeding, sucrose, skin-to-skin care, kangaroo care, and upright positioning are among the non-pharmacological strategies used to manage procedural pain in newborns (Benoit et al., 2017; Denise Harrison et al., 2016; Meek & Huertas, 2012; Shah et al., 2012). Additionally, the World Health Organization emphasized that infants should be breastfed during or shortly before the vaccination session, if it is culturally acceptable (WHO, 2015). One of the methods used to reduce needle-related pain is the ShotBlocker® application.

ShotBlocker® is an apparatus developed based on the Gate Control Theory to reduce pain by preventing pain transmission to the central nervous system (Cobb & Cohen, 2009; Drago et al., 2009)immunization injections cause negative short-term and long-term consequences for children. The Gate Control Theory of pain suggests that physical interventions (eg, rubbing the site. There exist varying results reported by studies in the literature investigating the effect of ShotBlocker® on pain management. In a study by Drago et al. (2009), ShotBlocker® was found to be effective in reducing the pain of intramuscular injection according to the evaluations of nurses and caregivers. On the other hand, Cobb and Cohen (2009) found that ShotBlocker® was not effective in terms of reducing acute pain.

The use of sucrose has been recommended by many clinical guidelines to prevent or treat procedural pain (vaccination, heel lancing, venipuncture, and intramuscular injection) (Gao et al., 2016; Gray et al., 2006; Matsuda, 2017) More than 100 studies evaluating the effect of sweet solutions have concluded that sucrose reduces pain during invasive procedures and reduces crying time (Despriee & Langeland, 2016; Denise Harrison et al., 2017; Kassab et al., 2020; Uzelli & Yapucu Güneş, 2015).

Nurses develop safe, easy-to-use, effective, and inexpensive non-pharmacological strategies to reduce procedural pain (Caglar et al., 2017). The methods used to reduce pain during IM vaccinations should be readily available, inexpensive, and easily tolerable by infants. For methods that can be applied during painful procedures, infant- and clinic-specific procedures should be established. In order to improve pain management during procedures, a comparison of commonly used non-pharmacological methods and how effective these methods are should be investigated. Although sucrose is a widely used non-pharmacological method to improve pain management during invasive procedures, its use is not appropriate in some groups such as children with hyperglycemia. In this case, it is necessary to use effective alternative methods in pain management. The sucrose method (with proven efficacy) was compared with other methods in relatively fewer studies. The superiority of different non-pharmacological methods in reducing pain has been investigated in many comparative studies. In this study, the pain reduction effect of sucrose, which is frequently used and whose effect has been determined by many studies, and ShotBlocker, which is used less frequently in vaccine applications and in reducing pain in neonates, was compared. It is important that the methods and/or equipment used to reduce pain during vaccination are practical, applicable in all settings, reusable, and low- or no-cost (Canbulat Sahiner et al., 2018). The fact that ShotBlocker is a practical method suggests that it will be an alternative method for sucrose in the pain management of infants. To our knowledge, no previous study has investigated the effectiveness ShotBlocker® by comparing it with sucrose in neonates during Hepatitis B (2nd Dose) vaccine administration.

Aim

The aim of this study was to compare the effectiveness of ShotBlocker® and sucrose interventions in pain management during vaccination. The study hypotheses were as follows:

Administration of sucrose in infants during vaccine administration will reduce vaccine-related pain compared to control and placebo groups.

Using ShotBlocker® during vaccine administration in infants will reduce vaccine-

related pain compared to control and placebo groups.

Using ShotBlocker® to reduce vaccine-related pain in infants will have an effect similar to using sucrose.

METHODS

Type of the Research

This is a randomized controlled study with placebo and control groups, designed to compare the effects of ShotBlocker® and sucrose on pain reduction during vaccine injections in infants.

Place of the Research

The study population consisted of infants admitted for Hepatitis B (2nd Dose) vaccinations at the end of the first month (at one month of age). Although the Hepatitis B vaccine is reported to be less painful than some other vaccines, it is one of the first painful experiences in healthy term neonates (Amiri Shadmehri et al., 2020) which was done in 2015 at the Nohom-e Dey Hospital of Torbat Heidariyeh, 90 eligible infants were randomly selected and divided into two intervention and one control groups. In the breast-milk odor group (n = 30. Taking this situation into consideration, babies who applied the Hepatitis B vaccine were evaluated in the study. The study was conducted to one of the three randomly-selected family health centres in a province in eastern Turkey between September 2019 and January 2020.

Universe/Sample of the Research

The sample size was estimated as 35 for each group (ShotBlocker® = 35), ShotBlocker®-placebo = 35, sucrose = 35, sucrose-placebo = 35 and control = 35). In order to test the adequacy of the sample size, a power analysis was performed with a post hoc test using the G * Power 3.1.3 program. The representation power of the sample was found as .99 with 175 sample sizes, .601 effect size, .05 error margin, and .909 common variances. A post hoc power analysis was used to determine whether the number of sample obtained after the completion of the study is sufficient for the statistical power of the study (Cohen, 1988). Eventually, 175 infants and their parents were included in the study and it was confirmed that the number of samples used was sufficient.

The eligibility criteria for the infants were as follows: (1) born at the term gestations of 38-42 weeks; (2) no redness, deteriorated skin integrity, or nerve damage in the area of application; (3) no history of any clinical injection excluding first vaccinations at birth. Infants with any diagnosed congenital abnormalities or neurological developmental impairment, or a history of analgesics or sedatives within the last 24 hours were excluded from the study. The eligibility criteria for the parents were as follows: (1) being literate; (2) (previously diagnosed) having no mental or physical disabilities. Parents who could not comply with the data collection procedures were excluded from the study.

In the study, a multi-stage randomization method was used as follows: 1) a random selection of the family health centres in the city in which the research was conducted; 2) a random selection of the parents and infants to be included in the study at each centre; and 3) a random assignment the participants to the groups using a computer-based block randomization method. First, all family health centres in the province where the study was conducted were listed, and three of them were selected according to computer-generated random numbers. Later, infants presented to these family health centres for Hepatitis B vaccine and their families, who met the inclusion criteria, were identified. Five sets were created for the block operation. Babies were assigned to

the groups according to the random list obtained by repeating the random numbers assigned to each set 35 times. The group represented by the random numbers was identified as a result of writing all the group names on a piece of paper and drawing lots.

Different blinding methods are used in studies to reduce bias. Due to the nature of the research, the present study could not be carried out completely blinded. However, each group was blinded within itself. In the ShotBlocker® group, which side of the apparatus is inverted and which side is effective is not explained to the assessors. For the sucrose group, water or sucrose was given to infants by the researcher, and the assessors rated the pain without knowing which child was given sucrose and which one was given sterile water. Assessors were blinded by not declaring the group in which infants were assigned within the group.

Data Collection Instrument-Validity and reliability information

Data were collected using a descriptive information form and the Neonatal Infant Pain Scale (NIPS). Blinded assessors (nurses, parents, and observers) independently assessed pain levels before and during the vaccination of each infant using the Turkish version of the NIPS. Assessors were trained to use the NIPS instrument just before the vaccination. Researchers trained parents before the procedure to evaluate NIPS parameters.

Descriptive Information Form: The descriptive information form prepared by the researchers asks for introductory information such as infant gender, length, and weight. In addition, pain scores assessed by the three different observers (nurse, parent, and observer) were recorded via this form.

Neonatal Infant Pain Scale (NIPS): The NIPS is a valid behavioural instrument that can be used to assess infants' response to pain. NIPS includes six behavioural responses to pain: facial expression, crying, breathing patterns, arms, legs, and state of wakefulness. The total pain scores range from 0 to 7. While the internal consistency of the original NIPS is within the range of .87 to .95, the internal consistency of the Turkish version is .83 (Curry et al., 2012; Uzelli & Yapucu Güneş, 2015).

Action/Intervention

In the study, injections were administered by the same nurse at each of the three family health centres. All three nurses had undergraduate-level training, at least seven years of Family Health Centre experience, training in vaccination, and took part in the study voluntarily without any conflicts of interest.

First, the neonates were placed in a supine position on a blanket while their arms were flexed, crossed over, and positioned close to their chest. Then, the injections were administered by nurses following a strict protocol. The skin was cleaned with an alcohol-soaked cotton before injection and allowed to dry for 30 seconds. Then, the Hepatitis B vaccine was administered via IM injection into the vastus lateralis muscle with a 1-inch, 23-gauge needle placed at a 90° angle while the tissue was held. The methods whose effectiveness were evaluated for vaccine administration are ShotBlocker® and sucrose.

ShotBlocker®

ShotBlocker® is a patented apparatus developed to reduce injection pain. It is intended for intramuscular and subcutaneous injections. It is used by holding it onto the skin surface during injection, and has no side effects. The ShotBlocker® has short, non-pointed, blunt

protrusions on the face that contact with the skin, and there is a hole in the middle of the apparatus that leaves the injection site exposed. The protruded surface of the apparatus is placed on the area of application just before injection (Caglar et al., 2017; Canbulat Sahiner et al., 2018).

Sucrose

In the study, 2 ml sucrose of 25% was used to reduce the pain level of the infants. Sucrose was administered to the infant orally via an injector. In the literature, the use of 25% 2 ml sucrose administration has been reported as effective in reducing pain in infants during vaccination (Kassab et al., 2012).

In infants randomized to the ShotBlocker® group

After cleaning the skin, the short, blunt, pointed part of the ShotBlocker® was kept in contact with the skin. The ShotBlocker® was pressed firmly to the skin for 20 seconds, as reported previously (Caglar et al., 2017; DeMore & Cohen, 2005). The injection was administered through the central opening of the ShotBlocker® (see Figure 1). After completing the injection and removing the needle, the ShotBlocker® was removed.

Figure 1. ShotBlocker®

In infants randomized to the ShotBlocker®-placebo group

After cleaning the skin, the flat, non-pointed part of the ShotBlocker® was kept in contact with the skin. The ShotBlocker® was held lightly on the skin for 20 seconds. The injection was administered through the central opening of the ShotBlocker® (see Figure 1). After completing the injection and removing the needle, the ShotBlocker® was removed.

In infants randomized to the sucrose group

In-line with the routine procedure, sucrose was administered to the infant two minutes before vaccine injection. Sucrose was 25% and 2 ml was used, because it has been reported in the literature that sucrose in the amount of 0.1-2 ml and 20%-25% concentrations is effective in reducing pain in infants during vaccinations (Gao et al., 2016; Kassab et al., 2012)neonates in neonatal intensive care units can be exposed to numerous painful procedures every day requiring multiple doses of sucrose. Some experiments have been performed to examine the efficacy and safety of repeated sucrose administration for repeated procedural pain; however, a systematic review of this topic has not yet been carried out. Objective To identify and assess the evidence demonstrating the efficacy and safety of repeated sucrose for repeated procedural pain in neonates. Method A systematic review was conducted using the Cochrane methodology. Pubmed, Cochrane Library, Web of Science, CINAHL (Cumulative Index to Nursing and Allied Health Literature.

In infants randomized to the sucrose-placebo group

In-line with routine procedure, 2 ml sterile water (instead of sucrose) was administered to the infant orally via an injector two minutes before

vaccine injection. The assessors rated the pain without knowing which child was given sucrose and which one was given sterile water.

In infants randomized to the control group

Infants presented for routine vaccine administration in the centres where the study was conducted were selected as the control group. No pain-reducing method is used during routine vaccine administration in the centres. In other words, in actual clinical practices, infants are not provided any pain management method in these centres. Vaccine injections were performed in accordance with the routine procedure.

Data Collection

In present study, 237 infants were assessed for eligibility; and, 175 infants who met the inclusion criteria were randomized into groups, 35 infants in each group (see Figure 2). The standard questionnaire was filled out by the researcher after the infants were randomly assigned to their groups.

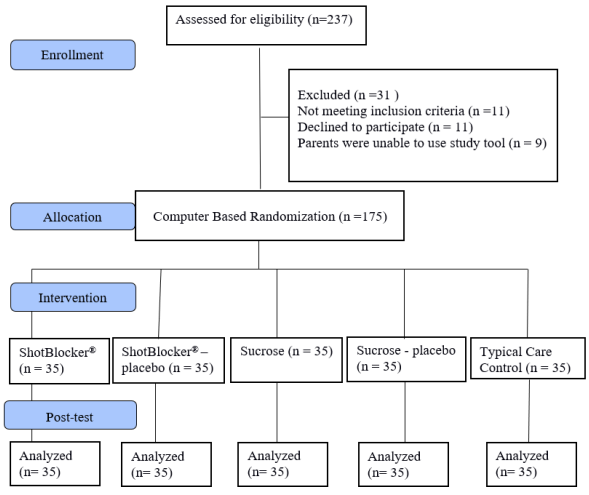

Figure 2. Consolidated Standards of Reporting Trials Diagram Showing the Flow of Participants Through Each Stage of a Randomized Trial.

Procedure

The researcher informed all parents about NIPS before the procedure. The babies of the parents in both the control and intervention groups were placed on the blanket and the parents stayed with the baby throughout the procedure. Firstly, the infant's pre-procedure pain levels were determined 1 minute before the injection by the nurses, parents, and observer through NIPS. Secondly, vaccine injections were administered by the nurses. Then, the process steps were applied on the basis of the infant's study group assignment. Lastly, perceived pain levels were measured by the nurses, parents, and observer during the administration of the vaccine injections (at the 1st minute of the procedure). The independent observer had completed undergraduate education in the field of nursing and working for nine years at a paediatric clinic. She was trained by the researcher to assess the infant's pain levels using NIPS.

Data Analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) version 22.0 for Windows (IBM Corp, Armonk, NY). Data were then analysed using descriptive statistics, chi-square test, ANOVA, and the Intraclass Correlation Coefficient (ICC). Shapiro–Wilk test was implemented to determine whether the sample data were normally distributed, and it was determined that all data were normally distributed. The chi-square and ANOVA tests were used to determine whether there was a difference between the groups based on gender, age, length, and weight of the new born. ANCOVA was used to determine whether there was a difference between the groups in terms of procedural pain. In addition, ANCOVA was used to eliminate the effect of gender and Body Mass Index (BMI) variables in the evaluation of the differences between groups. The ICC was used to determine whether there was a consistency between the observers in terms of the pain scores

of the newborns. The level of significance was set at p ≤ .05. Post-hoc pairwise comparisons with a Games Howell and Tukey HSD (p ≤. 05) were then performed. According to the literature, the impact size is "low" if the eta-square value is .01, "moderate" if it is .06, and "high" if it is .14 (Alpar, 2011).

Ethical Aspect of the Research

his study was designed with placebo and control groups in order to compare the effects of the interventions. At the time of commencing this study, we considered that this study was ethically justified based on current practices, i.e., nothing was done to alleviate pain in this setting.

Ethical approval for the study was obtained from the ethics committee of a university (Decision No: 2019/161; Date: 11.09.2019). The purpose of the research and the study methods were explained to the parents, and verbal and written informed consents were obtained before vaccination, observations, and measurements. The study was registered.

RESULTS

In this study, 53.1% of the infants were female, and 46.9% were male. The average weight and length of the infants were 4.08 ± .82 and 51.98 ± 2.67, respectively. There was no significant difference in infant age (30 days), weight, length, and gender among the five groups (Table 1).

Table 1. Characteristics of Newborns Included in the Randomized Controlled Trial (n=175)

Groups	Gender		Weight (kg)	Length (cm)
	Female n (%)	Male n (%)	Mean±SD	Mean±SD
Entire Sample (n=175)	93 (53.1)	82 (46.9)	4.08±.82	51.98±2.67
ShotBlocker® (n=35)	20 (57.1)	15 (42.9)	4.34±.94	51.88±2.92
ShotBlocker®-Placebo (n=35)	18 (51.4)	17 (48.6)	4.13±.78	51.28±2.61
Sucrose (n=35)	17 (48.6)	18 (51.4)	3.9±.87	52.68±2.89
Sucrose-Placebo (n=35)	20 (57.1)	15 (42.9)	4.16±.69	52.60±2.00
Typical Care (n=35)	18 (51.4)	17 (48.6)	3.87±.74	51.45±2.64
Test value	χ2=0.826		F=2.090	F=2.067
p values	p=.935		p=.084	p=.087

SD= Standard Deviation; χ2= chi- square test; F= ANOVA test

The level of procedural pain the infants experienced during injection was assessed by parents, nurses, and an independent observer. There was a statistically significant and high coherence between all measurements (ICC values of the groups respectively: ShotBlocker® = .900; Sucrose=.862; ShotBlocker®-Placebo=.740; Sucrose-Placebo= .817; Typical Care=.829, all p values < .001) (Table 2). The pre-injection pain scores of all infants in the study were found to be 0 (no pain) by all observers. There was no significant difference in pre-injection pain scores between groups (p > .05).

Table 2. Intraclass Correlation between the NIPS Score of Parent, Nurse and Observer (n=175)

Values	ShotBlocker®	Sucrose	ShotBlocker® -Plecebo	Sucrose -Placebo	Control (Typical Care)
ICC	.900	.862	.740	.817	.829
Lower Bound	.610	.511	.285	.415	.438
Upper Bound	.946	.758	.672	.753	.767
p	.000	.000	.000	.000	.000

SD= Standard Deviation; ICC= Intra-Class Correlation

There were statistically significant differences between the pain scores of the experimental and control groups, as determined by the parents, nurses, and the observer (all p values ≤ .001, Table 3).

The pain scores of the infants in the ShotBlocker® and sucrose groups were statistically lower than those in the placebo and control groups according to the Games Howell test results of the parents (p ≤ .001). Similarly, the pain scores of the infants in the ShotBlocker® and sucrose groups were statistically lower than those in the placebo and control groups according to the Tukey HSD test results of the nurses and the observer (p ≤ .001). For all observers, the children in the ShotBlocker® group had the lowest pain scores compared to the other two groups, but there was no statistically significant difference between the ShotBlocker® and sucrose pain scores (p > .05). According to the NIPS pain score averages, the eta-square values, showing the level of impact for all three assessments, were η^2 = .376 for the parents, η^2 = .502 for the nurses, and η^2 = .533 for the observer (indicating a high level of impact for all three assessments). According to the NIPS pain score averages in the gender control model, the eta-square values, showing the level of impact for all three assessments, were η^2 = .040 for the parents, η^2 = .054 for the nurses, and η^2 = .058 for the observer (Table 3). In addition, BMI has no effect on pain scores determined by parents, nurses and observer. According to the NIPS pain score averages in the BMI control model, the eta-square values were η^2 = .002 for the parents, η^2 = .004 for the nurses, and η^2 = .009 for the observer.

Table 3. Comparisons of Procedural Pain Scores among Groups

Groups	Parent- reported Mean±SD	Nurse- reported Mean±SD	Observer- reported Mean±SD
ShotBlocker® (n=35)	5.46±.95	4.71±.89	4.54±.88
Sucrose (n=35)	5.49±.81	4.74±.81	4.69±.75
ShotBlocker® -Placebo (n=35)	6.43±.69	6.11±.79	6.00±.80
Sucrose-Placebo (n=35)	6.37±.69	6.09±.78	6.09±.78
Control (Typical Care) (n=35)	6.83±.38	6.49±.56	6.49±.61
Test value	F=25.436	F=42.589	F=48.303
p value	p=.001	p=.001	p=.001
Effect size (η^2)	.376	.502	.533
Gender	F=7.005	F=9.174	F=10.451
	p=.009	p=.002	p=.001
Effect size (η^2)	.040	.054	.058

Covariate variable; gender, BMI (Body Mass Index) F; ANCOVA test statistics result SD= Standard Deviation; η2= Eta-square

DISCUSSION

Routine vaccination in childhood is considered a strong, safe, and cost-effective measure to eliminate and control infectious diseases; however, the pain experienced during vaccination is noted as an important barrier in terms of vaccine rejection by parents (Kumar et al., 2019; Taddio et al., 2017)many individuals either refuse or delay immunization because of pain from the needle puncture. Several methods have been employed to reduce injection pain during immunization in children.Methods: Study comprised of 210 healthy infants coming for immunizations. They were divided into three groups A, B and C having equal number of infants. Group A was given oral sucrose solution, group B was given topical

anaesthetic prior to immunization; whereas group C acted as controls. Response to pain was recorded among the three groups and findings were analyzed.Results: Infants enrolled in group A, i.e. those who were given 24% oral sucrose solution before immunization showed significant reduction in pain (measured by modified behaviour pain scale. The American Society for Pain Management Nursing reports that those who undergo painful interventions have the right to optimal pain management before, during, and after the procedure (Yilmaz Kurt et al., 2019). In this study, the effectiveness of ShotBlocker® and sucrose interventions in the management of pain during vaccinations in infants was evaluated using comparisons with placebo and control groups. No pain-reducing method is used during routine vaccine administration in the centres where the study was conducted. For this reason, the routine vaccination procedure of the clinic was evaluated as the control group. In this study, placebo/no treatment groups were used to draw attention to the fact that infants experienced high levels of pain due to vaccination without any pain-reducing method. However, for future infant pain studies it is recommended that there should be no placebo/no treatment groups because of the abundant strong evidence of sweet solutions. Thus, in the present study, it was also compared to the pain level of infants during routine vaccine practices with the intervention groups. For the infants in each group, parents, nurses, and an observer determined the pain scores.

Varying results have been reported for the effect of variables such as age, gender, and previous painful experiences on pain perception during invasive procedures in children. Some studies have stated that these variables affect perceived pain (Karakaya & Gözen, 2016; Yilmaz Kurt et al., 2019). In the present study, it was determined that all groups were homogeneous in terms of age, gender, weight, and length ($p > .05$). Thus, the influence possibility of these variables was reduced when evaluating the effect of the sucrose and ShotBlocker methods in reducing perceived pain. There are studies evaluating the effect of the position of infants on pain levels during vaccination (Lacey M Eden et al., 2014; Taddio et al., 2009).In our study, infants were in a supine position during vaccination. Studies evaluating different positions on vaccination pain can be applied.

Although there exist studies investigating the effectiveness of ShotBlocker® and sucrose in reducing pain during painful invasive procedures, there exist no studies comparing the effectiveness of these two frequently-used methods. In the intragroup comparison, there was a statistically significant strong correlation in the pain scores reported by the parents, nurses, and the observer. The same results reported by different observers indicate the strength of the research evidence. In addition, homogeneous groups were formed in order to increase the internal validity of the study; subjects were randomly assigned to groups; placebo and control groups were used; the researchers did not perform assessments in order to reduce expectation bias; and blinded assessments were made by those performing the pain assessments (parents, nurses, and the observer).

In the study findings, there was a statistically significant difference between the pain scores determined by the parents, nurses, and the observer for the ShotBlocker®, sucrose, ShotBlocker®-placebo, sucrose-placebo, and control groups (all p values $\leq .001$). The mean pain score determined by the parents, nurses, and the observer were found to be lower in the ShotBlocker® and sucrose groups than the control and placebo groups.

ShotBlocker® has an analgesic effect via peripheral transcutaneous electrical nerve stimulation according to the gate control theory (Binay et al., 2019). Different studies also found that ShotBlocker® relieves pain by providing electrical stimulation during painful procedures (Canbulat Sahiner et al., 2018; Çelik & Khorshid, 2015; Drago et al., 2009; Sivri Bilgen & Balcı, 2019; Taddio et al., 2009). Although there have been studies evaluating the effect of ShotBlocker in the last few years, none of them included the neonatal population or examined use during vaccine administration (Girgin et al., 2023; Gürdap & Cengiz, 2022; Savcı et al., 2022; Sivri et al., 2023. Canbulat Sahiner et al., (2018) reported that the pain scores of children in the ShotBlocker® group were significantly lower compared to the control group. Caglar et al., (2017) revealed that pain levels during vaccination in newborns were significantly lower when ShotBlocker® was used. All these research results support the present findings. In addition, the absence of decreased pain levels in the ShotBlocker®-placebo group compared to the controls, who underwent standard vaccination, also revealed the effect of ShotBlocker® on reducing pain caused by vaccine injection. In contrast, there exist varying results obtained in studies on the effectiveness of ShotBlocker®. For example, Cobb and Cohenimmunization injections cause negative short-term and long-term consequences for children. The Gate Control Theory of pain suggests that physical interventions (eg, rubbing the site (2009) did not support ShotBlocker® as an effective intervention to reduce children's pain during vaccination injections. These differences regarding the effectiveness of ShotBlocker® are believed to be due to differences in terms of age groups included these studies and the pain criteria used) (Canbulat Sahiner et al., 2018; Çelik & Khorshid, 2015; Drago et al., 2009; Sivri Bilgen & Balcı, 2019; Taddio et al., 2009).

More than 100 studies evaluating the effect of sweet solutions (sucrose or glucose) on reducing pain have shown that the use of small volumes of sweet solutions during painful procedures significantly reduces behavioural responses and pain scores in newborns and young infants (Gao et al., 2016; Denise Harrison et al., 2017; Matsuda, 2017; Stevens et al., 2016). Harrison et al. found that infants who received oral sucrose prior to procedures exhibited a lesser behavioural response to pain at the end of the procedure than those who received a placebo (Harrison et al., 2003). Similarly, Stevens et al. found that sucrose reduces pain during IM injection administration (Stevens et al., 2016) In their meta-analysis study, Liu et al. found that the combined use of non-nutritious suction and oral sucrose reduced pain scores and decreased crying time (Liu et al., 2017). In our study, it was found that the use of sucrose was effective in reducing pain in infants who received the Hepatitis B vaccine ($p < .001$, Table 3). The release of endogenous opioids is believed to be the mechanism underlying the analgesic effect of sucrose (Yilmaz et al., 2014). The reason behind the ineffectiveness of the sucrose-placebo (2 ml of sterile water) intervention in reducing pain can be attributed to this theory.

Different amounts of sucrose are applied to reduce pain in infants. In present study 25% 2 ml sucrose was used because it has been reported in the literature that 0.1-2 ml sucrose in 20%-25% concentrations is effective in reducing pain in infants during vaccinations (Gao et al., 2016; Kassab et al., 2012). However, it was reported that oral administration of a very small dose of sucrose (0.1 ml) appears to be equally effective at reducing pain in neonates during a single painful

procedure (Stevens et al., 2018). For this reason, it is recommended to apply a minimal effective dose of sucrose.

There were no statistically significant differences between the ShotBlocker® and sucrose pain scores for all observers in this study ($p > .05$). This finding suggests that both methods can be used effectively during infant vaccinations. These results have important implications for clinical practice. Although the effectiveness of sucrose in reducing procedural pain, particularly in vaccinations, has long been well-known, it is not routinely administered in clinical practices (Aydin & Avşar, 2019). The fact that ShotBlocker® and sucrose are practical, and relatively inexpensive methods can also increase its use in routine clinical practices. This information is important for healthcare professionals working with infants both in hospitals and outpatient settings, because these non-pharmacological methods are readily available, involve a very short start time for analgesia, and are economical and easy to use (Aydin & Avşar, 2019; Canbulat Sahiner et al., 2018; Matsuda, 2017; Stevens et al., 2018; Taddio et al., 2009).

Limitations

There were a few limitations to be considered when interpreting the findings of this study. First of all, because of the nature of the intervention, double-blinding was not possible in this study. Secondly, although a homogeneous sample increases internal validity, it may raise questions about the generalizability of these findings to children of different ethnicities and ages. Thirdly, immobilizing the child's leg during vaccination caused difficulties in evaluating leg movements, a category of NIPS. Lastly, no pain-reducing method is used during routine vaccine administration in the centres where the study was conducted. These infants receiving routine vaccine administration were selected as controls.

IMPLICATIONS FOR PRACTICE

In this study, it was concluded that the use of ShotBlocker® and sucrose reduced infant pain levels during vaccination according to all observers and that there was no statistically significant difference between these two methods. Therefore, both methods can be used effectively in infant vaccination practices. This study contributes valuable evidence supporting the effectiveness of ShotBlocker® and sucrose interventions in reducing pain during vaccination in infants, with implications for improving pain management practices in clinical settings. These methods are practical, relatively inexpensive, and readily available methods for pain management during vaccination. In addition, the present results also provide evidence that ShotBlocker® can be used safely as an alternative method when sucrose is not possible.

The study's findings provide important insights for healthcare professionals, indicating that these non-pharmacological methods can be easily incorporated into routine clinical practices to alleviate pain during vaccinations in infants. The study suggests that healthcare professionals should consider utilizing ShotBlocker® and sucrose interventions during infant vaccinations to minimize pain. This information is important for healthcare professionals working in infants both in hospitals and outpatient settings because these non-pharmacological methods are readily available, involve a very short start time for analgesia, and are low-cost and easy to use. Further research is needed to support these findings. However, for future infant pain studies it is recommended that there should be no placebo/no treatment groups because of the abundant strong evidence of sweet solutions as well as breastfeeding in infants aged ~1 month. In this

context, it may be suggested that further research should focus on whether there is a difference between the use of both methods and the use of sucrose alone. Further research could explore the effectiveness of these interventions in other age and different cultural groups or settings, as well as investigate the optimal dosage of sucrose for pain management.

Acknowledgement

We wish to thank all the parents who participated with their infants. A special thank you is also extended to the observer and nurses for providing practical assistance during the study. No conflict of interest has been declared by the authors. This research did not receive any specific grant from any funding agency neither in the public nor in the commercial or no-profit sectors. Approval for the study was obtained from the Ethics Committee of a university faculty of medicine (Date: 11/09/2019, #2019/161). Concept and Design: Z.C., M.Z., E.H.Y., and E.V., Data Collection and Processing: Z.C., M.Z., and E.V., Analysis and Interpretation: Z.C., M.Z., and E.H.Y., Literature Search: : Z.C., M.Z., E.H.Y., and E.V., Writing: Z.C., M.Z., and E.H.Y.

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