Pain Management Nursing 20 (2019) 54–61

Contents lists available at ScienceDirect

Pain Management Nursing

journal homepage: www.painmanagementnursing.org

Original Article

Oral Glucose and Listening to Lullaby to Decrease Pain in Preterm Infants Supported with NCPAP: A Randomized Controlled Trial

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ARTICLE INFO

Article history:
Received 13 October 2016
Received in revised form
18 February 2018
Accepted 4 April 2018

ABSTRACT

Background: Preterm infants spend the early days of their lives in neonatal intensive care units, where they undergo many minor painful procedures. There are many nonpharmacologic methods that can effectively reduce the pain response of neonates who undergo routine procedures.
Aims: This study aimed to investigate whether oral glucose and listening to lullabies could bring pain relief during the removal and reinsertion of the tracheal tube and also oronasopharyngeal suctioning in premature infants to whom nasal continuous positive airway pressure was applied.
Design: A double-blind, randomized controlled trial.
Setting: This study was conducted in the neonatal intensive care unit in the tertiary setting between November 2012 and September 2013.
Participants/Subjects: A total of 106 preterm infants were divided into three groups, including 37 infants in the control group, 35 infants in the lullaby group, and 34 infants in the glucose group.
Methods: All preterm infants were randomly assigned to either the intervention groups or the control group. Pain responses were assessed using the Neonatal Infant Pain Scale and the Premature Infant Pain Profile.
Results: An assessment of the pain severity of the preterm infants after the intervention indicated that the preterm infants in the lullaby and glucose groups had lower pain, whereas the preterm infants in the control group experienced more pain ($p < .05$).
Conclusion: The findings suggest that pain could be reduced significantly in preterm infants after the suggested intervention, although further studies are required to identify the benefits of lullabies or glucose in infants during other painful procedures.

Preterm infants spend the early days of their lives in the neonatal intensive care unit (NICU) (Ancora et al., 2013), where they are subjected to approximately 50 to 150 potentially painful procedures every day (Morais et al., 2016), totaling around 750 procedures (Page, 2004) throughout the period of hospitalization in the NICU. The most common procedures in clinical nursing practice are intubation, aspiration of the tracheal tube, collection of samples by arterial puncture, and venous access (Morais et al., 2016), although this may vary depending on the clinical status of the infant and the length of hospitalization (Morais et al., 2016; Standley & Swedberg, 2011).

One such painful procedure that is often required in preterm infants is nasal continuous positive airway pressure (NCPAP) (SUPPORT Study Group, 2010; Weiner & Zaichkin, 2016), which is associated with complications as nasal trauma, pain, gastric distention, and obstruction, imposing more burdens on health care team and resulting in overall perceived patient discomfort (Abdel-Hady, Shouman & Aly, 2011; Campbell, Shah, Shah, & Kelly, 2006; Shoemaker, Pierce, Yoder, & DiGeronimo, 2007). Changing the nasal cannula is one of the most common nursing procedures in preterm infants who are supported with NCPAP (Cignacco et al., 2008). The most common painful procedures include endotracheal and nasopharyngeal suctioning (Simons et al., 2003).

Several studies have reported that the use of CPAP alone reduces the need for surfactants in premature infants (SUPPORT Study Group, 2010; Weiner & Zaichkin, 2016). Manipulation of the CPAP prongs

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https://doi.org/10.1016/j.pmn.2018.04.008
1524-9042/

(insertion/reinsertion) is the most prevalent procedure, accounting for 24.3% of the total 27 documented procedures. It has been reported that in preterm infants the removal and insertion of CPAP prongs is a standard procedure after each change of the position of the neonate and also for nasopharyngeal suctioning. The second most common painful procedure is nasopharyngeal suctioning, followed by transcutaneous O_2 tape removal (Cignacco et al., 2009).

Recent studies have indicated that painful procedures experienced by newborns may lead to neurologic and behavioral changes (Morais et al., 2016). Neonates experience acute measurable physiologic, behavioral, metabolic, and hormonal responses to pain (Witt, Coynor, Edwards, & Bradshaw, 2016), and among these, physiologic responses to painful stimuli in preterm infants are manifested as acute increases in the heart rate, blood pressure, heart rate variability, and intracranial pressure, as well as decreased arterial oxygen saturation (Milazzo et al., 2011). Several studies that involved animals and neonates have reported that the responses of infants to painful stimuli in repeated and prolonged episodes may have long-term consequences, including adverse effects on neurologic and behavioral development (Morais et al., 2016; Young, 2005). This is associated with the fact that the pain occurs at a critical time of neurologic maturation (Witt et al., 2016). Grunau (2013) presented evidence of long-term associations among repeated pain in the NICU and altered brain development, neurodevelopment, programming of stress systems, and later pain perception in preterm infants. Premature infants have a higher risk (50%) of developmental disabilities, the most common types of which are cerebral palsy, hyperactivity, and specific learning disabilities (Standley & Swedberg, 2011).

Although there are many validated pain scoring systems, there is no universal method for the assessment of pain in this population, which could be problematic given the lack of ability of neonates to communicate verbally. Objective measurements, such as heart rate, blood pressure, and salivary cortisol, can be used in an objective assessment. However, most care providers usually rely on the grimace, crying, and overall demeanor. Furthermore, there is a lack of understanding of how neonates perceive pain and the resultant adverse sequelae that can occur when pain remains untreated (Witt et al., 2016). In 2006 the American Academy of Pediatrics and the Canadian Paediatric Society published a policy stating that each health care facility should establish a neonatal pain control program aimed at the routine assessment of pain, reduction in the number of painful procedures, and reduction and prevention of acute pain resulting from invasive procedures (American Academy of Pediatrics & Fetus and Newborn Committee, 2006).

Strategies for stress reduction and systematic pain management are the main issues in the NICU (Cignacco et al., 2007), in which pain management remains an interdisciplinary task (Cignacco et al., 2007; Morais et al., 2016; Witt et al., 2016). Pain relief increases the homeostasis and stability of neonates, and the care and support of immature infants are essential, given the distress associated with neonatal intensive care (Gaspardo, Miyase, Chimello, Martinez, & Linhares, 2008). National guidelines and experts both suggest that the pain assessment of neonates should be implemented routinely and that pharmacologic and nonpharmacologic methods should be used to reduce pain to avoid its detrimental effects in infants, particularly in preterm infants (American Academy of Pediatrics & Fetus and Newborn Committee, 2006; Harrison, Yamada, & Stevens, 2010b). In particular, the use of nonpharmacologic interventions is of great importance because they are based on clinical pain assessments performed by nurses and can be carried out by nursing staff (Cignacco et al., 2007).

Nonpharmacologic interventions are used alone or in combination with pharmacologic treatment modalities in repeated painful procedures among hospitalized neonates, and various nonpharmacologic pain prevention and relief interventions have been found to effectively reduce the pain response of neonates undergoing routine procedures (American Academy of Pediatrics & Fetus and Newborn Committee, 2006; Harrison et al., 2010b). These interventions include the use of oral sucrose/glucose, breastfeeding, kangaroo care, and listening to music (Gabriel et al., 2013; Gradin, Eriksson, Holmqvist, Holstein, & Schollin, 2002; Hartling et al., 2009; Johnston et al., 2014).

Currently the administration of sweet solutions (in particular, sucrose and glucose) is widely recommended for routine use before painful procedures in neonates (Deshmukh & Udani, 2002; Lindh, Wiklund, Blomquist, & Håkansson, 2003), although repeated use of oral sweeteners may have side effects on preterm infants (Slater et al., 2010). The administration of glucose is the most commonly investigated nonpharmacologic intervention for the relief of procedural pain among neonates (Cignacco et al., 2009). Kassab et al. (2012) investigated glucose solution with sterile water before vaccinations in healthy infants and found out that the mean full-lung crying time and mean total crying time were significantly shorter in the glucose group (Kassab, Sheehy, King, Fowler, & Foureur, 2012). In a study by Matar et al. (2016), neonates were given 2 mL of 10% glucose solution 2 minutes before the procedure (intervention group); researchers found that the mean Neonatal Pain Assessment Scale scores after venipuncture or nasopharyngeal suctioning were significantly lower in the intervention group than in the control group (Matar, Arabiat, & Foster, 2016). Kumari et al. (2017), investigating pain response using the Premature Infant Pain Profile (PIPP) score at 30 seconds after heel lance in preterm neonates, found no significant difference between the 25% glucose and 24% sucrose study groups with respect to PIPP scores, duration of crying, and rate of adverse events (Kumari, Datta, & Rehan, 2017). Glucose, which is more readily available in specific concentrations, has been suggested to have the same mode of action and similar analgesic effects to sucrose, and so can be proposed as a simple and cost-effective alternative to sucrose (Guala et al., 2001).

Over the past decade, several studies have examined the effects of music therapy on premature infants and have reported that music improves physiologic response (i.e., heart rate and oxygen saturation) and behavior in infants and reduces their stress during painful procedures (Alipour, Eskandari, Tehran, Hossaini, & Sangi, 2013; Garunkstiene, Buinauskiene, Uloziene, & Markuniene, 2014; Oh, Yang, Lee, Park, & Kim, 2013). To date, however, to our knowledge, there has been no study on the pain-relieving effects of glucose and lullabies during the removal and reinsertion of tracheal tubes and oronasopharyngeal suctioning. In the present study we investigated whether oral glucose and listening to lullabies had a pain-relieving effect during the removal and reinsertion of tracheal tubes and during oronasopharyngeal suctioning in premature infants to whom NCPAP is applied.

Methods

This double-blind, randomized controlled trial was conducted to evaluate the effects of recorded lullaby music and oral glucose on pain in premature infants hospitalized in the NICU during interventions.

Sample and Setting

This study was conducted in the NICU at a university hospital in Turkey between November 2012 and September 2013. The minimum sample size was computed as 30 for each group at a power of 80% and a margin error of 5%. As recommended by the biostatistician of the study, the final group size was considered as a minimum of 30 preterm infants. During the study period, a total of 289 preterm infants were admitted to the NICU, 188 of the patients underwent CPAP treatment, and 106 of the patients met the inclusion criteria. These infants were divided into three groups, including 37 infants in the control group, 35 infants in the lullaby group, and 34 infants in the glucose group. All preterm infants were randomly assigned to either the intervention or control groups, with randomization performed using a sealed envelope method to assign the preterm infants to one of the three groups: no application, oral glucose solution, and listening to lullabies.

The inclusion criteria were as follows: gestational age of 26-37 weeks; postnatal age of younger than 1 day and older than 9 days; Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) scores >5 at 5 minutes after birth; and appropriate body weight for gestational age. None of the infants received sedative drugs, such as phenobarbital, and none had intraventricular hemorrhage, sepsis, acute lung disease, congenital defects, hypersensitivity to sound, APGAR scores of ≤5 at 5 minutes after birth, neuromuscular dysfunction, or a history of maternal drug or alcohol abuse. The infants in the lullaby and glucose groups who experienced any significant medical problem, including laryngotracheal stenosis or handling, during the intervention were excluded from this study.

All participants met the inclusion criteria. Throughout the 9-month recruiting period, 106 (50 female; 56 male) preterm infants were included in the control (n = 37), lullaby (n = 35), and glucose (n = 34) groups. The mean gestational and postnatal age of the preterm infants were 30.80 ± 3.41 weeks and 2.31 ± 2.00 days, respectively. The mean birth weight of the preterm infants was 1603.25 ± 677.56 grams, and APGAR scores at 5 minutes ranged from 5 to 10. The mean postnatal age was 2.49 ± 2.12 days in the control group, 2.00 ± 1.91 days in the lullaby group, and 2.44 ± 1.98 days in the glucose group. A total of 51.4% of the preterm infants in the control group were male (n = 19), 51.4% of the preterm infants in the lullaby group were male (n = 18), and 55.9% of the preterm infants in the glucose group were male (n = 19). There was no statistically significant difference in the sex, gestational age, postnatal age, APGAR scores at 5 minutes, birth weight, birth height, or birth head circumference among the groups ($p > .05$; Table 1).

Data Collection Tools

A patient information form and an intervention follow-up form were used to collect data for this study. Pain responses were assessed using the Neonatal Infant Pain Scale (NIPS) and PIPP, both of which are used routinely in the NICU of our institution.

Patient Information Form

The patient information form was prepared by the researchers for the collection of data on the premature infants, including sex, gestational age, birth weight, birth height, and birth head circumference.

Intervention Follow-Up Form

The intervention follow-up form was prepared by the researchers to obtain physiologic data (i.e., oxygen saturation and heart rate) on the premature infants, recorded before, during, and after the intervention.

NIPS

The NIPS was developed for the evaluation of procedural pain or distress in a full-term or preterm infant (Lawrence et al., 1993; Lehr et al., 2015; Mathew & Mathew, 2003). The behavioral response of neonates to pain is assessed and rated with six subscales: facial expression, cry, breathing patterns, arm position, leg position, and state of arousal. Scores for behaviors in each subscale range from 0 (behaviors associated with no pain, such as the relaxed face, no crying) to 1 (behaviors often associated with pain such as the facial grimace and flexed or extended arms or legs). The subscale of cry has three levels with scores of 0-2. The neonatal behavior score is reached by adding the scores of each of the subscales, meaning a score range of 0-7 (Table 2). A score of 0-2 points indicates mild pain; 3-4 indicates moderate pain; and >4 points indicates severe pain. The Cronbach α coefficients were found to be .95, .87, and .88 before, during, and after the intervention, respectively, by Lawrence et al. (1993). In the present study the Cronbach α coefficients were found to be .77, .76, and .79 before, during, and after the intervention, respectively.

PIPP

The PIPP is a seven-indicator composite measurement scale that was developed at the University of Toronto and McGill University for the assessment of acute pain in preterm and term neonates (Ballantyne, Stevens, McAllister, Dionne, & Jack, 1999; Stevens, Johnston, Patrica, & Anna, 1996). The indicators include (1) gestational age, (2) behavioral state before painful stimuli, (3) altered heart rate during stimuli, (4) altered oxygen saturation, (5) brow bulge during painful stimuli, (6) eye squeeze during stimuli, and (7) nasolabial furrow during painful stimuli. The scores for each parameter range from 0 points to 3 points (Table 3). This tool also considers gestational age, and its validity and reliability were

Table 1
Comparison of the Control, Lullaby, and Glucose Groups According to the Information Characteristics of Premature Infants

Characteristics	Lullaby Group (n = 35)	Glucose Group (n = 34)	Control Group (n = 37)	Total	Test and *p*
	n (%)	n (%)	n (%)	N (%)	
Gender (male)[a]	19 (51.4)	18 (51.4)	19 (55.9)	56 (52.8)	$\chi^2 = 0.187$ $p = .911$
	mean ± SD	**mean ± SD**	**mean ± SD**	**mean ± SD**	
Gestational age (weeks)	31.57 ± 3.18	30.57 ± 3.47	30.26 ± 3.54	30.80 ± 3.41	F = 1.417 $p = .247$
Postnatal age (days)	2.00 ± 1.91	2.44 ± 1.98	2.49 ± 2.12	2.31 ± 2.00	F = 0.629 $p = .535$
5-minute APGAR score	8.31 ± 1.36	7.43 ± 1.42	7.83 ± 1.39	7.86 ± 1.42	F = 2.860 $p = .063$
Birth weight (g)	1774.14 ± 647.74	1582.50 ± 680.06	1460.67 ± 684.91	1603.25 ± 677.56	F = 1.985 $p = .143$
Birth height (cm)	40.78 ± 4.59	39.47 ± 4.88	38.26 ± 6.58	39.49 ± 5.49	F = 1.904 $p = .154$
Birth head circumference (cm)	29.61 ± 3.18	28.48 ± 3.77	28.26 ± 4.51	28.78 ± 3.87	F = 1.231 $p = .296$

SD = standard deviation; APGAR = Appearance, Pulse, Grimace, Activity, and Respiration.
[a] The percentage column is taken.

Table 2
Neonatal Infant Pain Scale (NIPS)

NIPS	0 Point	1 Point	2 Points
Facial expression	Relaxed	Contracted	—
Cry	Absent	Mumbling	Vigorous
Breathing	Relaxed	Different than basal	—
Arms	Relaxed	Flexed/stretched	—
Legs	Relaxed	Flexed/stretched	—
Alertness	Sleeping/calm	Uncomfortable	—

Maximal scores of 7 points, considering pain ≥4.

conducted by Akcan, Yigit, and Atici (2009). The total score is in the 0-21 point range, with higher scores indicate increased pain (Stevens et al., 1996). Within the scale, a score of 0-6 points indicates mild pain, 7-12 points indicates moderate pain, and 13-21 points indicates severe pain. The PIPP's Cronbach α coefficient was found to be .75 by Akcan et al. (2009), whereas the Cronbach α coefficient for the present study was found to be .73.

Procedures

This study protocol was approved by the Ethics Committee of Faculty of Medicine at Ataturk University, and the study was conducted in accordance with the principles of the Declaration of Helsinki. The aim and procedure of this study were briefly explained to the parents, and each parent then provided voluntary formal written consent. The demographic characteristics of the infants were garnered from hospital records, and neonatal medical charts were reviewed to ensure the absence of any contraindication to the intervention.

All interventions were performed by a single nurse because infants may perceive pain differently if the intervention is applied by different individuals. The infants in the control, lullaby, and glucose groups were placed in the supine position in an incubator. The tracheal tube was removed from the preterm infants to whom NCPAP was applied from one nostril, and the aspiration procedure was carried out from mouth and nose. After aspiration in the oronasopharyngeal area, a new tracheal tube was shortened, passed from a single nostril, and inserted into the pharynx, and the NCAP application was continued. The behavioral responses of the infants were recorded throughout the intervention with a video camera. None of the infants had heart rates >200 beats per minute (beats/min) or oxygen saturation <60%.

Physiologic parameters were recorded by a nurse using a monitor, while another nurse pushed the tension-measuring button at the same time as the removal and reinsertion of the tracheal tube and oronasopharyngeal suctioning. To record the baseline values, the video recording of the infant was started 3 minutes before the removal of the tracheal tube, and data, including oxygen saturation, heart rate, NIPS scores, and PIPP scores, were recorded. Other data, such as birth weight, birth height, birth head circumference, gestational age, postnatal age, and APGAR score at 5 minutes, were garnered from the medical records. During each session, the infant was observed every 3 minutes before, during, and after the intervention.

After completing the intervention, the intervention follow-up form was filled out by the investigator. Gestational age, behavioral state, heart rate, and oxygen saturation were assessed and recorded at the bedside.

Heart rate and oxygen saturation were recorded from the digital display on the bedside cardiac monitor (Nihon Kohden 2501K) connected to cardiac electrodes attached to the infant's chest according to the manufacturer's instructions, and an oximeter probe was placed on the right or left foot of each infant in three groups before the intervention. Heart rate and oxygen saturation levels were monitored continuously throughout the intervention, and the peak levels before, during, and after the intervention were recorded.

Facial actions were assessed, and the PIPP and NIPS scores were calculated. The video recordings of the applications were evaluated by four expert observers (a nurse specialized in child health and diseases, two neonatology specialists, and a pediatric neurologist) who were blinded to the group assignment. The evaluations were carried out independently from each other and in accordance with the aforementioned criteria. For each evaluation, the observers watched the videos of the infants and made PIPP and NIPS assessments before, during, and after the intervention. In addition, these observers were blind to each other and did not talk about the scores they gave. Scoring was made based on pain severity. The coefficient of concordance among the observers was calculated and was found to be at a good level (κ value = 0.67).

Intervention Groups

The Lullaby Group (n = 35)

The preterm infants were made to listen to lullabies through a portable speaker located around 30 centimeters away from their heads in the incubator. The thermal environment in the incubators (GE Giraffe) was managed with an air servo control to maintain the infants' body temperature when the isolate portals were open. The CD of lullabies chosen for the application was inserted into the CD player. During the reinsertion of the tracheal tube, the sound level of the CD player was modulated, and a lullaby was played in such a way that the sound level was 50-60 decibels in the incubator, in line with the findings of previous studies that investigated music therapy methods in infants (Alipour et al., 2013; American Academy of Pediatrics Committee on Environmental Health, 1997; Committee

Table 3
Premature Infant Pain Profile (PIPP)

Indicators	0 Point	1 Point	2 Point	3 Point
Gestational age	≥36 weeks	32-35 weeks and 6 days	28-31 weeks and 6 days	<28 weeks
Behavioral state	Active/awake Opened eyes Facial movements	Quiet/awake Opened eyes No facial movements	Active/sleep Closed eyes Facial movements	Quiet/sleep Closed eyes No facial movements
Heart rate (maximum)	0-4 beats/min increase	5-14 beats/min increase	15-24 beats/min increase	25 beats/min or more increase
Oxygen saturation (minimum)	0%-2.4% decrease	2.5%-4.9% decrease	5.0%-7.4% decrease	7.5% or more decrease
Brow bulge	None	Minimum	Moderate	Maximum
Eyes squeezed	None	Minimum	Moderate	Maximum
Nasolabial furrow	None	Minimum	Moderate	Maximum

None is defined as 0%-9% of the observation time; minimum, 10%-39% of the time; moderate, 40%-69% of the time; and maximum as 70% or more of the observation time. In this scale, scores vary from zero to 21 points. Scores ≤6 indicate absence of pain or minimal pain; scores >12 indicate the presence of moderate to severe pain (Stevens et al., 1996).
beats/min = beats per minute.

Table 4
Comparison of Lullaby, Glucose, and Control Groups Regarding Physiological Parameters before, During, and after the Procedure

Physiologic Parameters	Lullaby Group	Glucose Group	Control Group	Total	F; *p*
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Before Procedure					
Oxygen saturation	90.68 ± 6.60	92.70 ± 5.39	92.86 ± 5.22	92.09 ± 5.79	1.565; .214
Peak heart rate	151.77 ± 17.50	155.58 ± 20.13	144.43 ± 26.45	150.43 ± 22.10	2.416; .094
During procedure					
Oxygen saturation	82.91 ± 9.54	82.02 ± 9.31	82.56 ± 10.35	82.50 ± 9.67	0.072; .931
Peak heart rate	154.00 ± 23.02	152.02 ± 24.61	149.64 ± 23.14	151.84 ± 23.42	0.308; .736
After procedure					
Oxygen saturation	85.11 ± 8.36	83.08 ± 9.85	83.43 ± 7.83	83.87 ± 8.66	0.542; .583
Peak heart rate	160.88 ± 16.74	157.61 ± 22.13	157.43 ± 20.42	158.63 ± 19.75	0.336; .715

SD = standard deviation.

to Establish Recommended Standards for Newborn ICU Design, 2007; Dearn & Shoemark, 2014). Once the intervention was completed, the music was turned off. The intervention was made in the afternoon to reduce interference from environmental noise.

Glucose Group (n = 34)

One milliliter of 30% glucose was injected by syringe into the infant's mouth 1 minute before the intervention.

Control Group (n = 37)

No intervention was applied to the preterm infants in the control group aside from the routine application.

Statistical Analysis

The statistical analysis was performed using SPSS Version 18.0 software program (SPSS Inc., Chicago, IL, USA), and descriptive data were expressed as the mean and standard deviation and percentage. The normality of the data distribution was assessed using the Kolmogorov-Smirnov test, and an analysis of variance test was used to compare the control and intervention groups. A χ^2 test and a correlation in compatibility analysis between independent observers were used to analyze the collected data. A p value < .05 was considered statistically significant.

Results

Before the intervention, no statistically significant difference was identified in the mean peak heart rate and oxygen saturation among the groups ($p > .05$). After the intervention, the mean oxygen saturation was 85.11 ± 8.36% in the lullaby group, 83.08 ± 9.85% in the glucose group, and 83.43 ± 7.83% in the control group, which indicated no statistically significant difference ($p > .05$). The mean peak heart rate was 160.88 ± 16.74 beats/min in the lullaby group, 157.61 ± 22.13 beats/min in the glucose group, and 157.43 ± 20.42 beats/min in the control group, indicating no statistically significant difference ($p > .05$; Table 4).

No severe pain was experienced in the lullaby group, whereas 40% had mild pain and 60% had moderate pain. A comparison of the pain severity of the infants in the glucose group indicated that 35.3% had mild pain, 61.8% had moderate pain, and 2.9% had severe pain after the intervention. In the control group, 27% had mild pain, 64.9% had moderate pain, and 8.1% had severe pain. There was no statistically significant difference in the PIPP pain scores among the groups ($p > .05$; Table 5). A comparison of the pain severity of the infants in the lullaby group indicated that 82.9% had mild pain, 11.4% had moderate pain, and 5.7% had severe pain after the intervention. All infants (100%) in the glucose group had mild pain. In addition, none of the infants in the control group had severe pain, whereas 81.1% had mild pain, and 18.9% had moderate pain, indicating a statistically significant difference in the NIPS scores among the groups ($p < .05$; Table 5).

Before the intervention, there was no statistically significant difference in the PIPP scores among the groups, whereas the mean PIPP scores of the premature infants in the control group during the intervention (11.40 ± 1.99) were significantly higher than those of the infants in the lullaby and glucose groups (11.11 ± 2.86 and 9.97 ± 2.63, respectively) ($p < .05$). The mean PIPP scores of the premature infants in the control group after the intervention (8.35 ± 2.31) were significantly higher than the scores of the infants in the lullaby and glucose groups (6.77 ± 2.18 and 6.82 ± 2.27, respectively) ($p < .05$) (Table 6). According to the mean PIPP scores of the preterm infants after the intervention, the pain severity of the preterm infants in the lullaby and glucose groups were found to be lower, whereas the preterm infants in the control group experienced more pain. Before the intervention, no statistically significant difference was identified in the NIPS scores among the groups. The mean NIPS scores of the premature infants in the control group during the intervention (5.67 ± 0.81) were significantly higher than those of the infants in the lullaby and glucose groups (5.17 ± 0.92 and 4.20 ± 1.82, respectively) ($p < .05$). Also, the premature infants in the control group after the intervention (1.48 ± 1.04) had significantly higher mean NIPS scores than the infants in the lullaby and glucose groups (1.80 ± 1.38 and 0.58 ± 0.82, respectively) ($p < .05$) (Table 6). It can be understood from the mean NIPS scores after the intervention that the preterm infants in the glucose group had the least pain.

Discussion

In this study we investigated the effects of oral glucose and lullabies on pain severity during the removal and reinsertion of a tracheal tube and during oronasopharyngeal suctioning in premature infants to whom NCPAP was applied. The findings suggest that

Table 5
Comparison of Lullaby, Glucose, and Control Groups Regarding PIPP and NIPS Scores

Pain Level	Lullaby Group	Glucose Group	Control Group	Test; *p*
	n (%)[a]	n (%)[a]	n (%)[a]	
PIPP				$\chi^2 = 4.213$;
Mild: 0-6 points	14 (40)	12 (35.3)	10 (27)	.378
Moderate: 7-12 points	21 (60)	21 (61.8)	24 (64.9)	
Severe: 13-21 points	—	1 (2.9)	3 (8.1)	
NIPS				$\chi^2 = 11.089$;
Mild to no pain: 0-2 points	29 (82.9)	34 (100)	30 (81.1)	**.026**
Mild to moderate pain: 3-4 points	4 (11.4)	—	7 (18.9)	
Severe pain: >4 points	2 (5.7)	—	—	

Significant values are in bold.
PIPP = Premature Infant Pain Profile; NIPP = Neonatal Infant Pain Scale.
[a] The percentage column is taken.

Table 6
Comparison of Mean PIPP and NIPS Scores of Lullaby, Glucose, and Control Groups

Pain Level	Lullaby Group	Glucose Group	Control Group	F; p
	Mean ± SD	Mean ± SD	Mean ± SD	
PIPP				
Before the intervention	5.28 ± 2.06	5.32 ± 2.26	5.83 ± 2.45	0.666; .516
During the intervention	11.11 ± 2.86	9.97 ± 2.63	11.40 ± 1.99	**3.174; .046**
After the intervention	6.77 ± 2.18	6.82 ± 2.27	8.35 ± 2.31	**5.706; .004**
NIPS				
Before the intervention	0.22 ± 0.54	0.70 ± 1.24	0.45 ± 0.76	2.455; .091
During the intervention	5.17 ± 0.92	4.20 ± 1.82	5.67 ± 0.81	**12.416; .000**
After the intervention	1.80 ± 1.38	0.58 ± 0.82	1.48 ± 1.04	**11.048; .000**

Bold values are the statistically significant ($p < 0.05$) values.
PIPP = Premature Infant Pain Profile; NIPP = Neonatal Infant Pain Scale; SD = standard deviation.

the oxygen saturation and peak heart rate were higher in the lullaby group compared with the control group (Table 4). Previous studies have found that music therapy can have a significant clinical benefit for preterm infants in the NICU setting (Garunkstiene et al., 2014; Loewy et al., 2013). Garunkstiene et al. (2014) reported no changes in the oxygen saturation levels of preterm neonates when subjected to live or recorded lullabies, although Loewy et al. (2013) found out that music intervention improved physiologic measures, such as heart rate, respiration rate, oxygen saturation, and mean arterial pressure. Amiri et al. (2009) found that the mean change in the oxygen saturation level increased significantly in the music group, whereas Farhat et al. (2010) identified a significant difference in the oxygen saturation level during and after the intervention (Farhat, Amiri, Karbandi, Esmaily, & Mohammadzadeh, 2010). In another study, Jabraeili et al. (2016) reported a statistically significant increase in oxygen saturation in the lullaby group compared with the control group (Jabraeili, Sabet, Mustafa-Gharebaghi, Jafarabadi, & Ashadi, 2016). Taheri et al. (2017) reported that a recorded lullaby could increase oxygen saturation in neonates in the NICU, indicating that exposure to recorded lullabies can affect significantly oxygen saturation levels. Garunkstiene et al. (2014) found that lullabies effectively reduced heart rates in premature infants with a postpartum age of younger than 32 weeks. Wirth et al. (2016) found a significant decrease in heart and respiratory rates both during and after the intervention compared with the control group.

In the present study the mean oxygen saturation and heart rates of preterm infants in the intervention groups were found to be higher during and after the intervention compared with those in the control group, but no statistically significant difference was identified among the groups regarding the mean peak heart rate and oxygen saturation ($p > .05$). Uzelli and Yapucu Güneş (2015) also reported a lower mean oxygen saturation level in the control group during and after the intervention, although the heart rate in the control group was significantly higher than in the glucose group. In a similar study, an increase in the heart rate was identified with the administration of 30% glucose (Eriksson, Gradin, & Schollin, 1999), whereas other authors found no significant difference in the heart rates of the glucose and comparators (Bauer, Ketteler, Hellwig, Laurenz, & Versmold, 2004; Gharehbaghi & Ali, 2007; Gradin, 2005).

Listening to lullabies was found to reduce the immediate behavioral pain response rated with PIPP and NIPS scores compared with the control group in the present study (Table 6). Oh et al. (2013) also investigated the effects of music on response to pain during injection and found that the music group had lower NIPS scores compared with the control group. The results of the present study are consistent with previous findings (Dearn & Shoemark, 2014).

In the present study, 1 mL of 30% glucose reduced significantly the immediate behavioral pain response rated with PIPP and NIPS scores compared with the control group (Table 6). McCullough et al. (2008) studied pain response in preterm infants during nasogastric tube insertion and found out sucrose administered orally provided good pain relief (McCullough, Halton, Mowbray, & Macfarlane, 2008). Harrison et al. (2010a) supported this view, suggesting that sucrose and glucose reduced pain in infants up to 12 months of age. In another study, during subcutaneous injection, very preterm infants (28 to <32 weeks) were orally administered 0.3 mL of 30% glucose, and another group was administered 0.3 mL water; researchers recorded lower pain scores in the glucose group than in the water group (Fernandes, Campbell-Yeo, & Johnston, 2011). In another study, Kassab et al. (2012) suggested glucose as an effective analgesic for the immunization of pain in infants. Bergomi et al. (2014) also evaluated the effects of oral glucose and music during heel lance among premature infants and found that both glucose and music were well tolerated and effective in limiting pain increase compared with the standard procedure. Kumari et al. (2017) reported that the oral administration of 25% glucose affected pain in preterm infants during heel lance. Lima et al. (2017) also reported that neonates who received 25% glucose had lower NIPS scores than those in the non-nutritive sucking group. Similarly, the findings of the present study support the previously reported effectiveness of oral glucose in reducing pain. We recommend the use of a glucose solution as an analgesic before painful procedures given the ability of glucose concentrations to reduce pain. The glucose concentration is highly effective in reducing pain. According to the PIPP scores, oral sweet solutions (24%-30% sucrose and 25% glucose) provided higher analgesic effects, compared with heel lance, during gastric tube insertion in newborn infants. The use of small volumes of oral sweet solutions can therefore be recommended for use in clinical practice to decrease neonatal discomfort during gastric tube insertions (Chen, Zhang, Xie, Wen, & Harrison, 2017).

In contrast to the findings of the present study, Vezyroglou et al. (2015) investigated whether orally administered glucose reduced pain response during oropharyngeal suctioning in preterm infants while on NCPAP but could find no statistically significant difference in a comparison of the treatment effects, although this may be attributed to the gestational age of the study samples.

Implications for Nursing Research

Further studies are needed to examine the target feasibility, clinical utility, effectiveness, and safety of long-term use in many nonpharmacologic pain management interventions, and researchers may help health care professionals in promoting a stable approach to pain management by guiding practice. A large body of high-quality evidence supports the efficacy of glucose in the first month of life during commonly performed painful procedures. It should be noted that neonates who suffer from prolonged or persistent pain may not exhibit the usual behavioral signs of pain (American Academy of Pediatrics & Fetus and Newborn Committee, 2006). Reducing the exposure of premature and sick infants to painful procedures requires commitment, planning, and coordination at many levels of an organization, which includes a careful evaluation of the need for routine pathology testing, ensuring coordination of diagnostic and treatment modalities, reducing the need for multiple episodes of blood sampling, and judicious assessment of the need for such routine procedures as airway suctioning (Harrison et al., 2010b). In the present study we noted that the combined use of music and glucose led to lower pain scores than other methods.

The use of nonpharmacologic interventions, including glucose, lullabies, and breast milk, by nursing professionals before invasive procedures enhances the quality of care. Several studies have found that the use of these measures is dependent on knowledge of professionals about the effectiveness of these methods and, in particular, the use of protocols in the institution (Morais et al., 2016). Many studies have identified the ability of nonpharmacologic interventions to reduce pain in preterm infants, and these interventions should be used by all nurses who are working in a NICU setting for the management of medical conditions that result in moderate pain (Badr, 2012).

The nursing staff may be most familiar with the procedural pain behaviors of infants or young children, and pain management is one of the independent tasks of the nurse when dealing with painful procedures in infants. Accordingly, the nurse should evaluate the pain severity of the infant and should plan and administer the pharmacologic and nonpharmacologic pain management strategies developed with the health care team and assess their effectiveness.

We believe that our study results can contribute to the use of evidence-based and nonpharmacologic methods of pain management in pediatric nurses. Although there is limited evidence regarding the benefits of music therapy or lullabies during painful procedures, an environment that allows the parents of sick infants to individualize their infants' bedside environment and play their choice of music throughout the infant's stay is one of many ways to assist families and their infants during hospitalization (Harrison et al., 2010b). Guidelines should also highlight how to maintain the optimal effectiveness of sweet solutions over the course of prolonged procedures. Although listening to lullabies was found to be effective in reducing pain in preterm infants, the glucose group experienced less pain in the present study. In this regard, the application of oral glucose solutions during painful procedures can be used in NICUs.

Limitations of Study

There are some limitations to this study that should be noted. First, this study was conducted in a single center in a tertiary setting with relatively small sample size, and so the results of this study cannot be generalized for all preterm infants. Second, only one intervention (glucose, lullaby) was made in each infant, with each infant observed during and after the intervention. However, these interventions were not tested on all infants. Thus the interpretation of combined effects is precluded. Accordingly, further large-scale studies are required to assess the effects of glucose use and listening to lullabies on other physiologic parameters, such as crying time, through repeated measures.

Conclusions

The findings in this study indicate that pain could be significantly reduced in preterm infants, as measured by the NIPS and PIPP, and that the preterm infants in the glucose group experienced the least pain after interventions. This study suggests, therefore, that controlled interventions, such as lullaby music and glucose, could have positive effects on pain in premature infants. In this regard, we suggest the administration of glucose in addition to pharmacologic methods, especially before painful procedures during the neonatal period, because its application is simple, cost effective, and noninvasive. Further studies on the use of oral glucose and listening to lullabies are recommended in other areas of premature infant care.

Acknowledgments

This research was supported by Ataturk University Research Fund under project no. BAP 2012/404.

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