Effect of Auditory versus Olfactory Stimulation Interventions on Preterm Infants' Pain Response during Venipuncture

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Abstract

Background and Aim: Preterm infants' pain is prevalent in the Neonatal Intensive Care Units (NICUs), with numerous invasive procedures happening daily. Repeated and untreated pain have both short- and long-term sequelae. Therefore, the aim of this study was to investigate the effect of auditory versus olfactory stimulation interventions on preterm infants' pain response during venipuncture. **Method:** A quasi-experimental comparative research design was utilized. A purposive sample of 90 preterm infants was elected from the NICU at Mansoura University Children Hospital. Preterm infants were divided equally into three groups: auditory, olfactory and control groups. A Preterm Infant Assessment Tool, Premature Infant Pain Profile (PIPP), and Neonatal Infant Pain Scale (NIPS) were used for data collection. **Results:** There was a statistical significant difference between the control, music, and lavender groups concerning their PIPP total mean scores before and after venipuncture and their NIPS total mean scores during venipuncture ($p< 0.001$). **Conclusion:** Preterm infants in the music and lavender groups had a considerable reduction in their pain response compared to the control group during venipuncture. **Recommendations:** Auditory and olfactory stimulation interventions are recommended as simple, safe and low-cost non-pharmacological methods that facilitate positive effects for preterm infants during painful procedures at NICUs**.**

Keywords: Auditory, Olfactory, Pain, and Preterm infants.

Introduction

Preterm infants are defined as live newborns born before 37 weeks of gestation **(World Health Organization, 2018)**. Preterm infants have organ systems that are vulnerable and immature, and they might encounter further adverse health issues than full-term neonates **(Humberg et al., 2020).** Around fourty percent of preterm infants encounter a complex range of unfavorable neurodevelopmental results. Hence, prematurity is a significant matter for health plans and needs longitudinal medical attention in Neonatal Intensive Care Units (NICUs) **(Lee & Ra, 2021).** The preterm infants' debilitated development isn't only a result of the atypical early-life environment of them **(Filippa et al., 2021),** but it is additionally related to medical elements, involving pain exposure **(McPherson et al., 2020).**

Pain is a disturbing emotional and sensory experience related to potential or actual tissue harm **(Maya-Enero et al., 2022).** Besides, the pain has been characterized as the "fifth vital sign" that ought to be routinely observed during clinical assessment **(Williams & Lascelles, 2020).** Routine painful procedures are commonplace to the essential therapeutic management and nursing care. Preterm infants are routinely encountering on average 12–17 invasive procedures daily **(Campbell-Yeo et al., 2022)** and a few preterm infants during the NICU stay might encounter more than 3000 painful procedures and as a result pain exposure is higher. Further on, numerous of the preterm infants have inherent acute or chronic circumstances, exposing them to a large number of diagnostic and therapeutic procedures **(Yaprak et al., 2022).**

Venipuncture is one of the major repeated painful procedures performed in the NICUs **(Talebi et al., 2022).** Additionally, only sixty percent of venipuncture is influential in a single attempt, the preterm infant is being more

exposed to painful incentives because of the many trials before achieving success **(Silveira et al., 2021).** Regardless of the high frequency of painful procedures implemented in the NICU, ordinarily these procedures are done without pain prohibiting or alleviating measures and no efforts are made to evaluate or reduce pain during these procedures **(Olsson et al., 2021).**

It is emphasized that the unfavorable impact of pain within preterm infants has been well recorded. Recognizing persistent pain is critical, since it can unfavorably influence their development in various domains **(Shiff et al., 2021)** and may contradict with infant's growth, change subsequent perception of pain, impair behavioral and cognitive development and prolong hospitalization **(Rad et al., 2021).** Preterm infants manifest slower pain recovery from anybody. The pain exposure impacts can accumulate, as the preterm infants may not have had the opportunity to get better from one iatrogenic procedure prior exposure to the next one **(Kaur et al., 2019).** Furthermore, unalleviated, recurred pain can precipitate irreversible injuries involving the brain, lead to adverse physiological consequences in all systems and, potentially influencing long term development and functional abilities causing motor and sensorial impairment **(Clifford-Faugère et al., 2019).**

As stated by the evidence, painful stimuli influence infant's early life experiences and long-term life consequences. Thus, sufficient pain management is a crucial issue in the NICU, and it is necessary to prohibit short- and long-term pain consequences **(van der Vaart et al., 2021).** Preterm infants have the right to obtain effective, safe, and efficient pain relief to enhance health outcomes **(Karadag et al., 2022).** This fact has guided developmental based care, that concentrates on grouping interventions to minimally manipulate the preterm infants, treating pain and as possible preventing painful procedures **(Tanju & Kurt, 2021).**

To inhibit and relieve pain both pharmacologic and non-pharmacologic methods are utilized in order to decrease the pain adverse effects on the preterm infants **(McPherson et al., 2020).** Pharmacological pain management is available; however, it has many limitations and many studies have questioned their applications and safety for preterm infants **(Baudesson de Chanville et al., 2017).** Therefore, to decrease the pharmacological treatment, non-pharmacological methods are widely used and suggested **(Clifford-Faugère et al., 2019).**

Studies have revealed the efficiency of non-pharmalogical interventions in reducing procedural pain and proposed that it should be regularly applied prior to painful procedures **(Lin et al., 2022).** Non-pharmacological strategies have been implemented as it has almost no side effects **(Yaprak et al., 2022).** These methods involve different types of developmental care which shown proportional efficacy **(Filippa et al., 2021).** So, there is an intense propensity in order to employ non-pharmacological approaches, as safe and simple methods for alleviating pain in preterm infants and the nurse may use non-pharmacological means as effective approaches to reduce pain **(Hoarau et al., 2021).** Numerous techniques have already been executed to alleviate pain depending on five senses; among them, smell, and hearing **(Rad et al., 2021).**

At birth preterm infants' senses are entirely developed and they have sensory abilities enabling them to manipulate their environment, that grants them to react properly to olfactory and auditory stimulations. Moreover, research studies recommend sensory stimulation may produce the analgesia effects through concise painful procedures **(Lan et al., 2021).** The gentle stimuli generate descending inhibitory pathways activation and endorphins secretion mediated by intermediate interneurons, that buffer the response of painful impulse in the spinal cord, termed "gate control". Auditory and olfactory stimulation interventions are reasonable and acceptable for nurses **(Duchamp-Viret et al., 2021).**

Auditory strategies include exhibiting infants to soothing sounds. Recently, several researchers have tested the effect of music or calming sounds on preterm infant's pain response during several painful procedures **(Shiff et al., 2021).** Many research studies have shown the favorable impacts of listening to

music therapy in lowering preterm infant pain from painful procedures such as venipuncture **(Karadag et al., 2022).** Music can support the preterm infants in their behavioral and physiological self-regulation **(Ettenberger et al., 2021).**

Likewise, olfactory strategies include altering the environment of preterm infants by revealing them to a calming smell like lavender through painful procedures. At birth, the olfactory system is more developed than their other senses. In previous studies, preterm infants showed recognized responses to diverse odors **(Maya-Enero et al., 2022).**

Additionally, when preterm infants exposed to various smells, they were conveying preferences. Therefore, olfactory stimulation with a favored scent may be an initial intervention to produce a favorable stimulation for preterm infants. As claimed by a systematic review, a pleasant and familiar aroma had calming influences, involving diminished the irritable behaviors (motor and facial signs) and duration of crying during painful procedures **(De Clifford-Faugere et al., 2022).**

Lavender has spasmolytic and sedative characteristics and has been magnificently utilized in order to manage pain during venipuncture. In addition, olfactory stimulus with lavender presented soothing impacts for extremely decreased blood oxygen saturation and increased heart rate of preterm infants experiencing painful procedures **(Duchamp-Viret et al., 2021).** As declared by a randomized controlled trial that lavender decreases preterm infants' pain response both during and after venipuncture **(Lee & Ra, 2021).**

Neonatal nurses are the main advocates for the right of preterm infants to sufficient pain relief. They have an essential protector role to preserve preterm infants from absolute pain sensation **(Popowicz et al., 2021).** Also, NICU nurses are accountable for finding an efficient method for pain management; they must apply a powerful evidence-based assessment tool to assure best management of pain **(Stenkjaer et al., 2019).** As well as nurses play a vital function in provision of developmental care to preterm infants in NICUs to produce a secure environment which supports favorable development, reduces the pain negative impact and lowers harmful stimuli **(Adam et al., 2019).**

Significance of the study

Preterm infants pain is a common challenge. The existing worldwide predictable preterm birth incidence rate is approximately10.6 percent, and in all countries, it is constantly increased; being a preterm infant is the main cause of mortality and morbidity **(Pavlyshyn et al., 2023).** Moreover, iatrogenic pain is a consequence of life saving procedures created to assist the prematurity various challenges. Actually, the preterm infants' sensitive developing nervous systems have indicated short- and long-term variations in their pain response **(Marchal et al., 2021).** The incidence of behavioral and cognitive impairments stays noticeable in preterm infants. Several researchers indicated that persistent procedural pain is a common factor which affects development of motor and behavior patterns, cognition and neurological of preterm infants in NICUs **(Lavanga et al., 2021).**

Due to the venipuncture frequency in the NICUs, it's important to assess and manage the pain responses of such procedure **(Silveira et al., 2021).** Conversely, particularly in developing countries, many procedures of venipuncture are performed without suitable measures. Despite innovations in this area of knowledge, there is yet few evidence advocating measures of pain management for preterm infants **(Yaprak et al., 2022).** Preterm infant pain is hugely neglected, underestimated, unnoticed and sufficiently undertreated, because of gaps between pain evidence, practice and knowledge among NICU nurses. Evidence revealed that procedural pain is often deficiently managed in neonatal period, and many painful procedures are applied without any pain relief measures **(Shen et al., 2021).**

Therefore, health care providers' understanding of preterm infant's pain is a major issue to improve care quality, promote long term infant wellbeing and health and minimize morbidity and mortality **(Lin et al., 2022).** Each NICU ought to develop a policy to supply proper pain relieve involving using measures to alleviate procedural pain and

reducing the painful experiences number as possible, not only because it is an ethical issue but also should be viewed as an essential part of routine nursing care **(Kia et al., 2021).** Because of the distinctive role of nurses in care of neonates, they require to be knowledgeable about non-pharmacological measures of pain relief and routinely initiate pain control with those measures. In addition, auditory and olfactory stimulation interventions are highly applicable and inexpensive measures **(Talebi et al., 2022).**

During the researcher investigators' empirical observation and clinical practice in the NICU, it was noticed that nurses do not use any measures to alleviate pain for preterm infants while performing venipuncture procedure. Auditory and olfactory stimulation might play a significant role as non-pharmacological pain management interventions during venipuncture procedures. Interventions should continue to be evaluated and should attempt to consider the psychosocial and neurobiological portions of preterm vulnerability for pain protection and treatment approaches.

Also, in Egypt there are no studies conducted to compare the effectiveness of auditory versus olfactory stimulation interventions on preterm infants' pain response, so, it is necessary to investigate the efficiency of several types of intervention. A better knowledge of efficient interventions for preterm infants' pain management will direct future research and clinical practice. Therefore, this study is carried out to compare the effect of auditory versus olfactory stimulation interventions on preterm infants' pain response during venipuncture.

Operational definitions

Auditory stimulation intervention: The research investigator used a toy with musical sound beside the preterm infant's ear at least two minutes before venipuncture, continued during venipuncture, and at least two minutes after venipuncture procedure. Voice level was measured by decibel using a mobile application called decibel dB meter (sound level app) to ensure a reduced level of voice for preterm infants not exceeding 45 dB, as suggested by the American Academy of Pediatrics (AAP).

Olfactory stimulation intervention: In this study, the olfactory intervention consisted of placing a cotton ball saturated with a natural lavender oil odor placed three centimeter (cm) in proximity to the preterm infant's nose at least two minutes before venipuncture, continued during venipuncture, and at least two minutes after venipuncture. Natural lavender oil is colorless, insoluble in water, and has a density of 0.885 g/ml.

Venipuncture: In the current study, cannula insertion was performed, and blood sampling was withdrawn.

Aim of the study

This study aimed to investigate the effect of auditory versus olfactory stimulation interventions on preterm infants' pain response during venipuncture.

Research hypotheses

The present study hypothesizes the following:

H1: Preterm infants who will receive auditory stimulation intervention before venipuncture will have significantly lower pain scores than those in the control group.

H2: Preterm infants who will receive olfactory stimulation intervention before venipuncture will have significantly lower pain scores than those in the control group.

Method

Research design

A quasi-experimental comparative research design was utilized to conduct the current study. A quasi-experimental design is a type of experimental design that is very similar to the true experimental design, except there is a loss of one criterion: control, manipulation, or randomization **(Donald & Stanley, 2019).**

Setting

The present study was carried out at the NICU on the 6th floor of the Mansoura University Children Hospital (MUCH) which is affiliated to Mansoura University Hospitals. It consists of six rooms: two ordinary rooms and four intensive care units that provide care and treatment for full-term and high-risk neonates. The unit capacity consisted of 33 incubators

and 14 beds. The unit is well equipped and provides care for neonates all over the Delta Governorates.

Subjects and sampling

A purposive sample of 90 preterm infants was included in this study and divided equally into three groups: control group (30), auditory stimulation intervention group (30), and olfactory stimulation intervention group (30). Preterm infants who required venipuncture for blood sampling and cannula insertion were enrolled if they met the following inclusion criteria: gestational age 28 < 37weeks, both genders, conscious, in the first week of life, stability of vital signs before venipuncture, and no pain experience due to previous venipuncture for at least the last 6 hours. The exclusion criteria involved preterm infants with neurological disorders, birth trauma, asphyxia, neonatal sepsis, congenital or genetic abnormalities (central nervous system and cardiovascular systems), receiving painkillers, sedatives, and anticonvulsants for 12 hours before venipuncture; preterm infants whose mothers had a history of receiving opioids, antidepressants, and anticonvulsants during pregnancy; Apgar score of less than seven at the 10^{th} minute of life; grade III and/or IV intraventricular hemorrhage; and preterm infants on mechanical ventilation.

Relied on literature data **(Moselhi Mater et al., 2019)**, and considering a significance level of 5% and a study power of 80%, the sample size can be computed by the subsequent formula:

$$n = \frac{(Z\alpha/2 + Z\beta)^2 \times 2(SD)^2}{d^2}$$

Where SD = standard deviation obtained from the preceding study; Zα/2, for 5% this is 1.96; Zβ, for 80% this is 0.84 and d is the expected difference. Therefore,

$$n = \frac{(1.96 + 0.84)^2 \times 2(1.07)^2}{(0.78)^2} = =29.5$$

Depending on the above formula, the required sample size for each group was 30.

Data collection tools

Three tools were used for data collection.

Tool I: A Preterm Infant Assessment Tool was developed by the research investigators to collect data regarding preterm infants and was divided into two parts:

Part I: Characteristics of Preterm Infant as gender, gestational age, birth weight, age on admission, current age at study, method of feeding, and diagnosis.

Part II: Preterm Infant's Physiological Status: Vital signs (respiration, pulse, and temperature) and oxygen saturation before and after venipuncture

Part III: Venipuncture Procedure Assessment Sheet: It was developed by the research investigators to collect data about the reasons for the venipuncture procedure (blood sampling or cannula insertion), site of puncture, duration of procedure, number of puncture trial and procedure complications.

Tool II: The Premature Infant Pain Profile (PIPP) was developed and validated by **Stevens et al., (1996).** The PIPP tool was validated and revised for use in preterm infants with a gestational age of 26–37 weeks by **Gibbins et al., (2014).** It is presently the most validated clinical test for determining the pain level in preterm infants. It consists of seven indicators for pain assessment in preterm infants: three behavioral responses (brow bulge, eye squeeze, and nasolabial furrow), two physiological responses (heart rate and oxygen saturation), and two contextual responses (gestational age and behavioral state). Each indicator is scored on a four-point scale (0–3) to give a maximum total score of 21. A score of 0–6 indicates minimal or no pain, a score of 7–12 indicates slight to moderate pain, and a score greater than 12 indicates severe pain.

Tool III: The Neonatal Infants Pain Scale (NIPS) was developed by **Lawrence et al., (1993)** and it is recommended for newborns with a gestational age of 28–38 weeks for the procedural pain assessment. It is a practical tool with high significance for clinical utility because it is feasible, easy, and does not require additional monitoring to record heart rate and oxygen saturation.

It includes five behavioral components (crying, appearance of the face, upper and lower limb movements, and alertness) and one physiological indicator (breathing patterns). Each item, except crying, had a possible score of 0 or 1. The cry has a possible maximum score of 2 (0= no cry, l= whimper, 2= vigorous cry). The total score ranges from 0 to 7. Total pain scores from 0 to 3 indicate no to mild pain, 4 to 5 indicate moderate pain, and 6 to 7 indicate severe pain.

Tools validity and reliability

Tool (I) was thoroughly reviewed by three experts to examine content validity. Modifications were made according to the experts' judgments on sentences clarity, content appropriateness, and items sequence. The internal consistency of Tool (I) was tested by using Cronbach's alpha coefficient test; r = 0.82 and 0.71 for (parts 2 & 3 respectively).Tool II (PIPP) is a standardized and valid tool, and its reliability was 0.96 **(Stevens et al., 1996)**. Also, tool III (NIPS) is a highly reliable and valid standardized tool, and its Inter-rater reliability was 0.97 **(Lawrence et al., 1993).**

Pilot study

The pilot study was implemented on 10 percent of the sample (nine preterm infants) to examine the feasibility of the study tools, application of tools, clarification of sentences, and estimation of the time required to collect the required data; unnecessary items were omitted, and required modifications were made.

Ethical considerations

An ethical approval was obtained from the Research Ethical Committee at the Faculty of Nursing, Mansoura University to carry out the current study (Ref. No. P. 0267). All parents of preterm infants who contributed in the study were informed regarding the procedure, aim, benefits, and nature of the study, and a formal written consent was obtained from them. The researcher asserted that the obtained data were only used for the research purpose. The confidentiality and anonymity issues of the data were assured, and the parents had the right to withdraw their preterm infants from the study at any time without any effect on the care provided to them.

Procedure

Before carrying out the current study, an ethical approval was obtained from the Research Ethical Committee at the Faculty of Nursing, Mansoura University to conduct the study. Official permissions were obtained from the director of MUCH and from the head of the NICU, where a clear explanation was given about the aim, nature, and expected outcomes of the present study. The researcher contacted the preterm infants' parents during the unit visiting hours to clarify the purpose and nature of the study and to obtain their consent to involve their preterm infants in this study. After the parents agreed to involve their preterm infants in the study, the first 30 preterm infants with the inclusion criteria were allocated to the control group, the following 30 preterm infants were assigned to the olfactory stimulation intervention group, and the following 30 preterm infants were appointed to the auditory stimulation intervention group.

The researcher was present two days a week during the morning shift. All preterm infants were individually observed by the researcher throughout the study period. Characteristics and medical data of the preterm infants at the three groups were obtained from the neonatal records on an individual basis; it took approximately 10-15 minutes (Tool I).

Before the procedure, the research investigator ensured that the preterm infants' diapers were clean, not in a hunger state, having their feeding up to one hour before the procedure, and in a quiet and calm state. For the three groups, the venipuncture procedure was carried out by the assigned nurses on duty while following a standardized procedure; venipuncture was used for medical reasons and not for the study. After the infant's examination, a proper procedure site was selected to ensure skin intactness; the skin was cleansed with disinfectant and waited for two seconds. Venipuncture was performed using a 20/21 G needle.

All preterm infants who were involved in the study stayed at rest for at least 30 minutes,

without any kind of stimulation before the evaluations, that happened during the daytime because it was the greatest activity period in the unit. Before the procedure, the hands were washed and adjusted to the preterm infant's body temperature. The preterm infants were put on a warmer by servo control with normal skin temperature in a calm room. All circumstances, involving light, the injection device, and room temperature, were the same for the three groups, and the venipuncture procedure was performed by a qualified nurse. The oxygen saturation and baseline heart rate, respiration, of all preterm infants were checked and documented maximum two minutes before starting the intervention at the initial time, during the procedure and for two minutes after finishing the procedure (using a standard cardiac monitor and a pulse oximeter).

The study started with preterm infants in the control group, who didn't receive any intervention and only received routine NICU care during venipuncture. For preterm infants in auditory intervention group: a toy with musical sound was placed 20 cm from the preterm infant's head beside the ear; the correct position was constantly verified by the research investigator for two minutes before the venipuncture procedure, during and also for two minutes after completing the venipuncture procedure in accordance with the literature. Moreover, the toy did not exceed the recommended sound levels to prevent over-stimulation.

The nurse and the research investigator didn't use any odorous substances during the procedure for preterm infants in the olfactory intervention group. First, natural lavender oil was placed in a cotton ball, which was placed three centimeters away from the preterm infant's nose. This procedure was starting two minutes before venipuncture because its effect was better when its smell became familiar to the preterm infant and was continued until the procedure was completed and for two minutes after finishing the venipuncture in accordance with the literature.

The preterm infant's pain was evaluated in real time by the research investigator. Pain assessment occurred at three moments. The PIPP (Tool II) was used to measure the preterm infant's pain twice for the three groups: the first time was the baseline immediately 30 seconds before the venipuncture procedure and the second time was two minutes after finishing the venipuncture. Preterm infants' pain during the venipuncture procedure was measured using the NIPS (Tool III), and preterm infants were observed to fully assess each indicator of this tool. After the application of the bedside scales at the described times, total scores were calculated.

Statistical analysis

All statistical analyses were performed using SPSS for Windows (version 20.0; SPSS, Chicago, IL, USA). All continuous data were normally distributed and expressed as mean ±standard deviation (SD). Categorical data were expressed as numbers and percentages. Comparisons were performed using the student's t-test for two variables with continuous data and ANOVA for more than two variables with continuous data. The chi-square test or Fischer exact test was used for comparison of variables with categorical data, as appropriate. The correlation coefficient test was used to assess the correlation between variables with continuous data. The Cronbach's alpha test was performed to test the internal consistency of the tools used in the study. Statistical significance was set at $p<0.05$.

Results

Table (1) illustrated that there was no statistical significant difference between preterm infants characteristics in music, lavender and control groups regarding their gender, gestational age, weight, age on admission, current age at study, method of feeding and diagnosis g (p = 0.581, 0.642, 0.998, 0.857, 0.111, 0.503 & 0.679 respectively).

Table (2) revealed that, pre-venipuncture there were no statistical significant differences of preterm infants' pre intervention vital signs (respiration, pulse & temperature) (p = 0.087, 0.498 & 0.263respectively) and oxygen saturation (p = 0.147), but there were statistical significant differences of preterm infants' post intervention vital signs (respiration, pulse & temperature) (p< 0.001) and oxygen saturation (p = 0.043).

Table (3) demonstrated that, most venipuncture procedure in music, lavender and control groups were for blood sampling (80%, 90% & 83.3% respectively), the site of puncture was arm in (80%, 70% &73.3% respectively), the duration of venipuncture procedure (43.3%, 56.7% & 53.3% respectively) in music, lavender and control groups were lasted from one to three minutes and the number of puncture trail was one trial in 50% of music group, 70% of lavender group and 60% of control group. This table also detected that there was no statistical significant difference between three groups regarding venipuncture procedure assessment.

Table (4) showed that, (100%, 33.33% & 96.7% respectively) of the preterm infants in music, lavender and control groups had grimace facial expression and (100%, 36.7% & 90.0% respectively) of them had whimper crying. Regarding breathing pattern (83.3% & 93.3% respectively) of music and control groups had variable breathing, but 86.7% of them in lavender group had relaxed breathing. The preterm infants' arms were relaxed in 60% of lavender group and were restrained in (56.7% & 80.0% respectively) of music and control groups. The preterm infants' legs in music and lavender groups were relaxed in (86.7 & 90.0 respectively) , but it was restrained in 83.3% of control group. The state of arousal was (100% & 93.3 respectively) not fussy in music and lavender groups, but it was fussy in 70.0% of control group. Also this table conveyed that there were statistical significant differences between the three groups regarding all items of NIPS.

Table (5) reported that during venipuncture procedure, 46.7% of preterm infants in music group and 83.3% in lavender group had mild pain, on the other hand, 56.7% of them in control group had moderate pain. This table also showed that there was statistical significant difference in NIPS total mean scores between the three groups ($p< 0.001$) and detected that the total NIPS mean score in control group 5.4 ±0.5 was higher than those in music and lavender groups (3.5 ±0.5&2.4 ±0.6) respectively.

Table (6) revealed that pre the venipuncture procedure; a statistical significant difference was detected in the total mean score of PIPP between the three groups ($p< 0.001$) with higher total mean of control group 5.4 ±0.7 compared to music and lavender groups (2.6 ±1.0 & 2.9 ±1.2 respectively). The same table also represented that post the venipuncture procedure; there was statistical significant difference in the total mean score of PIPP between the three groups ($p<0.001$) with higher total mean of control group 6.3 ±0.9 than music and lavender groups (2.3 ±1.1 & 1.8 ±0.7 respectively).

Table (7) manifested that there was statistical significant negative correlation between preterm infants' gestational age and their NIPS during venipuncture procedure in lavender group, otherwise there were no statistical significant correlations between preterm infants' other characteristics (gestational age, weight, age on admission & current age) and their PIPP pre and post-venipuncture procedure at three groups.

Table (1): Percent distribution of the studied preterm infants according to their characteristics (n=90):

Preterm infants' characteristics	Music		Lavender		Control		Chi-Square / Fisher's exact test	
	n	%	n	%	n	%	$\chi 2$	*p*
Gender								
Male	11	36.7	15	50.0	13	43.3	1.086	0.581
Female	19	63.3	15	50.0	17	56.7		
Gestational age (Weeks)								
28 – 30	8	26.7	7	23.3	10	33.3	0.445	0.642
30 – 32	15	50.0	16	53.3	16	53.3		
32 – 37	7	23.3	7	23.3	4	13.3		
Mean ±SD	30.6 ±2.2		30.8 ±2.0		30.3 ±2.1			
Weight (Grams)								
< 1500	19	63.3	20	66.7	17	56.7	0.002	0.998
1500 – 2500	7	23.3	6	20.0	6	20.0		
> 2500	4	13.3	4	13.3	7	23.3		
Mean ±SD	1577.7 ±526.9		1569.7 ±585.8		1573.4 ±510.8			
Age on admission (Days)								
1	22	73.3	24	80.0	24	80.0	0.154	0.857
2 – 4	6	20.0	3	10.0	5	16.7		
5 – 7	2	6.7	3	10.0	1	3.3		
Mean ±SD	2.1 ±0.8		2.0 ±0.9		2.0 ±0.7			
Current age at study (Days)								
1	10	33.3	3	10.0	7	23.3	2.248	0.111
2 – 4	8	26.7	10	33.3	12	40.0		
5 – 7	12	40.0	17	56.7	11	36.7		
Mean ±SD	3.5 ±1.7		4.5 ±2.2		4.4 ±2.1			
Method of feeding								
Enteral	6	20.0	8	26.7	9	30.0	3.337	0.503
Parental	8	26.7	3	10.0	5	16.7		
Enteral & Parental	16	53.3	19	63.3	16	53.3		
Medical diagnosis								
RDS	22	73.3	23	76.7	20	66.7	0.775	0.679
Other	8	26.7	7	23.3	10	33.3		

Table (2): Comparison of mean physiological status of preterm infants between music, lavender and control groups at pre and post venipuncture (n=90):

Physiological status	Music Group	Lavender Group	Control Group	One Way ANOVA	
	Mean ±SD	Mean ±SD	Mean ±SD	F	*p*
Pre – venipuncture procedure					
Vital signs					
Respiration	39.7 ±6.0	42.5 ±4.3	41.9 ±4.8	2.513	0.087
Pulse	147.3 ±11.9	144.1 ±8.0	145.9 ±10.8	0.702	0.498
Temperature	37.0 ±0.2	36.9 ±0.1	36.9 ±0.2	1.358	0.263
Oxygen saturation	94.5 ±2.3	93.5 ±1.9	93.8 ±2.0	1.963	0.147
Post – venipuncture procedure					
Vital signs					
Respiration	34.6 ±4.6	34.7 ±3.3	52.6 ±3.4	221.653	<0.001*
Pulse	137.7 ±9.3	134.8 ±6.0	158.2 ±8.3	76.514	<0.001*
Temperature	36.9 ±0.3	37.0 ±0.2	37.6 ±0.2	75.882	<0.001*
Oxygen saturation	96.9 ±2.0	94.3 ±16.2	88.4 ±16.1	3.248	0.043*

* Statistical significant difference at $p< 0.05$

Table (3): Comparison of the venipuncture procedure assessment sheet between music, lavender and control groups (n=90):

Venipuncture procedure assessment	Music		Lavender		Control		Chi-Square / Fisher's exact test	
	n	%	n	%	n	%	$\chi 2$	*p*
Reason of venipuncture								
Blood sampling	24	80.0	27	90.0	25	83.3		
Cannula insertion	6	20.0	3	10.0	5	16.7	1.184	0.553
Site of puncture								
Arm	24	80.0	21	70.0	22	73.3		
Leg	6	20.0	9	30.0	8	26.7	0.818	0.664
Duration of procedure (Minutes)								
≤ 1	8	26.7	9	30.0	8	26.7		
1 – 3	13	43.3	17	56.7	16	53.3		
> 3	9	30.0	4	13.3	6	20.0	2.645	0.619
Number of puncture trail								
One	15	50.0	21	70.0	18	60.0		
Two	11	36.7	9	30.0	12	40.0		
Three	4	13.3	0	0.0	0	0.0	9.438	0.051

Table (4): Comparison of the Neonatal Infants Pain Scale (NIPS) between music, lavender and control groups during venipuncture procedure (n=90):

Neonatal Infants Pain Scale	Music		Lavender		Control		Chi-Square / Fisher's exact test	
	n	%	n	%	n	%	$\chi 2$	*p*
Facial Expression								
Relaxed	0	0.0	20	66.7	1	3.3		
Grimace	30	100.0	10	33.3	29	96.7	47.329	<0.001**
Cry								
None	0	0.0	19	63.3	3	10.0		
Whimper	30	100.0	11	36.7	27	90.0	37.660	<0.001**
Breathing pattern								
Relaxed	5	16.7	26	86.7	2	6.7		
Variable breathing	25	83.3	4	13.3	28	93.3	49.091	<0.001**
Arms								
Relaxed	13	43.3	18	60.0	6	20.0		
Restrained	17	56.7	12	40.0	24	80.0	10.005	0.006*
Legs								
Relaxed	26	86.7	27	90.0	5	16.7		
Restrained	4	13.3	3	10.0	25	83.3	44.903	<0.001**
State of arousal								
Not fussy	30	100.0	28	93.3	9	30.0		
Fussy	0	0.0	2	6.7	21	70.0	47.073	<0.001**

* Statistical significant difference at $p< 0.05$

Table (5): Comparison of the Neonatal Infants Pain Scale (NIPS) total mean scores between music, lavender and control groups during venipuncture procedure (n=90):

Neonatal Infants Pain Scale	Music		Lavender		Control		Chi-Square / Fisher's exact test	
	n	%	n	%	n	%	$\chi 2$	*p*
Mild pain	14	46.7	25	83.3	2	6.7		
Moderate pain	11	36.7	3	10.0	17	56.7		
Severe pain	5	16.7	2	6.7	11	36.7		
Total NIPS Mean ±SD	3.5 ±0.5		2.4 ±0.6		5.4 ±0.5		32.739	<0.001**

* Statistical significant difference at $p < 0.05$

Table (6): Comparison of the Premature Infant Pain Profile (PIPP) between music, lavender and control groups at pre and post venipuncture procedure (n=90):

Premature Infant Pain Profile	Music	Lavender	Control	One Way ANOVA	
	Mean ±SD	Mean ±SD	Mean ±SD	F	*p*
Pre-venipuncture procedure					
Gestational age (Weeks + Days)	0.71 ±0.25	0.73 ±0.25	1.19 ±0.43	21.413	<0.001**
Observe infant	0.58 ±0.21	0.56 ±0.19	1.21 ±0.43	46.386	<0.001**
Heart rate (beats/min increase)	0.14 ±0.05	0.16 ±0.05	0.23 ±0.08	17.631	<0.001**
Oxygen saturation (% decrease)	0.13 ±0.05	0.16 ±0.05	0.35 ±0.13	64.246	<0.001**
Brow bulge	0.36 ±0.13	0.42 ±0.14	0.84 ±0.30	7.576	<0.001**
Eye squeeze	0.35 ±0.12	0.40 ±0.14	0.84 ±0.30	52.766	<0.001**
Nasolabial	0.37 ±0.13	0.44 ±0.15	0.81 ±0.29	40.736	<0.001**
Total Mean ±SD	2.6 ±1.0	2.9 ±1.2	5.4 ±0.7	74.694	<0.001**
Post-venipuncture procedure					
Gestational age (Weeks + Days)	0.71 ±0.25	0.73 ±0.25	1.19 ±0.43	21.413	<0.001**
Observe infant	0.51 ±0.20	0.35 ±0.13	1.40 ±0.48	100.254	<0.001**
Heart rate (beats/min increase)	0.12 ±0.05	0.10 ±0.04	0.27 ±0.09	63.688	<0.001**
Oxygen saturation (% decrease)	0.11 ±0.04	0.10 ±0.04	0.40 ±0.14	114.605	<0.001**
Brow bulge	0.32 ±0.12	0.26 ±0.10	0.97 ±0.33	104.673	<0.001**
Eye squeeze	0.31 ±0.12	0.25 ±0.09	0.97 ±0.33	109.315	<0.001**
Nasolabial	0.33 ±0.13	0.28 ±0.10	0.94 ±0.32	93.990	<0.001**
Total Mean ±SD	2.3 ±1.1	1.8 ±0.7	6.3 ±0.9	205.825	<0.001**

* Statistical significant difference at $p< 0.05$

Table (7): Correlation between the preterm infants' characteristics and their NIPS during venipuncture procedure and PIPP at pre and post venipuncture procedure (n=90):

	Gestational age		**Weight**		**Age on admission**		**Current age**	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
NIPS during venipuncture								
Music group	0.099	0.602	0.100	0.597	0.058	0.759	0.224	0.234
Lavender group	-0.471	0.009*	-0.091	0.633	-0.290	0.120	-0.291	0.119
Control group	-0.315	0.090	0.213	0.258	-0.141	0.457	-0.065	0.734
PIPP at pre-venipuncture								
Music group	-0.066	0.730	0.083	0.662	0.288	0.123	0.008	0.965
Lavender group	0.099	0.602	-0.021	0.913	0.269	0.151	-0.297	0.110
Control group	-0.275	0.141	-0.277	0.139	0.091	0.634	-0.044	0.818
PIPP at post -venipuncture								
Music group	-0.314	0.091	0.274	0.143	0.183	0.333	-0.163	0.389
Lavender group	0.108	0.572	-0.047	0.806	-0.020	0.918	0.108	0.570
Control group	0.114	0.549	-0.007	0.971	-0.312	0.093	0.084	0.660

* Statistical significant difference at $p<0.05$

Discussion

The evidence proved that preterm infants perceive pain, more responsively and suffer from significant sequelae due to their neurological system immaturity **(Clifford-Faugère, Lavallée &Aita, 2017)** and the preterm infant's NICU experience is rife with invasive procedures and pain inducing experiences. Therefore, non-pharmacological techniques are suggested as the first-line treatment as stated by the neonatal pain management guidelines **(Balice-Bourgois et al., 2020),** additionally, it is becoming increasingly important for NICU nurses to use them for the purpose of controlling pain and enhancing quality of life for preterm infants. Therefore, the current study aimed to investigate the effect of auditory versus olfactory stimulation intervention on preterm infants' pain response during venipuncture, that can highlight current gaps in practice and knowledge and assist evidence-based clinical decision-making.

The current study revealed no statistical significant difference between preterm infants'

characteristics in the music, lavender, and control groups in terms of gender, gestational age, weight, age at admission, current age at the study, method of feeding, and diagnosis. This result is concurrent with a study titled music therapy with preterm infants and their caregivers, a randomized trial in which the three groups did not differ significantly in their socio-demographic or baseline data **(Ettenberger et al., 2014).** This result supports the current study's results as homogeneity between groups clarifies the difference in response to various interventions.

Regarding the preterm infants' vital signs (respiration, pulse, and temperature) and oxygen saturation pre venipuncture, the current study showed that there were no statistical significant differences between the music, lavender, and control groups, excluding other factors that may have initiated preterm pain before exposure to painful stimuli (venipuncture). However, there were statistical significant differences between the three groups post-venipuncture. This result agrees with that of a double-blind randomized controlled study on pain control with lavender oil in premature infants, which stated that there was a statistically significant difference between the two groups **(Usta et al., 2021).**

In addition, the study results are in line with those of previous research studies that investigated the short-term impacts of music on preterm infants, involving improvements in physiological status **(Haarika et al., 2017; Ragasivamalini & Ragupathy, 2019; Bayraktar &Tanyeri, 2020).** Another study about "Effect of recorded maternal voice, breast milk odor, and incubator cover on pain and comfort during peripheral cannulation in preterm infants" concluded that, there were statistically significant differences of preterm infants' means between groups **(Alemdar, 2018).** This result might be interpreted as both lavender oil and music work by activating the parasympathetic nervous system, that promotes relaxation and reduces stress. Additionally, pleasant smells and sounds may distract preterm infants from the pain that they experience during painful procedures.

Most venipuncture procedures in the music, lavender, and control groups were for blood sampling, the common site of puncture was the arm, the duration of venipuncture procedure in the music, lavender, and control groups lasted from one to three minutes and the number of puncture trials was one trial in 50% of the music group, 70% of the lavender group, and 60% of the control group, with no statistically significant difference between the three groups. This result is congruent with that of **Mohamed et al., (2019).** This result also excluded any factors that may interfere with differences other than those resulting from the current study interventions.

Regarding the response of preterm infants to the NIPS during venipuncture in the control, music, and lavender groups, the current study manifested that the group that received lavender oil smell as an intervention showed a greater relaxation effect than the control and music groups. This result is consistent with that of **Usta et al., (2021)** who reported that lavender aromatherapy was more effective than placebo or no intervention in reducing the pain in preterm infants.

The authors noted that the mechanism of action of lavender oil in pain relief is not fully understood but may be related to its effects on the Central Nervous System (CNS). The current study results are also supported by various previous studies that stated that aromatherapy has been used to manage pain in preterm infants, demonstrating an objective enhancement in NIPS scores, and recommended that lavender essential oil has disclosed benefits in minimizing pain during venipuncture procedure **(Akcan &Polat, 2016; Razaghi et al., 2015; López et al., 2017; Fitri et al., 2020; Razaghi et al., 2020).**

Otherwise, music therapy has also been investigated as a potential pain management intervention for preterm infants and the current study showed that it has better effect than control group. This result matches with that of **Yakobson et al., (2021),** who mentioned that music therapy had an improvement effect on preterm infants, including behavioral state (e.g., crying, facial expression, body movements) and pain scores; **Yue et al., (2021)** found that music therapy was efficient in relieving preterm infants' pain, but the effect was small. The authors noted that the

mechanism of action of music therapy in pain relief is also not fully understood, but it may be related to its effects on distracting attention from painful stimuli.

Overall, based on the available evidence from the current study, lavender oil may be more influential than music therapy in reducing preterm infants' pain. Additionally, lavender oil may have fewer potential side effects than music therapy, such as overstimulation or discomfort due to noise; however, it is important to note that both interventions may play a role in pain management for preterm infants, and the choice of intervention may depend on factors such as the specific circumstances of the procedure, the infant's individual needs and preferences, and the availability of resources.

Regarding the comparison of pain severity during venipuncture between the three groups, the current study showed that there was a statistical significant difference in NIPS total mean scores between the three groups. The current study also showed that the majority of preterm infants who received lavender oil as an intervention to relieve pain during venipuncture procedure had mild pain, while more than two-thirds of the group that received music had moderate to severe pain, and most of the control group suffered from moderate to severe pain. Thus, the current study hypotheses (1&2) were asserted as the preterm infants at auditory and olfactory stimulation intervention groups had lower pain scores than those in the control group.

This study result agrees with some evidence suggesting that preterm infants who receive lavender oil as an intervention for pain management may experience milder pain and have significantly lower pain scores than those who received standard care compared to those who received music therapy or standard care **(Beheshtipoor et al., 2017).**

This may be due to its effects on the CNS. Lavender scent has been shown to have a calming effect on the CNS, which can reduce stress and promote relaxation. This may facilitate reduction of pain perception in preterm infants. In contrast, music therapy may help to distract the attention of preterm infants from the painful stimulus, which may decrease pain perception. However, the effect of music therapy in preterm infants' pain management may rely on the specific type of music and the intensity and timing of the intervention.

Regarding comparison of the PIPP total mean scores between the study groups, the current results summarized that there was a statistical significant difference between control and interventions groups post intervention as total mean score of PIPP decreased in lavender and music groups than pre intervention while increased in the control group. Thus, the current study hypotheses (1&2) were asserted as the preterm infants at auditory and olfactory stimulation intervention groups had lower pain scores than those in the control group.

This result agrees with a randomized controlled trial which found that both the music therapy and lavender aromatherapy groups had significantly lower pain scores post-venipuncture compared to the control group. Specifically, the mean PIPP scores in the lavender group decreased more than the mean PIPP scores in the music therapy group and in contrast, the mean PIPP scores in the control group increased post-venipuncture.

The result also in agreement with randomized controlled trial which illustrated that lavender lower pain responding both during and after venipuncture **(Lee & Ra, 2021)** and previous studies stated that, the differences in pain scores between the intervention groups and the control group were statistically significant, indicating that lavender and music therapy were effective in reducing pain in preterm infants undergoing painful procedures such as venipuncture. Additionally, previous studies suggested that lavender may be more efficient than music therapy in decreasing pain severity **(Shen et al., 2022).**

Furthermore, the current study revealed that there were a statistically significant negative correlation between preterm infants' gestational age and their NIPS scores during venipuncture procedure in lavender group this result in contrast with **Menin & Dondi, (2020)** who indicated that there is a positive correlation between preterm infants' gestational age and the scores of NIPS, meaning that as the gestational age of the

infant decreases, the NIPS scores tend to be higher, indicating higher levels of pain. This correlation is thought to be due to several factors; first, preterm infants have immature CNS, which may make them more sensitive to pain and less able to regulate their responses to painful stimuli. Additionally, preterm infants may experience more painful procedures than term infants, as they may require more medical interventions and procedures due to their immature organ systems. This increased exposure to painful stimuli may result in higher NIPS scores, as the infants may have a lower threshold for pain and a heightened response to painful stimuli **(Perry et al., 2018).** It's necessary to account that while the positive or negative correlation between preterm gestational age and NIPS scores is well-established, it is not always a consistent relationship. Other factors, such as the individual differences in pain sensitivity and the type and duration of the painful stimulus, may also affect NIPS scores and pain perception in preterm infants.

Overall, accurate and timely assessment of pain in preterm infants is essential for effective pain management and improved health outcomes. Healthcare professionals should consider the gestational age and characteristics of the preterm infant, as well as the type and duration of the painful stimulus, when assessing pain and selecting appropriate pain management interventions. Additionally, pain responses of preterm infants are influenced by the use of non-pharmacological management, timing of painful procedures, the technique used, and the degree of professional expertise.

Conclusion

The current study results concluded that preterm infants in music and lavender groups had significant reduction in their pain response than control group during venipuncture procedure at NICU. However, the olfactory stimulation intervention using lavender oil is more effective to alleviate the venipuncture-related pain in preterm infants compared to auditory stimulation intervention using music. As non-pharmacological nursing intervention, olfactory stimulation with lavender is an inexpensive, easy-to-implement, and effective intervention for relieving pain in preterm infants.

Recommendations

1- Auditory and olfactory stimulation interventions are recommended as simple, safe and low-cost non-pharmacological methods that facilitate positive effects for preterm infants during painful procedures at NICUs without interfering with medical care.

2- Lavender essential oil and music should be suggested as non-pharmacological pain prevention method and as a routine care for controlling pain among preterm infants in NICUs.

3- Olfactory stimulation with lavender essential oil might be provided by the NICUs for preterm infants' painful procedures.

4- Further studies should be conducted to confirm the results of this study according to the clinical background of preterm infants and to evaluate both short- and long-term effects of lavender and music on preterm infants.

5- Further studies needed to evaluate the effect of auditory in combination with olfactory stimulation intervention on preterm infants' pain response.

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