



Non-Pharmacology Pain Management on Neonate: A Systematic Review

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ABSTRACT

Introduction: Neonates undergoing treatment often experience pain and painful procedures. Proper pain management needs to be done considering various cases in neonates with different pain experiences and causes. This study aimed to review the effect of non-pharmacological pain interventions on neonates. **Methods:** A systematic review was conducted to investigate the effect of non-pharmacology pain management in neonates. Studies were obtained from Proquest, Clinical Key for Nursing, Science Direct, and EBSCO databases. This study was limited to Randomized Control Trial studies published between 2015 and 2022, using subject headings and synonyms as keywords: neonate, neonatal, newborn, pain management, non-pharmacology pain management, and pain level. Next, JBI (Joanna Brings Institute) was used to evaluate journal quality, and thematic analysis was used as the data analysis method. **Results:** The search identified 659 relevant studies, and 19 studies have met the criteria. Nineteen articles show that various effective non-pharmacological pain management in premature and term infants are a sweet solution, skin stimulation, positioning, audio stimulation, and olfactory stimulation. Twelve journals discuss comparisons between interventions, and six journals discuss positions like facilitated tacking, hammock, swaddling, holding, and nesting. Five journals discuss combined pain management. Most of the journals (12 journals) discuss breastmilk odor stimulation and breastfeeding. The study also proved that multiple pain management was more effective than one type of intervention. **Conclusion:** The case-tailored practice of pain management in neonates and selecting the right combination of pain management will help reduce pain and increase comfort.

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INTRODUCTION

Exposure to pain in neonates is related to neuronal development. Exposure to pain obtained during treatment will have an acute or chronic impact on subsequent development. Pain experienced by premature babies is also a fundamental problem because the sensory development of pain is not perfect. Premature babies with exposure to pain are at risk for allodynia and inappropriate pain response and can also experience hyperalgesia, where the neonate experiences an excessive pain response. Neonates also felt discomfort during the procedure for taking venous blood. Venous blood sampling is a routine invasive procedure performed on hospitalized neonates. Neonates are particularly vulnerable to the adverse effects of this routine procedure. Some studies say that discomfort will affect heart

rhythm, cortisol levels, crying behavior, decreased oxygen, and increased motoric excess. According to anatomical studies, nociceptors receiving pain stimuli in neonates have the same or even denser density than adults. More than 90% of hospitalized neonates undergo invasive procedures such as venous blood. The results of data at the University of Muhammadiyah Malang Hospital in 2017, of 115 neonates, 93% were taken for venous blood collection at least once and a maximum of 6 times during hospitalization. The room nurse does not yet have the right action to manage the discomfort caused by the venous blood sampling procedure. The first year of the study showed that the average comfort level was 22.5, where the lowest score was five while the highest score in patients not using a ventilator was 25; if using a ventilator, the highest score was 30. The NIPS pain scale obtained an average result of 4.94 from the value range

1-7. The results of this study showed data that infants who were treated at the hospital experienced pain when taking venous blood and experienced discomfort with an average close to the maximum value. The results of another study showed that 50.3% of neonates experienced pain, and only 32% had pain management, both pharmacological and non-pharmacological. This finding shows that almost 70% of neonates do not receive pain management during treatment.

Efforts to prevent the long-term impact of discomfort and pain are significant. The study of non-pharmacological pain management, especially in neonates, has not been widely discussed, so this topic is needed to strengthen the study of non-pharmacological particular interventions in newborns who experience pain.

METHODS

Study Design and Literature Search Strategy

The research design used in this study is a systematic review. The literature search strategy and selection criteria

are as follows: In obtaining references in this study, the researchers searched for articles from several search sites, including Science Direct, Proquest, Clinical Key For Nursing, and EBSCO. The articles were searched based on the research title entitled Non-Pharmacology Pain Management on Neonate, so to get the desired journal, the researcher used keywords as described in table 1 below:

Table 1. Keywords used during Literature Search

| | P-I-O | Sinonim |
|-----------|--|----------------------------------|
| | P: Neonate | Boolean: OR Neonatal, Newborn |
| Keyword 1 | E: Pain Management Boolean: AND Non-pharmacology Pain Management | |
| Keyword 2 | O: Pain level | |

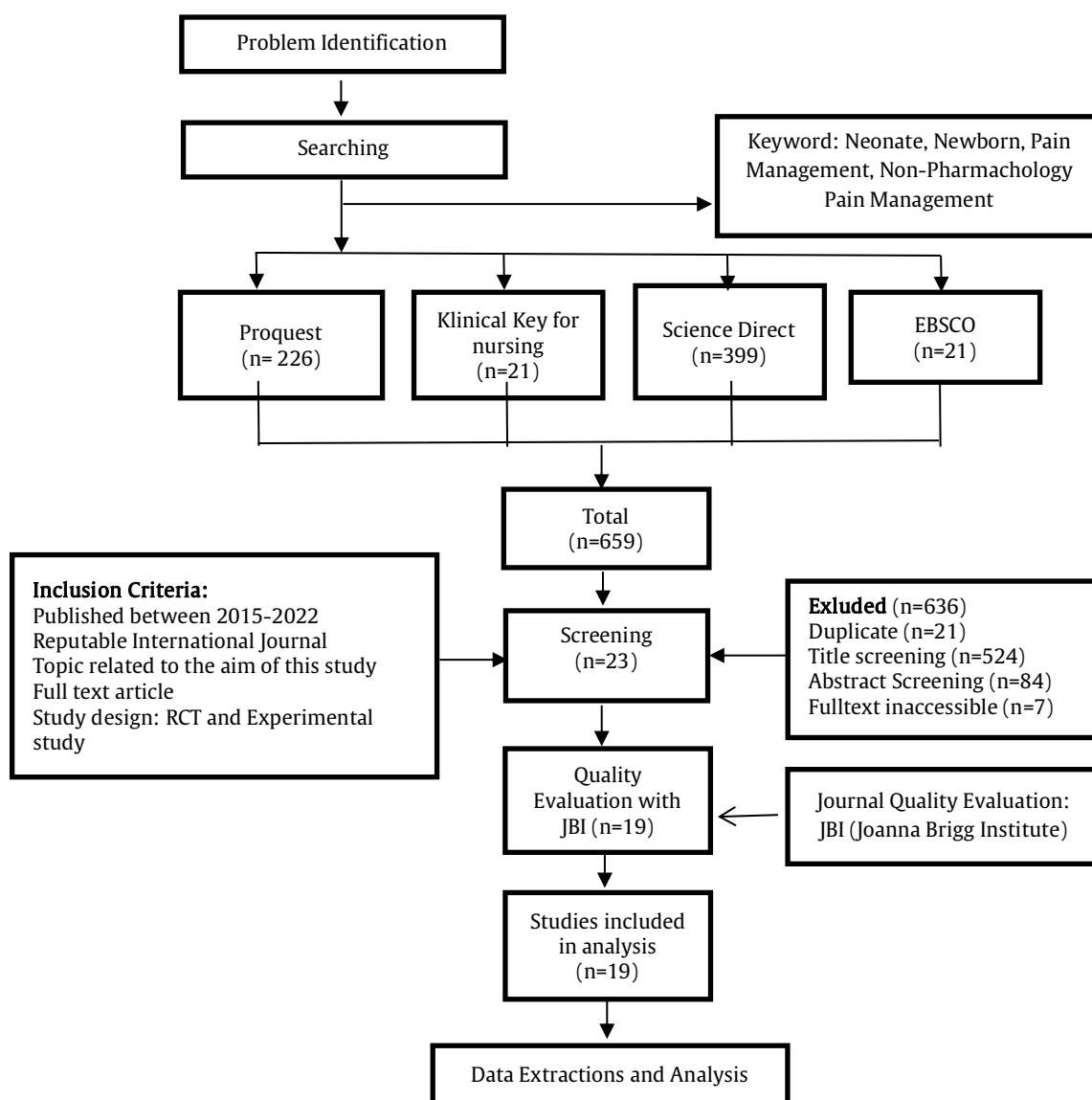


Figure 1. Prisma Flow Non-Pharmacology Pain Management on Neonate

Selection Criteria, Screening and Quality Evaluation

The topic of this study is Non-Pharmacology Pain Management on Neonate based on literature studies. This study used data filtering to select articles by the following provisions: articles from the last eight years (2015-2022), reputable international journals, accessible full text, experimental study, and randomized controlled trial study. In this study, quality assessment uses JBI critical appraisal tools. The assessment process must include information that matches the predetermined assessment criteria and at least meets the criteria of more than 50% (Aromataris & Munn, 2020). The literature search and screening process flow are generally described in figure 1.

Data Extraction and Analyze

This study extracted data related to the population, intervention, and outcomes (PIO components). To standardize this process and increase the validity of the results, researchers will compile data extraction tables and classify the data collected from research results based on research identities: title, year, author, research methods, and research results (Saltikov, 2012). Furthermore, the data analysis process is carried out using thematic analysis to saturate the information obtained from selected research journals. The data extraction and JBI score assessment areas are presented in Table 1 below.

Table 1. Data Extraction

| No | Tittle dan author | Method | Result |
|----|--|--|--|
| 1 | Diler Yilmaz, Sevil Inal. (2020). Effect on three different methods used during heel lance procedures on pain level in term neonates (Yilmaz & Inal, 2020). | <ol style="list-style-type: none"> 1. Desain : prospective, RCT 2. Sampel : New born aterm (160) yag dilakukan heel lancing 3. Variabel : Independen : Manajemen nyeri swaddling, holding, breast feeding Dependen : Pain Level 4. Instrumen : NIPS 5. Analisis : Pearson' s Chi-square | The difference in pain scores using the NIPS was lowest in the swaddling, holding, and breastfeeding group with a pain scale (4.47±1.19), then the swaddling and holding group (5.57 ±1.23), swaddling (5.85±0.86) and the control group (6.40 ±0.95). The difference in duration of crying and calming between the four groups had a significant difference in the swaddling and holding groups with a p-value < 0.1 compared to swaddling and holding (40.92 ± 28.83) and compared swaddling and holding (77.37 ± 44.01) with p-value = 0.000, swaddling group (69.75±33.43) with p-value = 0.001 (79.25±41.47) with p-value = 0.000. there was no significant difference in the comparison of the duration of crying in the four groups. The length of time to calm down there is a significant difference. In the swaddling, holding, and breastfeeding group (26.25 ± 25.75), the swaddling group (56.00 ± 36.65), swaddling and holding (65.75 ± 50.25), and the control group (60.27 ± 42.52) (p < 0.05). The swaddling group was compared to the control, swaddling+holding with control and swaddling and swaddling+holding, and there were no significant differences. |
| 2 | Camila Gemin Ribas, Marimar Gorette Andrezza, Valéria Cabral Neves and Silvia Valderramas. (2019). Effectiveness of Hammock Positioning in Reducing Pain and Improving Sleep Wakefulness State in Preterm Infants (Ribas et al., 2019) | <ol style="list-style-type: none"> 1. Design: prospective, RCT 2. Sample: Preterm neonates 30-37 weeks gestation (26 divided into two groups @13), stable and breathing spontaneously 3. Variables: Independent: Hammock Positioning Dependent: Pain Level and Sleep Wakefulness State 4. Instruments: PIPP, NFCS, BNBAS 5. Analysis: Mann-Whitney test and Student t-test according to the type of variable and the data distribution. The chi-square test was used for categorical variables. A significance level of P< .05 was used. Post hoc analysis of the statistical power was performed with G*Power 3.1 | The results of the hammock position group showed increased pain compared to the traditional position group (Premature Infant Pain Profile score, 2.62 ± 1.89 vs. 2.31 ± 1.97, P = .008) and sleep-wake status score (2.08 ± 0.64 vs 1.23 ± 0.44, P < .001), decreased heart rate (151.69 ± 5.44 vs 142.77 ± 5.18 beats/min, P < 0.001), respiratory rate (52.31 ± 4.05 vs 50.23 ± 2.55 beats/min, P = .024), and increased peripheral S _{po2} (94.69 ± 2.14 vs 98.00 ± 1.22%, P < .001) . |
| 3 | Monica Rita Hendricks, Prakash Amboiram, Mariam OJ, Suman Rao PN. (2021). Effect of Nurture Intervention on Neurodevelopmental Outcomes of Preterm | <ol style="list-style-type: none"> 1. Design: prospective, RCT 2. Sample: Preterm gestational age 26-34 weeks with an estimated sample size of 160 newborns in the NICU 3. Variables: Independent: Nurture Intervention | This study is a protocol study that will obtain data on the effect of nurture intervention on neonates on neuronal development, language development, and the risk of autism |

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| | Neonates: A Randomized Trial for Protocol Standardization. | Dependent: Neurodevelopment 4. Instruments: Ages and Stages Questionnaire (ASQ)-3-12 and Language Evaluation Scale Trivandrum (LEST) 5. Analysis: Independent t-test | |
| 4 | Hala M Obeidat, Mona A. Shurique. (2015). Effect of Breast-Feeding and maternal Holding in Relieving Painful Responses Full-Term Neonates. | 1. Design: RCT 2. Sample: 128 full-term newborn infants during heel lance blood drawing 3. Variables: Independent: Breast-feeding and maternal holding Dependent: Pain complete responses 4. Instrument: PIPPS (premature infant pain profiler scale) 5. Analysis: Independent T-test | The study results found a significant difference between breastfeeding and maternal holding, 9.65 (1.94), and maternal holding at 13.32 (2.75). The result of $t = -8.447$ and $p\text{-value} = 0.000$ |
| 5 | Soroosh Soltani, Dariush Zahoori, Mojtaba Adineh. (2018). Comparison of the effectiveness of Breastfeeding, oral 25% Dextrose, Kangaroo-Mather care method, and EMLA cream on pain score level following heel pick sampling in Newborns: a randomized clinical trial. | 1. Design: double-blind, controlled RCT 2. Sample: A total of 161 Newborn terms allocated breast milk feeding 42, oral dextrose 40, KMCM 38, and KMCM ointment 40 performed heel lancing 3. Variables: Independent: Pain management swaddling, holding, breastfeeding Dependent: Pain Level 4. Instrument: NIPS 5. Analysis: ANOVA and Chi-square | The results showed no significant difference between gender, weight, and baseline pain scores in the four groups ($p: 0.904$). The results of the lowest pain score were found in the breastfeeding group when compared to other groups, breast milk feeding (5.52 ± 2.22), Oral dextrose (6.45 ± 1.88), KMCM (6.84 ± 1.96), and KMCM ointment (7.37 ± 1.95) in data collection after heel-picked and there was a significant difference with $p\text{-value} = 0.001$ |
| 6 | Ayse Sener Tablecloth, Meral Bayat. (2020). Comparison of breast milk smell, white noise, and facilitated tucking applied to premature preterm infants during endotracheal suctioning on pain and physiological parameters (Taplak & Bayat, 2021). | 1. Design: Prospective, RCT 2. Sampel: Preterm infants (80). Gestational age of 26 weeks or more. In NICU 3. Variables: Independent: Breast milk smell, White noise, Facilitated tucking Dependent: Pain 4. Instrument: Premature Infant Pain Profile-Revised (PIPP-R) 5. Analisis : Chi-square and Kruskal-wallis test | It was found that the intervention of white noise and facilitated tucking applied was more effective in relieving infants before the endotracheal suctioning procedure ($p < 0.05$). No significant differences were found between groups in reducing pain during the endotracheal suctioning procedure ($p > 0.05$). The score analysis using PIPP-R in premature infants was divided into four groups: the group with breast mil smell, white noise, facilitated tucking applied, and control groups before the endotracheal suctioning procedure. While there was no significant difference between the groups in terms of measurements obtained 3 and 5 min before the procedure, there was a significant difference between the groups at 1 min ($p = 0.048$). After the procedure, the intervention group breast mil smell, white noise, and facilitated tucking applied and the control group while there was no difference between mean scores of premature infants were determined at 1 and 5 min on the PIPP-R; there was a significant difference between the mean scores of the PIPP-R determined at 3 min ($p = 0.047$). |
| 7 | Nahed Saied Mohamed El-Nagger, Orban Ragab Bayoumi. (2016). Effect of Applying Nesting Technique as a Developmental Care on Physiological Functioning and Neurobehavioral Organization of Premature Infants. | 1. Design : Quasi-Experimental 2. Sample: Preterm infants (80). Gestational age of 32-36 weeks. In NICU 3. Variables: Independent: Nesting technique, Development care, Neurobehavioral organization Dependent: Physiological function 4. Instruments: Premature Infants Assessment Sheet (PIAS), Neonatal Behavioral Assessment Tool (NBAT), and Neonatal Infants Pain Scale (NIPS) 5. Analysis: X^2 | found that the results of a high maturity significance between differences regarding physiological, behavioral, and neurological outcomes of premature infants concerning temperature, oxygen saturation (SaO ₂), infant crying, sleep, and juveniles' activity between the study and control groups. Regarding the physiological functioning of premature babies, it shows that 90%, 97.5% & 85% compared to 40%, 60% & 0% of mature babies, their temperature is normal in the supine position, side-lying, and prone positions in the study group and control group, respectively, which exhibited maturity difference insignificance ($X^2 = 23.14, 20.57$ & 14.06 at $p\text{-values} 0.00$, 0.00 , & 0.00) respectively. As regards respiratory rate, the analysis also explained that |

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| | | | <p>80% of infants were premature compared to 57.5%. They had normal respiratory rates during the supine position of the study group and control group, respectively, with a maturely significant difference ($X^2 = 5.33$, at a p-value of 0.05). Regarding SaO₂ during prone position, it was found that 100% and 90% of premature babies had a SaO₂ level of 95% in both. Regarding the behavior of premature infants, the responses in the form of a sleep/awake state stated that 82.5%, 87.5% & 100% were had a better sleep in supine, side-lying and prone positions compared to 20%, 20% & 10% in both study and control groups respectively. These results also showed that 80% and 90% of the premature infants were awake in the study group compared to 62.5% and 30% of those in the control group during the recumbent and prone positions, respectively, reflecting the significant difference in premature ($X^2 = 21.37$ & 10.14, at P-values of 0.00, 0.006) respectively. Minority (5%) mature infants in the study group cry on their stomachs position.</p> |
| 8 | <p>Sibel Kucukoglu, Sirin Kurt and Aynur Aytekin. (2015). The effect of the facilitated tucking position in reducing vaccination-induced pain in newborns (Kucukoglu et al., 2015).</p> | <ol style="list-style-type: none"> 1. Design: Randomized Controller Experimental Study 2. Sampel : Preterm infants (60). Gestational age of 37 weeks and over. In NICU 3. Variables: Independent: Holding position, Facilitated tucking position Dependent: Pain Level 4. Instrument: Neonatal Infants Pain Scale (NIPS) 5. Analysis: Chi-square, Independent t-test, and Cronbach's alpha coefficient calculation | <p>Results of comparing the descriptive characteristics of newborns in the control and treatment groups were found. There were no significant differences in maturity between the groups in terms of sex, gestational age, weight, height, method of delivery, and the number of previous children submitted by the child's mother.</p> <p>The mean NIPS pain score of infants in the treatment group (2.83 ± 1.18) was significantly lower than that of infants in the control group (6.47 ± 1.07, $p < 0.05$). While 50% of the infants in the treatment group had no pain, 93.4 % of the infants in the treatment and control groups experienced pain. When the physiological parameters of the newborn changed in the care and control groups the groups were examined, no differences were found between the groups in terms of fever, pulse, respiration, and oxygen saturation before and after the procedure ($p > 0.05$)</p> <p>The respiration rate of newborns in the control group was significantly higher than that of newborns in the treatment group during the procedure ($p < 0.05$)</p> |
| 9 | <p>Ayşe Kahraman, Zümrüt Basbakkal, Mehmet Yalaz, Eser Y. Sozmen. (2017). The effect of nesting positions on pain, stress and comfort during heel lance in premature infants.</p> | <ol style="list-style-type: none"> 1. Design: Experimental Study-Research 2. Sample: Preterm infants (33). Gestational age of 31-35 weeks. In NICU 3. Variables: Independent: Nesting position, Comfort, Stress Dependent: Cortisol Level 4. Instruments: Neonatal Infants Pain Scale (NIPS), COMFORneo Scale, 5. Analysis: The man-Whitney test, and The Kruskal-Wallis test | <p>It was found that 33 participants were premature babies, with an average of 33 weeks of gestation (min: 31 weeks, max: 35 weeks). The average birth weight of babies is 1757 g (min: 1230 g, max: 2450 g). 57.6% of neonates are women. The average fifth-minute Apgar score is 8.96 (min: 8, max: 10). The baby's average oxygen saturation (SatO₂) is 94.30 in the prone position during heel pike and 86.63 in the supine position. Average SatO₂ increased significantly during prone positioning ($p = 0.000$). Furthermore, the average SatO₂ increased significantly during the prone position five minutes before heel spear, 30 minutes before heel spear, and 30 min after heel spear ($p < 0.05$), which means heart rate (HR) was 146.09 during the prone positioning and 145.48 during the supine position, with no significant difference between the positions ($p = 0.166$); premature infants in the supine position cried because of longer time during heel spearing than those who were prone position ($p = 0.003$). Crying time was not significantly different in body weight, sex, and gestational age ($p > 0.05$).</p> <p>NIPS scores show significantly lower scores in the prone position than in the supine position ($p = 0.000$).</p> <p>The COMFORT neo scale scores showed a</p> |

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| | | | <p>significant decrease in scores in the prone position compared to the supine position. The NRS COMFORT neo pain score shows significantly lower scores in the prone position than in the supine position ($p = 0.000$). The median salivary cortisol level during the prone position five minutes before the heel spearing was significantly lower than in the supine position ($p = 0.006$). Thirty minutes after heel spearing, the salivary cortisol level during the prone position was significantly lower than in the supine position ($p = 0.001$). Five minutes before and 30 minutes after heel spearing, Median salivary melatonin levels during the prone position did not show a significant difference compared to the supine position ($p = 0.445$)</p> |
| 10 | <p>Hsueh-Fang Peng, Ti Yin, Luke Yang, Chi Wang, Yue-Cune Chang, Mei-Jy Jeng, Jen-Jiuan Liaw. (2017). Non-Nutritive Sucking, Oral Breast Milk, and Facilitated Tucking Relieve Preterm Infant Pain during Heel-Stick.</p> | <ol style="list-style-type: none"> 1. Design: Prospective, RCT 2. Sampel : Preterm infants (109). Gestational age of 29-37 weeks. In NICU level III 3. Variables: Independent: Non-nutritive sucking, Oral breast milk, Facilitated tucking Dependent: Pain 4. Instrument: Premature Infant Pain Profile (PIPP) 5. Analisis : Chi-square (Anova) | <p>The pain was measured by watching videotapes of infants undergoing heel-stick procedures and assessing pain at 1-minute intervals with premature PIPP. Data were collected through eight phases: baseline (phase 1, 10 min without stimulation before heel stick), during heel stick (phases 2 and 3), and 10 min recovery (phase 4-8). For infants receiving suckling and breast milk, the change in pain score from baseline in phases 2-8 was 2.634, 4.303, 2.812, 2.271, 1.465, 0.704, and 1.452 units lower than the change in the corresponding pain score in infants receiving routine care (all p-value < 0.05 except for phases 6 and 7). Similarly, for infants who received suckling, breastfeeding, and tucking, the pain scores from baseline were 2.652, 3.644, 1.686, 1.770, 1.409, 1.165, and 2.210 units lower than the corresponding changes in pain scores in infants receiving routine care in the second phase. 2-8 (all p values < 0.05 except for phase 4). After receiving suckling, breast milk, sucking, and sucking breast milk, the baby's risk of experiencing mild pain (pain score 6) was significantly decreased by 67.0% and 70.1%, respectively, compared with infants receiving routine care.</p> |
| 11 | <p>Mahnaz Jebreili, Hanieh Nashat, et al. (2015) Comparison of Breastmilk Odor and Vanilla Odor on Mitigating Premature Infants' Response to Pain During and After Venipuncture (Jebreili et al., 2015a)</p> | <ol style="list-style-type: none"> 1. Design: RCT 2. Sample: Infant (135) 3. Variables: Independent: Comparison of Breastmilk Odor and Vanilla Odor Dependent: Mitigating Premature Infants' Response to Pain 4. Instrument: Preterm Infant Pain Profile (PIPP) is a scale for pain score 5. Analisis : $p < 0.05$ was considered statistically significant | <p>The results showed that the smell of vanilla and breast milk could calm premature babies during a venipuncture, but only the smell of breast milk significantly calmed the baby after the venous function was performed. The mean results of the PIPP pain scale during venous puncture (7.31 ± 2.52) in the breast milk group and (9.21 ± 2.78) in the vanilla group with a p-value = 0.01. After the action, the results were (6.08 ± 2.67) in the breast milk group and (8.13 ± 2.93) in the vanilla group with a p-value = 0.021</p> |
| 12 | <p>Dilek Kucuk Alemdar and Funda Kardas Ozdemir (2017) Effects of Having Preterm Infants Smell Amniotic Fluid, Mother's Milk, and Mother's Odor During Hell Stick Procedure On Pain, Physiological Parameters, and Crying Duration (Alemdar & Ozdemir, 2017)</p> | <ol style="list-style-type: none"> 1. Design: Randomized Controlled Experimental Research 2. Sample: Preterm Infants (123) 3. Variables: Independent: Having Preterm Infants Smell Amniotic Fluid, Mother's Milk, and Mother's Odor Dependent: Procedure On Pain 4. Instruments: Apgar Score and Preterm Infant Pain Profile (PIPP) 5. Analysis: percentage distributions, means, standard deviation, chi-square test, Kruskal-Wallis, and Dunnett's test | <p>The results showed no significant difference in premature infants who underwent intervention in each group, both on the pain scale, saturation, duration of crying, and heart rate before, during, and after the procedure. However, the average value of the duration of crying in the amniotic odor group got the lowest score. Due to amniotic odor, there was a significant difference in oxygen saturation in term infants in each group.</p> |
| 13 | <p>Merve Cakirli, MSc and Ayfer Acikgoz, Ph.D. (2020) A Randomized Controlled Trial The Effect of Own Mother's Breast Milk Odor and</p> | <ol style="list-style-type: none"> 1. Design: RCT 2. Sample: Newborn (90) 3. Variables: Independent: Own Mother's Breast Milk Odor and Another Mother's | <p>The three groups did not have significant differences in the mean \pm SD HR, BP, and Sao2 before intervention ($P > 0.05$). However, after the intervention, the mean heart rate in groups A, B, and C was 146 ± 14.3, 153 ± 17.5 and 155 ± 17.7,</p> |

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| <p>Another Mother's Breast Milk Odor on Pain Level of Newborn Infants (Cakirli & Acikgoz, 2021).</p> | <p>Breast Milk Odor Dependent: Pain Level of Newborn Infants 4. Instrument: Neonatal Identification Information Form, Data Evaluation Form, and Neonatal Pain, Agitation, and Sedation Scale (N-PASS) Analysis;</p> | <p>respectively ($P = 0.012$). In addition, the mean PIPP scores in groups A, B, and C were 6.6 ± 1.3, 10 ± 2, and 11.4 ± 1.9, respectively ($P < 0.001$). No significant difference was found between groups in mean SaO₂, systolic, and diastolic blood pressure after intervention ($P > 0.05$)</p> |
| <p>14 Dilek Kucuk Alemdar. (2018) Effect of Recorded Maternal Voice, Breast Milk Odor, And Incubator Cover On Pain and Comfort During Peripheral Cannulation Preterm Infants.</p> | <p>1. Design: RCT 2. Sample: Preterm Infants (136) 3. Variables: Independent: Recorded Maternal Voice, Breast Milk Odor, And Incubator Cover On Pain and Comfort During Peripheral Cannulation Dependent: Preterm Infants 4. Instruments: Preterm Infant Pain Profile (PIPP) Score, Premature Infant Comfort Scale (PICS), and Apgar score 5. Analysis: Statistical package for social sciences 18.0 software whit parentage one-way ANOVA (between groups), Kaplan-Meier log-rank test, and the Post-Hoc advance analysis Bonferroni test</p> | <p>There is a significant difference between the PIPP scores during and after giving breast milk, recording the mother's voice ($0.00 < 0.05$)</p> |
| <p>15 Chiao-Hsuan Lin, Jen-Jiuan, et al. (2022). Efficacy of Breast Milk Olfactory and Gustatory Interventions on Neonates' Biobehavioral Responses to Pain during Heel Prick Procedures.</p> | <p>1. Design: double-blind, prospective, RCT 2. Sample: Neonates (114) 3. Variables: Independent: Breast Milk Olfactory and Gustatory Interventions Dependent: Neonates' Biobehavioral Responses to Pain 4. Instrument : Apgar Score 5. Analysis: G*power 3.1.9.2 software with within between interaction, MANOVA approach</p> | <p>Breast milk's smell and taste can stabilize biobehavioral responses to pain during heel puncture procedures in neonates.</p> |
| <p>16 Zahra Akbarian Rad, Parvin Azizneidroshan, et al. (2021) The Effect of Inhealing Mother's Breast Milk Odor on The Behavioral Responses to Pain Caused by Hepatitis B Vaccine in Preterm Infants: a Randomized Clinical Trial (Rad et al., 2021).</p> | <p>1. Desain: The single-blind randomized clinical trial 2. Sample: Neonates (90) 3. Variables: Independent: Inhealing Mother's Dependent: Preterm Infants 4. Instrument: Premature Infant Pain Profile (PIPP) Score 5. Analysis: The chi-square, ANOVA, ANCOVA, and PIPP score is between 0 and 6 points; the pain level is mild if between 7 and 12 points, it is moderate and if between 13 and 21 points are severe. $P < 0.05$ was considered significant in this study.</p> | <p>In the study, it was found that no significant difference was found between the three groups in the mean \pm SD HR, BP, and Sao₂ before intervention ($P > 0.05$). However, after the intervention, the mean heart rates in groups A, B, and C were ($A = 146 \pm 14.3$), ($B = 153 \pm 17.5$), and ($C = 155 \pm 17.7$), respectively. -respectively ($P = 0.012$). In addition, the mean PIPP scores of groups A, B and C were ($A = 6.6 \pm 1.3$), ($B = 10 \pm 2$), and ($C = 11.4 \pm 1.9$), respectively. respectively ($P < 0.001$). There was no significant difference between the groups in mean SaO₂, systolic blood pressure, and premature after intervention ($P > 0.05$).</p> |
| <p>17 Bircan Tasci and Tolay Kuxlu Ayyildz (2020) The Calming Effect of Maternal Breast Milk Odor on Term Infant: A Randomized Controlled Trial.</p> | <p>1. Design: Randomized aged study 2. Sample: Newborn (84) 3. Variables: Independent: Maternal Breast Milk Odor Dependent: Term Infant: Neurodevelopment 4. Instruments: Ages and Stages Questionnaire (ASQ)-3-12 and Language Evaluation Scale Trivandrum (LEST) Analysis :</p> | <p>The findings show that newborns in both groups were similar in sex, mode of delivery, weeks of gestation, birth weight, head circumference, length, Apgar score, and no premature difference. At the same time, in both groups, prematurely significant differences were detected between NIPS scores before, during, and after sampling (breastfeeding group, $p = 0.001$ and formula-fed group, $p = 0.001$). Although no prematurely significant differences were detected between the heart rates of the groups before sampling ($p = 0.571$), newborns in the breastfed group had a lower heart rate remit during ($p = 0.001$) and after ($p = 0.001$) sampling compared to the formula milk group. At the same time, in both groups, a prematurely significant difference was detected between heart rates before, during, and after sampling (breast milk group, $p =$</p> |

0.001 and formula milk group, $p = 0.001$. Although no significant differences were detected prematurely between the SpO2 levels of the two groups before sampling ($p=0.099$), newborns in the breast milk group had higher SpO2 levels during and after sampling compared to newborns in the formula milk group ($p = 0.001$). The duration of the crying of newborns sniffing milk formula was significantly longer during sampling than newborns who sniffed breast milk ($p = 0.001$). There was no prematurely significant difference between the groups in terms of salivary cortisol measurements prior to sampling ($p = 0.820$); the salivary cortisol levels of newborns in the breastfed group after sampling were found to be premature significantly lower than those of newborns in the breastfed group formula ($p = 0.004$).

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| 18 | Carren Usta, MS. Bilge Tanyeri Bayraktar, MD. And Suleyman Bayraktar, MD. (2020) Pain Control With Lavender Oil in Premature Infants: A Double Blind Randomized Controlled Study (Usta et al., 2021) . | <ol style="list-style-type: none"> Design: A Double-blind Randomized Controlled Clinical Study Sample: Premature Babies (61) Variables: Independent: Lavender Oil Dependent: Pain Control Instrument: Premature Infant Pain Profile-Revised (PIPP-R) pain score Analysis: a statistically significant ($p<0.05$) difference between two groups in terms of PIPP-R score during and after the sampling ($p=0.008$ and $p=0.03$) | A total of 61 infants were analyzed in the study, consisting of 29 girls (47.5%) and 32 boys (52.5%) aged 2–25 days (mean age 5.31 – 4.86 days). No significant difference was seen between the two groups regarding gestational age, birth weight, age at intervention, or mode of delivery ($p>0.05$). There was no difference in gender between groups ($p = 0.029$). In total, 20 (66.7%) and 12 (38.7%) infants were men in CG and LOG, respectively; it compares PIPP-R scores. There is a significant difference between the two groups regarding PIPP-R scores both during and after sampling ($p = 0.008$ and $p = 0.03$, respectively). PIPP-R scores at the start of the procedure were not found to be significantly different between groups ($p > 0.05$). No effects were observed during the study. |
| 19 | A Randomized Controlled Trial Comparing the Effects of Honey versus Sucrose as Analgesia during Venipuncture in the Newborns. | <ol style="list-style-type: none"> Design: A Double-blind Randomized Controlled Clinical Study Sample: 78 Newborn Full-term Variables: Independent: Honey versus sucrose Dependent: Pain and Cry Duration Instrument: Premature Infant Pain Profile (PIPP) pain score Analysis: Mann Whitney test | A Mann-Whitney U test was performed to test the difference in the PIPP score between both groups. The calculated p-value was 0.76. The median duration of total audible cry after venipuncture was 4 seconds for the sucrose group and 5.5 seconds for the honey-treated group. It gives a median difference of 1.5 seconds between both groups. The Mann Whitney U test showed a p-value of 0.803 when performed to test for the difference between both groups with the duration of crying time |

RESULTS

Table 2. General Characteristics of Studies

| Category | N | % |
|--|-----------|------------|
| Year of Published | | |
| 2015 | 3 | 17 |
| 2016 | 1 | 6 |
| 2017 | 3 | 17 |
| 2018 | 2 | 11 |
| 2019 | 1 | 5,5 |
| 2020 | 5 | 28 |
| 2021 | 2 | 11 |
| 2022 | 1 | 5,5 |
| Total | 18 | 100 |
| Study Design | | |
| Randomized Controlled Trial | 11 | 61 |
| Quasi-Experimental | 1 | 6 |
| Randomized Controller Experimental Study | 2 | 11 |
| Experimental Study Research | 1 | 5,5 |
| Single Blind Randomized Clinical Trial | 1 | 5,5 |
| Randomized Controlled Study | 1 | 5,5 |
| Randomized Controlled Clinical Study | 1 | 5,5 |

| Total | 18 | 100 |
|------------------------|-----------|------------|
| Sample | | |
| Aterm Newborn Infant | 7 | 39 |
| Preterm Newborn Infant | 11 | 61 |
| Total | 18 | 100 |
| Instrument | | |
| NIPS | 5 | 28 |
| PIPP | 6 | 33 |
| Behavioral Scale | 3 | 17 |
| et. al. | 4 | 22 |
| Total | 18 | 100 |
| Pain Management | | |
| Position | 4 | 22 |
| Odor | 7 | 39 |
| Combination | 4 | 22 |
| Voice | 2 | 11 |
| Environmental Setting | 1 | 6 |
| Total | 18 | 100 |
| Result | | |
| Signivicant | 13 | 72 |
| Not Signivicant | 5 | 28 |
| Total | 18 | 100 |

General Information of Studies

Based on a review of 19 journals related to pain management in neonates, the most journals were in 2020, with as many as five journals (28%). While the research design used was a randomized controlled trial of as many as 11 journals (64%). The sample characteristics are 61% are preterm newborn infants, the most instrument used is PIPP (33%), and the most common pain management is odor stimulation (39%). Based on data analysis, the intervention proved to be effective (72%), and five others (28%) obtained different trials that are

equally effective, or there are no differences with other interventions in the journal so that they can be recommended as appropriate pain management for this treatment.

Result of Data Analysis

We generated the reviews' findings into groups and subgroups themes, as shown in the Tabel 3 below. Keywords-Theme and Description

| Keywords | Theme | Description |
|---|-----------------------|--|
| swaddling holding Facilitated tacking Hammock KMC Nesting prone | Positioning | Six articles discuss position manipulation for reducing pain in a neonate with painful procedures. |
| Breast milk odor Vanilla odor Mother odor Amnion odor | Odor stimulations | Eight articles discuss odor stimulation for reducing pain in neonates with painful procedures. |
| Mother voice | Sound stimulations | Two articles discuss the mother's voice that affects the pain level of the painful neonate |
| Sucrose honey | Sweet solution | Three articles discuss the sweet solution that affects pain levels in the painful neonate |
| Non-nutritive sucking gustotomy | oral stimulation | Two articles discuss oral stimulation that affects pain levels in the painful neonate |
| Breastfeeding Nurturing intervention | Kombinasi | Six articles discuss more than one intervention that affects pain levels in the painful neonate |
| Developmental care Incubator cover | Modifikasi lingkungan | Two articles discuss environmental modified that affect pain levels in the painful neonate |

Table 3 above shows that the most common interventions for non-pharmacological pain management in neonates are odor stimulation in breast milk, mother odor, vanilla odor, and amnion odor. Next is the position set at the time of the action that causes pain in as many as six articles. Six articles discuss combination intervention, while three discuss sound stimulation. Articles that discuss the intervention of sound stimulation, oral stimulation, and modification of the treatment environment are two articles each.

DISCUSSIONS

This literature review shows that most interventions in overcoming pain in infants use odor stimulation. The journals found related to this topic were at most eight articles that explained the effect of smell with significant results. The odor in reducing pain with the most compelling evidence with the lowest average pain is the smell of breast milk, the smell of the mother, and the smell of the amnion. In contrast, the smell of vanilla and lavender aromatherapy is still less effective for reducing pain than breast milk but affects the duration of crying or calming. Smells that are familiar to babies, such as the smell of one's breast milk and the smell of non-mothers milk, both can significantly reduce pain scale (Alemdar, 2018; Cakirli & Acikgoz, 2021) in addition to having a calming effect on neonates, whereas amniotic odor is more effective in reducing the duration of crying in pain procedures. Breast milk odor can also stabilize the baby's behavior towards pain procedures, heart rate, and oxygen saturation and reduce the duration of crying.

Another intervention that is also quite effective in dealing with pain in neonates is positioning, where the swaddling,

holding, Facilitated tacking, Hammock, KMC, Nesting, and prone positions are proven to reduce pain during treatment procedures. The combined position of swaddling, holding, and breastfeeding is more effective in reducing pain. Maternal holding and breastfeeding positions are more effective in reducing pain than holding alone. Nesting in the prone position is more effective in increasing comfort in premature babies exposed to pain than in the supine position; besides that, facilitated tucking is also effective in reducing pain in premature babies vaccinated against newborns or heel-sticks. (Kucukoglu et al., 2015; Peng et al., 2017). As well as the hommcock position can also be effective in reducing pain and improving sleep-wake conditions, heart rate and respiratory rate, and oxygen supply in premature infants. It can be concluded that position manipulation such as nesting with a prone position, facilitated tucking, and hammock position can be an option for pain management in premature infants. The above findings also prove that combining more than one position is more effective in reducing pain. Swaddling and holding positions can be alternative pain management options for term infants, combined with breastfeeding to make it more effective.

The results of most journals with interventions that combine positioning, oral stimulation, suction, and the most combination are breastfeeding and smell stimulation, as well as environmental modifications, show evidence of being more effective in reducing pain in both premature and term infants.

Modification of the baby's environment which is part of developmental care by providing a comfortable environment such as in the womb, namely minimizing lighting, installing nesting, closing the incubator, minimizing sound sources, and providing longer rest periods will reduce stress, especially in premature babies and can reduce pain levels due to the procedure. treatment (Alemdar, 2018; El-Nagger & Bayoumi,

2016; Kahraman et al., 2018) . Nurture intervention is also very helpful in improving the quality of life of premature babies in care, where an intervention with a nurturing approach can reduce the baby's stress level. Premature babies with the immaturity of various organ systems are very susceptible to stress levels. Nurture intervention is a combination approach that is quite holistic in managing pain and stress in premature babies. Treatment by mothers with nurture intervention facilitates mothers to do firm, sustained touch, odor exchange, skin-to-skin contact with KMC, eye contact, and vocal shooting, which can effectively improve the quality of development of premature children.

Pain management that is also effective for premature and term babies is a sweet solution by giving 24% sucrose, and 25% dextrose, the type of honey has also been shown to have the same effect in reducing pain due to invasive procedures or other treatment procedures.

CONCLUSIONS

Based on the results of a *systematic review*, it can be concluded that non-pharmacological pain management is most effective in reducing pain in premature infants and term infants who experience pain due to treatment procedures. The themes obtained from data extraction results in non-pharmacological pain management in neonates were carried out by the smell, sound, oral stimulation, positioning, environmental modification, sweet solution, and interventions. The findings in this study prove that the combination of interventions has a more significant impact on reducing pain due to treatment.

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CONFLICT OF INTEREST

The principal researcher declares no conflict of interest in this research.

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