

Effect of Olfactory and Gustatory Stimulations on Preterm Neonates' Feeding Progression and Sniffing Away Feeding Tube

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Abstract

Prematurity is associated with feeding difficulties which remain a challenge for the neonatal nurses. Reaching full enteral feeding and increased weight are eligible criteria for sniffing away feeding tube and discharging from the Neonatal Intensive Care Unit (NICU). So, incorporating innovative olfactory and gustatory stimulations would enhance the preterm neonates' oral feeding abilities. Consequently, it leads to sniffing away the feeding tube, improve full enteral feeding and weight. **Aim:** The aim of the present study was to determine the effect of olfactory and gustatory stimulations on preterm neonates' feeding progression and sniffing away feeding tube. **Research design:** A quasi-experimental design was used. **Setting:** The study was conducted at the NICU of Damanhour National Medical Institute, Damanhour City, Al-Behira governorate, Egypt. **Subjects:** A convenience sampling of 60 preterm neonates who had hemodynamic and physiological stability and started tube feeding on the first day comprised the study subjects. Those neonates were equally divided into a study group (received olfactory and gustatory stimulations in addition to routine NICU care) and a control group (received NICU routine care without stimulations). **Tools:** Two tools were used to collect the necessary data namely; characteristics and medical history of the preterm neonates assessment tool and preterm neonates' feeding progression and sniffing away feeding tube assessment tool. **Results:** After the application of intervention, the mean time to reach full enteral feeding for the neonates in the study group was 18.77 ± 3.43 in comparison with 25.02 ± 3.95 for those in the control group and the difference was statistically significance ($P=0.000$ for each). The actual consumed milk relative to the total prescribed milk volume increased to be from 75% to less than 95% per feed for 40% of the neonates in the study group compared to only 16.7% for those in the control group with significant statistical difference ($P<0.037$). Moreover, the mean neonates' body weight was 1.926 ± 0.10 for the neonates in the study group compared to 1.864 ± 0.10 for the neonates in the control group and the difference was statistically significant ($P=0.045$). Furthermore, the mean time to sniffing away feeding tube (reach full sucking) was 11.13 ± 2.83 for preterm neonates in the study group compared to 15.49 ± 4.68 for those in the control group with significant statistical difference, where $P=0.000$. **Conclusion:** Preterm neonates who received olfactory and gustatory stimulations exhibited better abilities to organize oral –motor functions and shorter time to reach full enteral feeding. Olfactory and gustatory stimulations were effective in enhancement the volume of consumed milk, feeding tolerance and body weight with decreasing the occurrence of adverse effects during feeding. In addition, those preterm neonates exhibited shorter time to sniffing away feeding tube (reach full sucking). **Recommendations:** The olfactory and gustatory stimulations should be incorporated in the NICU policies and the written guidelines for caring of the preterm neonates.

Keywords: olfactory and gustatory stimulations, preterm neonates' feeding progression, sniffing away feeding tube.

Introduction

Prematurity is now the most important cause of death in the first month of life. It was estimated that 15 million neonates were born prematurely worldwide and more than one million of them die because of prematurity (World Health Organization, 2018). Most

preterm neonates stay in a Neonatal Intensive Care Unit (NICU) for weeks or months due to various problems related to respiration, nutrition, temperature and other disorders (Louyeh et al., 2020; Radwan & Mohammed, 2019).

Gastro-intestinal motility, digestion and metabolic control are major issues in nutrition of the preterm neonates (Beker et al., 2017). Preterm neonates are often unable to coordinate sucking, swallowing and breathing for oral feeding because of immaturity of their neurologic and digestive systems. However, most of these preterm neonates are fed through orogastric or nasogastric tube feeding until they are able to suck all of their feeds. They are fed with small volumes of milk, and this gradually increases depending on how well feeds are tolerated (Muelbert et al., 2019; Schriever et al., 2018). Once the tube feedings start, it significantly impact on the preterm neonate's survival, lead to long-term hospitalization and consequently increase hospital costs (Muelbert et al., 2019).

Immaturity presents a significant challenge to the provision of effective nutrition. Preterm neonates have rapid growth particularly of the brain and need high caloric. Furthermore enteral feeding is often poorly tolerated which may lead to delay the transition to full enteral feeds, growth failure and long-term neurodevelopmental impairment (Beker et al., 2021).

Oral nutrition is a golden standard for discharging a premature neonate from the NICU (Louyeh et al., 2020). It's important to improve preterm neonates feeding capabilities to meet their nutritional requirement and decrease the complications of delay feeding. Therefore, using cost effective interventions that hasten sucking behavior and accelerate transition to oral feeding (sniffing away feeding tube) and reach full enteral feeding such as olfactory and gustatory stimulations could be helpful for preterm neonates (Muelbert et al., 2019).

Smell and taste are powerful sensory inputs that develop during fetal life and are important in the transition to postnatal feeding (Beker et al., 2017). Olfactory receptor neurons (smell receptor) were developed in preterm neonates at 24–27 weeks of gestation and nasal chemoreception begins its function during the last gestational trimester (Schaal et al., 2020; Schriever et al., 2018). The Gustatory receptors (taste receptors) are present from 18 weeks' post menstrual age (PMA) and flavor

perception is established around 24 weeks' PMA (Beker et al., 2021). Smell and taste are primarily processed in the olfactory and gustatory cortex and then integrated with high brain function. They are important for the appreciation of food, but also they are strong stimulators of digestion and metabolisms which improve tolerance of enteral feeds by triggering reflexes in the brain refer to cephalic phase response (Beker et al., 2017; Lee, 2019; Muelbert et al., 2021).

Cephalic phase response is a pathway involved in digestion and in anticipation of food. It increases salivation, peristaltic movements; increase secretion of digestive enzymes and digestive-related hormones, the pancreas also releases insulin and glucagon into the bloodstream in response to sensory stimulation thereby the initiation of digestive process occurs before food reaches the stomach (Beker et al., 2021; Muelbert et al., 2019; Muelbert et al., 2021). The first sensory experience happen in utero, fetal smell and taste receptors are exposed to the components of amniotic fluid for many weeks before birth. Fetal swallowing of amniotic fluid starts by the end of the first trimester and reaches up to 750 mL/day by 34 weeks' gestation (Akcan & Polat, 2016; Muelbert et al., 2019; Park & Im, 2020).

Newborn infants can detect the odor of their mothers' nipples and get breast milk within the first days of their life (Aytekin et al., 2011; Neshat et al., 2016; Pouraboli et al., 2015). As the preterm neonate is feed through a tube the physiological connection between the odor and taste of nutriment, which initiate the cephalic phase, followed by sucking behavior and the satisfactory feeling of gastric filling is interrupted because preterm neonates who are fed by the tube may not experience the smell and taste of milk as the milk is placed directly into the stomach (Muelbert et al., 2019; Schriever et al., 2018).

Neonatal nurse has a proactive role in caring of preterm neonates. Providing safe feeding and appropriate nutritional support for preterm neonates is challenging for a neonatal nurse. It can be achieved through non-invasive and inexpensive approach as smell and taste of breast milk before each tube feeding. She can

train mothers to pump their breast milk to be used as an odor stimulus and also as a feeding to their preterm neonates. Furthermore she can use a piece of cotton socked with breast milk before each feeding to stimulate taste. Thus, neonates will not only be benefit from expressed milk for gavage feeding but also benefit from the stimulus effect of breast milk odor, and taste which enable them to quick transition to oral feeding (Aytekin et al., 2011; Beker et al., 2021).

Significance of the study:

Neonatal nurses are key persons involved in the neonates' care. They have a crucial role in the assessment and management of feeding problems among preterm neonates. So, they should be equipped with the most innovative evidences in the neonatal feeding interventions as a vital component of neonatal care. Olfactory and gustatory stimulations are one of these interventions to enhance the quality of neonatal care and maintain the best long-term outcomes of preterm neonates. Unfortunately, researches addressing the incorporation of olfactory and gustatory stimulations in NICU' policies are limited. Hopefully, the current study would implement olfactory and gustatory stimulations as feeding interventions to enhance the feeding outcomes of preterm neonates and faster achievement of independent oral feeding /sniffing away feeding tube.

This study aimed to:

Determine the effect of olfactory and gustatory stimulations on preterm neonates' feeding progression and sniffing away feeding tube.

Research Hypotheses:

- 1- Preterm neonates who receive olfactory and gustatory stimulations exhibit better feeding progression than those who do not.
- 2- Preterm neonates who receive olfactory and gustatory stimulations exhibit faster sniffing away feeding tube than those who do not.

Operational Definitions:

Olfactory Stimulation: In this study, refers to the stimulation of preterm neonate's

sense of smell via the inhalation of a piece of cotton soaked with fresh squeezed maternal breast milk.

Gustatory Stimulation: In this study, refers to the stimulation of preterm neonate's sense of taste via placing a few drops of maternal breast milk on neonate's lips -if he is sleep- or on his tongue -if he is awake- using a sterile syringe or a sterile pacifier.

Feeding Progression: In this study, refers to the progress of the preterm neonates' abilities to organize oral-motor functions, time to reach full enteral feeding, the volume of consumed milk relative to the prescribed volume per feed and body weight without feeding intolerance or the occurrence of adverse effects during feeding.

Sniffing Away the Feeding Tube: In this study refers to the principle criterion which denotes the improvement in the preterm neonates' oral feeding abilities and enhancement in sucking, swallowing and breathing coordination, consequently represents time to reach full sucking/ transfer from gavage to oral feeding.

Materials and method:

Materials

Research Design

A Quasi experimental research design was used to accomplish this study.

Setting

The study was conducted at NICU of Damanhour National Medical Institute affiliated to Ministry of Health in Damanhour City, Al-Behira governorate, in Egypt. The NICU consists of three rooms. Each room contains 10-15 incubators. It provides services for critically ill neonates in Al-Behira governorate.

Subjects:

- Epi-Info program was used to estimate the sample size using the following parameters:

- Population size =100 preterm neonates (representing the average number of neonates admitted to the previously mentioned setting in the last three months prior to data collection).
- Expected frequency = 50%.
- Acceptable error =5 %.
- Confidence coefficient =95%.

- Minimum sample size = 55 preterm neonates.
- A convenience sampling of 60 preterm neonates who fulfilled the following criteria comprised the study subjects:
 - Gestational age: Ranged from 28 to < 37 weeks.
 - At the first day of starting tube feeding i.e. Nasogastric or Orogastric tube.
 - Had hemodynamic and physiological stability.
 - Did not receive any sedatives or analgesics.
 - Free from any structural anomalies of GIT or neonatal sepsis.
 - Critically ill and those on mechanical ventilator were excluded.
- Eligible preterm neonates who fit the inclusion criteria were randomly divided into

two equal groups as illustrated in **Figure 1**, where one neonate was assigned to the study group and the next neonate was assigned to the control group alternatively.

Each group consisted of 30 preterm neonates as follows:

- **The study group:** where preterm neonates received olfactory and gustatory stimulations before and during tube feeding in addition to routine NICU care.
- **The control group:** where preterm neonates received routine NICU care (tube feeding without stimulation).

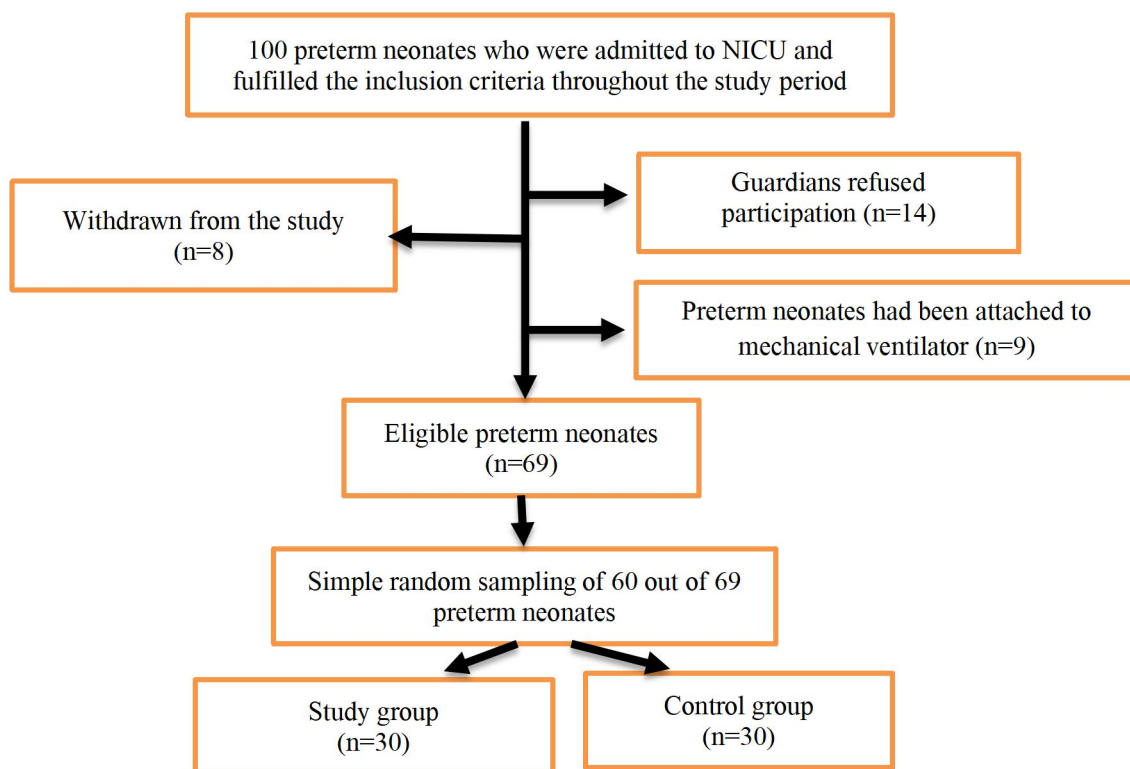


Figure-1: Flow chart of participants' recruitment process.

Tools:

Two tools were used to collect the necessary data.

Tool one: Characteristics and Medical History of the Preterm Neonates Assessment Tool:

This tool was developed by the researchers. It included two parts:

Part I: Characteristics of the Preterm Neonates as: Postnatal age, gender and birth weight.

Part II: Medical History of the Preterm Neonates, such as: gestational age, current diagnosis, type of delivery and length of hospital stay/ days (duration of hospitalization).

Tool two: Preterm Neonates' Feeding progression and Sniffing Away Feeding Tube Assessment Tool:

This tool was developed by the researchers after thorough review of the related and recent literature (Beker et al., 2021; Khodagholi et al., 2018; Lee, 2019; Muelbert et al., 2019). It was used to assess the preterm neonates feeding progression and sniffing away feeding tube. It included two parts:

Part I: Preterm Neonates' Feeding progression which involved:

A: Preterm Neonates' Abilities to Organize Oral-Motor Functions which involved:

- Open mouth promptly when lips are stroked at feeding onsets.
- Maintain a smooth, rhythmic pattern of sucking once feeding is under way.
- Maintain a stable rhythmic suck-swallow pattern.

B: Preterm Neonates' Time to Reach Full Enteral Feeding.

C: Preterm Neonates' Consumed Milk relative to the Prescribed Volume per Feed.

D: Preterm Neonates' Feeding Intolerance Criteria which entailed:

- Gastric residual volume > 50% of the previous feed (Baldassarre et al., 2019).
- Presence of vomiting.
- Presence of abdominal distension (increase in abdominal girth by 2 cm or more in between feedings) (Thomas et al., 2018).

E: Preterm Neonates' Occurrence of Adverse Effects during Feeding which involved:

- Desaturation (O₂ saturation is less than 90%).
- Bradycardia
- Aspiration, gagging, choking
- Apnea

F: Preterm Neonates' Weight: it was used to assess weight gain of the preterm neonates in grams from the first day of initiating tube feeding till the first day of initiating oral feeding.

Part II: Preterm Neonates' Time to sniffing away feeding tube (Reach Full Sucking): it included the preterm neonates' time of transfer from gavage to oral feeding.

Method

1. Approval from the Research Ethics Committee of the Faculty of Nursing, Damanshour University was obtained before carrying out this study.
2. An official letter from the Faculty of Nursing, Damanshour University was sent to the hospital administrative personnel in NICU at Damanshour National Medical Institute for permission to conduct the study with explanation of the aim of the study.
3. Tool one and tool two were developed by the researchers.
4. Tool one and tool two were submitted to a jury of five experts in the Pediatric Nursing field to assess their content validity. The content validity was 96% for tool one and 95% for tool two. There were no modifications.
5. Reliability of tool two was ascertained by measuring the internal consistency of its items using Cronbach's Alpha coefficient test and the result yielded 0.854 which is accepted.
6. A pilot study was carried out on 6 preterm neonates (10% of the total sample size) to test the applicability and clarity of the tools and no modifications were done. Those neonates were excluded from the study subjects.
7. The researchers attended both morning and evening shifts for data collection.
8. Initially, data considering the characteristics and medical history of each preterm neonate among both groups (study and control) were assessed using tool one.
9. Tool two was applied for all preterm neonates in the control group as follows:

first time (first assessment) at the first day of initiating tube feeding except **part I B** - the preterm neonates' time to reach full enteral feeding- and **part II**: preterm neonates' time to sniffing away feeding tube/ reach full sucking. Then, the preterm neonates were left for the NICU routine care without any intervention either before or during gavage feeding. After that, the assessment was done for the second time (second assessment) at the first day of initiating oral feeding using all parts of tool two.

10. Assessment of the preterm neonates' feeding progression and time to sniffing away feeding tube (reach full sucking) in the control group using tool two were applied as follows:

Part I: Preterm Neonates' Feeding progression which involved:

A-Neonates' Abilities to Organize Oral-Motor Functions were observed which involved opening mouth promptly when lips are stroked at feeding onsets, maintaining a smooth, rhythmic pattern of sucking once feeding is under way and maintaining a stable rhythmic suck-swallow pattern.

B-Preterm Neonates' Time to Reach Full Enteral Feeding was determined.

C- Preterm Neonates' Consumed Milk relative to the Prescribed Volume per Feed was measured.

D-Preterm Neonates' Feeding Intolerance Criteria were assessed which entailed increase gastric residuals volume > 50% of the previous feeding as well as presence of vomiting and abdominal distension (by measuring abdominal girth between feedings using measuring tape.

E-Preterm Neonates' Occurrence of Adverse Effects during Feeding were observed which involved the presence of desaturation (O₂ saturation is less than 90%) and bradycardia from cardiac monitor, aspiration, gagging, choking or apnea.

F-Preterm Neonates' Weight: The researchers weighed all the neonates as follows: the neonates were weighed naked

before the first feed at 9 am using digital scale on a daily basis from the first day of initiating tube feeding until the initiation of oral feeding.

Part II: Preterm Neonates' Time to sniffing away feeding tube (Reach Full Sucking): it included the preterm neonates' time of transfer from gavage to oral feeding.

11. The time spent to complete the assessment for each preterm neonate was about 15-20 minutes.
12. **For the study group:** The preterm neonates received both olfactory and gustatory stimulations as the following steps:
 - The fresh mothers' breast milk was collected in a sterile bottle for gavage feeding and kept in a refrigerator every 24 hours.
 - The stimulations were applied 5 minutes before starting and during gavage feeding three times /day (9 am, 12 MD and 3 pm) consecutively till the initiation of oral feeding.
 - The olfactory (smell) stimulation was applied as 1 cc volume of fresh squeezed mother's breast milk was taken using sterile syringe and poured on a piece of cotton placed within 1.5-2 cm away of a neonate's nasal septum which was removed after gavage feeding.
 - The gustatory (taste) stimulation was applied by placing a few drops of fresh squeezed mother's breast milk on a neonate's lips -if he was sleep- or on his tongue -if he was awake- using a sterile syringe or a sterile pacifier.
13. Tool two was applied for all preterm neonates in the study group with the same manner and at the same time sequences like mentioned previously for the control group.
14. Infection control measures were followed to prevent infection. They included hand hygiene and disinfecting of the study instruments as the digital scale and measuring tape with alcohol swab before and after use.
15. Comparison between two groups at completion of the study was done to

determine the effect of olfactory and gustatory stimulations on preterm neonates' feeding progression and time to sniffing away feeding tube.

16. The data were collected during a period of six months which started from the beginning of December 2020 to the end of May 2021.
17. Ethical considerations were considered all over the study phases as follows:
 - Written informed consents of the preterm neonates' parents were obtained after explaining the aim of the study.
 - Parents have the right to refuse the participation of their preterm neonates and to withdraw from the study at any time.
 - Confidentiality of the obtained data was assured, and participants' anonymity was respected. The preterm neonates' privacy was maintained during the implementation of the study.

Data Analysis

The Statistical Package for Social Sciences (SPSS) version 23 was utilized for data analysis. Descriptive statistics included number, percentage, mean and standard deviation to describe the preterm neonates' characteristics and medical history. The mean and standard deviation was also used to describe the preterm neonates' length of hospital stay/day, mean time to reach full sucking and full enteral feeding, gastric residual volume as well as preterm neonates' body weight. Kolmogorov-Smirnov test was used to check the normality of study variables, and it showed that they were normally distributed. In analytical statistics, Student t-test was used to compare the differences and test the significance between the preterm neonates' mean length of hospital stay/day, mean time to reach full sucking and full enteral feeding, gastric residual volume as well as preterm neonates' body weight. Moreover, the Chi-square and Fisher's Exact tests were used to compare the differences and test the significance between the preterm neonates' abilities to organize oral-motor functions and feeding intolerance. Furthermore, the Chi-square test was used to compare the differences

and test the significance between the preterm neonates' characteristics and occurrence of adverse effects during feeding. In addition, the Fisher's Exact test was used to compare the differences and test the significance between the preterm neonates' medical history and consumed milk relative to the prescribed volume per feed. All of the statistical analyses were considered significant at $P \leq 0.05$.

Results

Table 1: illustrates the characteristics of the preterm neonates in the study and control groups. The table shows that preterm neonates' age ranged from 1-7 days among 53.3 % of neonates in the study group and 66.7% of those in the control group. Regarding their gender it was revealed from the table that, female preterm neonates constituted 76.7% of the neonates in the study group and 66.7% of the neonates in the control group. The weight of 66.7% of neonates in both groups ranged from 2000 to less than 3000 grams.

Table 2: portrays the medical history of the preterm neonates in the study and control groups. The majority of neonates (86.7%) in both groups were late preterm. Their mean gestational ages were 34.5 ± 4.55 and 34.7 ± 4.51 weeks for the study and control groups respectively. The most common diagnosis encountered by preterm neonates in the study group and the control group was hyperbilirubinemia (63.3% and 60% respectively). The types of delivery was cesarean section for all preterm neonates in the study group and for the vast majority of those in the control group (93.3%) and the differences were not statistically significant.

The table also illustrates that the length of hospital stay is ranged from 14 to less than 21 days for slightly more than three quarters of neonates (76.7%) in the study group compared to 40.0% for those in the control group. On the other hand, all neonates in the study group discharged before 22 days of hospitalization while, almost one third of neonates in the control group (26.7%) were still hospitalized. The difference was statistically significant between both groups regarding their length of hospitalization ($P = 0.001$). The mean length of hospitalization was 16.32 ± 5.95 days for the study group and 25.19 ± 4.57 days for the

control group and the difference was statistically significant where, $P = 0.000$.

Effect of olfactory and gustatory stimulations on preterm neonates' abilities to organize oral-motor functions were clarified in **table 3**. Regarding neonates' abilities to open their mouth promptly when lips are stroked at feeding onsets, the first assessment revealed that 20% of the preterm neonates in the study group and 23.3% of those in the control group opened their mouth. While, 70% of the preterm neonates in the study group compared to 46.7% of those in the control group opened their mouth in the second assessment. However, the difference was not statistically significant. A very small percentage of preterm neonates in both groups (16.7% for study group and 13.3% for the control group) maintained a smooth, rhythmic pattern of sucking once feeding is under way in the first assessment. On the other hand, this percentage substantially increased to 80.0% in the second assessment for the study group compared to 36.7% for the control group with significant statistical difference, where $P < 0.001$. Additionally, 16.7% of the preterm neonates in study group and 20.0% of those in the control group were able to maintain a stable rhythmic suck-swallow pattern in the first assessment. Meanwhile, this percentage dramatically increased to 86.7% in the second assessment for the study group compared to 43.3% for the control group and the difference was statistically significant ($P < 0.000$).

Effect of olfactory and gustatory stimulations on preterm neonates' mean time to reach full enteral feeding was presented in **table 4**. The current study findings indicated that the preterm neonates in the study group reached the full enteral feeding almost seven days earlier than those in the control group (18.77 ± 3.43 and 25.02 ± 3.95 respectively). There was significant statistical difference between the study and control groups, where $P = 0.000$.

Effect of olfactory and gustatory stimulations on preterm neonates' consumed milk relative to the prescribed volume per feed were illustrated in **table 5**. In the first assessment, the consumed milk relative to the total prescribed volume was 25% to less than 50% per feed for 60% of the neonates in the

study group and 63.4% for those in the control group with no significant statistical difference between both groups. On the other hand, in the second assessment the consumed milk relative to the total prescribed volume was from 75% to less than 95% per feed for 40% of the neonates in the study group compared to only 16.7% for those in the control group. Also, the actual consumed milk relative to the total prescribed milk volume increased to be 95 % and more per feed for neonates in the study group and neonates in the control group (50% and 43.3% respectively) and the differences were statistically significant ($P < 0.037$).

Table 6 shows the effect of olfactory and gustatory stimulations on preterm neonates' feeding intolerance criteria. Regarding gastric residual volume, it was clear that the majority of the neonates in both the study and control groups (80% and 83.3% respectively) had less than 50% gastric residual at the first day of initiating tube feeding. At the first day of initiating oral feeding, 93.3% of the neonates in the study group and 86.7% of those in the control group had less than 50% gastric residual with no significant statistical differences between both groups. Moreover, the mean of gastric residual volume was 4.83 ± 3.39 for the neonates in the study group compared to 5.10 ± 3.76 of neonates in the control group at the first day of initiating tube feeding with no significant statistical difference. Meanwhile, the mean of gastric residual volume was 1.37 ± 4.26 for the neonates in the study group compared to 3.63 ± 5.35 of those in the control group at the first day of initiating oral feeding and the difference between the two groups was statistically significant ($P = 0.001$).

In addition, there was no vomiting for 56.7% of the neonates in the study group and 53.3% of the neonates in the control group in the first assessment with no significant statistical difference between the two groups. However, 93.3% of the neonates in the study group compared to 63.3% of those in the control group in the second assessment had no vomiting and the difference was statistically significance between the two groups, where $P < 0.005$.

Concerning abdominal distension, the same number of neonates in both groups had

no abdominal distension (63.3%) in the first assessment. On the other hand, all neonates in the study group (100%) had no abdominal distension compared to 76.7 % of the neonates in the control group with significant statistical difference between the two groups ($P < 0.011$).

Effect of olfactory and gustatory stimulations on preterm neonates' occurrence of adverse effects during feeding were reflected in **table 7**. It was observed that no desaturation occurred for all neonates in both groups (study and control) neither in the first assessment nor the second one. Regarding the other adverse effects in the first assessment, it was found that 30% of the neonates in the study group and 23.3% of those in the control group suffered from bradycardia. In addition, the equal number/ similar percentage of neonates (16.7%) in both the study and the control groups had aspiration, gaging and chocking. While, apnea occurred for 16.7% of the neonates in the study group and 20% of the neonates in control group. In the second assessment, bradycardia occurred for 33.3% of the neonates in the study group and 46.7% of the neonates in the study group. Aspiration, gaging and chocking happened for 26.7% of the neonates in the study group and 36.7% of the neonates in the study group. While, apnea found in 20% of the neonates in the study group and 16.7% of the neonates in the control

group. There were no significant statistical differences between the two groups either in the first or the second assessment in relation to the occurrence of adverse effects during feeding.

Table 8 portrays the effect of olfactory and gustatory stimulations on preterm neonates' weight. At the first day of initiating tube feeding (the first assessment), it was found that the mean body weight for the neonates of the study group was 1.760 ± 0.14 and 1.764 ± 0.11 for the neonates in the control group. The difference was not statistically significant. While, the mean body weight was 1.926 ± 0.10 for the neonates in the study group compared to 1.864 ± 0.10 for the neonates in the control group at the first day of initiating oral feeding (the second assessment) and the difference was statistically significant ($P = 0.045$).

Effect of olfactory and gustatory stimulations on preterm neonates' mean time to sniffing away feeding tube (reach full sucking) was illustrated in **table 9**. It can be seen that the mean time to sniffing away feeding tube (reach full sucking) for preterm neonates in the study group was 11.13 ± 2.83 days in comparison with 15.49 ± 4.68 days for neonates in the control group. There was significant statistical difference between the study and control groups, where $P = 0.000$.

Table 1: Characteristics of the preterm neonates in the study and control groups

Preterm Neonates' Characteristics	Study group (n=30)		Control group (n=30)		Test of Significance
	No.	%	No.	%	
Postnatal Age/ days					X = 1.111 P= 0.292
• 1-7.	16	53.3	20	66.7	
• 8-14.	14	46.7	10	33.3	
Mean ± SD	5.96 ± 3.95		5.23 ± 4.10		
Gender					X = 0.739 P= 0.390
• Male.	7	23.3	10	33.3	
• Female	23	76.7	20	66.7	
Birth weight / grams					-----
• 1000 –	10	33.3	10	33.3	
• 2000 -<3000	20	66.7	20	66.7	
Mean ± SD	1.760± 0.14		1.764± 0.11		

X² = Chi Square test P: P value of Chi Square * Significant at P ≤ 0.05

Table 2: Medical History of the preterm neonates in the study and control groups

Preterm Neonates' Medical History	Study group (n=30)		Control group (n=30)		Test of Significance
	No.	%	No.	%	
Gestational age					-----
• Moderately preterm (32 - < 34 weeks)	4	13.3	4	13.3	
• Late preterm (34 -< 37 weeks)	26	86.7	26	86.7	
Mean ± SD	34.5 ± 4.55		34.7 ± 4.51		
Current Diagnosis					FET = 0.232 P= 1.000
• Hyperbilirubinemia.	19	63.3	18	60.0	
• Infant of diabetic mother	9	30.0	10	33.3	
• Respiratory Distress Syndrome.	2	6.7	2	6.7	
Type of Delivery					FET = 0.246 P = 0.492
• Vaginal Delivery.	0	0.0	2	6.7	
• Cesarean Section	30	100	28	93.3	
Length of hospital stay/ days (Duration of hospitalization)					FET = 12.511 P = 0.001*
• 14-	23	76.7	12	40.0	
• 21-	7	23.3	10	33.3	
• 22-28	0	0.0	8	26.7	
Mean ± SD	16.32± 5.95		25.19 ± 4.57		t= 8.677 P= 0.000*

FET = Fisher's Exact Test
P: P value of Fisher's Exact test/ Student t- test

t= Student t- test
* Significant at P ≤ 0.05

Table 3: Effect of Olfactory and Gustatory Stimulations on Preterm Neonates' Abilities to Organize Oral-Motor Functions

Ability to Organize Oral-Motor Functions	Baseline data (1 st day of initiating tube feeding) (first assessment)					(1 st day of initiating oral feeding) (second assessment)				
	Study Group (n= 30)		Control Group (n=30)		Test of Significance	Study Group (n= 30)		Control Group (n=30)		Test of Significance
	No.	%	No.	%		No.	%	No.	%	
Open mouth promptly when lips are stroked at feeding onsets.	6	20.0	7	23.3	$X^2 = 0.098$ $P = 0.745$	21	70.0	14	46.7	$X^2 = 3.360$ $P < 0.067$
Maintain a smooth, rhythmic pattern of sucking once feeding is under way.	5	16.7	4	13.3	FET= $P = 1.000$	24	80.0	11	36.7	$X^2 = 11.589$ $P < 0.001^*$
Maintain a stable rhythmic suck-swallow pattern.	5	16.7	6	20.0	$X^2 = 0.111$ $P = 0.739$	26	86.7	13	43.3	$X^2 = 12.381$ $P < 0.000^*$

X²: Chi Square test

FET: Fisher's Exact

P: P value of Chi Square/ Fisher's Exact test

* Significant at $P \leq 0.05$.**Table 4:** Effect of Olfactory and Gustatory Stimulations on Preterm Neonates' Mean time to Reach Full Enteral Feeding

The time to reach Full Enteral Feeding	(1 st day of initiating oral feeding)		
	Study Group (n= 30)	Control Group (n=30)	Test of Significance
Mean time to reach full enteral feeding/days	18.77± 3.43	25.02± 3.95	$t = 7.337$ $P = 0.000^*$

t= Student t-test

P: P value of Student t-test

*Significant at $P \leq 0.05$.**Table 5:** Effect of Olfactory and Gustatory Stimulations on Preterm Neonates' Consumed Milk relative to the Prescribed Volume per Feed.

Consumed milk relative to the prescribed volume per feed (%)	Baseline data (1 st day of initiating tube feeding) (first assessment)					(1 st day of initiating oral feeding) (second assessment)				
	Study Group (n= 30)		Control Group (n=30)		Test of Significance	Study Group (n= 30)		Control Group (n=30)		Test of Significance
	No.	%	No.	%		No.	%	No.	%	
< 25	4	13.3	3	10.0	FET =0.579 $P = 1.000$	0	0.0	0	0.0	FET =8.279 $P < 0.037^*$
25-	18	60.0	19	63.4		1	3.3	6	20.0	
50-	3	10.0	4	13.3		2	6.7	6	20.0	
75-	5	16.7	4	13.3		12	40.0	5	16.7	
95 and more	0	0.0	0	0.0		15	50.0	13	43.3	

FET: Fisher's Exact Test

P: P value of Fisher's Exact test

* Significant at $P \leq 0.05$.

Table 6: Effect of Olfactory and Gustatory Stimulations on Preterm Neonates' Feeding Intolerance Criteria

Feeding Intolerance Criteria	Baseline data (1 st day of initiating tube feeding) (first assessment)					(1 st day of initiating oral feeding) (second assessment)				
	Study Group (n= 30)		Control Group (n=30)		Test of Significance	Study Group (n= 30)		Control Group (n=30)		Test of Significance
	No.	%	No.	%		No.	%	No.	%	
Gastric residual volume:										
<50%	24	80.0	25	83.3	X ² =0.111 P<0.739	28	93.3	26	86.7	FET = 3.625 P=0.671
50 % and more	6	20.0	5	16.7		2	6.7	4	13.3	
	4.83±3.39		5.10±3.76		t= 0.825 P= 0.413	1.37±4.26		3.63±5.35		t= 3.659 P= 0.001*
Presence of vomiting:										
No	17	56.7	16	53.3	X ² =0.067 P<0.795	28	93.3	19	63.3	X ² = 7.954 P< 0.005*
Yes	13	43.3	14	46.7		2	6.7	11	36.7	
Presence of abdominal distension:										
No	19	63.3	19	63.3	—————	30	100.0	23	76.7	FET = 8.951 P< 0.011 *
Yes	11	36.7	11	36.7		0	0.0	7	23.3	

X² = Chi Square test

FET = Fisher's Exact Test

t= Student t- test

* Significant at P ≤ 0.05

P: P value of Chi Square/ Fisher's Exact test/ Student t- test

Table 7: Effect of Olfactory and Gustatory Stimulations on Preterm Neonates' Occurrence of Adverse Effects during Feeding

Adverse effects during feeding	Baseline data (1 st day of initiating tube feeding) (first assessment)					(1 st day of initiating oral feeding) (second assessment)				
	Study Group (n= 30)		Control Group (n=30)		Test of Significance	Study Group (n= 30)		Control Group (n=30)		Test of Significance
	No.	%	No.	%		No.	%	No.	%	
Desaturation (O₂ saturation is less than 90%).	0	0.0	0	0.0	-----	0	0.0	0	0.0	-----
Bradycardia.	9	30.0	7	23.3	X ² =0.341 P<0.559	10	33.3	14	46.7	X ² =1.111 P<0.292
Aspiration, gaging, chocking.	5	16.7	5	16.7	-----	8	26.7	11	36.7	X ² =0.693 P<0.405
Apnea.	5	16.7	6	20.0	X ² =0.111 P<0.739	6	20.0	5	16.7	X ² =0.111 P<0.739

X²: Chi Square

P: P value of Chi Square

* Significant at P ≤ 0.05.

Table 8: Effect of Olfactory and Gustatory Stimulations on Preterm Neonates' Weight

Neonates' Weight	Baseline data (1 st day of initiating tube feeding) (first assessment)			(1 st day of initiating oral feeding) (second assessment)		
	Study Group (n= 30)	Control Group (n=30)	Test of Significance	Study Group (n= 30)	Control Group (n=30)	Test of Significance
Min-Max	1.00-1.50	1.00-1.52	t=- 0.060 P= 0.953	1.06-1.55	1.05-1.41	t= 2.067 P= 0.045*
Mean ± SD	1.760± 0.14	1.764± 0.11		1.926± 0.10	1.864± 0.10	

t= Student t-test

P: P value of Student t-test

*Significant at $P \leq 0.05$.**Table 9:** Effect of Olfactory and Gustatory Stimulations on Preterm Neonates' Mean time to sniffing away feeding tube (Reach Full Sucking)

The time to sniffing away feeding tube (Reach Full Sucking)	(1 st day of initiating oral feeding)		
	Study Group (n= 30)	Control Group (n=30)	Test of Significance
Mean time to sniffing away feeding tube / reach full sucking feeds/days	11.13± 2.83	15.49± 4.68	t= 18.655 P= 0.000*

t= Student t-test

P: P value of Student t-test

*Significant at $P \leq 0.05$.

Discussion

Oral feeding is a complex task for preterm neonates where it requires precise coordination between sucking, swallowing and breathing that does not develop before 32–34 weeks of gestation (Khodaghali et al., 2018; Osman et al., 2017). Safe and competent oral feeding requires proper integration of physical and neurophysiologic functions that may not be mature at the time of oral feeding introduction (Lau, 2015). The function of gastrointestinal tract among preterm neonates is impaired related to early interruption of gestation. Moreover, immature oral motor control, weak feeding reflexes and the presence of unpleasant oral stimulation as the insertion of feeding tubes are definitely hinder oral feeding process among preterm neonates (Mousa et al., 2017).

The prematurity of those neonates leads to long hospitalization and the imposition of emotional and financial burden on the family (Khodaghali et al., 2018). The consequent impact of neonatal oral feeding difficulties points to the critical need for more efficacious early interventions to facilitate the appropriate development of oral feeding skills in preterm neonates (El-Shahat et al., 2018). Olfactory and gustatory stimulations can improve preterm neonates' feeding performance and facilitate

transition from tube to oral feeding (Khodaghali et al., 2018). The main role for the neonatal nurses is accurate assessment of neonatal feeding readiness and thoughtful progression to full oral feeding (Nassar et al., 2021). Nurses can play an important role in enhancing oral feeding skills through combined olfactory and gustatory stimulations during preterm neonates' routine care. Few studies have examined whether combined olfactory and gustatory stimulations using maternal milk can be effective intervention for faster achievement of independent oral feeding and earlier hospital discharge. So, the current study was conducted to determine the effect of olfactory and gustatory stimulations on preterm neonate feeding progression, sniffing away feeding tube and length of hospitalization.

The development of efficient suckle-feeding depends on the maturation and coordination of neuronal central pattern generators (CPGs) controlling suck, swallow and breath. These CPGs are activated to varying degrees during non-nutritive suck (Shandley et al., 2020). Initially, the present findings illustrated that preterm neonates in both the study and the control groups are almost equal in their abilities to organize oral-motor functions at the first day of initiating tube feeding. While, preterm neonates in the

study group were improved at the first day of initiating oral feeding after the intervention in all parameters such as open mouth promptly when lips are stroked at feeding onsets, maintain a smooth, rhythmic pattern of sucking once feeding is under way and maintain a stable rhythmic suck-swallow pattern and the differences were statistically significant except in relation to open mouth promptly when lips are stroked at feeding onsets. Furthermore, the mean time to reach full sucking /sniffing away feeding tube for preterm neonates in the study group was less than the neonates in the control group with a significant statistical difference.

These results could be attributed to the positive effect of olfactory and gustatory stimulations as the maternal milk odor facilitates the initiation of breastfeeding by guiding the neonates to nipple and eliciting sucking-mouthing movements. Also, the gustatory stimulation with breast milk is an important component of the stereotyped sequence of prefeeding behavior which can lead to a better mother-neonate bonding and providing the experience of sucking. These results are congruent with the results of khodagholi et al. (2018) who found that the preterm neonates who received combined stimulation with maternal milk odor and taste stimulations with Non-Nutritive Sucking (NNS) achieved earlier development of oral motor skills. Also, Amer (2015) reported accelerated maturation of the sucking reflex and earlier readiness for bottle feeding when preterm neonates are presented with NNS opportunities during gavage feeding. Moreover, Shamsi et al. (2014) reported that olfactory stimulation of premature infants significantly reduced the transitional time from gavage to oral feeding. Conversely, Beker et al. (2017) and Yildiz et al. (2011) declared that there was no evidence of a clear effect of exposure to the smell and taste of milk during tube feedings on time to reach full sucking feeds. Additionally, the results of the present study are not in congruent with a Randomized Controlled Trial (RCT) done by Muelbert et al. (2019) who reported that the evidence from two trials suggested that exposure to the smell and taste of milk with tube feedings has no clear effect on time taken to reach full sucking feeds.

Tube feedings bypass the oral and nasal cavities, so tube-fed neonates have limited exposure to the smell and taste of their feeds. Therefore, there is little stimulation of the cephalic phase response of digestion and this might contribute to feed intolerance. It is obvious from the current study that there was statistical significance difference between the study and the control groups regarding the mean time to reach full enteral feeding as the preterm neonates in the study group reached seven days earlier than those in the control group. This finding could be justified in the light of the fact that the exposure to the smell and taste of milk during tube feeding may stimulate the cephalic phase response of digestion by increasing salivation, secretion of digestive enzymes and release of digestion related hormones such as ghrelin, leptin, gastrin, insulin and others (Zolotukhin, 2013).

This finding is consistent with the finding of khodagholi et al. (2018) who conducted a study entitled “the effect of non-nutritive sucking and maternal milk odor on the independent oral feeding in preterm infants” and found that large number of the neonates in the study group achieved independent oral feeding with full feeding. Moreover, Shamsi et al. (2014) and Yildiz et al. (2011) reported that maternal milk odor led to a faster achievement of full oral feeding among premature infants. Meanwhile, Schriever et al. (2018) used rose odor, vanilla odor and a control stimulus (placebo) in a prospective randomized controlled study to evaluate the effect of olfactory stimulation on oral nutrition in preterm infants. The study showed, that preterm infants in the vanilla-intervention group reached complete oral nutrition with average one week earlier than those in the control group.

The enteral feeds for preterm neonates are usually start at small volumes and are increased gradually until full enteral feeds are tolerated. Feeding intolerance is defined as the inability to digest enteral feedings in association with increased gastric residuals, abdominal distension, vomiting, or both (Moore & Wilson, 2011). The current study results reflected that preterm neonates in both groups are almost equal in their feeding intolerance at the first day of initiating tube feeding while,

preterm neonates in the study group were substantially improved at the first day of initiating oral feeding after the intervention in all parameters such as mean amount of gastric residual volume, absence of vomiting and abdominal distension and the differences were statistically significant.

These findings could be interpreted in the light of the fact that early priming of the olfactory and gustatory systems is critical, as the ability to taste chemical compounds guides the amount of milk consumed. Once food intake is expected or commenced, the brainstem and higher centres activate the cephalic phase response and release appetite hormones in saliva. These salivary hormones are postulated to play a role in metabolism in addition to increasing the triggering peristaltic movements of the gut (Beker et al., 2021; Muelbert et al., 2019; Zolotukhin, 2013). In this respect, Muelbert et al. (2019) emphasized that smell and taste have a significant role in assisting digestion and absorption of food. Therefore, providing some milk for the infant to smell and to taste when milk is given via an orogastric or nasogastric tube could potentially help them tolerate greater volumes of milk more quickly.

Milk transfer rate and the amount have been used as important quantitative indicators and predictors of successful oral feeding skills (Prade et al., 2016). The results of the present study revealed that approximately two thirds of the neonates in both groups consumed from 25% to less than 50% of milk volume relative to the prescribed volume per feed at the first day of initiating tube feeding. These results could be related to multiple factors that lead to poor feeding abilities among preterm neonates as neurological immaturity, poor muscle tone as well as less developed sucking and swallowing mechanisms. These factors could contribute to inadequate oral feeding intake among those preterm neonates (Salem et al., 2016).

Fortunately, the results of the present study reflected that the consumed milk volume relative to the prescribed volume per feed was significantly increased on the first day of initiating oral feeding among the preterm neonates in the study group compared to those

in the control group. These results could be justified by the improvement of the neonates' abilities to organize oral-motor functions, feeding abilities and sucking, swallowing, breathing coordination process. The improved sucking skills learnt by several sessions of providing olfactory and gustatory stimulations and the achievement of independent full sucking and oral feeding in the current study confirms the significant effect of the intervention. In this context, Yildiz et al. (2011) ascertained that in order to safely tolerate oral feeding, the preterm infant should be able to coordinate simultaneous sucking, swallowing, and respiration. The results of the current study go in line with the results of Beker et al. (2017) who conducted a RCT to determine the effect of smell and taste to improve nutrition in very preterm infants. The findings of RCT revealed that the smell and taste of milk improve milk tolerance in preterm infants.

The provision of smell and taste stimulations for the preterm infants receiving tube feedings is currently being applied in the care of some preterm infants based on the assumption that there is biological plausibility for a possible benefit. Potential adverse effects of this intervention could include aspiration, gagging, choking, bradycardia and desaturation (Muelbert et al., 2019). Regarding the occurrence of adverse effects during feeding, the present study results illustrated that no desaturation occurred for all neonates in both groups the study and the control neither in the first assessment nor the second one. In addition, there were no statistical significance differences between the two groups either in the first or the second assessment. However, the experience of adverse effects such as bradycardia, aspiration, gagging, choking or apnea during feeding was less among the preterm neonates in the study group compared to those in the control group. These results could be attributed to the positive effect of the intervention and its beneficial impact on feeding of preterm neonates without harm or detrimental effects among those neonates.

These results are in harmony with the findings of Beker et al. (2021) who concluded that regular exposure to the smell and taste of

milk is a simple and inexpensive intervention with potential benefits and no apparent adverse effects. Furthermore, the present study results are in the same line with Beker et al. (2017) who reported that no adverse effects related to smell and taste stimulations were observed. In this frame, Muelbert et al. (2021) elaborated that smell and taste are intimately connected to nutrition and the integration of taste and smell information arising from the peripheral sensory organs which is believed to occur in the orbitofrontal cortex. In addition, during sensory stimulation there is a rise in oxygen delivery to the brain cells, which leads to an increase in concentration of oxygenated hemoglobin in the cerebral cortex.

The findings of the current study confirmed the significant effect of olfactory and gustatory stimulations on the improvement of neonates' body weight as the mean body weight of preterm neonates in the study group was dramatically increased compared to those in the control group at first day of initiating oral feeding and at the end of the stimulations. This finding could be justified by the improvement in the preterm neonates' abilities to organize oral-motor functions, faster sniffing away feeding tube (reach full sucking) and reach full enteral feeding earlier and consumed more milk relative to the prescribed volume per feed with better feeding tolerance which are consequently associated with increased body weight among preterm neonates in the study group. The present study finding is in agreement with Beker et al. (2017) who found in RCT that the smell and taste of milk improve weight in preterm infants. The current study finding is contradicted with the finding of Beker et al. (2021) who conducted a RCT and elaborated that regular smell and taste of milk associated with tube feeding did not improve preterm infants' weight at discharge. Moreover, Khodaghali et al. (2018) reported that there were no statistically significant differences between the two groups in terms of daily weight gain in the two weeks of the intervention.

The early achievements of oral feeds by sniffing away feeding tube with better sucking, swallowing, and breathing coordination have resulted in early discharge from the hospital. In addition, the American Academy of Pediatrics

stated that neonates could be discharged when they achieved effective oral feeding; however, the path from gavage to total oral feeding can be difficult for preterm infants. Long-term gavage feedings can cause lack of tendency to breastfeeding that require long term hospitalization (Muelbert et al., 2019). The current study finding revealed that the mean length of hospitalization for neonates in the study group was significantly less than the mean of those in the control group and the preterm neonates in the study group were discharged nine days earlier than those in the control group. This finding could be interpreted in the light of the fact that the preterm neonates in the study group exhibited an improvement in their abilities to organize oral-motor functions, faster sniffing away feeding tube (reach full sucking) and enteral feeding earlier, consumed more milk relative to the prescribed volume per feed and displayed more feeding tolerance with substantial increase in mean body weight.

This finding is in congruent with the finding of Beker et al. (2017) and Yildiz et al. (2011) who found that infants who exposed to the smell and taste of milk with tube feedings had a shorter hospital stay than infants who not exposed to the intervention. Shamsi et al. (2014) reported that olfactory stimulation of premature infants significantly reduced the length of hospitalization more in intervention group. Khodaghali et al. (2018) found that combined stimulation with maternal milk odor and NNS can accelerate maturation in preterm infants and enable their earlier achievement of feeding skills and lead to earlier hospital discharge. Schriever et al. (2018) concluded that olfactory stimulation for preterm infants in the vanilla-intervention group could be discharged from the hospital on average 9 days before those in the control group. While, Muelbert et al. (2019) reported that there was very low-quality evidence demonstrating that exposure to the smell and taste of milk decreased duration of hospitalization by almost four days.

Conclusion

Based on the findings of the current study, it can be concluded that preterm neonates who received olfactory and gustatory stimulations exhibited better abilities to

organize oral –motor functions and shorter time to reach full enteral feeding. Olfactory and gustatory stimulations were effective in enhancement the volume of consumed milk, feeding tolerance and body weight with decreasing the occurrence of adverse effects during feeding. In addition, those preterm neonates exhibited shorter time to sniff away feeding tube (reach full sucking).

Recommendations

Based on the findings of the current study, the following recommendations were suggested:

- Educational programs should be provided for neonatal nurses about the olfactory and gustatory stimulations to enhance feeding progression among preterm neonates.
- The olfactory and gustatory stimulations should be incorporated in the NICU' policies and the written guidelines concerning the procedures for caring of the preterm neonates.

Acknowledgment

The authors are grateful to all neonates and their guardians who participated in this study. Besides, we thank all the nurses who are working in the NICU from Damanhour National Medical Institute for their cooperation.

Conflict of Interest

The authors have declared no conflict of interest

References

- Akcan, E., & Polat, S. (2016). Comparative effect of the smells of amniotic fluid, breast milk, and lavender on newborns' pain during heel lance. *Breastfeeding Medicine*, 11(6), doi:10.1089/bfm.2015.0174.
- Amer, H. (2015). Effect of prefeeding oral stimulation program on feeding performance of preterm infants. *Journal of Biology, Agriculture and Healthcare*, 28(4),1-13.
- Aytekin, A., Arıkan, D., Tastekin, A., & Gozum, S. (2011).The effect of the odor of breast milk on the time needed

for transition from gavage to total oral feeding in preterm infants. *Journal of Nursing Scholarship*, 43(3),265-73. doi:10.1111/j.1547-5069.2011.01410.x.

- Baldassarre, M. E., Di Mauro, A., Montagna, O., Fanelli, M., Capozza, M., Wampler, J. L., ... & Laforgia, N. (2019). Faster gastric emptying is unrelated to feeding success in preterm infants: randomized controlled trial. *Nutrients*, 11(7), 1670. <https://doi.org/10.3390/nu11071670>.
- Beker, F., Liley, H. G., Hughes, I. P., Jacobs, S. E., Macey, J., Twitchell, E., & Davis, P. G. (2021). Effects on growth of smell and taste of milk during tube feeding of preterm infants: A randomized clinical trial. *JAMA Pediatrics*, 175(11), 1115-23. doi: 10.1001/jamapediatrics.2021.2336.
- Beker, F., Opie, G., Noble, E., Jiang, Y., & Bloomfield, F. H. (2017). Smell and taste to improve nutrition in very preterm infants: A randomized controlled pilot trial. *Neonatology*, 111(3), 260-6.
- El-Shahat, H. T. M., Elsamman, G. A., Mohamed, A., Elwahab, A., & Mohamed, M. F. (2018). Effect of prefeeding oral stimulation technique on reaching to full oral feeding in preterm newborn in neonatal intensive care units in Ismalia city. *Journal of Nursing and Health Science*, 7(4), 50-8.
- Khodagholi, Z., Zarifian, T., Soleimani, F., Shariati, M. K., & Bakhshi, E. (2018). The effect of non-nutritive sucking and maternal milk odor on the independent oral feeding in preterm infants. *Iranian Journal of Child Neurology*, 12(4), 55-64.
- Lau, C. (2015). Development of suck and swallow mechanisms in infants. *Annals of Nutrition and Metabolism*, 66(Suppl. 5), 7-14.
- Lee, E. J. (2019). The effects of breast milk olfactory stimulation on physiological responses, oral feeding progression and body weight in preterm infants. *Journal*

- of *Korean Academy of Nursing*, 49(2), 126-36. doi: 10.4040/jkan.2019.49.2.126.
- Louyeh, Z., Naderifar, M., Faghihi, H., Knoll, L., & Mahmoodi, N. (2020). Comparing the effect of breast milk odor and incubator cover on nutritional adequacy of premature infants: A quasi-experimental. *Medical Surgical Nursing Journal*, 9 (2), doi : 10.5812/msnj.99993.
- Moore, T. A., & Wilson, M. E. (2011). Feeding intolerance: A concept analysis. *Advances in Neonatal Care*, 11(3), 149-54.
- Mousa, A., Yadollah, Z., Zoya, H. & Soraya, K. (2017). The effect of non-nutritive sucking on transcutaneous oxygen saturation in neonates under the nasal continuous positive airway pressure (CPAP): A review. *Int J Pediatr*, 5(39),4511-9.
- Muelbert , M., Bloomfield, F., Pundir, S., Harding, J., & Pook, C. (2021). Olfactory cues in infant feeds: volatile profiles of different milks fed to preterm infants. *Frontiers in Nutrition Journal*, 7. <https://doi.org/10.3389/fnut.2020.603090>.
- Muelbert, M., Lin, L., Bloomfield, F. H., & Harding, J. E. (2019). Exposure to the smell and taste of milk to accelerate feeding in preterm infants. *Cochrane Database of Systematic Reviews*, (7). CD013038. doi: 10.1002/14651858.CD013038.pub2.
- Nassar, H.M.I., Helmy, A.A., & Ayed, M.M.A. (2021). Effect of oral stimulation technique application on promoting feeding among preterm infants. *Egyptian Journal of Nursing and Health Sciences*, 2(2), 298-316.
- Neshat , H., Jebreili, M., Seyyedrasouli, A., Ghojzade. M., Hosseini, M., & Hamishehkar, H. (2016). Effects of breast milk and vanilla odors on premature neonate's heart rate and blood oxygen saturation during and after venipuncture. *Pediatrics & Neonatology Journal*, 57 (3). 225-31.
- Osman, A. A., Ahmed, E. S., Hassanein, F. E. S., Mohamed, H. S., & Brandon, D. (2017). Assessment of oral feeding readiness among preterm infants. *Assiut Scientific Nursing Journal*, 5(10), 116-21.
- Park, Y. A., & Im, Y. J. (2020). The effects of a continuous olfactory stimulation using breast milk (COSB) on behavioral state and physiological responses in Korean premature infants. *Journal of Pediatric Nursing*, 53, e114-e20. doi.<https://doi.org/10.1016/j.pedn.2020.02.042>.
- Pouraboli , B., Shamsi, A., & Iranmanesh, S. (2015). The effect of breast milk odor on first breast feeding time and weight gain in premature infants. *I-Manager's Journal on Nursing*, 5(3),27-34. doi:10.26634/jnur.5.3.3627.
- Prade, L., Bolzan, G., Berwig, L., Yamamoto, R., Vargas, C., Silva, A., & Weinmann, A. (2016). Association between readiness for oral feeding and feeding performance in preterm neonates. *Audiol., Commun. Res*, 21 (3), 33-5.
- Radwan, R.I.M., & Mohammed, A.A.A. (2019). Effect of nesting position on behavioral organization among preterm neonates. *International Journal of Novel Research in Healthcare and Nursing*, 6 (3), 803-18.
- Salem, E., El-Tohamy, E. & Darwish, O. (2016). Effectiveness of sensory-motor stimulation on oral feeding skills in preterm neonates. *Med. J. Cairo Univ*, 84(1), 493-8.
- Schaal, B., Saxton, T. K., Loos, H., Soussignan, R., & Durand, K. (2020). Olfaction scaffolds the developing human from neonate to adolescent and beyond. *Philosophical Transactions of the Royal Society B*, 375(1800). <https://doi.org/10.1098/rstb.2019.0261>.
- Schriever, V. A., Gellrich, J., Rochor, N., Croy, I., Cao-Van, H., Rüdiger, M., & Hummel, T. (2018). Sniffin'away the feeding tube: the influence of olfactory stimulation on oral food intake in newborns and premature infants. *Chemical Senses*, 43(7), 469-74. <https://doi.org/10.1093/chemse/bjy034>.

- Shamsi, A., Movahed, Z., Pouraboli, B., & Iranmanesh, S. (2014). The effect of olfactory stimulation with breast milk smell on the duration of feeding transitional time from gavage to oral feeding and hospital stay in premature infants hospitalized in neonatal intensive-care unit. *Med-Surg Nurs J*, 3(1), 17–23.
- Shandley, S., Capilouto, G., Tamilia, E., Riley, D. M., Johnson, Y. R., & Papadelis, C. (2020). Abnormal nutritive sucking as an indicator of neonatal brain injury. *Frontiers in Pediatrics*, 8. <https://doi.org/10.3389/fped.2020.599633>.
- Thomas, S., Nesargi, S., Roshan, P., Raju, R., Mathew, S., Sheeja, P., & Rao, S. (2018). Gastric residual volumes versus abdominal girth measurement in assessment of feed tolerance in preterm neonates: a randomized controlled trial. *Advances in Neonatal Care*, 18(4), E13-E19.
- World Health Organization. (2018). *Survive and thrive: transforming care for every small and sick newborn: key findings* (No. WHO/FWC/MCA/18.11). Retrieved from: <https://apps.who.int/iris/bitstream/handle/10665/276655/WHO-FWC-MCA-18.11-eng.pdf>.(Accessed on September 25th, 2021).
- Yildiz, A., Arıkan, D., Gözümlü, S., Taştekin, A., & Budancamanak, İ. (2011). The effect of the odor of breast milk on the time needed for transition from gavage to total oral feeding in preterm infants. *Journal of Nursing Scholarship*, 43(3), 265-73.
- Zolotukhin, S. (2013). Metabolic hormones in saliva: origins and functions. *Oral Diseases*, 19(3), 219-29.