Effect of Peppermint Inhalation on Chemotherapy Induced-Nausea and Vomiting in Children with Leukemia

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Abstract

***Background**: Today, leukemia is one of the most important health challenges in the world. Despite the many advances in malignancy treatment, children undergoing chemotherapy are still suffering from deliberating side effects. So, pediatric oncology nurses play a main role in the management of those children.* ***Objective:** this study aimed to identify the effect of peppermint inhalation on chemotherapy induced nausea and vomiting in children with leukemia.* ***Design**: A quasi-experimental research design.* ***Setting:** The study was conducted at the Inpatient and Outpatient Hematology/leukemia Unit at Smouha University Children's Hospital at Alexandria.* ***Subjects**: A convenience sampling of 50 children with leukemia comprised the study subjects, their ages ranged from 6-15 years and a healthy sense of smell, no history of asthma or chronic obstructive pulmonary disease; no allergy to plants or essential oils. The study subjects were randomly assigned equally into two groups (control and peppermint inhalation groups).* ***Tools**: Three tools were used: Tool I: Socio Demographic and Medical Data of Children with Leukemia Undergoing Chemotherapy Assessment Sheet, Tool II: Assessment of Nausea and Vomiting of Children with Leukemia Interview Schedule, and Tool III: Assessment of Severity of Nausea and Vomiting by Baxter Retching Faces (BARF) Scale.* ***Results**: The study revealed that children who received peppermint inhalation had a significantly lower mean total score of chemotherapy induced -nausea and vomiting through the three studied sessions compared to those in control groups (P =0.000).* ***Conclusion**: It can be concluded that the peppermint inhalation therapy may have significant antiemetic effects as alleviating the CINV for children with leukemia.* ***Recommendations**: Pediatric oncology nurses should incorporate peppermint inhalation therapy in pediatric oncology unit protocols for management of chemotherapy induced -nausea and vomiting.*

Keywords: Children, leukemia, Peppermint Inhalation, Chemotherapy Induced Nausea and Vomiting, Nursing

Introduction

leukemia is the most common type of malignancy in childhood, accounting for 25% of all malignancies that occur before the age of twenty (El-Zine et al., 2021). It is defined as a heterogeneous group of hematological cancers that predominantly involves the peripheral blood and bone marrow (Kouhpeikar et al., 2019). World Health Organization, (2018) reported the total new cases of leukemia in Egypt was 4.314 (3.74%) and the total mortality rate was 3.752 (4.84%). Additionally, according to Smouha University Children's Hospital Statistics in Alexandria 2022, the number of new cases with ALL was 300 children (Alexandria University Children's Hospital, 2022). There are four main types of leukemia where Acute Lymphoblastic Leukemia (ALL) is the most diagnosed type of in children. It accounts for approximately 26% of malignances in children (Inaba & Pui, 2021; Malczewska et al., 2022).

Chemotherapy is the main selected treatment modality for leukemia, it's a cancer treatment that uses to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. (Mohamed et al., 2022National Cancer Institute {NCI}, 2022;). Children with leukemia face harmful and unpleasant side effects from chemotherapy that includes, effects on the bone marrow, risk of infection, changes in taste and smell, mucositis, bowel changes, hair loss, fatigue, nausea and vomiting (Mondanaro et al., 2021).

Chemotherapy-Induced Nausea and Vomiting (CINV) is one of the most serious side-effects and a major concern in children with leukemia, occurring in 70% of children under chemotherapy and negatively affects the quality of lives (Beauchemin et al., 2020; Farhangi et al., 2022). Clinical evidence has shown that common chemotherapy regimens, even when complemented with the best antiemetic drugs, may still cause nausea and vomiting. So, to control CINV, it is critical to apply non- pharmacological beside pharmacological interventions from the beginning of treatment (Semerci et al., 2022).

Peppermint inhalation therapy is one type of aromatherapy. It has been utilized to promote healing, detoxification, stress reduction, antiemetics and improve quality of life (Elshafie & Camele, 2017). It is safe, non-invasive, and affordable treatment and inhaled through essential oils obtained from aromatic herbs. In the peppermint inhalation therapy, the aromatic essence stimulates the olfactory receptor cells and then transmits them to the limbic system and causes a positive effect (Farahani et al., 2019). Peppermint inhalation can help treat CINV due to their effects on the central nervous system, specifically the amygdala and hippocampus providing an emotional connection to scents and promoting well-being (Aćimović, 2021).

The pediatric oncology nurses have a great responsibility to the children and their family begins with identifying the diagnosis of leukemia, continuing to provide high-quality care during their treatment, managing side effects, and offering continuous support and information. Thus, they have a pillar role through regular assessment, monitoring, and evaluation of children's conditions (Hockenberry & Wilson, 2018). Hence, this study was undertaken to help in management of CINV, which are associated with higher compliance for chemotherapy regimen and fewer complications and thus improve children's quality of life and their health outcomes. So, there is a need to incorporate peppermint inhalation in nursing interventions for the management of those children.

Aims of the Study

This study was aimed to determine the effect of peppermint inhalation on Chemotherapy Induced Nausea and Vomiting among children with leukemia.

Research hypotheses

Children with leukemia who receive peppermint inhalation exhibit less Chemotherapy Induced- Nausea and Vomiting than those who don't.

Materials and Method

Materials

Design: A quasi experimental research design was used to conduct this study.

Settings This study was conducted at inpatient and outpatient Hematology/ leukemia Units at Smouha Children's University Hospital (AUCH) at Alexandria.

Subjects: A convenience sampling of 50 children with leukemia received the second chemotherapy session and their age ranged from 6 to 15 years old, and free from other disorders such as respiratory diseases, allergic diseases were comprised the study subjects. The study subjects were randomly assigned into two equal groups, 25 in each group (control, and peppermint inhalation groups). The first child was assigned to the control group, and the second child was assigned to the peppermint inhalation group, etc. The sample size was calculated using Epi-info7 program based on the following parameters: population size = 50/3months, expected frequency =50%, acceptance error

=5%, confidence coefficient =95%, design effect=1 and power=80%.

Tools: Three tools were used to collect the needed data:

Tool One: "Socio Demographic and Medical Data of Children with leukemia Undergoing Chemotherapy Assessment Sheet":

This tool was developed by a researcher to assess socio-demographic and medical data of children who underwent chemotherapy. It was included two parts:

Part I: Socio-Demographic Data of Children: It included age, gender, residence, and level of education.

Part II: Medical Data of Children: It included onset of disease, type of leukemia, prescribed chemotherapy drug, and antiemetic prescribed medication.

Tool Two: "Assessment of Nausea and Vomiting of Children with Leukemia Interview Schedule":

This tool was adapted from Ahmad (2016), to assess nausea and vomiting for children received chemotherapy. It was translated into an Arabic language. It consists of 24 items divided into three subscales namely, the experience of anticipatory nausea and vomiting, the experience of acute nausea and vomiting and the experience of delayed nausea and vomiting. Each subscale consists of eight items capturing all the characteristics of nausea and vomiting such as experiences, duration, severity and frequency of nausea and vomiting, and estimation of the amount of vomiting.

Scoring system: each item was scored as following: questions that had Yes (1) and No (0), questions about duration; less than one hour (1), and more than an hour (2), questions about frequency scored the same times, questions about severity scored as 1 for mild, 2 for moderate 3, for sever and 4 for intolerable, questions about amount was scored as 1 for small, 2 for moderate and 3 for large amount. The total scored was calculated.

In the current study CINV is categorized into:

- **Anticipatory nausea and vomiting**: (ANV) that occurs before the chemotherapy session treatment during child's preparation.
- **Acute nausea and vomiting**: that occur within the first 24 hours after chemotherapy is given.
- **Delayed nausea and vomiting**; that occurs more than 24 hours after chemotherapy (on 2nd and 3rd day after chemotherapy session).

Tool Three: "Baxter Retching Faces (BARF) Scale":

This scale was developed Baxter et al., (2011) to measure the severity of nausea and vomiting in children. It is a self-reporting tool that is used to report subjective data concerning nausea and vomiting. It has six faces with assigned scores ranging from zero to ten with a score difference of two between each face which represents a continuum of intensity as illustrated in Fig. (1). It is a verbal descriptive scale and categorized as following:

- Zero=No nausea and vomiting.
- one to less than four=Mild nausea and vomiting.
- From four to less than seven=Moderate nausea and vomiting.
- From seven to less than ten= Severe nausea and vomiting.
- Ten=Unbearable nausea and vomiting

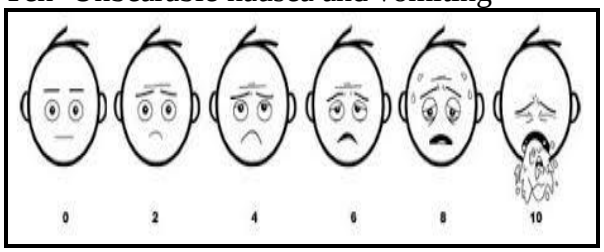

Figure (1): Baxter Retching Faces (BARF) scale (Baxter et al., (2011).

Method

Approval from the Ethical Research Committees of the Faculty of Nursing, Alexandria University was obtained before carrying out this study. An official letter was sent from the Faculty of Nursing to the director of the Alexandria University Children's Hospital to facilitate research implementation. Tool one was developed by a researcher. Content validity of the

study tools (one and two) was tested by five experts in the pediatric nursing field and necessary modifications were made. Reliability of the study tools (one and two) was ascertained by researcher by using appropriate statistical analysis test (Cronbach's Alpha test = 98). A pilot study was carried out on five children with leukemia to test the feasibility, applicability, and clarity of the tools. Necessary modifications were made. Those children were excluded from the study. The data were collected over a period of eight months from January 2022 to Augustus 2022.

At the initial contact, children's socio-demographic and medical data were reviewed by using tool one. Before each chemotherapy session, children with leukemia were assessed for ANV by using tools two and three for all children in two study groups.

For Peppermint Inhalation Group: The researcher applied two drops (0.2ml) of 2% essential oil of peppermint on a piece of cotton. Each child was instructed to take three breaths of the essence that had been put on a piece of cotton before starting chemotherapy session with three minutes (Evans et al., 2018). In addition, the piece of cotton with peppermint essence was kept at bed side table to use by child as needed throughout the chemotherapy session. Inhalation of peppermint essence was applied for three consecutive chemotherapy sessions. as needed with good compliance of use by children and parents, beside routine hospital care (ondansetron and dexamethasion).

For Control Group: The children in the control group received routine hospital care regarding chemotherapy induced nausea and vomiting (prescribed antiemetic medications).

Chemotherapy induced nausea and vomiting were assessed and recorded daily for three consecutive days immediately following each chemotherapy session along three chemotherapy sessions by using tool two and three among all children with leukemia of two study groups to identify acute (within first 24 hours after chemotherapy session) and delayed nausea and vomiting (on 2nd and 3rd days after chemotherapy session). Comparison was done between the two groups of the study to determine the effect of peppermint inhalation on chemotherapy induced nausea and vomiting among children with leukemia.

Ethical considerations:

Written informed consent was obtained from every child's parent after explaining the aim of the study and voluntary participation of their children and the right to withdraw from the study at any time. Children and parents were ascertained about confidentiality of children's data.

Statistical Analysis

The collected data were organized, tabulated, and statically analyzed using the statistical package for social studies (SPSS) Version 25.0. Qualitative data were described using numbers and percentages. Quantitative data were described mean ± standard deviation. Finally, analysis and interpretation of data were conducted. P-values of 0.05 or less were considered statistically significant.

Results

Table 1 illustrates the characteristics of children with leukemia undergoing chemotherapy. It was found that 72.0% and 80.0% of children were less than ten years in control and peppermint inhalation groups, respectively, it was showed that around two thirds of children were male in control and peppermint inhalation groups (68%, 64%, respectively). It was also portrayed that nearly three quarters of studied children in control group were living in rural area (68%) compared to 56% of children in peppermint inhalation group.

Figure 2 portrays the prescribed chemotherapy drugs for children with leukemia among the study groups. It was

found that the highest percentage of children in control group were administered with Methotrexate medication through the first, second and third session (64%, 72% & 60%, respectively. It was also showed that more than half of peppermint inhalation children (56%) were prescribed Methotrexate medication in the first session and increased to more than three quarters of in the second and third session (76% & 80%, respectively).

Table 2 reflected the positive effect of peppermint inhalation on experiences of ANV, duration, frequency, and severity besides to amount of vomiting compared to control group.

Children who received peppermint inhalation revealed a significant reduction in experiences of acute nausea and vomiting through the three studied sessions as noticed in table 3.

Table 4 shows the beneficial effect of peppermint inhalation on experiences of delayed nausea and vomiting on second and third days of chemotherapy administration compared to control group with reduction in its duration, severity, frequency, and amount of vomiting. where no child experienced delayed nausea and vomiting on third session of chemotherapy in peppermint inhalation group.

Table 5 illuminates that means total score of anticipatory nausea and vomiting, acute nausea and vomiting and delayed nausea and vomiting among children in control group are significantly high through the three sessions of chemotherapy compared to peppermint inhalation group (P=0.000). Additionally, children who inhaled peppermint reported lower total score of CINV than those who don't, nearly less than half of their total score through the three studied sessions.

Discussion

Leukemia is the most common malignancy in children, accounting for one-fourth of all childhood cancers (Weiner et al., 2023). Chemotherapy-Induced Nausea and Vomiting is a highly unpleasant side effect associated with chemotherapy treatments (Aapro, 2018). It was ranked as the fourth most prevalent and bothersome treatment-related side effect of chemotherapy. Despite recent advancements in the management of CINV, these side effects continue to be common and unpleasant in pediatric oncology patients (Ruggiero et al., 2018). However, all children undergoing chemotherapy were prescribed for antiemetic drugs (Table1), All children in this study suffered from nausea and vomiting after chemotherapy administration (table 5), This finding can be justified as Ezzo et al (2006) stated that after the introduction of 5-HT_3 receptor antagonists, the incidence of nausea may have risen despite the reduction in the incidence of vomiting.

Anticipatory nausea and vomiting can be explained by the classical conditioning model, chemotherapy as an unconditioned stimulus that naturally produces an unconditioned response (nausea, vomiting) is paired with a conditioned stimulus. Potential conditioned stimuli can include context of the sights and smells of the clinic, the nurses, the treatment room, etc. After repeated pairings of the unconditioned stimulus with this conditioned stimulus, exposure to the conditioned stimulus alone is sufficient to elicit the conditioned response (nausea, vomiting). So, the more chemotherapy sessions a child has, the more likely it is that ANV will occur (Kamen et al., 2014).

The findings of the present study revealed that the percentages of children who inhaled peppermint essence experienced an ANV through the three studied sessions with a significant decline were noticed in second and third sessions. These findings can be explained by containing the peppermint oil on Spearmint (*M. spicata*) and menthol. So, peppermint inhalation relaxes of the stomach muscles (Ali et al., 2015). Additionally, inhaled peppermint is a personal relaxation effect; this effect will decrease personal anxiety. The decrease of personal anxiety shall decrease the risk of anticipatory nausea and vomiting incidences (Ertürk & Taşcı, 2021). Similarly, Briggs et al., (2016) showed that the peppermint oil was significantly reduced the frequency of nausea, vomiting, retching

and the severity of nausea in cancer population undergoing chemotherapy (Efe Ertürk & Taşcı, 2021).

The findings of present study clarified that sixty percent of children in peppermint inhalation group experienced mild acute nausea and vomiting, two times for less than one hour during first and second sessions of study. Moreover, peppermint inhalation revealed a significant decline in the percentage of children who experienced acute nausea and vomiting during third session of study to less than one quarter of them with improvement in its frequency and severity (Table 3).

These findings may be justified as mechanism of peppermint action involves integration of essential oils into a biological signal of the receptor cells in the nose when inhaled, and rapidly absorbed by the bloodstream and exerts its rapid effects. The signal is transmitted to limbic and hypothalamus parts of the brain via olfactory bulb. These signals cause brain to release neuro messengers like serotonin, endorphin *etc*., to provide a feeling of relief. Hence, peppermint applies its antiemetic effect partially by acting as an antagonist on the 5-HT_3 receptor (Ahmadi et al., 2020; Rajabalizadeh et al., 2022). This result is congruent with Tayarani (2013) results reported that there was a significant decrease in the intensity and frequency of CINV within first 24 hours by using peppermint essential oil compared control group. In the same vein, another study which conducted by Zorba and Özdemir (2018) exhibited that inhalation of aromatic mixture including peppermint oil significantly reduced CINV.

On the other hand, the present study showed that peppermint inhalation has gradually decreased incidence of delayed nausea and vomiting among children with statistically significant improvement was observed between first and third sessions (Table4). These findings can be explained as menthol is thought to decrease nausea and vomiting by relaxing the smooth muscles of the gastrointestinal tract. Additionally, it is utilized as a remedy for spasm, cramp, headache, migraine, indigestion, nausea, and flatulence, and has antibacterial activity. These results congruent with Jafarimanesh et al. (2020) study reported that the peppermint oil reduced the frequency and duration of late-stage nausea and vomiting. Therefore, the findings of this study powered that peppermint inhalation therapy has a reasonable effect on reducing CINV for children undergoing chemotherapy (Table 5).

Conclusion

Based upon the findings of the current study, it could be concluded that peppermint inhalation therapy may have significant antiemetic effects as alleviating the CINV for children with leukemia.

Recommendations

In line with the findings of the study, the following recommendations are made:

- Replicating the study on a large probability sample is recommended for generalization of the findings.

Table 1: Characteristics of Children with Leukemia Undergoing Chemotherapy:

Children's Characteristics		Control Group (n=25)		Peppermint Inhalation Group (n=25)		Sig.	
		N	%	N	%	Z	P
Age/Year	– ≥ 10	18	72.0	20	80.0	-0.472	0.637
	– ≤10	7	28.0	5	20.0		
	– M±SD	7.760±1.588		7.560±1.502			
	– Min-Max	6-10					
Sex	– Male	17	68.0	16	64.0	-0.296	0.768
	– Female	8	32.0	9	36.0		
Residence	– Rural	17	68.0	14	56.0	-0.865	0.387
	– Urban	8	32.0	11	44.0		
Level of education	– Primary	25	100	25	100	----------	
	– Preparatory	0	0.0	0	0.0		
Type of leukemia	– ALL	25	100	25	100	----------	
Duration of Disease/ Months	– M±SD	4.480± 1.194		4.040± .978		-1.283	0.199
	– Min-Max	3-6					
Onset of Treatment/ Months	– M±SD	4.480± 1.194		4.040± .978		-1.283	0.199
	– Min-Max	3-6					
Antiemetic Medication	– Ondansetron	25	100.0%	25	100.0%	----------	

*** Significant at P < 0.05** **Z: Mann-Whitney U test** **P: significant between two groups of study**

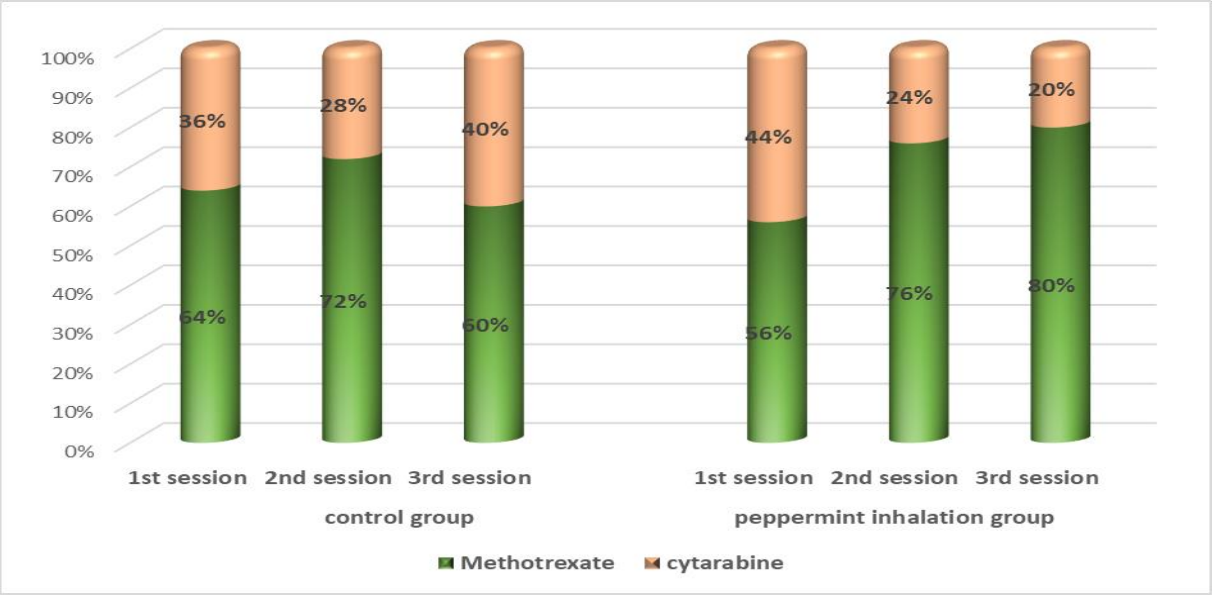

Figure 2: Percentage Distribution Prescribed Chemotherapy Drugs for Children with Leukemia among the Study Groups.

Table 2: Effect of Peppermint Inhalation on Chemotherapy Induced Anticipatory Nausea and Vomiting among Children with Leukemia before Chemotherapy Administration.

Chemotherapy Induced Anticipatory Nausea and Vomiting		1st session				2nd session				3rd session			
		Control Group		Peppermint Inhalation Group		Control Group		Peppermint Inhalation Group		Control Group		Peppermint Inhalation Group	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Experience of nausea	-Yes	13	52	5	20	22	88	13	52	22	88	2	8
	-No	12	48	20	80	3	12	12	48	3	12	23	92
	Sig. Z(P)	-2.333 (0.020)				-2.750 (0.006)				-5.604 (0.000)			
If yes:		**N=13**		**N=5**		**N=22**		**N=13**		**N=22**		**N=2**	
Duration/hrs	-<1hr.	0	0	0	0	0	0	0	0	0	0	0	0

	-≥ 1hr.	13	100	5	100	22	100	13	100	22	100	2	100
	-Mean ± SD. -Min.- Max.	2.96 ± 3.31 0.0 – 10		1.20 ± 2.61 0.0 – 10		5.56 ± 3.14 0.0 – 12		3.00 ± 3.23 0.0 – 10		5.12 ± 2.76 0.0 – 10		0.40 ± 1.38 0.0 – 5	
	Sig. Z(P)	-2.353 (0.019)				-2.746 (0.006)				-5.427(0.000)			
Worst degree	-Mild	1	8	5	100	5	23	11	85	5	23	2	100
	-Moderate	12	92	0	0	17	77	2	15	17	77	0	0
	-Severe	0	0	0	0	0	0	0	0	0	0	0	0
	-Intolerable	0	0	0	0	0	0	0	0	0	0	0	0
	Sig. Z(P)	-2.967 (0.003)				-4.144 (0.000)				-5.729 (0.000)			
Frequency	-Once	0	0	0	0	0	0	3	23	0	0	0	0
	-Twice	2	15	5	100	2	9	10	77	0	0	2	100
	-Three and more	11	85	0	0	21	91	0	0	22	100	0	0
	-Mean ± SD. -Min.- Max.	1.96 ± 2.11 0 - 6		0.44 ± 0.92 0 – 3		3.76 ± 2.37 0 – 12		0.92 ± 0.95 0 - 3		3.60 ± 2.36 0 – 12		0.16 ± 0.55 0 – 2	
	Sig. Z(P)	-2.831 (0.005)				-4.977 (0.000)				-5.708 (0.000)			
Experience of vomiting	-Yes	6	24	3	12	10	40	4	16	11	44	0	0
	-No	19	76	22	88	15	60	21	84	14	56	25	100
	Sig. Z(P)	-1.439(0.150)				-1.871 (0.061)				-3.718(0.000)			
If yes:		**N=6**		**N=3**		**N=10**		**N=4**		**N=11**		**N=0**	
Severity	- Mild	3	50	3	100	5	50	4	100	6	55	0	0
	-Moderate	3	50	0	0	5	50	0	0	5	45	0	0
	-Severe	0	0	0	0	0	0	0	0	0	0	0	0
	-Intolerable	0	0	0	0	0	0	0	0	0	0	0	0
	Sig. Z(P)	-1.219(0.223)				-2.094 (0.036)				-3.689 (0.000)			
Frequency	-Once	0	0	1	33	0	0	3	75	0	0	0	0
	-Twice	0	0	2	67	1	10	1	25	1	10	0	0
	-Three and more	6	100	0	0	9	90	0	0	10	90	0	0
	-Mean ± SD. -Min.- Max.	0.88 ± 1.69 0 - 6		0.20 ± 0.58 0 - 2		1.24 ± 1.59 0 - 4		0.20 ± 0.50 0 – 2		1.36 ± 1.60 0 – 4		0 ± 0 0 – 0	
	Sig. Z(P)	-1.348 (0.178)				-2.321 (0.020)				-3.694 (0.000)			
Amount	-Small amount	4	67	3	100	8	80	4	100	9	82	0	0
	-Moderate amount	2	33	0	0	2	20	0	0	2	18	0	0
	-Large amount	0	0	0	0	0	0	0	0	0	0	0	0
	Sig. Z(P)	-1.177 (0.239)				-1.958 (0.050)				-3.138 (0.002)			

*** Significant at P < 0.05** **Z: Mann-Whitney U test** **P: significant between two groups of study**

Table 3: Effect of Peppermint Inhalation on Chemotherapy Induced Acute Nausea and Vomiting among Children with Leukemia before Chemotherapy Administration.

Chemotherapy Induced Anticipatory Nausea and Vomiting		**1st session**				**2nd session**				**3rd session**			
		Control Group		**Peppermint Inhalation Group**		**Control Group**		**Peppermint Inhalation Group**		**Control Group**		**Peppermint Inhalation Group**	
		No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Experience of nausea	-Yes	25	100	15	60	25	100	15	60	25	100	6	24
	-No	0	0	10	40	0	0	10	40	0	0	19	76
	Sig. Z(P)	-3.500 (0.000)				-3.500(0.000)				-5.480(0.000)			
If yes:		**N=25**		**N=15**		**N=25**		**N=15**		**N=25**		**N=6**	
Duration	-<1hr.	0	0	15	100	0	0	0	0	0	0	6	100
	-≥ 1hr.	25	100	0	0	25	100	15	100	25	100	0	0
	-Mean ± SD. -Min.- Max.	10.64 ± 4.27 6 - 24		4.12 ± 3.98 0 - 12		7.24 ± 2.15 3 - 12		2.92 ± 2.47 0 – 5		6.88 ± 2.57 3 – 14		1.20 ± 2.18 0 - 5	

	Sig. Z(P)	-4.876(0.000)				-5.640(0.000)				-5.969(0.000)			
Worst degree	-Mild	0	0	11	73	0	0	15	100	0	0	6	100
	-Moderate	8	32	4	27	7	28	0	0	6	24	0	0
	-Severe	15	60	0	0	16	64	0	0	17	68	0	0
	-Intolerable	2	8	0	0	2	8	0	0	2	8	0	0
	Sig. Z(P)	-5.931(0.000)				-6.288(0.000)				-6.382(0.000)			
Frequency	-Once	0	0	0	0	0	0	6	40	0	0	2	33
	-Twice	0	0	15	100	0	0	9	60	0	0	4	67
	-Three and more	25	100	0	0	25	100	0	0	25	100	0	0
	-Mean ± SD. -Min.- Max.	5.80 ± 2.04 3 - 10		1.20 ± 1.00 0 - 2		4.84 ± 1.43 3 – 8		0.96 ± 0.89 0 – 2		4.88 ± 1.24 3 – 6		0.40 ± 0.76 0 - 2	
	Sig. Z(P)	-6.202(0.000)				-6.167(0.000)				-6.312(0.000)			
Experience of vomiting	-Yes	25	100	15	60	25	100	15	60	25	100	6	24
	-No	0	0	10	40	0	0	10	40	0	0	19	76
	Sig. Z(P)	-2.092(0.036)				-2.092(0.036)				-3.210(0.001)			
If yes:		**N=25**		**N=15**		**N=25**		**N=15**		**N=25**		**N=6**	
Severity	- Mild	1	4	13	87	1	4	15	100	1	4	6	100
	-Moderate	22	88	2	13	22	88	0	0	22	88	0	0
	-Severe	2	8	0	0	2	8	0	0	2	8	0	0
	-Intolerable	0	0	0	0	0	0	0	0	0	0	0	0
	Sig. Z(P)	-5.901(0.000)				-6.329(0.000)				-6.485(0.000)			
Frequency	-Once	0	0	1	7	0	0	10	67	0	0	3	50
	-Twice	0	0	12	80	0	0	5	33	1	4	3	50
	-Three and more	25	100	2	13	25	100	0	0	24	96	0	0
	-Mean ± SD. -Min.- Max.	4.32 ± 1.11 3 - 6		1.24 ± 1.09 0 – 3		3.52 ± 0.59 3 - 5		0.80 ± 0.76 0 - 2		3.32 ± 0.75 2 – 6		0.36 ± 0.70 0 - 2	
	Sig. Z(P)	-6.063(0.000)				-6.204(0.000)				-6.348(0.000)			
Amount	-Small amount	8	32	12	80	9	36	14	93	9	36	6	100
	-Moderate amount	17	68	3	20	16	64	1	7	16	64	0	0
	-Large amount	0	0	0	0	0	0	0	0	0	0	0	0
	Sig. Z(P)	-4.487(0.000)				-4.877(0.000)				-5.886(0.000)			

*** Significant at P < 0.05** **Z: Mann-Whitney U test** **P: significant between two groups of study**

Table 4: Effect of Peppermint Inhalation on Chemotherapy Induced Delayed Nausea and Vomiting among Children with Leukemia before Chemotherapy Administration.

Chemotherapy Induced Anticipatory Nausea and Vomiting		**1st session**				**2nd session**				**3rd session**			
		Control Group		**Peppermint Inhalation Group**		**Control Group**		**Peppermint Inhalation Group**		**Control Group**		**Peppermint Inhalation Group**	
		No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Experience of nausea	-Yes	25	100	14	56	25	100	9	36	25	100	5	20
	-No	0	0	11	44	0	0	16	64	0	0	20	80
	Sig. Z(P)	-3.500(0.000)				-4.183(0.000)				-5.715(0.000)			
If yes:		**N=25**		**N=14**		**N=25**		**N=9**		**N=25**		**N=5**	
Duration	-<1hr.	0	0	0	0	0	0	0	0	0	0	0	0
	-≥ 1hr.	25	100	14	100	25	100	9	100	25	100	5	100
	-Mean ± SD. -Min.- Max.	12.76 ± 6.15 2 – 20		3.68 ± 3.63 0 – 10		10.48 ± 3.02 4 – 20		2.00 ± 2.80 0 – 10		10.64 ± 2.29 6 – 14		1.40 ± 3.07 0 – 10	
	Sig. Z(P)	-4.893(0.000)				-5.897(0.000)				-5.931(0.000)			
Worst degree	-Mild	1	4.0	12	86	1	4.0	9	100	1	4	5	100
	-Moderate	24	96	2	14	23	92	0	0	23	92	0	0

	-Severe	0	0	0	0	1	4.0	0	0	1	4.0	0	0
	-Intolerable	0	0	0	0	0	0	0	0	0	0	0	0
	Sig. Z(P)	-5.969(0.000)				-6.436(0.000)				-6.573(0.000)			
Frequency	-Once	0	0	3	21	0	0	4	44	0	0	2	40
	-Twice	0	0	10	71	0	0	5	56	0	0	3	60
	-Three and more	25	100	1	8	25	100	0	0	25	100	0	0
	-Mean ± SD. -Min.- Max.	5.64 ± 2.02 3 – 10		1.04 ± 1.02 0 – 3		5.00 ± 1.47 3 - 8		0.56 ± 0.82 0 – 2		4.80 ± 1.55 3 - 8		0.32 ± 0.69 0 - 2	
	Sig. Z(P)	-6.113(0.000)				-6.210(0.000)				-6.307(0.000)			
Experience of vomiting	-Yes	22	88	8	32	21	84	2	8	21	84	0	0
	-No	3	12	22	0	4	16	23	8	4	16	25	100
	Sig. Z(P)	-4.001				-4.213(0.000)				-4.498(0.000)			
If yes:		**N=22**		**N=8**		**N=21**		**N=2**		**N=21**		**N=0**	
Severity	- Mild	13	59	8	100	12	57	2	100	12	48	0	0
	-Moderate	9	41	0	0	8	38	0	0	8	32	0	0
	-Severe	0	0	0	0	1	5	0	0	1	4	0	0
	-Intolerable	0	0	0	0	0	0	0	0	0	0	0	0
	Sig. Z(P)	-4.424(0.000)				-5.292(0.000)				-5.510(0.000)			
Frequency	-Once	0	0	4	50	0	0	1	50	0	0	0	0
	-Twice	0	0	4	50	0	0	1	50	0	0	0	0
	-Three and more	22	100	0	0	21	100	0	0	21	100	0	0
	-Mean ± SD. -Min.- Max.	3.60 ± 1.83 0 – 8		0.48 ± 0.77 0 - 2		2.80 ± 1.41 0 – 6		0.12 ± 0.44 0 – 2		2.76 ± 1.30 0 - 4		0.04± 0.20 0 - 1	
	Sig. Z(P)	-5.311(0.000)				-5.574(0.000)				-5.665(0.000)			
Amount	-Small amount	14	64	6	75	6	29	2	100	15	71	0	0
	-Moderate amount	8	36	2	25	15	71	0	0	6	29	0	0
	-Large amount	0	0	0	0	0	0	0	0	0	0	0	0
	Sig. Z(P)	-4.364(0.000)				-5.276(0.000)				-5.522(0.000)			

*** Significant at P < 0.05** **Z: Mann-Whitney U test** **P: significant between two groups of study**

Table 5: Mean Total Score of Chemotherapy Induced Nausea and Vomiting Among Children with Leukemia of Study Groups.

Mean Total Score	1st session		2nd session		3rd session	
	Control Group	Peppermint Inhalation Group	Control Group	Peppermint Inhalation Group	Control Group	Peppermint Inhalation Group
	M±SD	M±SD	M±SD	M±SD	M±SD	M±SD
Anticipatory Nausea	5.69 ± 2.69	3.64 ± 1.32	8.38 ± 1.94	4.52 ± 1.56	8.23 ± 1.96	3.24 ± 0.83
Sig. Z(P)	-2.964(0.003)		-4.995(0.000)		-5.717(0.000)	
Anticipatory Vomiting	3.62 ± 2.69	2.32 ± 0.90	3.69 ± 2.32	2.36 ± 0.86	4.0 ± 2.35	2.08 ± 0.40
Sig. Z(P)	-0.986(0.324)		-2.317(0.020)		-3.383(0.001)	
Acute Nausea	9.77 ± 1.88	4.56 ± 2.16	8.77 ± 1.54	4.16 ± 1.84	8.92 ± 1.19	2.88 ± 1.62
Sig. Z(P)	-5.960(0.000)		-6.126(0.000)		-6.264(0.000)	
Acute Vomiting	8.62 ± 1.61	3.88 ± 2.05	7.92 ± 0.76	3.28 ± 1.54	7.77 ± 0.93	2.28 ± 1.46
Sig. Z(P)	-6.002(0.000)		-6.140(0.000)		-6.183(0.000)	
Delayed Nausea	10.60± 2.08	8.48 ± 2.29	10.00± 1.50	9.20 ± 2.74	9.80± 1.52	10.12 ± 2.19
Sig. Z(P)	-6.102(0.000)		-6.204(0.000)		-6.296(0.000)	
Delayed Vomiting	5.77 ± 2.28	2.80 ± 1.22	5.0 ± 2.12	2.04 ± 0.93	5.15 ± 2.27	1.92 ± 0.70
Sig. Z(P)	-5.287(0.000)		-5.468(0.000)		-5.562(0.000)	
Total CINV	44.07 ± 6.73	25.68 ± 5.63	43.76 ± 5.60	25.56 ± 5.29	43.87 ± 6.12	22.52 ± 3.23

Sig. Z(P)	-6.076(0.000)	-6.071(0.000)	-6.100(0.000)

*** Significant at P < 0.05** **Z: Mann-Whitney U test** **P: significant between two groups of study**

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