Effect of Chlorhexidine in Prevention of Oral Lesions in Leukemic Children Receiving Chemotherapy

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Abstract: Leukemia is the most common childhood cancer. Untreated leukemia results in death from infections or hemorrhage. The primary treatment of ALL is chemotherapy which is usually associated with a number of side effects among which is oral mucositis (stomatitis). It is one of the most debilitating complications following chemotherapy treatment administration. These lesions may produce discomfort and pain which interfere with eating, patient compliance to treatment and potential risk of oral infection. Good and consistent oral hygiene is one of the basic roles of the pediatric nurse to prevent and reduce the complication of oral infection. It includes oral assessment before the initiation of chemotherapy treatment and during its administration followed by creating an oral care plan. Chlorhexidine gluconate is effective in the prevention of oral lesion and in decreasing the severity of stomatitis. The aim of the present study is to determine the effect of using chlorhexidine gluconate in the prevention of oral lesions in leukemic children receiving chemotherapy. The study was conducted at the Haematology Unit of Alexandria University Children`s Hospital at EL-Shatby and at the Oncology department at the Health Insurance Student Hospital in Alexandria. The subjects of this study comprised 50 children of both sexes with acute lymphoblastic leukemia. Children were divided into two groups: group 1 (study group) received 0.1 % of chlorhexidine gluconate and group II (control group) who was left to the routine hospital care. Tool consisted of three parts to collect the study data: Children's Bio socio-demographic data; Children's Medical data; Oral assessment guide (OAG) tool. The main result showed that children among the study group had healthier oral cavity and lower degree of oral mucositis no one developed severe oral mucositis compared to the children in the control group following 10 days of chemotherapy administration. The main recommendation is to creat an oral care plan to each child individually involving cleaning teeth by using a mouth wash with Chlorhexidine gluconate. This is important for preventing oral complications, decreasing severity of oral mucositis and treating gingivitis (swelling, redness and bleeding of the gums).

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1. Introduction:

Malignant diseases are one of the most common causes of death among children below the age of 15 years after accidents [(1)] . Among childhood malignancies, leukemia, is the most common childhood cancer accounting for about one third of pediatric malignancies [(2,3)] .

Chemotherapy is usually associated with a number of side effects mainly nausea, vomiting, anorexia, alopecia, neuropathy, constipation, hemorrhagic cystitis, moon face, mood changes and oral mucositis[(4,5)] . Oral mucositis (stomatitis) is one of the most debilitating complication following chemotherapy administration. Stomatitis is an inflammation of the oral mucosa which may include the cheek, lips, tongue, palate and floor of the mouth [(6,7)]. Oral mucositis can occur in any region of the mouth but more frequently affects non-keratinized regions such as the buccal mucosa, soft palate and the floor of the mouth[(8)].

Oral mucositis normally lasts for 3 weeks. It begins on the 3rd-5th day from starting chemotherapy with a peak on the 7th -14th day after chemotherapy. [(9,10)] Mucositis is caused by direct effect of chemotherapy by interfering with actual cell production, maturation and replacement and indirectly due to bone marrow depression during which neutropenia and thrombocytopenia lead to increased risk of bleeding and infection [(11,12)] .The severity of oral mucositis depends on the type of chemotherapeutic drug, dosage, frequency of drug administration,the child's age, neutrophil count and level of oral care [(11,12)] .

Preventive care for oral mucositis is very important especially in patients receiving high-doses of chemotherapy. Consistent oral hygiene is one of the basic roles of the pediatric nurse in the prevention and reduction of the severity of oral mucositis and oral infection. It includes oral assessment before the initiation of chemotherapy and daily assessment

during chemotherapy administration then creating an oral care plan [13].

There are different substances used in mouth care such as hydrogen peroxide, saline rinse, and herbal medicine as chamomile[14]. Other preparations that are used to prevent or treat mucositis include 12% Chlorhexidine gluconate because of its dual action against candidal and bacterial infection [15, 6] .

Chlorhexidine gluconate is a biguanide antiseptic and disinfectant. It is effective against both gram-positive and gram-negative bacteria but more effective against Gram-positive bacteria. It has been shown to have an immediate bactericidal action and a prolonged bacteriostatic action. It inhibits some virus and it is also active against some fungi. It acts by disrupting the bacterial cells plasma membrane. Chlorhexidine gluconate is used to treat gingivitis (swelling, redness, and bleeding of the gums). [16,17] It is often used as an active ingredient in mouthwash designed to kill dental plaque and other oral bacteria so it is used to improve bad breath. [16] The mouth of the child should be rinsed by chlorhexidine and kept in contact with the mucosal membrane for at least 30-90 seconds to be effective. For best effectiveness food, drink and mouth rinses should be avoided for at least one hour after use.[16, 18]

Poor oral health has significantly negative effects on systemic health so the pediatric nurse has an important role in providing oral care to children to reduce the impact of oral microbial flora, reduce cancer therapy related to mucositis, maintain nutritional status and to prevent soft tissue infections that may have systemic sequlea [5, 11] .

Aim of the work:

The aim of the study is to determine the effect of using chlorhexidine in the prevention of oral lesions in leukemic children receiving chemotherapy.

Research Question

What are the effect of using chlorhexidine in the prevention of oral lesions in leukemic children receiving chemotherapy?.

2. Subjects and Methods

Research design*:*

It is a quasi-experimental study.

Setting:

The study was conducted at the Haematology Unit in Children`s University Hospital at EL-Shatby and at the Oncology Department of Sporting Student's Hospital in Alexandria.

Subjects:

A Convenient sample of 50 children with acute lymphoblastic leukemia were selected according to the following criteria:

- Both sexes
-Free from any other disease.
-Free from any oral lesion.
-Age ranged from 2-16 years.
-Children were taken in the first day of starting chemotherapy either during induction or intensification phase.

The subjects of the study were divided into two groups by simple randomization:-

Group I (Treated group)

It Included 25 children with acute lymphoblastic leukemia who received oral hygiene by 0.1 % of chlorhexidine gluconate when they started chemotherapy.

Group II (Controlled group)

It included 25 children with acute lymphoblastic leukemia who received routine hospital care of oral hygiene.

Tool : It consisted of:

Children's Bio socio-demographic data, such as: name, age, sex, and residence area.

Children's Medical data, such as:

1-Type of ALL:
-B.ALL
-T.ALL

2-Platelet (PLT) count which was classified into:
- Severe thrombocytopenia (PLT < 20.000).
-Moderate thrombocytopenia (PLT 20.000- 40.000).
-Mild thrombocytopenia (PLT > 40.000). [19]

3-White blood cells (WBCs) count which was classified into:
- WBCs ≥ 50.000.
- WBCs < 50.000. [19]

4-Clinical manifestation: Hepatomegaly, Splenomegaly, Hepato- splenomegaly.

5- Protocol of treatment which was classified into high risk and low risk protocol.

-High risk protocol (age 1-9 years with initial WBCS ≥50.000/u/L or age >10 years and < 21 years with any WBCs count or with T-cell Acute lymphoblastic leukemia (ALL) or with overt testicular leukemia at diagnosis or had center nervous system (CNS) disease at diagnosis). [19]

-Low risk protocol (age 1-9.99 years or initial WBCS < 50.000/u/L or with T-ALL are not eligible or with overt testicular leukemia at diagnosis are not eligible or had CNS disease at diagnosis are not eligible). [19]

6- Stage of chemotherapy included induction or intensification phase.

- **Oral assessment guide (OAG) tool**

It was developed by Eilers *et al.* [9] to assess the condition of oral cavity and the degree of stomatitis for leukemic children.

The tool consists of 8 items: Voice; Swallow.; Lips and angle of the mouth; Tongue; Saliva ; Mucus membrane ; Gingiva and Teeth.

The scoring system of the tool is as follows:

Each of the eight items of oral assessment guide is scored as 1, 2 or 3; where:

Score 1 for normal findings.

Score 2 for mild abnormality without compromise of either mucosal integrity or loss of function.

Score 3for severe abnormality with compromise of either mucosal integrity or loss of function.

Scoring system for assessment of each part of oral cavity:

Score of voice

Communicate with patient and listen whether:

Score 1: The voice is normal.

Score 2: The voice is deep /raspy (hoarse).

Score 3: Patient has difficulty in talking, crying or had painful cry.

Score of swallow reflex

Ask patient to swallow and observe whether:

Score 1: The swallowing is normal.

Score 2: Patient experiences some pain on swallowing.

Score 3: Patient is unable to swallow.

Score of lips

Observe lips and feel tissue, assess whether they are:

Score 1: Smooth, pink, moist.

Score 2: Dry or cracked.

Score 3: Ulcerated or bleeding.

Score of tongue

Observe the tongue and assess whether it is:

Score 1: Pink, moist, and papillae present.

Score 2: Coated or there is loss of papillae with a shiny appearance, with or without redness.

Score 3: Blistered or cracked.

Score of saliva

Insert depressor into mouth, touching the centre of the tongue and the floor of the mouth and observe whether:

Score 1: The saliva is watery.

Score 2: The saliva is thick; or ropy.

Score 3: There is absence of saliva.

Score of mucous membrane

Observe the mucous membrane in the oral cavity and determine if it is:

Score 1: Pink and moist.

Score 2: Reddened or coated (increased whiteness) without ulceration.

Score 3: Ulcerated with or without bleeding.

Score of gingiva (Gums)

Gently press the gums with end of spatula and observe whether:

Score 1: They are pink and firm.

Score 2: They are oedematous with or without redness.

Score 3: There is spontaneous bleeding or bleeding with pressure.

Score of teeth or denture bearing area

Observe the appearance of the teeth or denture bearing area and determine whether:

Score 1: They are clean with no debris.

Score 2: There are plaques or debris in localized area (between teeth if present).

Score 3: There are plaques or debris generalized along gum line or denture bearing area.

The eight subscale scores of oral assessment guide are summed to obtain an overall assessment score that ranging from 8-24.

The total assessment score was categorized as follows:

- If an overall assessment score was 8 or less than 9, it denotes healthy oral cavity.
- If an overall assessment score ranges from 9-16, it denotes moderate mucositis.
- If an overall assessment score ranges from 17-24, it denotes severe mucositis [(7)] .

Method

1. Official written approval consent for conducting the study was obtained from the responsible administrative personel.
2. Informed consent was obtained from the parents after explaining the aim of the study.
3. Confidentiality was ascertained.
4. Oral assessment guide tool that was developed by Eilers *et al.* (1988) was adopted.
5. Tool was tested for content validity by 5 experts in the pediatric nursing field and the validity of the tool was 100%.
6. A pilot study was conducted on 5 children with acute lymphoblastic leukemia who received chemotherapy and was satisfying the prescribed criteria to test the clarity and applicability of the tool. These patients were excluded from the studied subjects.
7. The children were divided into two groups by simple randomization: Group1 (treated group), and Group II (controlled group).
8. All leukemic children, either treated group or controlled group, were assessed for oral cavity by inspection and digital palpation of the oral mucosa using oral assessment guide (OAG) tool on the first day of starting chemotherapy and after 10 days.
9. Group1 (study group) received oral hygiene with 0.1% Chlorhexidine gluconate on the first day of starting chemotherapy 2 times daily in the form of mouth rinse for old children . For young children, it was applied by cotton pad immersed in the used solution for one minute ,30 minutes after breakfast and the second time of mouth

wash 30 minute after the last meal time on the buccal, labial mucosa, lateral surface of the tongue and the soft, hard palate. The children and their mothers were instructed about avoiding food and drink for at least one hour after using mouth wash. This procedure was done every day from the first day of starting chemotherapy and lasted for 10 consecutive days.

10. Group II (controlled group) received routine hospital care of oral hygiene.
11. Evaluation of the degree of stomatitis was categorized according to whether the child had normal oral cavity (scored 8), moderate stomatitis (scored 9-16) or severe stomatitis (scored 17-24).
12. A comparison was done between the two groups, for determining the effect of chlorhexidine gluconate on prevention of oral lesion in oral cavity.
13. The data collection was done during the period from November 2008 to August 2009.

Statistical analysis:

Data were coded and transferred into specially designed formats to be suitable for computer feeding. Following data entry, checking and verification processes were carried out to avoid any errors during data entry. Data were analyzed using a personal computer with statistical package for social sciences (SPSS) version 13.

The following statistical measures were used:

- Descriptive measures included: Percentage, Mean, Standard deviation.
- Chi square test, Fisher's Exact Test, T test was used for test of significance.
- The 0.05 levels was used as the cut off values for statistical significance ($p \leq 0.05$)

3. Results:

Table (I) illustrates the socio demographic characteristics of the studied subjects. 54 % of the subjects was in the preschool age i.e. age 2-6 years, while 20 % of the subjects was in the adolescence age i.e. Age 12-16 years. Moreover, the mean age of the subject was 6.94±4.474 year.

Regarding sex, it was observed from this table that the highest frequencies (66%) of studied subjects were boys, while 34 % were girls.

Concerning the residence, 60 % of the studied subjects were from urban areas and 40 % of them were from rural areas.

Table (II) shows the percentage distribution of the studied subject according to their clinical data. It was found that equal percentage (80%) of studied and controlled groups had leukemia type (B.ALL). As regards clinical manifestation, nearly half of the studied group (48%) compared to 24% of the controlled group had Hepato-Spleenomegaly, While 44% of the controlled group and 24% of the studied group did not suffer from Hepato-spleenomegaly. There was no statistically significant difference between the two groups.Concerning platelets (PLT) count, 72 % of the studied group compared to 68% of the controlled group had mild thrombocytopenia. i.e. (PLT count > 40.000). On the other hand, 12% of the studied group compared to 20% of the controlled group had Severe thrombocytopenia (PLT count <20.000). There was no statistically significant difference between the two groups. The mean of PLT count of the studied and the controlled groups was 132160±131454 and 176800±165293 respectively. No statistically significant difference was found between the means of both groups.

Concerning white blood cells (WBCs) count, equal percentage (92%) of the studied and the controlled groups had WBCs count <50.000. The mean WBCs count of studied and controlled groups was 9788±17065 and 9922.4±14963 respectively. There was no statistically significant difference between the mean of both groups.

Regarding protocol of treatment, 64 % of the controlled group and 60% of the studied group received standard risk protocol of treatment. There was no statistically significant difference between both groups. Concerning stage of chemotherapy, equal percentage (68%) was found in the treated and the controlled groups during the induction phase.

As classified in table III which portrayed post 10 days chemotherapy oral assessment categories of studied and controlled groups, it was found that the studied group had more normal oral assessment concerning most of their oral assessment categories than that of the controlled group. As regards voice, the majority of the studied group (96%) had normal voice compared to 68% of the controlled group. On the other hand, none of the studied group had difficulty in talking, crying or had painful cry compared to 20% of the controlled group. Statistically significant difference was found between both groups where P=0.027. Concerning swallowing, the majority of the treated group (96%) had normal swallowing compared to 52% of the controlled group. Only 4% of the studied group suffered from some pain during swallowing compared to nearly one third of the controlled group (32%). None of the studied group suffered from the inability to swallow compared to 16% of the controlled group. The difference was statistically significant between both groups where P=0.002. Concerning lips, about three quarter of the studied group (76%) had smooth, pink and moist lips compared to 32% of the controlled group. 64% of the controlled group had dry or

cracked lips compared to about one quarter (24%) of the studied group. Statistically significant difference was found between both groups where P=0.007.

Regarding tongue, the children who had pink and moist tongue constituted the highest frequency in studied group (92%) while 44% were in the controlled group. Nearly half of the controlled group (52%) had coated tongue or loss of papillae compared to 8% of the studied group. None of the studied group had blistered or cracked tongue compared to 4% of the controlled group. There was statistically significant difference between both groups where P=0.001.Regarding saliva, 96% of the studied group had watery saliva compared to 64% of the controlled group. On the other hand, only 4% of the studied group had thick or ropy saliva compared with 36 % of the controlled group. Statistically significant difference was found between the studied and controlled groups where P=0.004.Concerning mucous membrane, it was found that the majority of the studied group (88%) and nearly half of the controlled group (48%) had pink and moist mucous membrane .However, 8% of the controlled group had ulcer with or without bleeding in mucous membrane compared to none of the treated group. Statistically significant difference was found between both groups where P=0.023.In the gingival of children, the results showed that slightly less than half of the controlled group (48%) had edema with or without redness in gingival, while 16% was found in the studied group. Statistically significant difference was found between both groups where P=0.02. Concerning teeth, 20% of the controlled group had plaque or debris in localized area along gum compared to only 4% of the studied group. No statistically significant difference was found between both groups.

Total scores of post 10 days chemotherapy oral assessment of the studied and the controlled groups are presented in table (IV). As classified in this table, nearly three quarters of the studied group (76%) had healthy oral cavity (OAG score=8) compared to 24% of the controlled group. On the other side, 16% of the controlled group had severe mucositis (OAG score from 17-24) compared to none of the treated group. There was statistically significant difference between both groups where P=0.005.

Table (V) shows the comparison between the total percent scores of treated and controlled groups regarding oral assessment guide (OAG) following 10 days of chemotherapy and their age.It was observed from this table that three quarters (75%) of children of the treated group whose age ranged from 2-6 years, had healthy oral cavity compared to 20% of the controlled group. None of the treated group whose age ranged from 2-6 years suffered from severe mucositis compared to 6.7% of the controlled group and there was no statistically significant difference. As Regards children whose age ranged from 6-12 years, it was found that 71.4 of the treated group had healthy oral cavity compared to 16.7% of the controlled group. On the other hand, none of the treated group whose age ranged from 6-12 years suffered from severe mucositis compared to one third (33.3%) of the controlled group and there was no statistically significant difference between them .Regarding children whose age ranged from 12-16 years it was found that the majority (83.3%) of the treated group had healthy oral cavity compared to half (50%) of the controlled group. No one of the treated group whose age ranged from 12-16 years suffered from severe mucositis compared to 25% of the controlled group and there was no statistically significant difference.

Table (VI) reveals the comparison between the total percent scores of treated and controlled groups regarding oral assessment guide (OAG) following 10 days of chemotherapy and their sex. It was found that 70 % of boy of the treated group had healthy oral cavity compared to 46.15 % of the controlled group. No one of the boys of the treated group suffered from severe mucositis compared to 7.7% of the controlled group. There was no statistically significant difference. Regarding girls, all the treated group had healthy oral cavity compared to no one of the controlled group. None of the treated group had severe mucositis compared to 25 % of the controlled group. Statistically significant difference was found between both groups where P=0.000.

Table (VII) illustrates the comparison between the total percent scores of treated and controlled groups regarding oral assessment guide (OAG) following 10 days of chemotherapy and their protocol of treatment. It was found that 73.3% of the treated group who received standard risk protocol of treatment had healthy oral cavity compared to 18.8% of the controlled group. However, no one of the studied group who received standard risk protocol of treatment suffered from severe mucositis compared to 18.7% of the controlled group. Statistically significant difference was found between both groups where P=0.004. On the other hand, the majority of the studied group (80%) who received high risk protocol of treatment had healthy oral cavity compared to one third (33.3%) of the controlled group, while 20% of the studied group who received high risk protocol of treatment suffered from moderate mucositis compared to more than half (55.6%) of the controlled group There was no statistically significant difference between both groups.

Table (VIII) clarifies the comparison between the total percent scores of studied and controlled

groups regarding oral assessment guide (OAG) following 10 days of chemotherapy and their stage of chemotherapy. It was found that slightly more than three quarters (76.5%) of the studied group during the induction phase had healthy oral cavity compared to nearly one quarter (23.5%) of the controlled group. No one of the studied group during the induction phase suffered from severe mucositis compared to 23.5% of the controlled group. Statistically significant difference was found between both groups where P=0.005. On the other hand, three quarters (75%) of the studied group, during the intensification phase, had healthy oral cavity compared to only one quarter (25%) of the controlled group. 25% of the studied group, during the intensification phase, suffered from moderate mucositis compared to 75% of the controlled group. Statistically significant difference was found between both groups where P=0.041.

Table (I): Bio socio-demographic characteristics of the studied subjects.

Socio-demographic Characteristics	Treated group (N=25)		Controlled group(N=25)		Total	
	No	%	No	%	No	%
1- Age /years						
• Pre-school age (2-6)	12	48	15	60	27	54
• School age (6-12)	7	28	6	24	13	26
• Adolescence age (12-16)	6	24	4	16	10	20
Total	25	100	25	100	50	100
Mean ± S.D	7.24±4.702		6.64±4.31		6.94±4.474	
t-value	0.470					
p	0.640					
2- Sex						
• Male	20	80	13	52	33	66
• Female	5	20	12	48	17	34
Total	25	100	25	100	50	100
3- Residence						
• Urban	14	56	16	64	30	60
• Rural	11	44	9	36	20	40
Total	25	100	25	100	50	100

Table (II): Percentage distribution of the studied subjects according to their clinical data:

Clinical Data	Treated group (N=25)		Controlled group (N=25)		X^2	P
	No	%	No	%		
1. **Type of leukemia**						
• B.ALL	20	80	20	80	0.000	1.000
• T.ALL	5	20	5	20		
Total	25	100	25	100		
2. **Liver and spleen** (clinical manifestation)						
• Hepatomegaly	2	8	1	4		
• Spleenomegaly	5	20	7	28	4.137	0.247
• Hepato-spleenomegaly	12	48	6	24		
• None	6	24	11	44		
Total	25	100	25	100		
3. Platelet count						
• Mild thrombocytopenia (PLT > 40.000)	18	72	17	68	0.571	0.715
• Moderate thrombocytopenia (PLT 20-40.000)	4	16	3	12		
• Severe thrombocytopenia (PLT <20.000)	3	12	5	20		
Total	25	100	25	100		
Mean± S.D	132160±131454		176800±165293			
t- value	1.057					
P	0.296					
4. WBCs count						
• Low risk (WBCs<50.000)	23	92	23	92	0.001	1.000
• High risk (WBCs≥50.000)	2	8	2	8		
Total	25	100	25	100		
Mean± S.D	9788±17065		9922.4±14963			
t- value	0.032					
p	0.977					

5. Protocol of treatment						
• Standard risk	15	60	16	64	0.085	0.771
• High risk	10	40	9	36		
Total	25	100	25	100		
6. Stage of chemotherapy						
• Induction phase.	17	68	17	68	0.000	1.000
• Intensification phase.	8	32	8	32		
Total	25	100	25	100		

Table (III): Post 10 days chemotherapy oral assessment categories of treated and controlled groups

Categories	**Treated group N=25**		**Controlled group N=25**		**X^2**	**P**
	No	**%**	**No**	**%**		
1-Voice						
• Normal	24	96	17	68		
• Deeper or raspy	1	4	3	12	7.195	0.027*
• Difficulty talking ,crying or had painful cry	0	.0	5	20		
2-Swallow						
• Normal swallowing	24	96	13	52		
• Some pain on swallowing	1	4	8	32	12.715	0.002*
• Unable to swallow	0	.0	4	16		
3-lips						
• Smooth , pink and moist	19	76	8	32	10.027	0.007*
• Dry or cracked	6	24	16	64		
• Ulcerated or bleeding	0	.0	1	4		
4- Tongue						
• Pink, moist and papillae present	23	92	11	44	13.302	0.001*
• Coated or loss of papillae	2	8	13	52		
• Blistered or cracked	0	.0	1	4		
5- Saliva						
• Watery	24	96	16	64	8.0	0.004*
• Thick or ropy	1	4	9	36		
• Absent	0	.0	0	.0		
6- Mucous membrane						
• Pink and moist	22	88	12	48	7.513	0.023*
• Reddened or coated without ulceration	3	12	11	44		
• Ulceration with or without bleeding	0	.0	2	8		
7- Gingival						
• Pink and firm	21	84	13	52	5.882	0.02*
• Edematous with or without redness	4	16	12	48		
• Spontaneous bleeding or bleeding with pressure	0	.0	0	.0		
8- Teeth						
• Clean and no debris	24	96	20	80	3.030	0.082
• Plaque or debris in localized area along gum	1	4	5	20		
• Plaque or debris generalized along gum	0	.0	0	.0		
Total	25	100	25	100		

Table (IV) Total percent scores of post 10 days chemotherapy oral assessment of treated and control groups:

Oral assessment guide score (OAG)	**Treated group No=25**		**Controlled group No=25**		**X^2**	**P**
	No	**%**	**No**	**%**		
Healthy oral cavity (OAG =8)	19	76	6	24	10.617	0.005*
Moderate mucositis (OAG score= 9-16)	6	24	15	60		
Severe mucositis (OAG score =17-24)	0	0	4	16		
Total	25	100	25	100		

***** Statistically significant $p \leq 0.05$

Table (V) Comparison between the total percent scores of treated and controlled groups regarding oral assessment guide (OAG) following 10 days of chemotherapy and their age.

Total percent scores of oral assessment guide (OAG)	Age											
	Preschool 2-6 years				School 6-12 years				Adolescence 12-16 years			
	Treated group		Controlled group		Treated group		Controlled group		Treated group		Controlled group	
	NO	%	NO	%	NO	%	NO	%	NO	%	NO	%
Healthy oral cavity (OAG =8)	9	75	3	20	5	71.4	1	16.7	5	83.3	2	50
Moderate mucositis (OAG score= 9-16)	3	25	11	73.3	2	28.6	3	50	1	16.7	1	25
Severe mucositis (OAG score =17-24)	0	0	1	6.7	0	0	2	33.3	0	0	1	25
Total	12	100	15	100	7	100	6	100	6	100	4	100
FET	4.993				4.286				2.061			
P	0.069				0.114				0.667			

Table (VI) Comparison between the total percent scores of treated and controlled groups regarding oral assessment guide (OAG) following 10 days of chemotherapy and their sex.

Total percent scores of oral assessment guide (OAG)	Sex							
	Boys				Girls			
	Treated group		Controlled group		Treated group		Controlled group	
	NO	%	NO	%	NO	%	NO	%
Healthy oral cavity (OAG =8)	14	70	6	46.15	5	100	0	0
Moderate mucositis (OAG score= 9-16)	6	30	6	46.15	0	0	9	75
Severe mucositis (OAG score =17-24)	0	0	1	7.7	0	0	3	25
Total	20	100	13	100	5	100	12	100
FET	2.75				14.857			
P	0.204				0.000*			

Table (VII) Comparison between the total percent scores of treated and controlled groups regarding oral assessment guide (OAG) following 10 days of chemotherapy and their protocol of treatment.

Total percent scores of oral assessment guide (OAG)	Protocol of treatment							
	Standard risk protocol of treatment				High risk protocol of treatment			
	Treated group		Controlled group		Treated group		Controlled group	
	NO	%	NO	%	NO	%	NO	%
Healthy oral cavity (OAG =8)	11	73.3	3	18.8	8	80	3	33.3
Moderate mucositis (OAG score= 9-16)	4	26.7	10	62.5	2	20	5	55.6
Severe mucositis (OAG score =17-24)	0	0	3	18.7	0	0	1	11.1
Total	15	100	16	100	10	100	9	100
FET	9.587				4.269			
P	0.004*				0.097			

Table (VIII) Comparison between the total percent scores of treated and controlled groups regarding oral assessment guide (OAG) following 10 days of chemotherapy and their Stage of chemotherapy.

Total percent scores of oral assessment guide (OAG)	Stage of chemotherapy							
	Induction phase				Intensification phase			
	Treated group		Controlled group		Treated group		Controlled group	
	NO	%	NO	%	NO	%	NO	%
Healthy oral cavity (OAG =8)	13	76.5	4	23.5	6	75	2	25
Moderate mucositis (OAG score= 9-16)	4	23.5	9	53	2	25	6	75
Severe mucositis (OAG score =17-24)	0	0	4	23.5	0	0	0	0
Total	17	100	17	100	8	100	8	100
FET	10.286				4.186			
P	0.005*				0.041*			

4. Discussion:

Chemotherapy treatment continues to be the mainstay in the treatment of leukemia. but is usually associated with a number of side effects mainly nausea, vomiting, anorexia, alopecia, neuropathy, constipation, hemorrhagic cystitis, moon face, mood changes and mucosal ulceration[20] .

Oral mucositis (stomatitis) is one of the most debilitating complications following chemotherapy administration. Chemotherapy effects on highly proliferative tissues remain significant. Oral mucositis affects up to 40% of patients undergoing chemotherapy per year in the United States [21] . Mucositis affect all mucous membrane covered surfaces from the mouth to the rectum. It significantly reduces the quality of life and patients` compliance with treatment. Unresolved or untreated mucositis can lead to infections, impaired nutritional status, speech, comfort and other complications that can increase morbidity, and impact patient outcomes. Mucositis is a dose-limiting toxicity for both chemo and radio therapy, and therefore can directly impact survival[20, 22- 25] .

The sites of mucositis lesions induced by both radiotherapy and chemotherapy are the non-keratinized mucosa, such as the buccal and labial mucosa, the ventral and lateral surfaces of the tongue, the floor of the mouth, and the soft palate [18] .

Oral complications may be prevented by oral assessment prior to the initiation of chemotherapy and then at least daily following the administration of chemotherapy. Adherence to a mouth care protocol and using mouth wash helps to maintain the moisture in the mouth, removes the remaining debris and toothpaste, and reduces the accumulation of plaque and infection[18] .

Chlorhexidine gluconate 0.12% is used against candidal and bacterial infection. It inhibits some viruses and it is active against some fungi [4, 16, 26] .

The biological characteristics of the present study reflect that the incidence of leukemia was high in preschool age (Table I). This result was in line with Sherif *et al* .[27] who conducted a study about demographic characteristics and history of risk exposure among acute leukaemic children in Alexandria. He reported that most of the acute leukemic children are belonging to the age of 2-5 years. Poncher *et al.* [28]who conducted a study about treatment of acute leukemia in children with and without folic acid antagonists also reported that Preschool age children were primarily affected.

It was noticed from the current study that the majority of the studied subjects were boys (Table I). The result was consistent with Jackson *et al.* [29] who conducted a study about why acute leukemia is more common in boys. The finding could be justified by the fact that the presence of a sex responsive gene near to the ABO blood group gene locus on chromosome '9' which relatively protects group O among girls against acute leukemia. The finding of the present study is also supported by many authors who mentioned that acute leukemia occurred more frequently in boys than girls [4,30]. Furthermore, Zorlu *et al.* [31] who conducted a study about evaluation of risk factors in children with acute lymphoblastic leukemia also reported that the risk of the development of ALL was found to be higher among boys than girls.

The result of the present study revealed that leukemic children from urban areas were more than rural areas (Table I). This result could be attributed to the fact that urban areas are more advanced in using high technology than rural areas. So there was more exposure to chemical substances and X-ray. Accidental exposure to Electro Magnetic Fields (EMF), as X-ray and drug especially during first trimester of pregnancy may be contributing factors to leukemia. This result was in agreement with Freda *et al.*[32] in their study about aggregation of childhood leukemia in geographic areas of Greece. They reported that there was high association between incidences of childhood leukemia and localized environmental exposure in urban areas to a lesser extent in semi urban areas. Tilinca *et al.*[33] who conducted a study about accidental ionizing radiation exposure and its impact on the population also found that incidence of leukemia in urban areas is more than that in rural areas. On contrary to the finding, Koushik[34] conducted a study about an ecologic study of childhood leukemia and population mixing in Canada. He found that population growth in rural areas was associated with an increased risk of leukemia particularly for ALL subtype due to population mixing which is not observed in urban areas.

The result of the present study revealed that the majority of the subjects had B.ALL (Table II). This result was in agreement with Magnani *et al.*[35] who conducted a study about increasing incidence of childhood leukemia in northwest Italy, and found marked increase in B cellsof ALL cases. Rios *et al.*[36] also reported B-cell precursor ALL showed high frequency than T lineage ALL.

The current study revealed that the majority of treated and controlled groups had low white blood cells count (Table II). This finding could be explained by the fact that in all types of leukemia the proliferating cells depress bone marrow production of the formed elements of the blood by competing for and depriving the normal cells of the essential

nutrients for metabolism which lead to neutropenia (decrease WBCs counts) resulting in infection. [37]

The result of the present study showed significantly higher percentage of the treated group having normal post 10 days chemotherapy oral assessment concerning most parts of their oral cavity compared to the controlled group (Table III). These findings could be attributed to using chlorhexidine for the treated group that had the ability to control gingivitis. It was often used as an active ingredient in mouthwash designed to kill dental plaque and other oral bacteria [38,39] . This result is in accord with many authors who reported that there was a significant decrease in the incidence and severity of oral mucositis and ulceration in children who received the preventive oral protocol using 0.12 % chlorhexidine mouth wash compared to the controlled group and reported the value of chlorhexidine mouth rinses in the prophylaxis of oral candidiasis in the myelosuppressed patient [8,10,13,40,41]. Moreover Vickars and Spinelli[42] who conducted a study about efficacy of chlorhexidine and nystatin rinses in prevention of oral complications in leukemia mentioned that potential bacterial and fungal pathogens were identified less frequently in the patients using chlorhexidine oral rinse. Contrary to the finding of the present study , Pitten *et al.* [43] who conducted a study about whether cancer patients with chemotherapy-induced leukopenia benefit from an antiseptic chlorhexidine-based oral rinse, reported that the chlorhexidine-based product did not provide a clinical benefit for cancer chemotherapy patients. Spijkervet *et al.*[44] who conducted a study about chlorhexidine inactivation by saliva also reported that chlorhexidine mouth rinsing was of limited value in decontaminating the oral cavity. Furthermore, Wahlin[45]who conducted a study about effects of chlorhexidine mouth rinse on oral health in patients with acute leukemia reported that there was increase in number of patients who had a burning sensation in the mouth, and a tendency toward increased numbers of salivary enterococci, enterobacteria, and/or Pseudomonas in patients who rinsed with chlorhexidine so did not support using of chlorhexidine.

It was noticed that the majority of studied subject had ulcerative lesions present in lips, tongue and mucous membrane as shown in (Table III). Similar to the findings found by Cheng *et al.*[[46]who conducted a study about prevention of oral mucositis in pediatric patients treated with chemotherapy: a randomised crossover trial comparing two protocols of oral care reported that most of the ulcerated lesions were located in the buccal mucosa and labial mucosa.

It was noticed from Table IV that the controlled group significantly had higher percentage of stmatitis at post 10 days chemotherapy oral assessment compared to treated group (Table IV). This could be attributed to the dual effect of chemotherapy on the oral mucosa; direct and indirect. The direct effect mediated by the treatment-induced stomatotoxicity resulting in mucosal atrophy and the indirect effect is through the systemic effects of chemotherapy, such as bone marrow suppression which affects the severity of oral complications [11] . This finding was in accord with Pinto *et al.* [8]who conducted a study about Prevention of oral lesions in children with acute lymphoblastic leukemia and reported that there was a high frequency of mucositis in children with ALL who did not receive chlorhexidine.

Concerning the degree of stomatitis, it was found that the children who used chlorhexidine had healthy oral cavity. 24% of treated group suffered from moderate oral mucositis and no one suffered from severe oral mucositis (Table IV). This might be attributed to the fact that the chlorhexidine had the ability to control, prevent, kill dental plaque and other oral bacteria [4] . Many authors were in line with the results of the present study who reported that chlorhexidine mouth rinse significantly reduced the incidence of oral mucositis in the treated group and the severity of oral mucositis was less compared to control group [10,40,47] . Moreover, Cheng *et al.*[46] cited that on their study about the prevention of oral mucositis in pediatric patients treated with chemotherapy: a randomized crossover trial comparing two protocols of oral care, also reported that OAG scores for mucositis in patient who use chlorhexidine was 8-13 (moderate mucositis) .

The present study revealed that the majority (73.9%) of children of controlled group developed moderate and severe mucositis during neutropenia compared to 26.1% of treated group who developed moderate oral mucositis (Table VII). This result was in harmony with Cheng *et al.* [10] who performed a study about evaluation of an oral care protocol intervention in the prevention of chemotherapy-induced oral mucositis in pediatric cancer patients. The study revealed that the majority of the children of controlled group during neutropenia developed oral ulcerative lesions and only one third of the subjects using the oral care protocol (chlorhexidine mouth rinse and 0.9% saline rinse) developed oral ulcerative lesions.

Conclusion

Based on the findings of the present study, it was concluded that Chlorhexidine was an effective solution in preventing and decreasing oral mucositis and gingivitis (swelling, redness, and bleeding of the gums) in leukemic children receiving chemotherapy. However, children in the treated group had healthier

oral cavity and lowest moderate degree of oral mucositis and no one of them developed severe oral mucositis compared to children in controlled group following 10 days of chemotherapy administration and significant differences were illustrated.

Recommendations

- Based on the findings of the present study the following recommendations are suggested:
- Responsibility of the nurses toward all children being treated from leukaemia and receiving chemotherapy is preventing and decreasing oral complication of chemotherapy through assessing oral cavity by using standardized grading system as an oral assessment guide (OAG) tool prior to the initiation of chemotherapy and at least daily following the administration of it.
- Creating an oral care plan to each child individually involving cleaning the teeth by using a mouth wash with Chlorhexidine gluconate is an important recommendation in preventing oral complications and decreasing severity of oral mucositis and treating gingivitis (swelling, redness and bleeding of the gums).
- Leukemic children receiving chemotherapy and their mothers should be informed about the possible oral complications of chemotherapy, how to detect and decrease the incidence of mucositis, and how to maintain oral hygiene.
- Direct family involvement in children oral care should be encouraged for maximum treatment compliance of their leukemic children.

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