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Oral health status and selected salivary physicochemical characteristics among a group of patients with acute lymphocytic leukemia undergoing chemotherapy (longitudinal study)

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Abstract

Background: Acute lymphoblastic leukemia is fast growing cancer of the white blood cell. Chemotherapy which has been used to treat malignant conditions has a negative impact on oral health condition among cancer patients. This observational study was conducted to determine the level of selected salivary physicochemical characteristics including flow rate and total antioxidant) in addition to evaluation of oral health status (dental plaque and gingival health condition) among a group of patients with acute lymphoblastic leukemia.

Materials and methods: The present study included thirty patients with acute lymphoblastic leukemia aged (14-17) years old. Those patients attended Medical City in Baghdad and were admitted to the Hematological Center at Teaching Baghdad Hospital. All patients fullfitted certain inclusion criteria. Salivary sample collection and oral examination were carried at three visits: the first visit was carried out before receiving chemotherapy (at the day of admission)(baseline data), while the second visit was carried out at the day 15 (after starting chemotherapy), and the third visit was done at the day 30 (after starting chemotherapy). Stimulated salivary samples were collected and salivary flow rate was determined. Dental plaque was assessed according to criteria of plaque index by Sillness and Löe (1964) and gingival health condition was assessed according to the criteria of Modified Gingival Index for Lobene et al (1986). Salivary samples then were chemically analyzed for the detection of salivary total antioxidant.

Results: In this study, salivary flow rate decreased with time (visits) (1.44±0.14, 1.27±0.16, 1.02±0.53) with statistically highly significant differences ($p<0.01$). On the other hand, the mean values of plaque and gingival indices increased with time (visits) (0.89± 0.39, 1.22± 0.58, 1.82 ±0.75) (0.98± 0.49, 1.13± 0.46, 1.38 ±0.84) respectively and the differences were statistically highly significant ($p<0.01$). While salivary total antioxidant decreased with time (visits) (0.94±0.25, 0.92±0.21, 0.82±0.21) with statistically significant differences ($p<0.05$).

Conclusion: Acute lymphoblastic leukemia, its treatment and duration of treatment have direct and indirect impact on the oral health status of leukemic patients. Those patients had poor oral hygiene with high rate of gingivitis in addition to change in salivary physicochemical properties, thus, an organized, comprehensive oral health preventive and educational programs in addition to intense oral hygiene program before and during the first month of treatment with cytotoxic

drug (chemotherapy) are essential to improve their oral health condition and prevent oral problems and complications.

Key words: salivary antioxidant, gingival health condition, leukemic patients.

Introduction

Acute lymphocytic leukemia is "a fast growing cancer of the white blood cell where the bone marrow makes lots of unformed cells called blast that normally would develop in to lymphocytes. However, the blasts are abnormal. They do not develop and cannot fight infections" [1].

It develops quickly and need to be treated urgently. Treatment of leukemia includes multiagent chemotherapy alone or in combination with radiotherapy or surgery. Chemotherapy is the use of anticancer drugs designed to slow or stop the growth of rapidly dividing cancer cell in the body [2]. It has an effect on general health, as it induces toxicity, infection and hemorrhage which are the major causes of treatment related mortality in acute leukemia [3,4]. It also affects person's oral health resulting in difficulty in eating, talking, chewing or swallowing [5].

Sonis and Fey (2002) reported controversial result related to the side effect of different oncologic drugs on the oral cavity [6]. Most of the antineoblastic drugs act indiscriminately on the basal cells of oral epithelium, altering its renewal capacity, this in turn, leads to the appearance of series of systemic and local side effects such as gingivitis, xerostomia, infection, hemorrhage and mucositis [7,8].

Human saliva is an important biological fluid that plays a critical role in the maintenance of oral health [9,10]. Saliva through its physical properties like flow rate, and chemical composition affects oral health status [11]. Cancer patients undergoing treatment for their disease often experience severe difficulties in maintaining such functions [12].

Saliva is rich in antioxidant compounds which are the most important defense mechanisms in saliva [13]. Antioxidants play an important role in normal cell differentiation. It is a well known fact that activated oxygen species (AOS) are generated as a result of oxygen metabolism and energy production; they are also implicated in tumor progression. On the other hand, antioxidants have anticarcinogenic potential [14]. The aggressive chemotherapy is the cornerstone of cancer therapy and it was suggested that antioxidants are reduced in patients with cancer [15].

As far as there was no previous Iraqi longitudinal study concerning the patients with acute lymphoblastic leukemia, this observational study was designed and conducted to assess the oral health status and selected salivary physicochemical parameters among those patients to gain knowledge about possible oral problems and complications during the first month of treatment with chemotherapy, this in turn may aid in improving the oral health and preventing the oral problems and complications through the application of organized preventive and educational oral health programs with intense oral hygiene programs before and during the first month of treatment.

Materials and methods

The sample of this study consisted of thirty patients with acute lymphocytic leukemia of both gender (males and females) aged 14-17 years. The age was recorded according to the last birthday (WHO, 1997) [16]. They were the patients who attended Medical City in Baghdad and were admitted to the Hematological Center at Teaching Baghdad Hospital where they diagnosed with acute lymphocytic leukemia, the diagnosis was established by bone marrow aspiration and biopsy.

Oral examination and recording of oral variable (dental plaque and gingival indices) in addition to saliva collection for assessing salivary physicochemical characteristics (salivary flow rate, determination of salivary total antioxidant) were performed at three visits by the researcher during the period of hospitalization:

1. The first visit was at the day of admission to the hospital (day 0) before treatment with chemotherapy (baseline data).
2. The second visit was performed after two weeks of admission (day 15) i.e patient on chemotherapy.
3. The third visit was performed at the day 30 of admission to the hospital (patient still undergo treatment with chemotherapy).

The collection of stimulated salivary samples was performed according to the instructions cited by Tenovuo and Lagerlöf (1994) and it was expressed as milliliter per minute (ml/min) [17]. Then the salivary sample was centrifuged at 3000 r.p.m for 10 minutes and the clear supernatants was separated by micropipette and stored at -20 C^0 in a deep freeze till the time of biochemical analysis. Dental plaque was evaluated according to Sillness and Löe index (1964) [18], gingival health condition according to modified gingival index (1986) [19]. The salivary total antioxidant was measures spectrophotometrically. Data analysis was conducted through the application of the SPSS. The analysis of data included: Paired t- test, one way ANOVA repeated measure, least significant differences (LSD) pair wise (repeated measure) test.

Results

The results showed that the mean values of salivary flow rate and total antioxidant decreased with time. Statistically, highly significant differences were found in mean values of salivary flow rate among visits and significant differences in mean values of total antioxidant among visits as show in Table (1). LSD test showed that there were statistically highly significant differences in salivary flow rate and total antioxidant between each pair of visits ($p<0.01$) except between the first and second visits regarding total antioxidant in which the differences was statistically not significant ($p>0.05$) Table (2). From the result of this study, it was found that the mean values of plaque and gingival indices increased with time. Statistically, highly significant differences were found in mean values of plaque and gingival indices among visits as show in Table (3). LSD test showed that there were statistically highly significant differences in plaque and gingival indices between each pair of visits ($p<0.01$) except between the first and second visits regarding gingival index where there was statistically significant difference ($p<0.05$) as show in Table (4).

Discussion

In recent decades, there was an increase in incidence rate of leukemia in various countries around the world

[20]. Acute lymphocytic leukemia affects general health, causing series of clinical and oral manifestations [21]. Furthermore, the toxicity associated with the use of chemotherapy and its side effects have a negative impact on patient's quality of life [22], as it develops systemic and local (oral) complications which may result in significant morbidity, impaired nutrition, treatment delays and dose reduction which are affecting the prognosis of the primary disease [23] .

Salivary flow rate and selected constituents were determined in this study as saliva through it physiochemical properties plays an essential role in maintaining the integrity of soft and hard tissue in the oral cavity [24]. Data of the present study showed a reduction in salivary flow rate among leukemic patients with time, this may be attributed to the effect of chemotherapy which causes xerostomia and reduced salivary flow rate [25]. Additionally, reduced salivary flow rate may be typically caused by anticholinergic medication utilized to control nausea and emesis [26].

Further explanation for this reduction in salivary flow rate was the anxiety and emotional stress in patients with ALL. Such patients are known to be very anxious when cytotoxic therapy starts [27]. Fever is another reason for reduction of the salivary flow rate as it is commonly present in many of ALL patients [28]. This result was also reported by previous studies [29,30]

The current study revealed a reduction in salivary TAO in leukemic patients among three visits this may be attributed to high level of free radicals in leukemic patients undergoing chemotherapy which cause oxidative stress and lead to depletion of TAO (degradation of antioxidants resulting from oxidative stress induced by chemotherapy). Furthermore, it is possible that cancer process itself causes the observed dysfunction of antioxidant system [31]. Another explanation for reduced TAO among three visits is the low intake of exogenous antioxidant, as nutritional intake can be severely compromised by the pain associated with sever oral mucositis and taste change occur due to chemotherapy that limits food intake [32]. Previous studies also reported this decline in TAO capacity in saliva of leukemic patients during chemotherapy [33,34].

In this study the mean values of dental plaque increased with time with statistically highly significant differences between three visits, which may be related to reduced salivary flow rate (due to chemotherapy) which favors dental plaque accumulation [29]. This result could be explain by the fact that the salivary flow rate may play an important role in relation to dental plaque accumulation since decrease of salivary flow rate leads to decrease of washing action of saliva and oral dryness as well as protective constituents decreased with decreased salivary flow rate [35]. Another explanation for increased dental plaque accumulation among leukemic patients during visits is the neglect or poor oral health measures, as most of patients reported their afraid from brushing their teeth due to bleeding and susceptibility to infections [29]. Several studies also revealed that patients with ALL showed a significant increase in plaque accumulation [36,37].

The result of the present study showed an increased in the mean values of gingival index during visits with statistically highly significant differences among three visits. This may be attributed to poor oral hygiene among ALL patients; this is supported by the results of the present study which revealed an increase in the mean values of dental plaque index among

three visits. It was reported that dental plaque plays an important role in the etiology and progression of gingival disease [38]. Another explanation for this increase in gingivitis is decreased salivary flow rate in leukemic patients among three visits and this could explain by the fact that salivary flow rate plays an important role in relation to plaque accumulation [39]. Also several studies reported that the severity of gingivitis was significantly higher in leukemic patients undergoing chemotherapy [36,37].

In conclusion, the findings of the present study revealed that patients with ALL undergoing chemotherapy during the first month of the induction phase are at a high risk of developing oral problems and complications, thus an organized, comprehensive oral health preventive and educational programs before and during the first month of treatment with cytotoxic drug (chemotherapy) are essential to improve the oral health status of the patients and prevent oral complication and this in turn will decrease the risk of local and systemic infections which may pose a threat to the patient's life.

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Table 1: Salivary physicochemical parameters of the sample among three visits.

Statistical analysis			Visits			Salivary parameter
			Third	Second	First	
P- value	F	df	Mean±SD	Mean±SD	Mean±SD	
0.00**	58.32	1.14	1.02±0.53	1.27±0.16	1.44±0.14	Flow rate (ml/min)
0.04*	4.20	1.12	0.82±0.21	0.92±0.21	0.94±0.25	Total antioxidants (mmol/l)

Table 2: Comparison of significance of salivary physicochemical parameters of the sample.

Sig.	Mean Difference	Visits		Salivary parameter
0.00**	0.17	Second	First	Flow rate (ml / min)
0.00**	0.41	Third		
0.00**	0.24	Third	Second	
0.64#	0.02	Second	First	Total antioxidant (mmol/L)
0.03**	0.12	Third		
0.00**	0.09	Third	Second	

Table 3: Plaque and gingival indices of sample among three visits.

Statistical analysis			Third visit	Second visit	First visit	Variable
P- value	F	Df	Mean±SD	Mean±SD	Mean±SD	
0.00**	51.48	1.40	1.82 ±0.75	1.22± 0.58	0.89± 0.39	PlI
0.00**	17.02	1.31	1.38 ±0.84	1.13± 0.46	0.98± 0.49	GI

Table 4: Comparison of significance of plaque and gingival indices among three visits.

P- value	Mean Difference	No. of Visit		Variable
0.00**	-0.33	Second	First	PlI
0.00**	-0.93	Third		
0.00**	-0.60	Third	Second	
0.01*	-0.16	Second	First	GI
0.00**	-0.40	Third		
0.00**	-0.25	Third	Second	