

The Common Complications of Chemotherapeutic Agents and the Effect of Xylitol Chewing Gum on Oral Dental Hygiene in Patients Having Malignant.

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ABSTRACT

Aims: The aim of this study were to estimate the percentage of general and oral complications among patients receiving chemotherapeutic agents and correlate the oral complications with the age of the patients and with the drugs either used singly or in combination with the other chemotherapeutic agent and the effect of xylitol chewing gum on oral dental hygiene in patients having malignant diseases.

Materials and Method: In this clinical trial, 70 patients with ages ranging between 7–65 years treated with different cancer chemotherapy for a duration from 3 months to 3 years. The patients were selected from those who treated in Hazim Al-Hafith center for treatment cancer in Mosul City. General and oral complications of chemotherapeutic agents were recorded and the agent recorded either used singly or in combination with the other chemotherapeutic agent. Twenty patients from those who had oral complications were examined and the plaque and gingival indices were measured according to Silness and Loe (1963) at the base line. Then those patients were instructed to take xylitol chewing gum (4 grams/day); four times immediately after eating. The plaque and gingival indices were measured again after 3 weeks of using the chewing gum. **Results:** The results of this study revealed that approximately half of the patients have general and oral complications while the others either had only general complications or had no complications (48.57%, 27.14%, 24.29% respectively). The incidence of oral complications correlated with the increasing in patients' age ($P < 0.01$). The distribution of general and oral complications were correlated with the agent used either singly or in combination, where 100% of patients medicated with single therapy had general and oral complications while the patients medicated with multiple therapy 70.69% of them had general and oral complications and 29.13% had no significant complications. The patients who had taken xylitol chewing gum had a significant reduction in plaque index while there is no significant reduction in gingival index ($p < 0.01$). **Conclusions:** the study concluded that the general and oral complications arising in cancer patients can be attributed to the various modalities of cancer chemotherapy. Routine oral hygiene and elimination of preexisting dental disease and sources of mucosal irritation with a giving of salivary substitutes like xylitol reduce the incidence and severity of a number of oral complications of chemotherapy.

Key words: Chemotherapy, oral complication, xylitol chewing gum.

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INTRODUCTION

Cancer chemotherapeutic agents are used clinically to destroy and suppress the growth and spread of malignant cells.^(1,2) Most chemotherapeutic agents have common adverse effects include, nausea, vomiting, diarrhea, alopecia, fever and allergic reaction.^(3,5,7)

Oral complications are frequently encountered in patients receiving chemotherapy include, mucositis, infection, hemorrhage and xerostomia.⁽⁴⁾ Oral complications always occur as a consequence of treatment for head and neck cancer and may be unpleasant and even life-

threatening complications.^(6,7) Several factors play a role in the development of these problems include, the type of malignancy, patient age, type and dosage of chemotherapy and oral hygiene level before and during therapy.^(8,9)

Oral mucositis is a universal oral complication in patients receiving high-dose systemic cancer chemotherapy.^(8,10) In addition, oral mucositis represent a significant risk factor for systemic infection, particularly in neutropenic patient, consecutive protraction or termination of chemotherapy may lead to treatment failure and result in increases in therapeutic

expenses.⁽¹¹⁾

Xerostomia is a common complication in patients receiving cancer chemotherapy and radiation therapy.⁽¹²⁾ Cancer chemotherapy can cause decrease in salivary secretion which is usually much less severe and transient.⁽¹³⁾ Furthermore, dry mouth results in tissue with reduced barrier function which contributes to increased mucosal irritation and infections.⁽¹⁴⁾

Oral infections associated with cancer therapy can be caused by fungal, viral and bacterial organisms.⁽⁴⁾ These infections can cause tissue damage directly or increase the damage due to secondary infection of oral mucositis.⁽¹⁵⁾ The effects of chemotherapy on bone marrow and oral flora coupled with the patient's immunosuppressed state and altered oral microbial flora predispose these patients to oral mucositis, infection and hemorrhage.⁽¹⁶⁾ In addition to that, chemotherapeutic agents may secondarily induce thrombocytopenia which is the usual cause of intraoral hemorrhage.⁽¹⁷⁾

Oral hygiene is an important factor in therapy of oral mucosa.⁽¹⁸⁾ The care of oral health plays a role in prevention and reduces the severity of oral complication.⁽¹⁹⁾ Improving the effectiveness of oral hygiene by cleaning the oral cavity with different forms of lotion and mouth washes and using a variety of products some form of pain relief, anti-inflammatory treatment as required and aggressive antimicrobial treatment for any new mouth infection.^(2,10)

Sugar free xylitol gum is a chewing gum made with xylitol which is the popular sweetener substance that looks and tastes like sugar.⁽²⁰⁾ The beneficial effects of xylitol on oral health: it reduces the quantity of plaque and the number of bacteria that cause tooth decay.⁽²¹⁻²⁴⁾ Furthermore, sugar free gum has a beneficial means of saliva stimulation for people suffering from Xerostomia.⁽²⁵⁾

The aims of this study were to estimate the percentage of general and oral complications among patients receiving chemotherapy and correlate the oral complication with the age of the patients and correlate the complications with the agent either used singly or in combination, and compare the effect of xylitol chewing gum

before and after taking in relation to their ability to control plaque formation and gingival inflammation.

MATERIAL AND METHODS

Seventy patients were participated in this study, their age ranged between 7–65 years. All patients treated with different chemotherapeutic agents either single or multiple therapy including methotrexate, cyclophosphamide, 5-fluorouracil, Bleomycin, Doxorubicin, Cisplatin and Paclitaxel.

A special case sheet was designed for each patient containing the following data: patients age, type of malignance, type of chemotherapy, dosage, duration, general and oral complications, measurements of plaque and gingival indices before and after treatment with xylitol chewing gum. The study was conducted in Hazim Al-Hafith center for treatment cancer in Mosul City for the period from February 2006 to July 2006.

Oral examination was performed to look for signs of complications and patients were asked for any symptoms of oral and general complications of therapy. 48.57% of patients had general and oral complications of the therapy. 27.14% of patients had only general complication including nausea, vomiting, diarrhea, alopecia and allergy. Oral complications including xerostomia, mucositis, infection and hemorrhage. The others 24.29% of patients had no significant complications according to the intraoral examination and patients questionnaire.

Patients about 58.82% from those who had oral complications were examined plaque and gingival indices and measured according to Loe and Silness (1963). The results for plaque index were recorded as occurrence of plaque grade zero (no plaque in gingival area); grade 1 (a film of plaque adherent to the gingival margin and the adjacent area of the tooth, the plaque may only be recognized by running a probe across the tooth surface); grade 2 (a moderate accumulation of soft deposit within the gingival pocket or on the tooth and gingival margin, this can be seen with naked eyes); grade 3 (a heavy

accumulation of plaque within gingival pocket or on the tooth and gingival margin).

The estimation of gingival index is same as for plaque index. The criteria for gingival index include grade zero (normal gingiva); grade 1 (mild inflammation, slight change in colour, slight oedema, no bleeding on probing); grade 2 (moderate inflammation, redness, oedema, bleeding of the gum on probing); grade 3 (sever inflammation, marked redness, oedema, ulceration and there is a tendency for spontaneous bleeding).

Those 58.82% of patients were asked to take xylitol chewing gum (4 grams/day); four times immediately after eating, they were instructed to brush their teeth during treatment. Plaque and gingival indices were taken at the base line and after three weeks of using the gum.

Statistical analysis in this study included descriptive statistics; that's, calculation of frequencies and percentage. Chisquare test was used. The level of significance was recorded at $p < 0.05$, paired t-test was used to compare the effect of xylitol chewing gum on plaque and gingival indices before and after treatment ($p < 0.05$).

RESULTS

The patients in this study either had oral and general complications or had only general complications or had no complications.

The percentage distribution of complications of chemotherapy was shown in Figure (1), where 48.57% of patients had general and oral complications, 27.14% had only general complications while 24.29% had no complications.

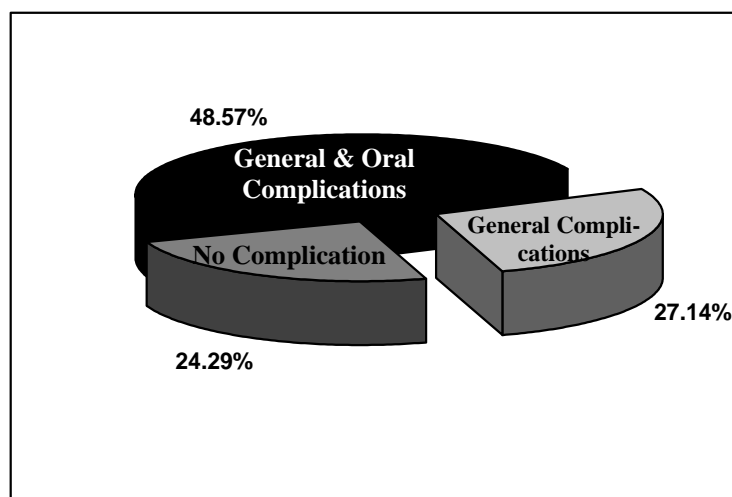


Figure. (1) Percentage distribution of complication in the studied group.

The percentage distribution of some common general complications among studied group were illustrated in Figure (2), where 60.38% had nausea and vomiting, 9.43% had diarrhea, 20.76% had alopecia and 9.43% had allergy ($p < 0.001$).

The percentage distribution of oral complications among studied group were represented in Figure (3) where 82.36% had xerostomia, 11.77% had mucositis, 8.83% had fungal infection and 2.94% had hemorrhage ($p < 0.001$).

The percentage distribution of oral

complications according to age represent 17.65% of patients had oral complication in age between (1–20 years), 20.59% in young age (21–40 years) and 61.67% in older age (41–65 years) was illustrated in Figure (4) ($p < 0.01$).

The percentage distribution of general and oral complications according to the agent used either singly or in combination were shown in Figure (5), where 100% of patients medicated with single chemotherapeutic agent had general and oral complications, while only 70.69% of patients

medicated with multiple chemotherapeutic agent had general and oral complications.

However, 29.31% had no complications ($p < 0.05$).

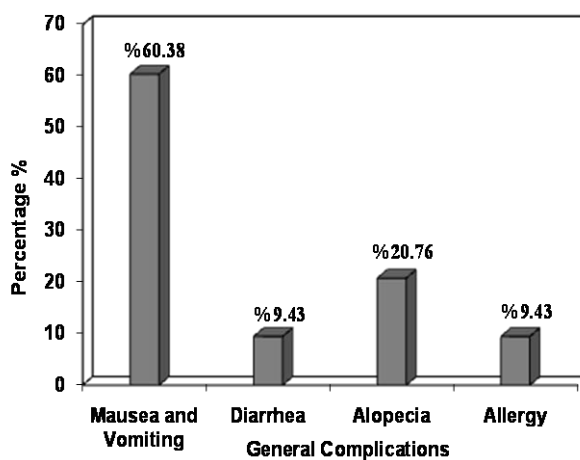


Figure (2) Percentage Distribution of some general complications according to patients with chemotherapy ($p < 0.001$).

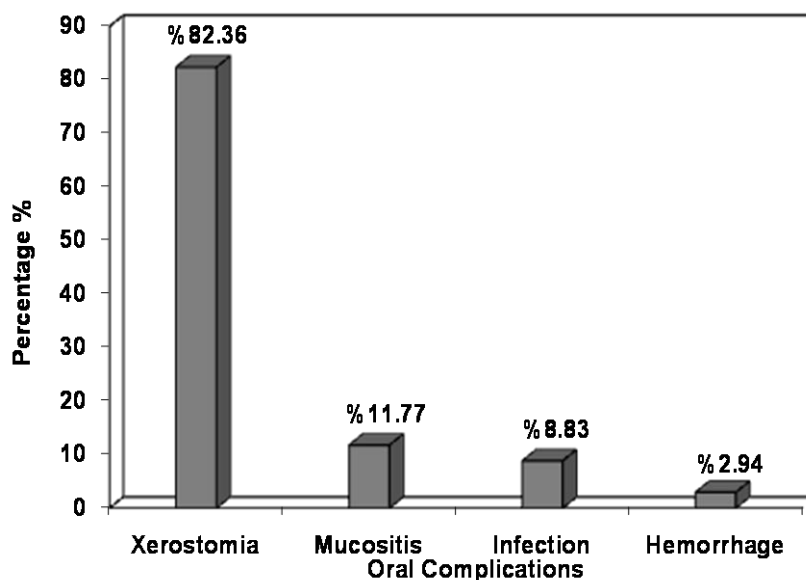


Figure (3) Percentage Distribution of oral complications according to patients with chemotherapy ($p < 0.001$).

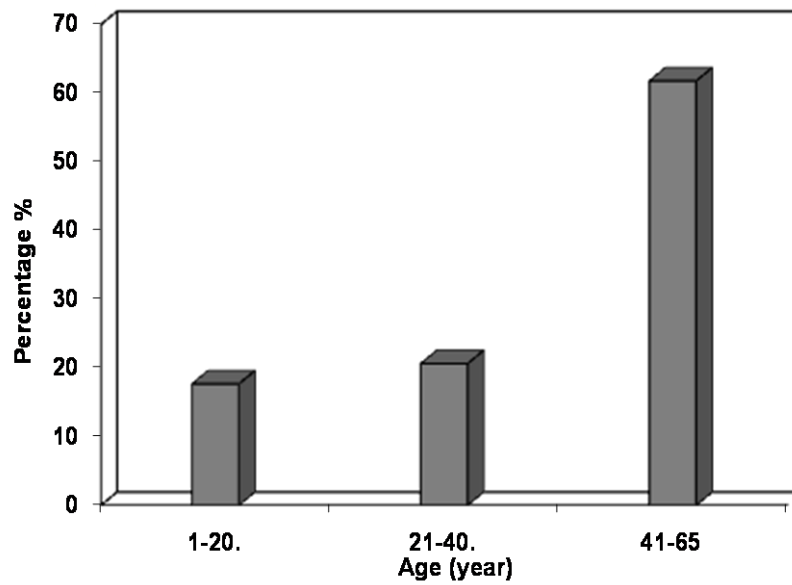


Figure (4) Percentage Distribution of oral complications according to age of the patients ($p < 0.01$).

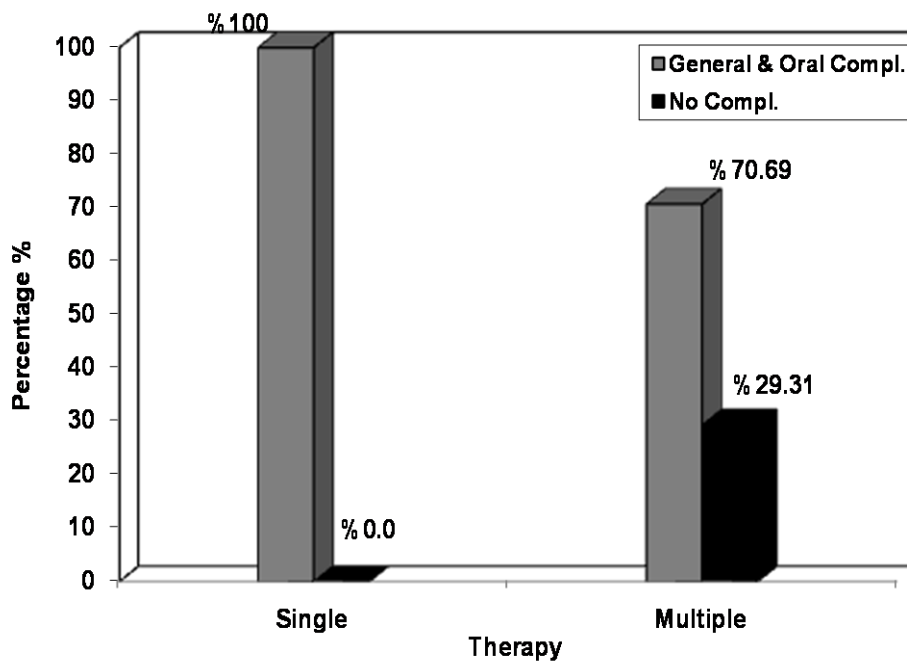


Figure (5) Percentage Distribution of general and oral complications according to the agents used either singly or multiply ($p < 0.05$)

The differences in plaque and gingival indices before and after taking xylitol chewing gum in only 35% of patients who can come for follow up from 58.82% of

patients who instructed to take chewing gum were illustrated in the Table (1), where there was significant reduction in plaque index after taking gum at ($p <$

0.001). However, there was no significant reduction in gingival index after taking gum.

Table (1) The Differences in plaque and gingival indices before and after taking xylitol chewing gum ($p < 0.001$).

Parameters	Mean \pm SD		<i>p</i> -value
	Before	After	
Plaque index (n=7)	1.71 \pm 0.49	0.86 \pm 0.38	0.001
Gingival index (n=7)	1.43 \pm 0.79	1.57 \pm 0.53	not significant

DISCUSSION

Patients receiving cancer chemotherapy often suffer from oral and general complications as a result of their disease and its treatment.⁽¹⁶⁾ Oral complications remain the dose-limiting toxicity of a variety of chemotherapeutic regimens and may result in significant morbidity, impaired nutrition, treatment delays and dose reductions.^(27, 28)

In this study the common general complication are gastrointestinal problems. This may be explained by the fact the gastrointestinal tract is a tissue that is rapidly turning over and the sloughing of the gastrointestinal mucosa can produce many disturbances like nausea, vomiting, and hemorrhagic diarrhea.⁽¹⁾ In addition to that, alopecia occur to lesser or greater extent during therapy with antineoplastic agents but the hair usually regrows when therapy is discontinued.⁽³⁾

Moreover, some antineoplastic agent like cisplatin, paclitaxel and interferons causes hypersensitivity ranging from skin rash to anaphylaxis because these drugs including foreign particles causes allergic reaction. Therefore, these patients requiring premedication with dexamethasone to overcome the allergicity.⁽²⁾

Acute and chronic complications of oral tissues and changes in physiologic process frequently accompany cancer therapies.⁽⁸⁾ The initial effect of chemotherapy is on rapidly proliferating cells of oral epithelium. As a consequence the epithelium may show atrophy and ulceration.⁽¹⁴⁾

In this study xerostomia was the most common oral problem associated with chemotherapy this certainly explained by the fact that cytotoxic agent affect salivation by different mechanisms that includ-

ing alteration in flow rate, electrolyte balance and some time salivary function but are generally reversible and transient.^(12, 13)

Therefore, were instructed the patients by rinsing their mouth frequently and giving sugar less or xylitol chewing gum for stimulation the salivation that act as protective layer to minimize dental plaque and caries and minimize bacterial and fungal infections.^(21, 22)

In this study 11.77% of patients suffered from mucositis and inflammation of oral cavity and ulceration. This may be due to many factors that affect oral cavity like high dose of chemotherapy giving to the patients, age of the patients, type of chemotherapy and a changes in oral environment and xerostomia caused by chemotherapy.⁽⁶⁾ These results were in agreement with other studies that explained mucositis as dose-limiting complication in patients receiving chemotherapy, bone marrow transplantation and local irradiation for tumours in the head and neck area.⁽¹¹⁾ In addition, oral mucosa is comprised of membranes of a high mitotic index with rapid epithelial turnover and maturation rates, this causes the mucosa to be vulnerable to adverse effects of chemotherapy.⁽⁴⁾

Fungal infection was encountered in 8.83% of patients at the palate and buccal mucosa. This may be explained by the fact that indirect effect of chemotherapy may include granulocytopenia with reduced salivary secretion, so that the protective mucin coating of the epithelium is compromised and these changes result in tissue with reduced barrier function and impaired ability to heal and to resist entry of pathogens, thus increasing the risk of systemic infection.^(14, 16) Moreover, oral bleeding can be manifested in 2.94% of patients

with malignant disease due to thrombocytopenia resulting from chemotherapy induce marrow suppression.^(16, 17)

Oral complications in this study showed to have incremental increase with age. This result was in agreement with several studies demonstrated that increases the potential for developing oral complications with age, type of malignancy, nutritional state and the level of oral health before and during therapy.^(4, 6, 9)

In this study all patients medicated with single therapy developed general and oral complication and more than half of the patients who received multiple chemotherapy also developed general and oral complication. These results were supported by other study⁽²⁸⁾ which showed that, the frequency and severity of complications are related to such factors as whether an agent is used singly or in combination, the dose and schedule of drug administration, the degree of myelosuppression and administration of many chemotherapy regimens may be complicated by toxicities that limit clinician's abilities to deliver the most effective doses of active agents.⁽²⁹⁾ However, 24.29% of patients who had no complications suffered from non-head and neck malignance and received low doses of multiple chemotherapeutic agents. This result was in agreement with other studies^(6,9) which reported that approximately 40% of patients with non head and neck malignancies developed oral problems following exposure to chemotherapy.

From 48.57% of patients, who had oral complication, 58.82% of them were educated and coming for receiving chemotherapy continuously, were examined and plaque and gingival indices were measured as a base line and giving xylitol chewing gum, only 35% of patients came to follow up after three weeks of taking gum and measured plaque and gingival indices because some of them stopped the drugs and others changing the time of receiving the drugs. The results showed that there were significant differences in plaque index after taking the gum. These results were in consistence with other studies presented that, xylitol reduces the quantity of plaque and insoluble carbohydrates. Hence, the resulting plaque is less adhesive on the

teeth enabling easier removal through stimulation of saliva by chewing gum.^(21, 30)

Moreover, the unique beneficial effect of xylitol on oral health are largely due to its 5. carbon chemical structure which is not recognized by mutans streptococci, oral bacteria that cause tooth decay.^(21, 22, 24)

CONCLUSIONS

Individual under going cancer therapy may be at a risk for a wide variety of complications that can affect morbidity and mortality. Acute oral complications associated with cancer chemotherapy are a frequent and potentially serious problem. Therefore, pretreatment oral assessment of those patients is an opportunity to identify and eliminate potential sources of sepsis and irritation. Routine oral hygiene has been accepted as an important component of oral care protocols for patients receiving cancer therapy and the patients should be motivated about good oral hygiene as well as their hospital and out hospital surrounding.

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