

Changes in Oral Microflora Related to Immunosuppressive Chemotherapy in Denture Wearing Cancer Patients

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Abstract

Objective: To investigate changes in oral microflora in oral cavity from denture wearing cancer patients within seven days of the first course of chemotherapy, and the association between these changes and the distressing oral problems of the patients.

Material and methods: Prospective uncontrolled study design was carried out with sixty cancer patients were enrolled in this study. Oral microflora of the buccal mucosa was cultured from two saliva samples before chemotherapy and after receiving the first dose of chemotherapy. Convenience-based sampling method was used based on the patient availability on recruitment days. Informed consent was obtained from the patients for enrollment in the present study.

Results: The results from this study have shown that in general, no statistically significant differences were found in the existence of bacteria between before and after chemotherapy, there is no association between the changes of bacterial types and chemotherapy. Types and number of oral bacteria were found to correlate to degree of oral health care or oral hygiene, saliva, and gender, and there is a direct relation between chemotherapy and decrease saliva amount and viscosity and the development of bad oral habits after chemotherapy in these patients.

Conclusion: the results of this study indicate that there were no changes in the microflora in the oral cavity in denture wearing cancer patients within seven days of the first dose of chemotherapy. No correlations between oral mucositis and specific microorganisms were assessed.

Key Words: Oral microflora, Denture, Cancer patients, Chemotherapy

Background

The oral cavity comprises multiple habitats which offer a number of ecological niches to a variety of microorganism [1]. Most of which are harmless commensal organisms. Others, however, are pathogenic and are involved in the development of many oral diseases as caries, periodontal diseases, and mucosal infections.

The colonization of habitats in the oral cavity is regulated by inter bacterial competition, nutrient supply, and the physicochemical environment (pH, temperature, etc.) [2], and any interruption in these parameters may cause shifting in oral microflora.

The oral defense mechanisms are compromised by cytotoxic chemotherapy, either by direct mucosal damage or by immunosuppression resulting from neutropenia related to cancer or to the chemotherapy used to treat it [3], potentially causing an overall shift in oral microflora.

The cancer treatment caused alterations in oral microbiota which may lead to the emergence of potential pathogens and subsequent other systemic health problems to the patients. Hence clinical guidelines and recommendations have been presented to control oral microbiota in patients with cancers, but also in this area, the scientific evidence is weak. More controlled studies are needed for further conclusion [4].

In the Gaza strip, there are many types of cancer, but until now no one has studied the relationship between changes in oral microflora and chemotherapy.

In the current study, the researchers intend to explore changes in some of the oral microflora expected in cancer patients during chemotherapy courses.

Materials and Methods

Study design

The prospective uncontrolled study design was carried out.

Study setting and patients recruitment

The study was conducted from 1 to 31 December 2018 and involved 60 patients who are wearing a denture and were received chemotherapy at al-Rantisi hospital. Inclusion criteria were history of no medical problems and a history of no medications. The samples were obtained twice from the same patient (before chemotherapy and after one week from receiving the first dose of chemotherapy). Informed consent was obtained from the patients for enrollment in the present study. In addition, all patients were interviewed and answered a closed-ended questionnaire which was designed especially for this study and containing personal, demographic and medical history information.

Clinical specimens' collection

A sterile swab was used for sampling from the buccal mucosa salivary flow in all patients before chemotherapy and after one week from receiving chemotherapy from the same area.

Collection of clinical data

A total of 120 salivary swabs were collected from the buccal mucosa of each patient before chemotherapy (60 swabs) and after one week (60 swabs) from receiving chemotherapy from the same area and convenience-based sampling method was used based on the patient availability on recruitment days.

Microbiological investigation

The swabs were plated on blood agar media, the blood agar media was prepared as following step: 40 g weighted blood base agar powder was completely dissolved in 1000 ml distilled water, then the media was sterilized by autoclaving technique, and the end poured media was solidified in sterile Petri dishes (*Figure 1*). The swab specimen was spread on blood agar for the cultivation of bacteria by using a quadrant streaking method. Then incubate at 37°C for 24 hrs, and the colony morphology was observed, as *Streptococci* show as pinpoints shape, *Staphylococci* show bigger than *Streptococci*, also type of hemolysis (Alpha, Beta or Gama) was observed. A catalase test was used to differentiate between *Streptococci* and *Staphylococci*.

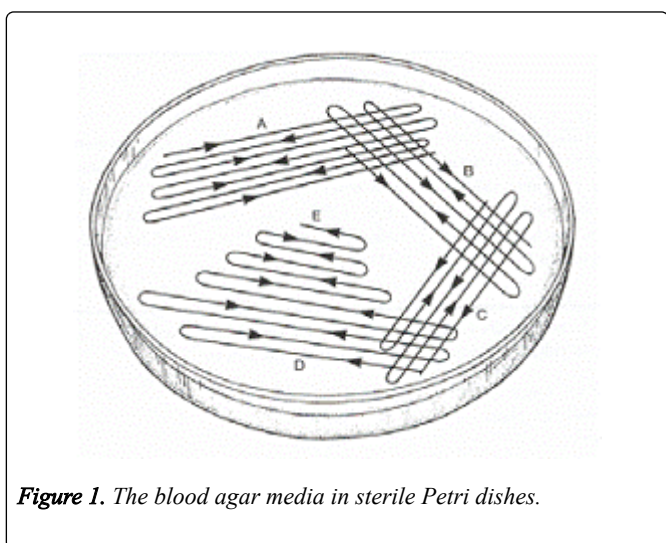


Figure 1. The blood agar media in sterile Petri dishes.

Statistical analysis

All subject data was encoded and analyzed using SPSS Statistics (version 24). Descriptive, frequencies, MacNemar analysis, and chi-square, to establish the statistical significance of the differences observed in distributions (significance level: $p < 0.05$).

Result

Descriptive analysis

In the present study, 60 cancer patients (23 male and 37 female), were involved: 16 patients aged (45-59 years), 21 patients aged (60-79 years), and 23 patients aged (79-83 years). The oral hygiene, dental practices and bacterial existence in the patient's oral samples were evaluated and compared to their counterparts' values after the chemotherapy protocol.

This research was done on patients having one of the four types of cancer, namely; breast, ovary, prostate, and lung. 43.3% of patients selected have breast cancer, 28.3% of them have prostate cancer, 20% of them have ovary cancer, and 8.3% of them have lung cancer.

Each one of these patients is treated with one of the drugs, namely; AC-T, BEP*3, and Zometa and Zoladex. 31 patients are treated with AC-T, 12 patients are treated with BEP*3, and 17 patients are treated with Zometa and Zoladex.

Statistical analysis

In general, no statistically significant differences were found in the existence of bacteria between before and after chemotherapy [5], there is no association between the changes of bacterial types and chemotherapy. Types and number of oral bacteria were found to correlate to the degree of oral health care or oral hygiene, saliva, and gender.

Table 1 shows a statistically significant association between changes in oral hygiene habits and chemotherapy.

Table 1. Significant test between changes in oral hygiene habits and chemotherapy.

	Oral hygiene and Oral hygiene "AF"
N	60
Chi-Square	4.645
Asymp. Sig.	0.031

- McNemar Test
- Binomial distribution

$p\text{-value} < 0.05$ a statistically significant difference between chemotherapy and oral hygiene was recorded in *Table 2*. Also, there is a direct relation between chemotherapy and decrease in saliva amount and change/decrease in saliva viscosity.

Table 2. A significant relation between chemotherapy and oral hygiene.

	Saliva viscosity and Saliva viscosity AF
N	59
Chi-Square	4.654
Asymp. Sig.	0.031

- McNemar test
- Binomial distribution

$p\text{-value} < 0.05$, so there is a statistically significant relationship between chemotherapy and saliva viscosity (*Table 3*).

Although there is no association between chemotherapy and changes in some bacteria type, there is a significant change in the presence of *Staphylococci* after chemotherapy.

Table 3. A significant relation between chemotherapy and the presence of *Staphylococci*.

	<i>Streptococci</i> and <i>Streptococci</i> "AF"	<i>Staphylococci</i> and <i>Staphylococci</i> "AF"
N	60	60
Exact Sig. (2-tailed)	1.000 ^b	0.019 ^b

- McNemar test
- Binomial distribution

Also, as mentioned before, there is a direct effect of chemotherapy on the patient's oral hygiene habits, we found

that chemotherapy adversely affects oral hygiene habits (Table 4). Patients with good oral hygiene before chemotherapy, unfortunately, showed bad oral hygiene after chemotherapy (70.97%) of the test group.

Table 4. the relationship between chemotherapy and hygiene habits.

Oral hygiene	Oral hygiene "AF"	
	Bad	Good
Bad	20	9
Good	22	9

In addition, we found that chemotherapy decreases saliva viscosity in most of the patients in our test group, patients who have viscous saliva before chemotherapy, unfortunately, showed watery saliva after CTX was (79.17%) of test group (Table 5).

Table 5. The relationship between chemotherapy and saliva viscosity.

Saliva viscosity	Saliva viscosity AF	
	Watery	Viscous
Watery	28	7
Viscous	19	5

Discussion

Chemotherapy (CTX) is a type of cancer treatment that uses cytotoxic drugs to kill cancer cells. Unfortunately, these drugs can inadvertently damage your healthy cells, too. Healthy cells throughout your body can be damaged, including the ones inside your mouth. This can lead to a variety of distressing oral side effects which may make it difficult to keep wearing your dentures; here are many side effects that chemotherapy patients with dentures should be prepared for. After few days of having chemotherapy, sore spots develop in the oral cavity. These spots cause pain when the pressure created by denture placement is applied. So that patients feel comfortable when they take off the denture. CTX also lowers your white blood cell count. This is a problem because your white blood cells play a key role in fighting off infections. Without enough white blood cells, you are more susceptible to oral fungal infections like oral candidiasis (thrush). The lesions may be sore and may make wearing dentures painful. CTX drugs can lead to thrombocytopenia, a lower than normal platelet count. Thus, people with thrombocytopenia experience increased bleeding and more difficulty stopping this bleeding. The friction of your dentures on your gum tissue may lead to excessive bleeding inside your mouth, making it hard for you to wear your dentures [6].

There is no consensus regarding quantitative and qualitative changes in oral microflora during cancer treatment or a clear pattern of association between mucositis and changes in oral microflora [2].

We have studied two types of bacteria; *Streptococci* and *Staphylococci* before and after chemotherapy. There was no high change on *Streptococcus*; the ratio of patients who have *Streptococcus* before and after CTX was 90.74%.

Chemotherapy showed change on the number of *Staphylococcus*; patients who have *Staphylococci* before and still have it after chemotherapy was 44.44% of the test group.

The viscosity of saliva increases the retention of the denture. Chemotherapy lessens the saliva viscosity; patients who were with viscous saliva and showed watery saliva after CTX was 79.17% of the test group. Oral hygiene impacts the number of oral bacteria, chemotherapy makes the patients down and this may make patients tend to not care about their oral hygiene; patients who are shown good oral hygiene before chemotherapy and shown bad oral hygiene after chemotherapy was 70.97% of test group. The severity ranges from localized to generalized erythema to frank ulceration and hemorrhage, the initial condition is often described as a burning sensation or tingling sensation making the mouth hypersensitivity to food and as the condition progress eating, swallowing and talking become increasingly difficult, and those make the patient hardly to wear the denture as a form of iatrogenic stomatitis [7,8].

Our results showed that there was no direct relationship between number and type of bacteria found in mouth and chemotherapy. Number and type of bacteria found in the mouth are directly related to oral hygiene and saliva viscosity.

Oral/dental health care is clearly more complex in cancer patients. Therefore, oral and dental care before, during and following chemotherapy are an important part of cancer treatment and are best provided by educated and experienced dental provider for treatment and/or prevention of oral complications [9], with good communication with oncology team can significantly improve patient quality of life and reduce health care costs. So, for the dentist, don't provide an emergency dental treatment to a patient currently received chemotherapy [10], before contacting patient's oncology team to find out whether treatment can be carried out safely. If this was not possible, refer the patient urgently to dental care specialist. It's advisable for the patient who has dry mouth to take frequent sips of water (every 10 minutes) and melt ice chips in the mouth for comfort, additionally one may consider using artificial salivary spray (eg. xerotin) and mouth moisturizing gel (eg. Biotene oral balance).

Residual salivary gland activity and salivary flow rate may be increased by saliva-stimulating tablets and medications like pilocarpine. Patients are recommended to use sorbitol chewing gum for salivary flow.

Finally, patients should be cautioned against coffee, tea, soft drink and mouth rinse with alcohol as they dehydrate the mouth [11].

The dentist can solute the problem of denture which can't fit well anymore by temporary fix (soft reline to the denture during treatment) or by permanent fix (3 to 6) months after finishing treatment.

Conclusion

Our study was done on a small sample size which is a limitation, and it shows that no significant changes in the microflora in the oral cavity which may cause mucositis in cancer patients wearing denture after treating by chemotherapy. It requires more patients to increase reliability

and accuracy of the results, and it's necessary to do more detailed studies to get the relationship between chemotherapy, changes in oral microflora, and the presence of mucositis in denture-wearing patients. Molecular biological techniques can be used to get better characterization of alterations and magnitude of oral microflora and this technique is not found in Gaza. This would help our understanding of the potential role of oral microflora in the development and aggravation of oral mucositis in denture-wearing patient.

Disclosure

The authors report no conflicts of interest in this work.

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