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ORIGINAL RESEARCH

FREQUENCY AND PATTERNS OF ORAL MANIFESTATIONS IN BREAST CANCER PATIENTS UNDER CHEMOTHERAPY

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ABSTRACT

Objective: The objective of this study was to assess the prevalence and character of the oral manifestations among a group of Iraqi women who had received different chemotherapy treatments.

Methods: A cross-sectional study of 150 patients treated Paclitaxel, Tamoxifen, 5-Fluorouracil or Capecitabine was done. To evaluate dysphagia reported by patients, changes in oral mucosa color, ulceration, cheilitis, and oral mucosa color, a standardized clinical examination was conducted.

Results: Oral complications were extremely common, and only 58 patients did not exhibit the change in mucosal colour; the most frequent was redness (n=40). In 60 patients, oral ulceration was seen and most of them complained about painful lesions (n=41). The most common overall result was cheilitis and over one-third of the cohort (n=54) had cheilitis. Fourty-six patients reported difficulty in swallowing. The rate of these manifestations differed depending on the chemotherapeutic agent with the highest rates being seen with 5-Fluorouracil and dysphagia and paclitaxel and cheilitis and mucosal whitening respectively.

Conclusion: The oral toxicities, especially mucositis, ulceration, cheilitis, and dysphagia are extremely frequent and regimen-related adverse effects of the chemotherapy in Iraqi women. These circumstances play a major role in patient morbidity, and they are a huge clinical liability. The results highlight the urgent necessity of agent-specific risk evaluation, preemptive patient education, and the use of stringent oral care guidelines before and during chemotherapy to prevent and reduce as well as manage these debilitating complications, which will positively impact the quality of life and compliance to treatment among oncology patients.

***Keywords*:** Oral ulcers, dysphagia, cheilitis, Iraqi women, Chemotherapy

INTRODUCTION

Cancer chemotherapy is an essential part of oncological treatment, it is linked to a remarkable range of both systemic and localized side effects that greatly affect the quality of life and morbidity in patients[1]. Oral complications are especially frequent, debilitating, and dose-limiting among them and may substantially reduce the effectiveness of treatment and its outcomes [2]. Oral mucositis is a condition which is highly vulnerable to the oral cavity because of high rate of mitotic activity of the basal epithelial cells in the mouth [3].

Oral chemotherapy is a paradigm shift in cancer care, which is typified by a higher convenience of patients, the need to visit healthcare facilities less, and a sense of agency. These therapeutics, a sub-division of both conventional cytotoxics and molecularly targeted agents, are becoming increasingly utilized in the treatment of a range of solid tumors and hematologic tumors. Nevertheless, the advantages of this treatment form are moderated by a unique and in many cases a significant adverse effect profile, the spectrum, onset, and clinical management of which may vary significantly as compared to parenteral treatment regimens [4].

With the development of oral chemotherapy, oncologic care has changed to be more convenient to the patient, with less frequent visits to the hospital and more autonomy. These agents both traditional cytotoxic and new targeted therapy are now being used in the treatment of various malignancies such as breast, colorectal, and

lung cancer and also hematologic neoplasms. Despite these benefits, oral chemotherapeutic regimens are often associated with severe toxicities with a characteristic profile, timing, and necessitating alternate management practices when compared to conventional intravenous delivery [5].

MATERIALS AND METHOD.

Data were collected through direct clinical examinations, with oral morphological signs recorded, such as color changes (redness, blackening, whitening), ulcers (painful or painless), chapped lips, difficulty swallowing, and changes in taste. The data were statistically analyzed to determine the relationship between the type of chemotherapy and the prevalence of these morphological markers.

RESULTS

The most common observed oral manifestation in all types of chemotherapies was the lack of any change in color, which was seen in 58 of the patients. The most frequent changes of the alterations were: redness of the oral mucosa (40 cases), whitening (34 cases), and darkening (18 cases). Mucosal changes occurred differently with chemotherapeutic agents. The most frequent rate of redness was noticed using 5-Fluorouracil and 11 cases each using Capecitabine. The highest number of cases that had their mucosa whitened was linked to paclitaxel. Capecitabine was the regimen that had the smallest percentage of patients with no change table 1.

Table 1. Distribution of oral mucosa color changes by chemotherapy type

Type of chemotherapy	Redness of mucous	Darkness of mucous	Whitening of mucous	No change	Total
Paclitaxel	**10**	**5**	**11**	**25**	**51**
Tamoxifen	**8**	**3**	**7**	**11**	**29**
5-Fluorouracil	**11**	**6**	**8**	**14**	**39**
Capecitabine	**11**	**4**	**8**	**8**	**31**
Total	**40**	**18**	**34**	**58**	**150**

Oral ulcers were a typical clinical observation as observed in 60/150 patients. Most of these ulcers were said to be painful, of these cases 41 were reported whereas painless cases were less, at 19. Depending on the chemotherapeutic agent, the distribution of ulcers was different. The number of painful ulcers with 5-Fluorouracil, and Capecitabine was a close tie at the highest. The treatment that had the greatest percentage of patients without ulcers was the treatment involving Paclitaxel and Capecitabine had the highest prevalence of ulceration table 2.

Table2. Distribution of oral ulcers by chemotherapy type

Type of chemotherapy	Painful ulcer	Painless ulcer	No ulcer	Total
Paclitaxel	**10**	**6**	**35**	**51**
Tamoxifen	**8**	**3**	**18**	**29**
5-Fluorouracil	**12**	**6**	**21**	**39**
Capecitabine	**11**	**4**	**16**	**31**
Total	**41**	**19**	**90**	**150**

On the other hand, the cracked lips or cheilitis was also found to be a very common oral presentation with 54 out of 150 patients having it. The incidence of this condition was also different between the various chemotherapeutic agents. The highest cases were linked to paclitaxel, then 5-Fluorouracil, and Tamoxifen. The minimum incidence of the regimens studied was observed in the patients who received Capecitabine as a treatment regimen table 3.

Table 3. Distribution of Cracked Lips by Chemotherapy Type

Type of chemotherapy	Chapped Lips	No Chapped Lips	Total
Paclitaxel	**18**	**33**	**51**
Tamoxifen	**12**	**17**	**29**
5-Fluorouracil	**15**	**24**	**39**
Capecitabine	**9**	**22**	**31**
Total	**54**	**96**	**100**

The table (4) describes the prevalence of patient-reported dysphagia in 150 Iraqi women receiving various chemotherapy regimens. 46 of 150 patients had dysphagia. It was discovered that the rate of dysphagia was different in the various chemotherapeutic regimens. The maximum frequency was noticed in patients undergoing the 5-Fluorouracil treatment, then proceeded to the Paclitaxel, Tamoxifen, and Capecitabine.

Table 5. Distribution of Swallowing Difficulty by Chemotherapy Type

Type of chemotherapy	Dysphagia	No Dysphagia	Total
Paclitaxel	12	39	51
Tamoxifen	9	20	29
5-Fluorouracil	16	24	39
Capecitabine	9	21	31
Total	46	104	150

4. DISCUSSION

The results of this investigation suggest that changes of the color of oral mucosa are a common phenomenon among Iraqi women under chemotherapy with a significant proportion of the sample (91 patients) showing some sort of variation. The mucosal redness or erythema is high and this observation is in line with the existing body of literature which credits the observation to mucositis as a result of chemotherapy which is a typical inflammatory side effect of cytotoxic therapy [6]. The processes include the direct harm to the fast-dividing epithelial cells of the oral mucosa that result in atrophy, inflammation, and erythema, which may be the antecedent of ulceration [7].

The mucosa observed to be whitened could be due to a variety of mechanisms that could include hyperkeratosis, oral candidiasis, or epithelial dysplasia as a result of the immunosuppressive impacts of chemotherapy. The observed high rate among patients who are taking paclitaxel should prompt additional research on the topic of mucosal toxicity profile of this drug [8]. The blackness of the oral mucosa might be related to post-inflammatory hyperpigmentation that is among the negative side effects of some chemotherapeutic agents; however, this was the least prevalent in the current cohort.

It is remarkable that several patients did not show any color changes, which confirms the personal differences of susceptibility to oral toxicities. Genetic predisposition, general health condition, and oral healthcare practices during treatment may be among the factors that cause this variability. According to the data, the incidence of patients with no mucosal changes was lowest when using Capecitabine, which would indicate that this regimen has a possibly higher mucotoxic profile than the others in this group, which is consistent with the side effects of the former [9]. The findings emphasize the need to enforce strict pre- and intra-treatment oral evaluation and preventive measures that oncologists and dental professionals are required to adopt in order to counter these frequent and sometimes painful complications, thus enhancing the quality of life of such patients undergoing chemotherapy.

The prevalence of oral ulceration and especially painful ulcers in this cohort highlights the high cost of oral mucositis which is a major dose limiting toxicity of cancer chemotherapy. The preponderance of painful lesions is a significant clinical issue, as it is directly related to patient morbidity, such as pain, dysphagia, nutritional deficiency, and poor quality of life, and could have to require a reduction or pause of life-saving cancer treatment, the gravity plays pathophysiologically through direct cytotoxic impact of chemotherapeutic agents on the basal epithelial cells, which inhibits normal regenerative potential of the oral mucosa and causes

tissue destruction and development of ulcers [10].

The observation that many patients never had ulcers points to the significance of personal risk factors, such as genetic polymorphisms, oral microbiome and application of preventive oral care procedures. The relative lack of prevalence among patients undergoing the use of Paclitaxel could be explained by its distinct mode of action, which could not be as harmful to the oral mucosa when compared to the antimetabolites. These findings underscore the significance of agent-specific risk management and the necessity of preventive measures specific to individuals with 5-Fluorouracil, excessive oral hygiene, and alike, in order to minimize the number and the severity of this disabling complication [11].

The difference in the prevalence of ulcers according to the different chemotherapeutic regimens is its adherence to the toxic profiles. Such increased incidence of ulcers, especially painful ulcers with the use of 5-Fluorouracil and Capecitabine is predictable because of the mechanism of action that is very toxic to mucositis since the two antimetabolite agents act on the most rapidly dividing cells , the fact that painless ulcers are less frequent but still to be carefully differentially diagnosed and should put the clinical suspicion on other ailments such as viral infections (e.g., cytomegalovirus) or neutropenic ulcers [12].

The dysphagia is a complex complication, which may be caused by severe mucositivities of the oral cavity and oropharyngeal ulceration, which is accompanied by much pain during the swallowing (odynophagia), and by direct neurotoxic action of chemotherapeutic agents that may lead to the loss of the complex neuromuscular coordination of the swallowing process [13]. Dysphagia has more than just a painful impact because it can be extremely dangerous when it comes to dishydration, malnutrition, and aspiration pneumonia as a potential result that may threaten the well-being of patients, in general, as well as their treatment results, in particular [14].

The result that 5-Fluorouracil was related to the most cases of dysphagia is in line with its propensity to induce serious mucosal damage across the entire upper aerodigestive tract. Swallowing reluctance and difficulty is mainly caused by the pain of widespread mucositis. The striking occurrence among all agents, with Tamoxifen included indicates dysphagia as a non-specific, yet prevalent cytotoxic therapy class effect, which may be enhanced by other co-morbid factors such as xerostomia [15].

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Competing Interests

The authors have no competing interests to declare.

Informed Consent

Not applicable.

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