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Periodontal disease and cancer patients undergoing chemotherapy

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Objective: The aim of this study was to evaluate periodontal status after periodontal treatment in patients with different malignant solid tumours submitted to chemotherapy. **Methods:** Fifty-four patients with newly diagnosed early-stage solid tumour malignancy treated by surgery and eligible for adjuvant chemotherapy were enrolled in this study. Clinical periodontal parameters obtained by a single calibrated examiner were evaluated before chemotherapy (T0), 21 days after chemotherapy (T1) and 210 days after chemotherapy (T2). Patients were grouped into healthy or periodontally diseased subjects. All patients received oral hygiene instructions, and the diseased patients received periodontal treatment at baseline. Comparisons between the groups were performed using the McNemar test ($P > 0.05$) and the Wilcoxon test with Bonferroni correction ($P < 0.02$) using SPSS software. **Results:** Of 54 patients enrolled in the study, two did not present to the third assessment (T2). The prevalence of periodontitis was 35.2% at baseline and no significant difference was found in the follow-up assessments. There was a statistically significant reduction in probing depth (PD), plaque index (PI) and bleeding on probing (BOP) between baseline and follow-up assessments. The attachment level (AL) did not vary significantly between the different follow-up periods ($P \geq 0.06$). **Conclusions:** Periodontal treatment was effective in reducing PI, BOP and PD and in maintaining AL in periodontitis cancer patients undergoing chemotherapy.

Key words: *Chemotherapy, cancer patients, periodontitis, periodontal treatment*

INTRODUCTION

Although priority is often given to the treatment of the malignancy itself, focus should also be directed at prevention and amelioration of complications that may occur as a result of the disease and/or its treatment. Chemotherapeutic agents are drugs designed to have a selective toxicity towards the tumour cells. Unlike surgery and radiation therapy, whose usages are limited to cancers confined to specific areas of the body, chemotherapy targets widespread or metastatic cancer. Current chemotherapeutic agents are often cytostatic or cytotoxic in nature to prevent the rapid division of the malignant cells and/or destroy them in the process, but these agents also act on normal cells with a high turnover rate[1]. Cancer treatment can cause a variety of problems in patients, including the maintenance of their daily oral hygiene. Before chemotherapy for malignancy it is necessary to perform careful screening for orodental diseases and conditions as these may generate acute problems and compromise the patients' medical care. Mucositis, dysgeusia, neurosensory and saliva changes, and oral and dental infections are among the reported oral adverse effects of chemotherapy[2,3]. These oral acute or chronic complications may arise throughout and after cancer treatment. The occurrence, severity and duration of these oral adverse effects show a wide variability depending on cancer diagnosis and disease stage, in addition to different dose-intensities and combinations of chemotherapeutic drugs. These complications impact quality of life. Hence, every effort should be focused on prevention. Accordingly, the management of oral toxicities is necessary to ensure optimal long-term oral health and general well-being[4]. In particular, hyposalivation and increased bacterial counts, along with dietary changes and oral hygiene difficulties, favour the development of dental caries and periodontal disease[5,6]. Substantial evidence supports an association between chronic infections/inflammation and cancer[7]. Periodontitis is a chronic inflammatory disease associated with Gram-negative anaerobic bacteria in the dental biofilm. It leads to irreversible destruction of tissues supporting teeth, clinically detectable as

periodontal pockets and alveolar bone loss. Most importantly, treatment of periodontal infections has been shown to prevent and reverse systemic adverse events[8]. Therefore, the aim of this study was to investigate the changes in periodontal clinical parameters in patients undergoing chemotherapy for the treatment of different solid tumours up to 7 months after cancer treatment.

MATERIALS AND METHODS

Fifty-four patients with newly diagnosed early-stage solid-tumour malignancy treated by surgery and eligible for adjuvant chemotherapy were enrolled in this study after giving informed consent. There were 25 male patients and 29 female patients, ranging in age from 25 to 72 years. Inclusion criteria were: older than 18 years of age; of either gender; at least six teeth in the oral cavity; no distant metastases at the time of inclusion; and undergoing chemotherapy. Patients were excluded if they had previously received radiotherapy or chemotherapy, had a diagnosis of Sjögren's syndrome and if dental treatment could not be performed before the initiation of cancer therapy as a result of timing issues. The study was conducted at the Day Hospital Oncology Unit, 'Fiorini' Hospital, Terracina, Latina. The research was conducted in full accordance with the World Medical Association Declaration of Helsinki and the study was approved by the Medical Ethical Committee of Sapienza University of Rome. All patients enrolled in this study signed an informed consent. The distribution of solid tumours was as follows: breast ($n = 16$), stomach ($n = 6$), oesophagus ($n = 7$), ovary ($n = 5$), colorectal ($n = 9$) and lung ($n = 11$). Patients with breast cancer received an adjuvant standard dose of cyclophosphamide, epirubicin and 5-fluorouracil (CEF) if pre- or perimenopausal or cyclophosphamide, methotrexate and 5-fluorouracil (CMF) if postmenopausal; patients with stomach, oesophageal or ovarian cancer received a dose of epirubicin, cisplatin and 5-fluorouracil (ECF); patients with colorectal cancer received a dose of Mayo Treatment (5-fluorouracil and folinic acid); and patients with lung cancer received a dose of cyclophosphamide, adriamycin and vincristine (CAV). The chemotherapy was administered for a total of six cycles. A full-mouth assessment of periodontal conditions was made using a millimetre-scale periodontal probe (model PCP-UNC 15R; Hu-Friedy, Chicago, IL, USA). Plaque index (PI), bleeding on probing (BOP), probing depth (PD) and attachment level (AL) were recorded at six different sites (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual and distolingual) on each tooth[9]. Teeth with class II and III degrees of mobility[10] and/or periodontal pockets with a PD of ≥ 6 mm, teeth with involvement of furcation (grades I, II and III)[9], dental extrusion or compromised interocclusal space were indicated for extraction based on clinical and radiographic assessments. These teeth were extracted before the first periodontal assessment. PI was determined for all surfaces of all teeth, which were classified according to the presence (score 01) or absence (score 00) of visible dental biofilm[11]. BOP was assessed in a dichotomous manner (present/absent), 30–60 seconds after probing[9]. All patients were examined by a single trained investigator (VC). Patients with periodontitis were classified according the CDC Working Group criteria, based on two or more interproximal sites with AL ≥ 4 mm or two or more interproximal sites with PD ≥ 5 mm (not on the same tooth)[12]. Periodontal evaluation was performed at three different time points – before chemotherapy (baseline), 21 days after the sixth cycle of chemotherapy and 210 days after the sixth cycle of chemotherapy, referred to as T0, T1 and T2, respectively. All patients received oral hygiene instructions on brushing and interdental cleaning, coronal scaling with an ultrasonic instrument and polishing. Those diagnosed with periodontitis also received root planing. As an additional precaution, the patients were prescribed chlorhexidine mouthwash. The use of other mouthwashes was not allowed to avoid confounding the effects of scaling and root planing. The patients were followed up every 3 weeks after every cycle of chemotherapy. At each patient visit, coronal polishing, topical application of 1% neutral fluoride gel and reinforcement of oral hygiene were provided.

Statistical analysis

All statistical tests were performed using the SPSS® software (version 17.0 for Windows; IBM, Milan, Italy). The prevalence of healthy and periodontitis patients over time was compared using the McNemar test ($P < 0.05$). For each patient, the PD and AL mean values were obtained by dividing the sum of these clinical parameters by the number of sites examined. These values were then compared over time using the Wilcoxon signed-rank test. The same test was also used to compare the frequencies of PI and BOP. Bonferroni correction was used to determine the statistical significance of differences between groups whenever appropriate ($P < 0.02$).

RESULTS

From 54 patients enrolled in the study, two did not present to the third assessment (T2). The prevalence of periodontitis was 35.2% at baseline and no significant difference was found in the follow-up (*Table 1*). There was a statistically significant reduction in PD between T0/T1 ($P = 0.02$) and T0/T2 ($P = 0.00$). AL

Table 1 Numbers of healthy and periodontal patients at each periodontal evaluation

Evaluationtime point	Total number of patients	Healthy patients*n* (%)	Periodontal patients*n* (%)
T0	54	35 (64.8)	19 (35.2)
T1	54	35 (64.8)	19 (35.2)
T2	52	34 (65.4)	18 (34.6)

T0, baseline; T1, 21 days after chemotherapy; T2, 210 days after chemotherapy.

Table 2 Comparisons between probing depth (PD) and attachment level (AL) at each periodontal evaluation

Evaluationtime point	PD(mm)	AL(mm)
T0	2.29 ± 0.40	2.53 ± 0.45
T1	2.11 ± 0.35	2.39 ± 0.37
T2	1.96 ± 0.30	2.41 ± 0.41

Values are given as mean ± SD.
T0, baseline; T1, 21 days after chemotherapy; T2, 210 days after chemotherapy.

Table 3 Comparisons between plaque index (PI) and bleeding on probing (BOP) at each periodontal evaluation

Evalutationtime point	Mean PI(%)	Mean BOP(%)
T0	69.0	17.0
T1	37.0	3.8
T2	24.0	9.0

T0, baseline; T1, 21 days after chemotherapy; T2, 210 days after chemotherapy.

did not vary significantly between the different follow-up periods ($P \geq 0.06$) (*Table 2*). *Table 3* shows the frequencies of PI and BOP, which were significantly lower in the T1 and T2 assessments than at baseline ($P < 0.001$). There was no difference between T1 and T2 for each parameter.

DISCUSSION

The oral cavity has the potential to be a major source of short-term and long-term complications from cancer therapy. Appropriate evaluation and elimination of potential sources of oral infection before cancer therapy is vital because oral bacteria are a known source of bacteraemia and septicaemia during cancer therapy. Chemotherapy-related oral infections contribute significantly to the morbidity and mortality in cancer patients. Mucosae, periodontium and teeth are the three anatomical sites most commonly associated with these complications[1]. It has been found that pathogenic microorganisms located subgingivally or in periradicular areas may cause acute exacerbations of pre-existing periodontal or periradicular infections[13] when the granulocyte count dips below 1,000/mm^3. Periodontitis results in the continuous release of bacterial and inflammatory markers into saliva and blood[14]. Furthermore, periodontal pathogens and inflammatory cytokines travel with saliva and blood from the affected tissues to distant sites and thus may adversely affect systemic health[15–17]. The changes in the clinical periodontal parameters observed in this study show that decreased PD and stabilised AL may be achieved in patients undergoing chemotherapy when oral hygiene procedures are intensified and reinforced through regular periodontal maintenance. The number of individuals with periodontitis did not change significantly. This could be explained because of the cases of periodontitis defined by AL, which also did not change from baseline to T2. AL may be a reflection of the past history of pathology, and periodontitis does not necessarily remain in the active phase[12]. A statistically significant reduction in the frequency of PI was observed between the baseline assessment and the final evaluation. This may be explained by frequent visits and oral hygiene reinforcement that were employed in our study. Intra-oral bleeding is a complication associated with chemotherapy. The bleeding can be spontaneous, traumatically induced or an effect from existing pathology. It can also be the result of thrombocytopenia secondary to suppression of haematopoietic tissues[1]. The reduction of BOP may be caused by a reduction in PI values, which decreased from 69.0% at T0 to 24.0% at T2. In our study, over the same length of time, the mean PD decreased from 2.29 mm to 1.96 mm, and a statistically significant difference was found between baseline and the other assessments. It has also been shown that supragingival plaque control alters the subgingival microflora and improves both PI and clinical periodontal parameters (BOP, PD and AL) in patients with moderately deep pockets, as in our study[18]. The reduction in PD may have occurred because of a decrease in inflammation resulting from periodontal treatment; AL remained stable across all three assessments. In conclusion, our findings confirm the hypothesis that patients undergoing chemotherapy do not show aggravation of their clinical periodontal status for up to 7 months after cancer treatment if they receive periodontal therapy and maintenance. In patients with solid tumours, chemotherapy may result

in a short-term depression in white cell counts with recovery before the next course of chemotherapy. Dental and periodontal treatment should be provided when white counts are not suppressed, typically 2–3 weeks following a course of chemotherapy, before the next dose of chemotherapy[5]. Normal oral flora comprises a variety of bacteria, some of which may become pathogenic with immunosuppression. Sepsis of unknown origin may possibly be the result of oral infections (e.g. Viridans streptococci, *Prevotella* species, *Fusobacterium*, *Aggregatibacter actinomycetemcomitans* and *Actinomyces* species)[19]. Given the patient's condition, meticulous oral hygiene practice is fundamental. It should be noted that evaluation, treatment and prevention of any pre-existing oral and dental pathology contribute significantly to an overall favourable treatment outcome for cancer patients; for this reason, the patient's oral health status should be stabilised/optimised to ensure minimally predictable complications[20]. The short follow-up time and the small number of patients are the main limitations of this study. A longer follow-up with a greater number of patients is advised to confirm our findings.

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Competing Interest

None declared.

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