ORIGINAL ARTICLE

Comparison of chemotherapy and hematopoietic stem cell transplantation pre and postterm DMFT scores: A preliminary study

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Abstract

Aims: Chemotherapy is frequently used as a conditioning regimen to destroy malignant marrow cells before transplantation. Xerostomia, dysphagia, altered taste perception, mucositis, soft-tissue ulceration, and infection are common adverse oral effects of chemotherapy. The study was aimed to compare decayed, missing, filled teeth (DMFT) scores before and after hematopoietic stem cell transplantation (HSCT) and chemotherapy.

Materials and Methods: Thirty-six patients undergoing HSCT were included in the study. A pre-HSCT dental treatment protocol was implemented that consisted of restoration of all active carious lesions, treatment of periodontal infections, and extraction of all teeth with advanced periodontal disease. Upon completion of dental treatment, the importance of rigorous and effective oral hygiene was reemphasized, and patients were recalled 6 months later. DMFT scores were calculated prior to the initiation of HSCT treatment and 6 months after transplantation.

Statistical Analysis Used: Regression analysis was used to evaluate the effects of HSCT and chemotherapy on DMFT scores.

Results: Wilcoxon T test showed a statistically significant difference in DMFT scores before and after HSCT ($P < 0.001$).

Conclusions: DMFT scores were found to increase after chemotherapy and HSCT, suggesting that the risk of infection is higher among HSCT patients when compared to other individuals. The results emphasize the need for dental examinations as an integral part of examination and treatment planning for patients undergoing HSCT and chemotherapy.

Key words: Chemotherapy, decayed missing filled teeth scores, hematopoietic stem cell transplantation

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Introduction

Hematopoietic stem cell transplantation (HSCT) is a curative treatment option for many hematological malignancies; including lymphomas, acute and chronic leukemias, aplastic anemia, multiple myeloma, neuroblastoma, some solid tumors, severe combined immunodeficiency, inherited immune disorders, and myelodysplastic syndromes.[1-5]

Chemotherapy with or without total body irradiation is frequently used to destroy malignant marrow cells prior to transplantation. These cytoreductive regimens used for immunosuppression rapidly destroy dividing cell

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populations, particularly hematopoietic progenitor cells and mucosal epithelial cells. At the same time, the agents used in chemotherapy may destroy metabolically active normal tissue cells; thereby adversely affecting the kidneys, heart, skin, immune system, and gastrointestinal track; including the oral cavity. The constant exposure of oral tissue to physical, chemical, thermal, and microbial injury makes the mouth a primary site of complications associated with chemotherapy.[6] The most common adverse oral effects include xerostomia, dysphagia, altered taste perception, mucositis, soft-tissue ulceration, and infection as well as gingivitis due to secondary pancytopenia associated with drug-induced myelosuppression. Xerostomia may lead to increased plaque accumulation and lower the pH of residual saliva,[7] increasing susceptibility to dental caries and thus requiring extensive preventive care.[6]

Because patients undergoing chemotherapy and HSCT have an increased susceptibility to infection during and after transplantation, it is important to eradicate all sources of infection prior to treatment.[3,8] Together with the entire gastrointestinal tract (GIT), the oral cavity is an important point of entry for systemic infection, mainly by gram-positive anaerobic microorganisms which can cause apical lesions and periodontal diseases.[9,10] Dental caries is an infectious microbiologic disease of the teeth that results in localized dissolution and destruction of calcified tissue. Dental caries and periodontal disease are probably the most common chronic diseases in the world.

Preexisting dental conditions may cause local and systemic complications during medical treatment.[11] Local dental infections that may remain inactive in healthy individuals can cause serious systemic complications in severely immunocompromised hosts as well as in patients undergoing HSCT.[3,12] Although new advances have been made in all areas of supportive care;[1] oral complications such as gingivitis, severe mucositis, and ulcerations continue to remain important causes of morbidity and mortality when not properly treated.[3]

Studies have reported that 29-72% of patients undergoing HSCT had at least one oral infection that required treatment before transplantation.[9,12,13] In order to identify and treat all potential sources of infection, dental evaluation of patients prior to HSCT has become routine. One previous study reported that early dental intervention significantly reduced the incidence of oral complications associated with immunosuppression regimens from approximately 40 to 12%.[3] Given their key role in the diagnosis, prevention, and treatment of complications stemming from the oral cavity, dentists should be included on the treatment team from pretransplantation through recovery of immune competence.[1]

The most common epidemiologic measure of caries is an evaluation of the number of permanent teeth that are decayed, missing, or filled. 'DMF' (referred to as 'dmf' in primary teeth) may be recorded in terms of either affected teeth ('DMFT') or affected tooth surfaces ('DMFS').[14] This study aimed to compare pre- and posttreatment dental status of patients undergoing HSCT and chemotherapy by examining their pre- and posttreatment DMFT scores.

Materials and Methods

This study was conducted with 36 patients (27 male, 9 female) undergoing HSCT who were referred to our clinic at the Department of Oral Diagnosis and Radiology over a 2-year period for pre-and posttransplantation dental evaluations and oral health management. The ethical committee of our faculty gave approval for the study and Declaration of Helsinki have read and the guidelines followed in this investigation.

Pretransplantation evaluation included both clinical and radiographic examinations with appropriate ethical committee was obtained prior to the start of the study and that subjects were volunteers who had given informed, written consent. Oral hard and soft tissues were assessed, and dental characteristics (number of decayed, filled and missing teeth; impacted and semi-impacted third molars; periapical and periodontal infection; retained roots) were recorded. Panoramic radiographs were taken of all patients, and in cases where suspicious periapical lesions were identified or superposition of contact surfaces occurred, either bitewing or periapical radiographs were also taken. Oral hygiene status was assessed through use of plaque index, as described by Löe and Silness.[15] Clinical and radiographic findings of periodontal disease, erupting third molars, unerupted third molars covered by soft tissue only, periapical radiolucency, retained root fragments with existing infection, deep dental caries more than half of the distance from the enamel to the pulp chamber, caries under restorations, and periodontal breakdown were considered to be potential foci of infection.

The CDC's Guideline for Preventing Opportunistic Infection Among Hematopoietic Stem Cell Transplantation Recipent[16] recommends maintaining oral health, removing lesions that can easily lead to dental infections, extracting teeth affected by moderate or severe periodontal disease, and removing dentures and orthodontic appliances during cancer treatment.[16] According to the guidelines, a pre-chemotherapy and HSCT dental treatment protocol was followed that included restoration of all active carious lesions, treatment of periodontal infections, and extraction of all teeth with advanced periodontal disease. As the first and most important step of the treatment protocol, medical consultation with the patient's hematologist was conducted in order to establish the degree of immunosuppression and antibiotic coverage

required to prevent any oral or generalized infection and hemorrhage. Prophylactic treatment, including periodontal scaling and root planning, was performed as necessary, and periodontally questionable or hopeless teeth were extracted. Semi-retained third molars and infected root fragments were also extracted, and faulty dental restorations were replaced, repaired, or if necessary, extracted so as to avoid any potential soft-tissue irritation or periapical infection during the course of HSCT therapy. To ensure adequate wound healing, all extractions were performed at least 1 week before initiation of therapy. To as great extents as possible, extractions were atraumatic, and care was taken to reduce sharp ledges and achieve maximal soft-tissue closure. Retained roots and fully impacted teeth with no clinical or radiological symptoms were left in place. In view of the prolonged healing period for 2 weeks[11] and extensive oral hygiene regime required during healing, no elective periodontal surgery was performed. Upon completion of dental treatment, the importance of rigorous and effective oral hygiene, including the use of fluoride-containing toothpaste and mouthrinse, was reemphasized, and the patient was recalled 6 months later.

Following 6 months of chemotherapy and HSCT therapy, patients were again referred to our clinic for detailed clinical and radiographic examinations. In order to evaluate the effects of HSCT and chemotherapy on dental status, DMFT indexes were calculated before and after transplantation, and DMFT scores were compared using Wilcoxon T test.

Results

A total of 36 patients (27 male, 9 female) whose diagnoses included acute myelogenous leukemia (19 patients), acute lymphocytic leukemia (5 patients), aplastic anemia (4 patients), and various other conditions (9 patients) undergoing HSCT were examined for the study. Thirty-four patients were treated with allogeneic SCT, and the remaining two patients were treated with autologous transplantation.

Mean patient age was 32 years (mean age: 31.8 ± 12.4). Distribution of the patients included in the study and the DMFT scores pre and posttreatment is given in Table 1. Overall pre- and posttransplantation mean DMFT scores were 7.0 and 8.83, respectively. While the median score of DMFT was 29.00 (26.00-30.75) before transplantation, it was found to be 28.00 (24.25-29.00) after HSCT. Wilcoxon T test showed the decrease in DMFT scores following HSCT to be statistically significant ($P < 0.001$).

Whereas at least one potential dental focus of infection was identified either radiographically or clinically in 34 of 36 patients and treated prior to HSCT and chemotherapy, dental foci of infection were found in only 29 of 36 patients following 6 months after HSCT and chemotherapy. No correlation was found between dental status and age, sex, or underlying disease.

Gingival inflammation caused by dental plaque was recorded in 80% of the patients prior to chemotherapy and HSCT. Postchemotherapy and HSCT examination gingivitis was found in 69.4% of the patients, despite patient counselling on the importance of oral hygiene and the elimination of preexisting oral pathosis to the greatest extent possible. Prior to chemotherapy and HSCT, 4 of 31 impacted third molars, 6 of 10 semi-impacted third molars, and 6 of 13 retained root fragments were extracted due to existing infection or the risk of infection.

Pre- and posttransplantation D-M-F components are given in Table 2 separately. Of the 80 teeth with active carious lesions, 54 of them were restored ideally and 26 of them extracted due to advanced caries lesions extending more than half of the distance of enamel to pulp chamber. Besides, 14 teeth were also extracted because of periodontal problems. The percentage of decayed teeth was 7.9% prior to HSCT and chemotherapy and it increased to 8.9% following treatment. In terms of number of individuals, the number of decayed teeth was found to have increased in 22.2% patients.

Table 1: Distribution of the patients included in the study and the DMFT scores pre and post treatment

Diseases	Patients (*n* (%))	Pre-DMFT scores (median)	DMFT scores after 6 months (median)
Acute myelogenous leukemia	19 (52.8)	7.0	8.0
Aplastic anemia	4 (10.3)	7.0	7.5
Myelodysplastic syndrome	1 (2.8)	3.0	19.0
Acute lymphocytic leukemia	5 (13.9)	5.0	8.0
NK cell lymphoma	1 (2.8)	11.0	12.0
Myelofibrosis	1 (2.8)	4.0	4.0
Multiple myeloma	3 (8.3)	9.0	14.0
B cell lymphoma	1 (2.8)	3.0	9.0
Lenfoblastic lymphoma	1 (2.8)	4.0	4.0
Total	36 (100.0)	5.0	8.0 ($P<0.001$)

DMFT=Decayed, missing, filled teeth; Nk=Neutral killer

Table 2: Distribution of the D-M-F components pre and posttreatment

	D (*n* (%))	M (*n* (%))	F (*n* (%))	Total (*n* (%))
Pretreatment	80 (31.6)	133 (52.6)	40 (15.8)	253 (100.0)
Posttreatment	51 (16.0)	173 (54.4)	94 (29.6)	318 (100.0)

D-M-F=Decayed, missing, filled

Discussion

Significant progress in medical management of cancer patients has been reported in recent years.[7,17] Improvements in diagnostic techniques and emphasis on early cancer detection have led to an increase in posttreatment life expectancy. As a result, it has become more common for dentists to treat patients who are currently undergoing or who have previously undergone treatment for cancer.[7] Treatment options for cancer patients include chemotherapy, radiotherapy, HSCT, surgical excision, or a combination of these procedures. Ideally, a dentist should be consulted for dental management before the initiation of cancer therapy, since good oral health is considered to be one of the most important components in improving mortality and morbidity rates. The optimal goal is to eliminate any potential dental focus of infection before cancer therapy begins and to maintain dental health during and after treatment.[18]

The oral cavity has been well documented as a source of septicemia in leukemia patients.[19,20] Rates of HSCT recipients with at least one oral infection that required treatment prior to transplantation have been reported to range from 29-72%.[9,12,13] In our study, 34 of the 36 patients had at least one potential focus of infection prior to HSCT.

HSCT patients are usually pancytopenic before and immediately after transplantation and neutropenic for 6-12 months after engraftment.[21] During this time, oral infection may result in severe consequences. In view of the serious consequences of bacteremia and septicemia, it is widely accepted that a pre-HSCT dental evaluation should be conducted, including both clinical and radiographical examination, a complete medical and dental history, evaluation of the patient's level of oral hygiene and dental awareness, an assessment of the patient's motivation, and ability to perform effective oral hygiene measures.[22] In line with the recommendations of CDC's Guideline for Preventing Opportunistic Infection Among Hematopoietic Stem Cell Transplantation Recipients,[16] the patients in our study underwent detailed clinical and radiographic evaluation, including orthopantomographs and, if necessary, bitewing and periapical radiographs. Baseline dental and periodontal health was recorded, and any existing oral pathosis was eliminated to the greatest extent possible. Our dental treatment protocol included restoration of all active carious lesions, treatment of periodontal infections and extraction of any teeth with advanced periodontal disease or periapical infection, semi-retained third molars, and teeth with infected root fragments. Retained roots and fully impacted teeth with no clinical or radiological symptoms were left in place. Patients were also instructed in oral hygiene techniques, including tooth brushing and flossing, and advised to use antimicrobial mouth rinse. Moreover, nutritional counseling was provided in order to help reduce the likelihood of dental caries and soft-tissue trauma and minimize the adverse side effects of any xerostomia that might result from HSCT therapy.[22]

In the present study, the DMFT index was used to evaluate the effects of HSCT on dental status. The DMFT is a cumulative index that includes the number of teeth with active caries ('D'), that is, bacterial infection, as well as the number of extractions ('M') and restorations ('F'), which are presumed to represent teeth that were at some point affected by dental caries. It is important to distinguish between the DMFT's 'M' and 'F' components, which are historical markers of the presence of past disease, and the 'D' component, which represents active disease, and to keep in mind that DMF rates do not provide a true measure of caries prevalence, but in fact, overestimate the prevalence of active caries.

Despite the counselling provided to patients in the present study regarding the importance of oral hygiene, DMFT scores increased significantly after HSCT treatment. It is possible that, patients ignored dental hygiene instructions and/or that the increase in DMFT scores was a result of xerostomia, one of the side effects of chemotherapy.

Studies have shown that oral and periodontal assessment and management reduce the risks of infection and fever associated with oral complications.[11,23,24] A study carried out by Melkos *et al*.,[3] with 58 patients, found a lower rate of complications among patients who received dental treatment before HSCT compared to those who did not receive dental treatment. In our study, the first step of the pre-HSCT dental treatment protocol was to motivate and instruct patients (and their parents) in maintaining an appropriate level of oral hygiene. Instruction in oral hygiene consisted of more than simply telling patients to brush their teeth; rather, it included a demonstration of the specific type of toothbrush to be used, the method of brushing and flossing, and the areas to be reached.[25] All the patients are instructed to brush their teeth with fluoride toothpaste after each meal and at bedtime, along with flossing once a day. Besides, they are advised to clean their tongue gently with a toothbrush or tongue scraper in order to keep their mouth as clean as possible.

Leukocytopenia associated with cancer treatment may increase susceptibility to orogenic bacteremia, eventually causing sepsis and even death. Although many cancer therapy protocols recommend the cessation of all oral hygiene procedures during this period, several authorities state that the risk of plaque-associated bacteremia requires

the continuation of gentle oral hygiene measures during therapy. This may include the wiping of teeth with cotton swabs or sponges and/or the use of brushing sticks dipped in an antimicrobial agent.[26,27]

For optimal transplantation management, appropriate patient selection must be accompanied by an optimal dental evaluation, pretreatment elimination of all infection sources, prompt management of complications during the immunosuppression period and regular posttransplantation follow-up.[3,28-31] In addition, gentle and frequent professional removal of dental plaque and calculus is often advised in order to maintain optimal oral hygiene and oral health. Long-term oral sequelae such as rampant caries can be prevented by regular dental check-ups, fluoride regimens, and the encouragement of home care oral hygiene. The successful achievement of this preventive period depends, to a large extent, on the compliance of the patient. The most critical issue is to keep the oral cavity as clean as possible. In the literature, it is reported that mouth rinses are widely used as an adjunct to maintain oral hygiene.[23,32] Fluoridated mouth rinses with a fluoride concentration of 0.05% is optimal for regular use.[33] Also, xylitol, which is a naturally occurring, low calorie sugar substitute with anticariogenic properties, is advised for the patients since the ability of plaque to produce acids by the metabolism of sugars is reduced by xylitol. As an important point to decrease dental decays, the presence of fluoride or xylitol in the mouthrinse is contributed to the reduction of *Streptococcus mutans* in plaque.[34] The ultimate goals of all these efforts is to reduce the incidence and frequency of oral complications, improve patient comfort, and help reduce the overall cost of care.

Conclusions

This study found that DMFT scores increased following chemotherapy and HSCT, indicating that HSCT patients are at a higher risk of infection since the oral cavity can act as the site of origin for dissemination of pathogenic organisms to distant body sites, especially in immunocompromised hosts such as patients suffering from malignancies, diabetes, or rheumatoid arthritis; or having corticosteroid or other immunosuppressive treatment. Within the limitations of this preliminary study that was limited by a small number of subjects, our findings emphasize the need for dental examinations as an integral part of examination and treatment planning for patients undergoing HSCT and chemotherapy.

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