Dental Care of the Pediatric Cancer Patient

Marcio A. da Fonseca, DDS, MS

Dr. da Fonseca is clinical associate professor, Department of Orthodontics and Pediatric Dentistry, University of Michigan School of Dentistry, Ann Arbor, Mich.
Correspond with Dr. da Fonseca at marcio@umich.edu

Abstract

Although the rate for childhood cancer has remained relatively stable for the past 2 decades, there have been drastic declines in mortality due to early diagnosis and improvements in therapy. Now over 75% of children diagnosed with cancer survive more than 5 years. The pediatric dental professional plays an important role in the prevention, stabilization, and treatment of oral and dental problems that can compromise the child's health and quality of life before, during, and after the cancer treatment. This manuscript discusses recommendations for the dental care of the pediatric oncology patient. (*Pediatr Dent.* 2004;26:53-57)

KEYWORDS: CHILDHOOD CANCER, ACUTE LYMPHOID LEUKEMIA, PEDIATRIC DENTISTRY, DENTAL CARE, PEDIATRIC ONCOLOGY

Received July 11, 2003 Accepted August 11, 2003

Cancer is the leading cause of disease-related fatalities for children between 0 and 14 years of age in the United States, affecting approximately 1 in 7,000 children every year.[1] The incidence is greatest in the first year of life, with a second peak at 2 to 3 years of age, followed by a decline until age 9 and then steadily increasing through adolescence.[1] Boys are more affected than girls, except in the first year of life, while white children show a 30% higher frequency than blacks, particularly during the first 5 years of life.[1] Acute lymphoid leukemia (ALL) is the most common malignancy (24% of all childhood malignancies), followed by central nervous system (CNS) tumors (22%) and sarcomas.[1-2] In the 1990s, 3-year survival rates exceeded 80% and 5-year survival was beyond 75% as a result of improvement in treatment.[1]

Unfortunately, the medical profession's lack of understanding of ways to modify the molecular mechanisms that occur during a malignant transformation has hindered the development of selective and highly effective cancer therapy, which is still largely empirical. The multimodality approach uses surgery and radiotherapy to control local disease and chemotherapy to eradicate systemic disease. The development and use of chemotherapy have evolved from clinical experience, with the goal to interfere with the synthesis or function of the vital nucleic acids in all cells.[2] The objective of radiation therapy is to cause DNA damage in cancerous cells, with minimal harm to adjacent tissues, which is critical in pediatric patients.[3] Rapidly dividing cells are more sensitive and show earlier cell death than regularly dividing cells, with the nondividing ones being insensitive to radiation.

Radiotherapy is given over a number of weeks in a series of equal-sized fractions, usually spaced by 24 hours to allow for repair of the normal tissues and positively affect the radioresponsiveness of tumors.[3] The total dose required to achieve local tumor control depends on the tumor type, amount of radiation given at each session, and overall number of treatments.[3] Although improvements in chemotherapy and ionizing radiation have led to less radical and less mutilating surgical intervention, surgery may still be necessary for initial staging of a tumor, biopsies, resection, and second- or third-looks. Immunotherapy uses leukocytes, monoclonal antibodies, and cytokines for tumor destruction with potential for target specificity and, hence, may spare children of the major side effects seen currently with standard oncology therapies. The acute and long-term side effects have been discussed elsewhere and will not be reviewed here.[4-5]

ALL accounts for about 75% of all childhood leukemias with a peak incidence at 4 years of age.[6] The most common signs and symptoms are anorexia, irritability, lethargy, anemia, bleeding, petechiae, fever, lymphadenopathy, splenomegaly, and hepatomegaly. Bone pain and arthralgias, caused either by leukemic infiltration of the perichondral bone or joint or by leukemic expansion of the marrow cavity, may occur, leading the child to present with a limp or

refusal to walk.[6] The most common head, neck, and intraoral manifestations of ALL at the time of diagnosis are lymphadenopathy, sore throat, laryngeal pain, gingival bleeding, and oral ulceration.[7] The overall cure rate for childhood ALL is about 80%. Patients who relapse during treatment are given intensive chemotherapy followed by bone marrow transplant. The treatment of ALL is based on clinical risk and is usually divided in four phases:

1. Remission induction—generally lasts 28 days and consists of 3 or 4 drugs (eg, vincristine, prednisone, and L-asparaginase), with a 95% success rate. Achievement of remission is a known pre-requisite for prolonged survival.
2. CNS preventive therapy/prophylaxis—CNS can act as a sanctuary site for leukemic infiltrates because systemically administered chemotherapeutic drugs are not able to cross the blood-brain barrier. Cranial irradiation and/or weekly intrathecal injection of a chemotherapeutic agent, usually methotrexate, are used. This presymptomatic treatment can be done in each phase as well.
3. Consolidation or intensification—designed to minimize the development of drug cross-resistance through intensified treatment, in an attempt to kill any remaining leukemic cells.
4. Maintenance—aimed to suppress leukemic growth through continuous administration of methotrexate and 6-mercaptopurine. The optimal length of this phase has not been established yet, but usually lasts 2.5 to 3 years.

Despite the current understanding that optimal oral health of the child means lower risks of complications during cancer therapy and lower hospital costs, many medical teams and dental clinicians still use outdated approaches to oral and dental care. This manuscript discusses contemporary recommendations for management of the pediatric cancer patient in the dental setting.

Recommendations for dental care

Oral and dental infections may complicate the oncology treatment as well as delay it, leading to morbidity and an inferior quality of life for the child. Early and radical dental intervention reduces the frequency of problems, minimizing the risk for oral and associated systemic complications.[4,8-10] Therefore, the dental consultation on a newly diagnosed patient should be done at once so that enough time is available for care to be completed before the cancer therapy starts. Every patient should be dealt with on an individual basis, and appropriate consultations with physicians and other dental specialists should be sought before dental care is instituted.[4]

The patient's medical history

The pediatric dentist should gather information about the underlying disease, time of the diagnosis, modalities of treatment the patient has received since the diagnosis (chemotherapy, radiotherapy, surgeries, etc.), and complications, including relapses. Hospitalizations, emergency room visits, infections (both oral and systemic), current hematological status, allergies, medications, and a review of systems (heart, lungs, kidneys, etc.) should be noted.

Today, most patients have a central line, which is an indwelling catheter inserted into the right atrium of the heart, useful for obtaining blood samples and administering chemotherapeutic agents, among others. They can be partially implanted (eg, Broviac, Hickman catheters) or subcutaneously implanted (eg, MediPort, Portacath, BardPort) and their presence dictates the use of antibiotics against endocarditis, even if the patient is already using antibiotics for prevention of systemic infections due to their immunosuppression.

The patient's hematologic status

Prolonged bleeding in childhood cancer may be caused by chemotherapy-induced myelosuppression, certain medications, and disorders of clotting and platelets related to the baseline disease. The normal platelet count is between 150,000 to 400,000/mm^3 but clinically significant bleeding is unlikely to occur with a level of >20,000/mm^3 in the absence of other complicating factors.[11] Trauma associated with oral function and damage to the mucosa, such as in herpetic infections, increase the risk of bleeding.[4] Particular attention should be paid to patients with coagulation disorders and liver tumors or liver dysfunction because they are at high risk for prolonged postoperative bleeding.[11] In those cases, additional blood tests should be ordered such as the activated partial thromboplastin time, which measures the intrinsic and common pathways of coagulation, and the prothrombin time, which evaluates the extrinsic and common pathways.[11,12] Their normal levels vary from lab to lab.

The neutrophils are the body's first line of defense, therefore the incidence and severity of infection are inversely related to their number. When the absolute neutrophil count is <1,000/mm^3, elective dental work should be deferred because the risk for development of infections increases greatly.[13]

Oral hygiene, diet, and caries prevention

Routine oral care is important to reduce the incidence and severity of oral sequelae of the treatment protocol, therefore aggressive oral hygiene should be done throughout the entire oncology treatment, regardless of the child's hematological status.[4,8-10,12-19] Many dental and medical professionals still erroneously believe that tooth-brushing increases the risk of bacteremia and bleeding, and advocate the discontinuation of oral hygiene with a regular toothbrush when the child is thrombocytopenic and/or neutropenic. Thrombocytopenia should not be the sole determinant of oral hygiene, as patients are able to brush without bleeding at widely different levels of platelet count.[15] Most importantly, there is evidence that patients

who do intensive oral care have a reduced risk of developing moderate/severe mucositis, without causing an increase in septicemia and infections in the oral cavity.[4,17-18]

A regular soft toothbrush or an electric brush used at least twice daily is the most efficient means to reduce the risk of significant bleeding and infection in the gingiva. [4,8,10,15-16] Sponges, foam brushes, and supersoft brushes cannot provide effective mechanical cleansing due to their softness; therefore, they should be used only in cases of severe mucositis when the patient cannot tolerate a regular brush.[15-16,19] Brushes should be air dried between uses and a toothpaste without heavy flavoring agents should be considered because they can irritate the tissues.[19] During neutropenic periods, the use of toothpicks and water-irrigating devices should be avoided because they may break the integrity of the tissues, creating ports of entry for microorganism colonization and bleeding. Ultrasonic brushes and dental floss can be used if the patient is properly trained.[19]

Patients who present poor oral hygiene or periodontal disease can use chlorhexidine rinses daily until the gingival health has been restored or until the mucosa shows signs of the initial stages of mucositis. At that point, rinses containing alcohol should be avoided because they can dry the mucosa and bring discomfort to the patient. Periodontal infection is a major concern because colonizing organisms have been shown to lead to bacteremias.[4]

The oncology child may be at high risk for dental caries from a dietary standpoint for a number of reasons. The caretakers may indulge the child with frequent unhealthy snacks. The patients may also be prescribed daily nutritional supplements rich in carbohydrate to maintain or gain weight such as Pediasure. Furthermore, many oral pediatric medications contain high amounts of sucrose (eg, nystatin). Despite the fact that nystatin is often prescribed, it cannot be recommended for prophylaxis and prevention of *Candida* infections in immunodepressed patients because its effect is similar to that of a placebo on fungal colonization and inferior to fluconazole in the prevention of invasive fungal infection and colonization.[4,20] It is important to make caretakers and the medical team aware of this risk factor so that medications are used in a manner that minimizes the caries risk. For example, children should not be allowed to fall asleep immediately after rinsing with nystatin or a clotrimazole troche that is not sugar free. Vomiting is often seen as a side effect of the cancer therapy, so the patient should rinse after emesis episodes with tap water or any bland solutions to remove the gastric acid which is irritating to the oral tissues and may cause enamel decalcification. Fluoride supplements and neutral fluoride rinses or gels are indicated for those patients who are at risk for caries.

Identification of existing and potential sources of infections and dental treatment

The patient's dental history should be reviewed, and a thorough examination of the head, face, neck, intraoral soft and hard tissues should be performed, complemented by radiographs when indicated. If spontaneous gingival bleeding is present, the physician must be notified because it may be a sign of internal hemorrhage. Some patients may complain of paresthesias caused by leukemic infiltration of the peripheral nerves. Others may report dental pain mimicking irreversible pulpitis in the absence of a dental/periodontal infection. This can be a side effect of vincristine and vinblastine,[2] commonly used chemotherapeutic agents.[4] In this case, the patient should avoid situations that exacerbate the discomfort, such as thermal stimuli or sweets, and analgesics should be prescribed for pain control. Reassurance that the pain will disappear within a few days after the cessation of the causative chemotherapy is important.

Patients may also complain of dental hypersensitivity usually brought on by cold or hot stimuli. The mechanism for the sensitivity is not well understood and can be treated with topical fluoride or a desensitizing toothpaste.[4] Furthermore, the clinician should be familiar with the possible acute and long-term oral/dental side effects of cancer therapy to anticipate problems, and provide expert diagnosis and treatment.[4-5]

The patient's blood counts normally start falling 5 to 7 days after the beginning of each treatment cycle, staying low for approximately 14 days before rising again. However, these time guidelines may vary from protocol to protocol; thus, it is important for the pediatric dentist to be familiar with the patient's cancer treatment plan. When time is limited for dental care before the oncology therapy starts, treatment priorities should be infections, extractions, periodontal care and sources of irritation before the treatment of carious teeth, root canal therapy for permanent teeth, and replacement of faulty restorations. Temporary restorations can be placed and nonacute dental treatment can be delayed until the patient's health is stabilized.[4,12,21]

Overall, routine dental care can be done when the ANC is >1,000/mm and platelet count is >50,000/mm^3. Some authors[4] recommend that endocarditis prophylaxis be prescribed when the ANC is between 1,000 and 2,000/mm^3 and optional platelet transfusions be considered pre- and 24 hours postoperatively when the level is between 40,000 and 75,000/mm.[3] During immunosuppression, all elective dental procedures should be avoided. In an emergency situation, the dentist should consult with the medical team, which may choose to prescribe platelet transfusions and additional antibiotic coverage, despite the lack of scientific evidence of its usefulness.[12]

When there is time prior to the initiation of cancer therapy, dental scaling and prophylaxis should be done, defective restorations repaired and teeth with sharp edges polished. Although there have been no studies to date that address the safety of performing pulp therapy in primary teeth prior to the initiation of chemotherapy and/or radiotherapy, it is prudent to provide a more radical treatment in the form of extraction to minimize the risk for oral and systemic complications. Despite the high rate of success of

pulpotomies and pulpectomies in healthy subjects, pulpal/periapical infections during immunosuppression periods can have a significant impact on cancer treatment.[4] Teeth that have already been pulpally treated and are clinically and radiographically sound present no threats. Symptomatic nonvital permanent teeth should receive root canal therapy at least 1 week before initiation of cancer therapy. If that is not possible, extraction is indicated. Endodontic treatment of permanent teeth with asymptomatic periapical involvement can be delayed if the patient is neutropenic.[12,21] During immunosuppression, swelling and purulent exudate may not be present, masking some of the classical signs of odontogenic infections, leaving them clinically undetected.[12,22] In this situation, radiographs are vital to determine periapical pathologies.

Fixed orthodontic appliances and space maintainers should be removed if the patient has poor oral hygiene or the treatment protocol carries a risk for the development of moderate to severe mucositis. Appliances can harbor food debris, compromise oral hygiene, and act as mechanical irritants, increasing the risk for secondary infection. However, a few contemporary protocols, particularly for ALL, may pose very little risk for the development of mucositis; thus, removing orthodontic appliances may not be necessary for patients who have good oral hygiene. Removable appliances and retainers may be worn as long as tolerated by the patient who shows good oral care.

Partially erupted molars can become a source of infection due to pericoronitis, so the overlying gingival tissue should be excised if the dentist believes it is a potential risk.[22] Loose primary teeth should be left to exfoliate naturally and the patient counseled not to play with them to avoid bacteremia. If the patient cannot comply with this recommendation, the teeth should then be removed. Impacted teeth, root tips, partially erupted third molars, teeth with periodontal pockets >5 mm, teeth with acute infections, and nonrestorable teeth should be removed ideally 3 weeks before cancer therapy starts to allow adequate healing.[12,14] If that is not possible, other authors suggest at least 4 to 7 days.[21,22]

If a permanent tooth cannot be extracted for medical reasons at that point in time, the pediatric dentist can consider amputation of the crown above the gingiva, followed by initial root canal treatment with antimicrobial medicament sealed in the root canal chamber. Antibiotics should follow for 7 to 10 days afterwards with the extraction subsequently done when the patient's hematological status is normal.[4] Particular attention should be given to extraction of permanent teeth in patients who will receive or have received radiation to the face because of the risk of osteoradionecrosis. Surgical procedures must be as atraumatic as possible, with no sharp bony edges remaining and satisfactory closure of the wounds.[4,12,14,22] A platelet count of 50,000/mm^3 is advisable for minor surgeries (eg, simple extractions), whereas a minimum level of 100,000/mm^3 is desirable for major surgeries (eg, removal of impacted teeth).[11]

The pediatric dentist should be ready to provide local measures to control bleeding such as pressure packs, sutures, use of a gelatin sponge, topical thrombin or microfibrillar collagen. If local measures fail, the physician must be contacted immediately. For patients who need a platelet transfusion before dental treatment, it is important to note that the peak concentration of platelets is achieved 45 to 60 minutes following transfusion.[11]

When the patient is in the maintenance phase of treatment and the overall prognosis is good, it is likely that his/her health status is close to normal. Dental procedures can be done routinely, but not before checking the blood count and prescribing antibiotics for SBE prophylaxis if a central line is in place. Orthodontic treatment may start or resume after completion of all therapy and after at least a 2-year disease-free survival.[23] By then, the risk of relapse is decreased and the patient is no longer using immunosuppressive drugs. However, the clinician must assess any dental developmental disturbances caused by the cancer therapy, especially in children treated under 6 years of age.[4,5,24] A panoramic radiograph should be obtained every 12 to 18 months to monitor the dental changes and plan dental rehabilitation accordingly.

Dahllof et al[24] described the following strategies to provide orthodontic care for patients with dental sequelae:

1. use appliances that minimize the risk of root resorption;
2. use lighter forces;
3. terminate treatment earlier than normal;
4. choose the simplest method for the treatment needs;
5. do not treat the lower jaw.

However, specific guidelines for orthodontic management, including optimal force and pace, remain undefined.[19] The role of growth hormone in the development of the craniofacial structures in pediatric cancer patients is not fully established.

Conclusions

The key to success in maintaining a healthy oral cavity during cancer therapy is patient compliance. Consequently, it is vital to educate the caretaker and child about the importance of oral care to minimize discomfort and maximize the chances for a successful outcome. Discussion should also include the deleterious effects of indulging the child with unhealthy foods, the potential cariogenicity of pediatric medications and nutritional supplements, and late effects of the conditioning regimen on the craniofacial growth and dental development. It is important for the pediatric dentist to realize that these issues are rarely discussed by the physicians and nurses involved in the patient's care. Furthermore, the participation of a pediatric dentist in the hematology/oncology team is of irrefutable importance.

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