Guideline on Dental Management of Pediatric Patients Receiving Chemotherapy, Hematopoietic Cell Transplantation, and/or Radiation

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Purpose

The American Academy of Pediatric Dentistry recognizes that the pediatric dental professional plays an important role in the diagnosis, prevention, stabilization, and treatment of oral and dental problems that can compromise the child's quality of life before, during, and after the cancer treatment. Dental intervention with certain modifications must be done promptly and efficiently, with attention to the patient's medical history, treatment protocol, and health status.

Pediatric patients undergoing chemotherapy and/or radiotherapy for the treatment of cancer or in preparation for hematopoietic cell transplantation (HCT) may present many acute and long-term side effects in the oral cavity. Furthermore, because of the immunosuppression they experience, any existing or potential oral/dental infections and trauma can compromise the medical treatment, leading to morbidity, mortality, and higher hospitalization costs. It is also imperative that the pediatric dentist be familiar with the oral manifestations of the patient's underlying condition and the treatment differences between patients undergoing chemotherapy only and those who will receive an HCT.

Methods

This guideline is based on a review of the current dental and medical literature related to dental management of pediatric patients receiving chemotherapy, hematopoietic cell transplantation, and/or radiation. A MEDLINE search was conducted using the terms "pediatric cancer", "pediatric oncology", "hematopoietic cell transplantation", "bone marrow transplantation", "mucositis", "stomatitis", "chemotherapy", "radiation therapy", "acute effects", "long-term effects", "dental care", "pediatric dentistry", and "clinical practice guidelines". Expert opinions and best current practices were relied upon when sufficient scientific data were not available.

Background

The most frequently documented source of sepsis in the immunosuppressed cancer patient is the mouth; therefore, early and radical dental intervention, including aggressive oral hygiene measures, reduces the risk for oral and associated systemic complications.[1-13] In a consensus conference on oral complications of cancer therapies sponsored by the National Institutes of Health in 1989, the most important recommendations were that all patients with cancer should have an oral examination before initiation of the oncology therapy, and that treatment of pre-existing or concomitant oral disease was essential to minimize oral complications in this population.[6] The underlying success in maintaining a healthy oral cavity during cancer therapy is patient compliance. Thus, the child and the caretakers should be educated regarding the possible acute side effects and the long-term sequelae in the oral cavity.[1-6,8,14,15] Younger patients present more oral problems than adults.[2] Because there are many oncology and HCT protocols, 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.[5]

Recommendations

Dental and oral care before the initiation of cancer therapy

Objectives

The objectives of a dental/oral examination before cancer therapy starts are two-fold:

1. to identify and stabilize or eliminate existing and potential sources of infection, local irritants, and irregular surfaces that may complicate the cancer therapy and HCT—without needlessly delaying the cancer treatment or inducing complications; and
2. to educate the patient and caretakers about the importance of optimal oral care in order to minimize oral

problems/discomfort during and after treatment and about the possible acute and long-term effects of the therapy in the craniofacial complex.

Initial evaluation

Medical history review: should include, but not be limited to, type of cancer, treatment protocol, medications, allergies, and immunosuppression status. For HCT patients, include type of transplant, conditioning protocol, and graft versus host disease (GVHD) prophylaxis. The presence of an in-dwelling venous catheter (ie, central line) dictates the need for endocarditis prophylaxis following the American Heart Association (AHA) recommendations[16]; however, this recommendation is empirical.[5,10]

Dental history review: includes information such as habits, trauma, symptomatic teeth, previous care, preventive practices, etc.

Oral/dental assessment: should include thorough head, neck, and intraoral examinations, oral hygiene assessment and training, and radiographic evaluation based on history and clinical findings.

Preventive strategies

Oral hygiene: Oral hygiene includes brushing of the teeth and tongue 2 to 3 times daily with regular soft brush or electric toothbrush, regardless of the hematological status.[4,5,8,9,13,17] Ultrasonic brushes and dental floss should be allowed only if the patient is properly trained.[1,8] Patients with poor oral hygiene and/or periodontal disease can use chlorhexidine rinses daily until the tissue health improves or mucositis starts. The high alcohol content can cause discomfort and dehydrate the tissues.

Diet: Dental practitioners should encourage a non-cariogenic diet and advise caretakers about the high cariogenic potential of dietary supplements rich in carbohydrate and oral pediatric medications rich in sucrose.

Fluoride: Preventive measures include the use of fluoridated toothpaste, fluoride supplements if indicated, neutral fluoride gels/rinses, or applications of fluoride varnish for patients at risk for caries and/or xerostomia. A brush-on technique is the most convenient technique making patients more compliant.[8]

Trismus prevention/treatment: Patients who receive radiation therapy to the masticatory muscles may develop trismus. Thus, daily stretching oral exercises/physical therapy should start before radiation is initiated and continue throughout treatment. Therapy also may include prosthetic aids to reduce the severity of fibrosis, trigger-point injections, analgesics, muscle-relaxants, and other pain management strategies.[3,5,10]

Reduction of radiation to healthy oral tissues: In cases of radiation to the head and neck, the use of lead-lined stents, prostheses, and shields, as well as beam-sparing procedures, should be discussed with the radiation oncologist.

Education: Patient/caretaker education includes the importance of optimal oral care in order to minimize oral problems/discomfort during and after treatment and the possible acute and long-term effects of the therapy in the craniofacial complex.

Dental care

Hematological considerations:

1. Absolute neutrophil count (ANC)
   - >1,000/mm^3: no need for antibiotic prophylaxis.[10] However, some authors suggest[5] that antibiotic coverage (AHA recommendations) may be prescribed when the ANC is between 1,000 and 2,000/mm^3. If infection is present or unclear, more aggressive antibiotic therapy may be indicated and should be discussed with the medical team.
   - <1,000/mm^3: defer elective dental care until the ANC rises. In dental emergency cases, discuss antibiotic coverage beyond endocarditis prophylaxis with medical team before proceeding with treatment. The patient may need hospitalization for dental management.[12]
2. Platelet count[5,10]
   - >75,000/mm^3: no additional support needed but be prepared to treat prolonged bleeding by using sutures, hemostatic agents, pressure packs, gelatin foams, etc.
   - 40,000 to 75,000/mm^3: platelet transfusions may be considered pre- and 24 hours post-operatively
   - <40,000/ mm^3: defer care. In dental emergency cases, contact physician before proceeding. Consider platelet transfusion and hospital admission for treatment.
3. Other coagulation tests may be in order for individual patients.

Dental procedures:

1. In general terms, most oncology/hematology protocols (exclusive of HCT, which will be discussed later) are divided into phases (cycles) of chemotherapy, in addition to other therapies (radiotherapy, surgery, etc). The patient's blood counts normally start falling 5 to 7 days after the beginning of each cycle, staying low for approximately 14-21 days, before rising again to normal levels for a few days until the next cycle begins. Ideally, all dental care should be completed before cancer therapy is initiated. But, when that is not feasible, temporary restorations can be placed and non-acute dental treatment can be delayed until the patient's hematological status is stable, usually in the few days between treatment cycles.[5,8,10,11]
2. Prioritizing procedures: When all dental needs cannot be treated before cancer therapy is initiated, priorities should be infections, extractions, periodontal care (eg, scaling, prophylaxis), and sources of tissue irritation before the treatment of carious teeth, root canal therapy for permanent teeth, and replacement of faulty restorations.[10] The risk for pulpal infection and pain determine which

carious lesions should be treated first.[8] Incipient to small caries can be treated with fluorides and sealants until definitive care can be accomplished.[5] It is also important to be aware that the signs and symptoms of periodontal disease can be decreased in immunosuppressed patients.[5]

3. Pulp therapy in primary teeth: 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, many clinicians choose to provide a more radical treatment in the form of extraction because pulpal/periapical/furcal infections during immunosuppression periods can have a significant impact on cancer treatment and become life-threatening.[5,8,11] Teeth that already have been treated pulpally and are clinically and radiographically sound present minimal risk.
4. Endodontic treatment in permanent teeth: Symptomatic non-vital permanent teeth should receive root canal treatment at least 1 week before initiation of cancer therapy to allow sufficient time to assess treatment success before the chemotherapy.[5,10] If that is not possible, extraction is indicated. Extraction is also the treatment of choice for teeth that cannot be treated by definitive endodontic treatment in a single visit. In that case, the extraction should be followed by antibiotic therapy (penicillin or for penicillin-allergic patients, clindamycin) for about 1 week.[5,10,12] Asymptomatic endodontic needs in permanent teeth can be delayed until the hematological status of the patient is stable.[10,11,18] It is important that the etiology of periapical lesions associated with previously endodontically treated teeth be determined because they can be caused by a number of factors including pulpal infections, inflammatory reactions, apical scars, cysts, and malignant lesions.[8] If a periapical lesion is associated with an endodontically treated tooth and no signs or symptoms of infection are present, there is no need for retreatment or extraction since the radiolucency likely is due to an apical scar.[18]
5. Orthodontic appliances and space maintainers: Appliances should be removed if the patient has poor oral hygiene and/or the treatment protocol or HCT conditioning regimen carries a risk for the development of moderate to severe mucositis, except for smooth appliances such as band and loops and fixed lower lingual arches.[1,8] Removable appliances and retainers that fit well may be worn as long as tolerated by the patient who shows good oral care.[5,8,19] If band removal is not possible, vinyl mouth guards or orthodontic wax should be used to decrease tissue trauma.[8]
6. Periodontal considerations: Partially erupted molars can become a source of infection because of pericornitis. The overlying gingival tissue should be excised if the dentist believes it is a potential risk and if the hematological status permits.[8,10]
7. Extractions: There are no clear recommendations for the use of prophylactic antibiotics for extractions. Recommendations generally have been empiric or based on anedoctal experience. 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.[5,8,10-12] If there is documented infection associated with the tooth, antibiotics, ideally chosen with the benefit of sensitivity testing, should be administered for about 1 week.[5,8,10,12]
   - Loose primary teeth should be left to exfoliate naturally and the patient should be counseled to not play with them in order to avoid bacteremia. If the patient cannot comply with this recommendation, the teeth should be removed if the hematologic parameters allow.
   - Impacted teeth, nonrestorable teeth, root tips, teeth with periodontal pockets >6 mm, and teeth exhibiting acute infections, significant bone loss, involvement of the furcation, or mobility should be removed ideally 2 weeks (or at least 7 to 10 days) before cancer therapy starts to allow adequate healing.[1,5,8,10,11]
   - Some practitioners prefer to extract all third molars that are not fully erupted, particularly prior to HCT, while others favor a more conservative approach, recommending extraction of third molars at risk for pulpal infection or those associated with significant periodontal infection, including pericoronitis.[9]
   - If a permanent tooth cannot be extracted for medical reasons (eg, severe thrombocytopenia), then the crown should be amputated above the gingiva and root canal therapy should be initiated on the remaining root fragment to minimize the risk of disseminating infection through the systemic circulation. The root canal chamber should be sealed with an antimicrobial medicament.[5] Antibiotics should follow for 7 to 10 days afterwards with the extraction subsequently performed when the patient's hematological status is normal.[5]

Dental and oral care during immunosupression periods

Objectives

The objectives of a dental/oral care during cancer therapy are three-fold:

1. to maintain optimal oral health during cancer therapy;
2. to manage any oral side effects that may develop as a consequence of the cancer therapy; and
3. to educate the patient and caretakers about the importance of optimal oral care in order to minimize oral problems/discomfort during treatment.

Preventive strategies

Oral hygiene: Intensive oral care is of paramount importance because it reduces the risk of developing moderate/severe mucositis without causing an increase in septicemia and infections in the oral cavity.[1-12] 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.[8,9,13] Patients should use a soft nylon brush 2 to 3 times daily.[8] Fluoridated toothpaste can be used but, if the patient does not tolerate it during periods of mucositis, it can be discontinued and water or saline solution can be substituted. If moderate to severe mucositis develops and the patient cannot tolerate a regular toothbrush or an end-tufted brush, foam brushes or super soft brushes soaked in aqueous chlorhexidine can be used, although they do not provide efficient cleaning.[9,17] The use of a regular brush should be resumed as soon as the mucositis improves.[8] Brushes should be air-dried between uses.[8] Electric or ultrasonic brushes are acceptable if the patient is capable of using them without causing trauma and irritation.[1,8] If patients are skilled at flossing without traumatizing the tissues, it is reasonable to continue flossing throughout treatment.[8] Toothpicks and water irrigation devices should be avoided when the patient is pancytopenic.[8,10]

Diet: Dental practitioners should encourage a non-cariogenic diet and advise caretakers about the high cariogenic potential of dietary supplements rich in carbohydrate and oral pediatric medications rich in sucrose.

Fluoride: Preventive measures include the use of fluoridated toothpaste, fluoride supplements if indicated, neutral fluoride gels/rinses, or applications of fluoride varnish for patients at risk for caries and/or xerostomia. A brush-on technique is the most convenient technique making patients more compliant.[8]

Lip care: Lanolin-based creams and ointments are more effective in moisturizing and protecting against damage than petrolatum-based products.[8,11]

Education: Patient/caretaker education includes the importance of optimal oral care in order to minimize oral problems/discomfort during treatment and the possible acute and long-term effects of the therapy in the craniofacial complex.

Dental care

Only conservative emergency dental care should be provided during immunosuppression, and only after consultation with the medical team in regards to platelet and antibiotic therapy. Patients who are using plant alkaloid chemotherapeutic agents (eg, vincristine, vinblastine) may present deep, constant pain (mostly in the mandible) in the absence of odontogenic pathology.[5,8,10] The pain resolves with discontinuation of the drugs and no treatment is necessary. The patient should be seen not less often than every 6 months for an oral health evaluation during treatment, preferably in times of stable hematological status and always after reviewing the medical history and the need for endocarditis coverage if a central line is still in place.

Management of oral conditions related to cancer therapies:

Mucositis: Mucositis care remains focused on palliation of symptoms and efforts to reduce the influence of secondary factors on mucositis.[5,10,12] The International Society for Oral Oncology has published guidelines for treatment of mucositis.[20] Most studies do not demonstrate a prophylactic impact of chlorhexidine on mucositis.[7,12]

Oral mucosal infections: The signs of inflammation and infection may be greatly diminished during neutropenic periods. Thus, the clinical appearance of infections may differ significantly from the normal.[1,10] Close monitoring of the oral cavity allows for timely diagnosis and treatment of fungal, viral, and bacterial infections. Prophylaxis with nystatin for fungal infections is not effective.[5,21] Oral cultures and/or biopsies of all suspicious lesions should be performed and prophylactic medications should be initiated until more specific therapy can be prescribed.[1,5,8-12]

Oral bleeding: Oral bleeding occurs due to thrombocytopenia, disturbance of coagulation factors, and damaged vascular integrity. Treatment should consist of local approaches (eg, pressure packs, antifibrinolytic rinses, gelatin sponges) and systemic measures (eg, platelet transfusions).

Dental sensitivity/pain: Tooth sensitivity could be related to decreased secretion of saliva during radiation therapy and the lowered salivary pH.[5,8,10]

Xerostomia: Sugar-free chewing gum, candy, sucking tablets, special dentifrices for oral dryness, saliva substitutes, frequent sipping of water, bland oral rinses, and/or oral moisturizers are recommended.[8,22] Saliva stimulating drugs are not approved for use in children. Fluoride rinses and gels are recommended highly for caries prevention.

Dental and oral care after the cancer therapy is completed (exclusive of HCT)

Objectives

The objectives of a dental/oral examination after cancer therapy ends are two-fold:

1. to maintain optimal oral health; and
2. to educate the patient and caretakers about the importance of optimal oral care in order to minimize oral problems/discomfort after treatment and about the possible acute and long-term effects of the therapy in the craniofacial complex.

Preventive strategies

Oral hygiene: Patients should resume normal tooth brushing 2 to 3 times daily. Brushes should be air-dried between uses.[8] Patients should continue/resume daily flossing.

Diet: Dental practitioners should encourage a non-cariogenic diet and advise caretakers about the high cariogenic potential of dietary supplements rich in carbohydrate and oral pediatric medications rich in sucrose.

Fluoride: Preventive measures include the use of fluoridated toothpaste, fluoride supplements if indicated, neutral fluoride gels/rinses, or applications of fluoride varnish for

patients at risk for caries and/or xerostomia. A brush-on technique is the most convenient technique making patients more compliant.[8]

Lip care: Lanolin-based creams and ointments are more effective in moisturizing and protecting against damage than petrolatum-based products.[8,11]

Education: Patient/caretaker education includes the importance of optimal oral care in order to minimize oral problems/discomfort after treatment and the possible acute and long-term effects of the therapy in the craniofacial complex.

Dental care

Periodic evaluation: The patient should be seen at least every 6 months (sooner if more imperative issues such as xerostomia and trismus are present). Patients who have experienced chronic or severe mucositis should be followed closely for malignant transformation of their oral mucosa (eg, oral squamous cell carcinoma).[23]

Orthodontic treatment: Orthodontic care may start or resume after completion of all therapy and after at least a 2 year disease-free survival when the risk of relapse is decreased and the patient is no longer using immunosuppressive drugs.[19] A thorough assessment of any dental developmental disturbances caused by the cancer therapy must be performed before initiating orthodontic treatment. The following strategies should be considered 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, and (5) do not treat the lower jaw.[24] However, specific guidelines for orthodontic management, including optimal force and pace, remain undefined.

Oral surgery: Oral surgical procedures such as an extraction or excisional biopsy may require pre-operative and post-operative hyperbaric oxygen to avoid osteomyelitis if the patient has had previous cranial radiation therapy to the involved maxillary or mandibular area.

Hematopoietic cell transplantation

Specific oral complications can be correlated with phases of HCT.[8,14,15]

Phase I: Pre-transplantation

The oral complications are related to the current systemic and oral health, oral manifestations of the underlying condition, and oral complications of recent medical therapy.

Dental and oral care before the transplant: Most of the principles are similar to those discussed for pediatric cancer. The 2 major differences are: 1) in HCT, the patient receives all the chemotherapy and/or total body irradiation in just a few days before the transplant, and 2) there will be prolonged immunosuppression following the transplant. Elective dentistry will need to be postponed until immunological recovery has occurred, which may take as long as 9 to 12 months after HCT, or longer if chronic GVHD or other complications are present.[5,8] Therefore, all dental treatment must be completed before the child is admitted in order to eliminate disease that could lead to complications during and after the transplant.

Phase II: Conditioning/neutropenia

The oral complications are related to the conditioning regimen and medical therapies, approximately to day 30 post-transplant.[8] Mucositis, xerostomia, oral pain, oral bleeding, opportunistic infections, and taste dysfunction can be seen. The patient should be followed up closely during the hospitalization period to monitor and treat the oral changes and reinforce the importance of optimal oral care. Dental care usually is not allowed in this phase.

Phase III: Initial engraftment to hematopoietic reconstitution

The intensity and severity of complications begin to decrease normally 3 to 4 weeks after transplantation. Oral fungal infections and herpes simplex virus infection are most notable. Oral GVHD can become a concern for allogeneic graft recipients. A dental/oral examination should be performed and invasive dental procedures, including dental cleanings and soft tissue curettage, should be done only if authorized by the HCT team because of the patient's continued immunosuppression.[8] Patients should be encouraged to continue optimal oral hygiene and avoid a cariogenic diet. Attention to xerostomia and oral GVHD treatment (including topical application of steroids or cyclosporine, and oral psoralen and ultraviolet A therapy) are a must. HCT patients are particularly sensitive to thermal stimuli between 2 and 4 months post-transplant.[8] Topical application of neutral fluoride helps reduce the sensitivity.

Phase IV: Immune reconstitution/ late posttransplantation

After day 100 post-HCT, the oral complications predominantly are related to the chronic toxicity associated with the conditioning regimen, including salivary dysfunction, craniofacial growth abnormalities, late viral infections, oral chronic GVHD, and oral squamous cell carcinoma.[8] Regular dental examinations with radiographs can be performed routinely, but invasive dental treatment should be avoided in patients with profound impairment of immune function.[8] Orthodontic treatment considerations are the same as discussed in the previous section.

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