Oral complications in children with cancer

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ABSTRACT. Background Childhood cancer and its treatment are often associated with significant oral complications. Malignant disease may manifest in the oral region, and aggressive cancer therapy may lead to painful oral mucositis and potentially life-threatening infectious complications. In addition, high-dose chemotherapy, conditioning regimens for haematopoietic stem cell transplantation, and radiation therapy to the head and neck region may cause damage to salivary glands, putting the child at risk of infections, including candidiasis, caries and periodontal diseases. Both chemotherapy and irradiation to the head and neck area may have long-term effects on developing dentofacial structures. This article reviews acute and chronic oral complications in paediatric oncology and recent insights into the pathogenesis of these problems. In addition, the role of dental professionals, within a multidisciplinary approach to the management of these complications, is discussed.

KEYWORDS: Childhood cancer, Oral complications, Mucositis, Late effects, Dental abnormalities.

Introduction

Paediatric dentists and other dental professionals providing dental care to children and adolescents can play an important role in the management of oral complications of cancer and its therapy. Firstly, they can contribute to early diagnosis because malignancies may present with signs and symptoms in the head and neck area. Secondly, once diagnosed most children will undergo aggressive treatment regimens associated with oral complications. Treatment of childhood cancer is performed in specialised cancer centres providing a multidisciplinary setting that ideally includes an experienced dental team. The paediatric dentist may be asked to perform preventative oral and dental care prior to cancer treatment or between chemotherapy cycles. Last and most importantly, he or she should be aware of the need of prevention of late oral complications and the growth and developmental disorders that may manifest in long-term survivors.

This article will briefly review epidemiologic aspects of cancers in children, oral signs and symptoms that may be present and basic principles of current treatment strategies. In addition, acute and chronic complications associated with cancer treatment and preventive and management approaches will be discussed.

Epidemiological considerations of childhood malignancies. In Western countries 1 out of every 500 to 600 children develops childhood cancer before reaching the age of 15 years. The type and distribution of malignancies occurring in children differ markedly from those in adult populations. Leukaemia is by far the most common malignancy in children (about one third of all childhood cancers). In children with Down’s syndrome, the relative risk to develop leukaemia is estimated to be 10-20 times higher than in children without this congenital condition [Goldacre et al., 2004; Ravindranath, 2005]. Acute leukaemia is the most common malignancy in children, approximately 85% of acute lymphoblastic leukaemia (ALL) and 15% acute myeloid leukaemia (AML). It may develop at any age, but the highest frequency is reported in children between 2 and 6 years of age. In boys leukaemia is more frequent than in girls. In addition to leukaemia, tumours of the brain and sympathetic nervous system, the lymphatic system (Hodgkin and non-Hodgkin lymphoma), kidneys, bone and soft tissue are among the most frequently occurring malignancies in childhood.

Current treatment strategies. In the past three decades survival from childhood cancer has improved
remarkably and the overall cure rate currently exceeds 70%. These results have been achieved mainly by the introduction of chemotherapy and the use of high-intensity combination chemotherapy regimens in conjunction with improved supportive care.

Depending on the type of malignancy, other treatment options apart from chemotherapy may include surgery and local irradiation. The radiation dose for solid tumours in the head and neck area (e.g., rhabdomyosarcoma, retinoblastoma, nasopharyngeal carcinoma, and brain tumours) is typically between 45 and 55 Gray (Gy). However, the recognition of the need to control for metastatic disease and pharmacologic advances has resulted in an increasing use of chemotherapy. Nevertheless, radiotherapy to the head and neck area can still form part of the treatment strategy in solid childhood malignancies. In addition, craniospinal irradiation (dose 18-24 Gy) may be indicated to treat leukaemia with central nervous system involvement, whereas prophylactic craniospinal irradiation is no longer performed in most cancer centres. In selected cases haematopoietic stem cell transplantation (HSCT) is indicated. Autologous HSCT (using the patient’s own haematopoietic stem cells) is performed as a rescue after high-dose chemotherapy in therapy-resistant malignancies. Most haematopoietic stem cell grafts, however, are allogeneic and derived from a matched sibling donor, or if not available from an unrelated donor. In the conditioning phase (the different phases of HSCT are reported in Fig. 1), myeloablative, high-dose chemotherapy and/or total body irradiation (TBI) is administered. When given as single-dose TBI, the radiation dose varies from 7 to 12 Gy. The total dose can be up to 14 Gy when TBI is delivered fractionated. Subsequently, the haematopoietic stem cell graft is infused intravenously to the patient (day 0).

Children undergoing HSCT remain highly susceptible to infection and bleeding until successful engraftment occurs marked by increasing peripheral blood cell counts, and have a compromised immune response and healing potential for up to 6-12 months.

**Signs and symptoms of malignant disease in the head and neck area**

In leukaemia, malignant cells compete with the proliferation of normal blood cells in the bone marrow. As a result patients may become anaemic, thrombocytopenic, and develop a lack of functioning peripheral white blood cells. Common symptoms include fatigue, pallor, bruising easily, fever, and bone pain. The disease often manifests in the orofacial...
region [Scully and MacFarlane, 1983]. There may be oropharyngeal pain and local lymph nodes may be swollen. The gingiva may be pale or scarlet red, swollen, bleeds easily, and ulceration or necrosis may be present. In addition, oral mucosal petechiae may develop [Barrett, 1986]. AML may be associated with gingival infiltration and proliferation of malignant cells, resulting in gingival enlargement [Sonis and Sonis, 1981].

Hodgkin lymphoma is generally associated with regional lymph nodes above the diaphragm, and commonly involves cervical or other head and neck nodes. Clinical characteristics of non-Hodgkin lymphoma (NHL) include lymphadenopathy in the Waldeyer ring and other head and neck nodes. NHL can also present extranodally as a tissue mass in the gingiva, the oral mucosa, or in the jaw bones. Patients may complain of bleeding and pain and teeth may become mobile.

The endemic type of Burkitt’s lymphoma is a common childhood malignancy in Africa. It is a rapidly progressing tumour that has a preference to the head and neck region. Most often it presents with swelling.

Sarcomas arising in various tissues may occur in the head and neck of paediatric patients. Rhabdomyosarcoma, a rapidly growing tumour, can be localized in the soft oral tissues, and metastasise to local lymph nodes. In rare cases, Ewing’s sarcoma (a bone tumour) can develop in the mandible and metastasize to the gingiva [McGlumphy et al., 1987]. Jaw lesions associated with Langerhans’ cell histiocytosis can be painful and cause jaw expansion, gingival swelling and “floating teeth”. Most patients, however, are asymptomatic, and one or more irregularly marginated lytic lesions are found on routine radiographs [Egeler and D’Angio, 1995]. Retinoblastoma can involve one or two eyes. Clinically, it can present as a light or whiteness reflected in the pupil.

Epithelial tumours are known to occur late following radiotherapy and potentially following chemotherapy, and may present in the oral mucosa.

Although the majority of children survive childhood cancer, they are at increased risk for development of secondary malignancies.

**Oral complications**

The pathogenesis of oral complications of cancer therapy is complex. It includes direct toxicity to oral tissues, the presence of a diverse oral microflora, and altered local and systemic host defences. The most common acute oral complications are mucositis, infection, hyposalivation, bleeding, and taste disorders, each of which may lead to significant secondary complications and have a negative impact on the quality of life. For example, during immunosuppression the oral cavity can become a major source of potentially life-threatening systemic infections. Oral pain and difficulties with swallowing may result in compromised nutritional state and speech. In addition, there may be psychosocial implications; the mouth is an important organ for finding comfort in young children and children may become depressed and isolated because of the inability to communicate.

**Oral mucositis.** Oral mucositis is a significant acute complication of intensive chemotherapy, myeloablative regimens for HSCT, and head and neck radiation. The condition is characterised by mucosal damage presenting as redness and ulceration (Fig. 2). Mucositis is reported by patients as one of the most painful and debilitating complications significantly reducing their quality of life [Bellm et al., 2000; Rose-Ped et al., 2002]. In addition, it has been established as a dose-limiting toxicity of cancer chemotherapy and can thus directly affect patient survival. Oral mucositis represents a risk factor for systemic infectious complications, and is associated with a significant increase in the duration of hospitalisation and the need for supportive care measures, leading to higher costs [Elting et al., 2003]. The first clinical signs and symptoms emerge 7-10 days after the start of chemotherapy and 2 to 3 weeks following radiation.

![Intra-oral photograph showing ulcerative oral mucositis during haematopoietic stem cell transplantation. The patient needed opioids for pain management. In addition, the lesion represents a portal of entry for microorganisms to translocate into the blood stream. This picture is kindly provided by Dr. S.T. Sonis.](image-url)
therapy. Labial and buccal mucosa, tongue, floor of mouth, and soft palate are usually more severely affected than keratinised tissues such as the hard palate and the attached gingiva.

Risk factors have not been clearly identified. Young children as well as elderly people are considered to be most susceptible. Generally the condition resolves more rapidly in children than in adults. Potential variables influencing mucositis include genetic polymorphisms, gender, body mass, pre-existing oral condition, level of oral hygiene, quantitative or qualitative salivary alterations and mechanical trauma induced by mastication [reviewed by Barasch and Peterson, 2003]. Acute Graft versus Host Disease (GvHD) may cause oral lesions occurring simultaneously or overlapping with mucositis, but should be considered as a separate condition (see below).

The pathogenesis is not completely understood. It is clear that mucositis is not solely the result of non-specific toxic effects of chemotherapy on dividing mucosal epithelial cells. Virtually all of the cells and tissues that comprise the oral mucosa are affected in the loss of integrity of the mucosal barrier [Sonis, 1998; Sonis et al., 2004]. Secondary infection may exacerbate the severity of mucositis, and in neutropenic patients complications may arise from bacteria penetrating through ulcerated mucosa into the bloodstream. Healing of mucositis occurs spontaneously. In myelosuppressed patients the condition usually resolves concomitantly with bone marrow recovery. However, despite normal appearance, healed oral mucosa is more susceptible for mucositis to develop as a result of subsequent chemotherapy or radiation.

Oral infection. A normal healthy mouth harbours hundreds of different microbial species. As a result of malignant disease, antibiotic regimens, and cancer therapy, the host-microbial equilibrium can be disturbed at many different levels. Loss of mucosal integrity promotes colonisation and overgrowth of microorganisms which may be part of the normal oral flora, or may be hospital-acquired species. In addition, reduction of saliva volume and alteration in salivary constituents including antimicrobial substances may develop [Dens et al., 1996]. In such an environment, it is important to treat pre-existent oral infection [Cheatham and Henry, 1994], reduce the oral microbial load by interventions prior to cancer treatment and avoid accumulation of dental plaque by maintaining good oral hygiene during cancer treatment.

The systemic infections that affect neutropenic paediatric cancer patients most frequently have changed during the last two decades with the Gram-negative bacilli gradually being replaced by the Gram-positive bacteria, and may be associated with significant morbidity [Ahmed et al., 2003]. Oral mucositis is acknowledged to be the principal risk factor for bacteraemia due to viridans streptococci [Donnelly, 2000].

In addition, oral mucosal infections may be associated with a wide variety of other microorganisms, including bacteria, fungal and viral pathogens. Overgrowth of Candida albicans resulting in clinical infection is common in paediatric cancer patients. Common oral findings include white adherent pseudomembranous plaques as well as red (erythematous) changes. The appearance of the lesions, including size, distribution, and colour, may contribute to the differential diagnosis [Epstein and Chow, 1999], but it is essential to recognize that in many cases it is difficult to diagnose infections based on clinical presentation alone. Comorbid oral conditions such as attenuated inflammatory response, mucositis and acute GvHD increase the difficulty to differentiate infection from non-infectious conditions.

In addition to infections related to the oral mucosa, those associated with the dentition may give rise to complications during myelosuppression. These infections typically involve the periodontium, the dental pulp/periapical area, and the soft tissues around erupting teeth. In addition, mobile primary teeth may act as a portal of entry for systemic infection.

Hyposalivation and xerostomia. The protective and homeostatic role of saliva has been well documented. Important salivary functions include physical cleansing of the oral cavity, facilitation of swallowing and speech, antimicrobial activities and buffering of acidic bacterial metabolic by-products, and remineralization of teeth. Radiation therapy can lead to irreversible damage to salivary glands within the radiation field. Xerostomia and hyposalivation are also common in patients treated with chemotherapy, but typically these problems are temporary. In HSCT recipients, who underwent TBI, hyposalivation may be more permanent [Dahllof et al., 1997a and b]. In addition, chronic GvHD may contribute to decreased salivary production. Hyposalivation predisposes to dental caries, periodontal diseases, mucosal infection and trauma, altered speech, reduced and altered taste, and inability to take certain foods by mouth.

Taste alterations. Children receiving chemotherapy and radiation to the head and neck region often experience a distressing alteration in taste or a reduction in taste sensation. Taste changes may vary from food tasting like cardboard or metal to salty,
Supplement to European Journal of Paediatric Dentistry • 3/2005

sweet, sour or bitter; or no taste at all. Taste dysfunction can last from days to months, but is usually reversible. The exact aetiology for this process is unknown but may be associated with several factors including diffusion of chemotherapy agents into the oral cavity or secretion in saliva [Epstein et al., 2002], the tumour itself, direct toxicity of chemotherapy or irradiation to replicating taste buds, neurotoxicity, hyposalivation, infection, GvHD-associated injury directed against taste receptors and psychologic changes, including conditioned food aversions. Taste dysfunction can result in emesis, reduced appetite and weight loss, and it can significantly reduce the child’s quality of life.

Oropharyngeal pain. Cancer patients, particularly those treated with high-dose chemotherapy can experience mild to excruciating oral pain due to a variety of causes. The malignancy itself may induce pain in the oral region. Oral mucositis is by far the most frequent cause, and the level of pain has been shown to correlate well with the severity of mucositis [Cella et al., 2003]. Pain often requires opioid analgesics for control. Oral infection is also a common cause of pain; particularly candidiasis and viral causes including reactivation of latent viruses such as herpes simplex (HSV) and varicella zoster virus. In addition, acute necrotising gingivitis and periodontitis or exacerbations of pre-existent chronic periodontal and/or dental infection may cause pain.

Selected classes of cytotoxic agents, including the vinca-alkaloids vincristine and vinblastine can cause peripheral neuropathy. Deep mandibular pain may develop resembling acute pulpsitis. A thorough dental history and oral examination should be performed to ensure proper diagnosis. The pain usually resolves within a week after cessation of the neurotoxic agent and no interventions other than pain management are necessary. Children on chemotherapy may also develop dental hypersensitivity within weeks after the initiation of treatment. Symptoms may range from “itching teeth” to mild pain and generally resolve spontaneously after several weeks.

Oral bleeding. Oral bleeding may occur during profound thrombocytopenia either as a result of the underlying disease or secondary to chemotherapy-induced myelosuppression. When the platelet count is above 40,000/mm³ clinically significant bleeding is rare, while at counts below 10,000/mm³ the risk of spontaneous oral haemorrhage increases significantly (Wandt et al., 1998). Although haemorrhage does not appear to be directly associated with oral mucositis, ulcerative lesions may increase the risk of haemorrhage, when submucosal blood vessels are exposed to trauma. In addition, HSV infection can significantly increase the bleeding risk due to profound mucosal breakdown. Similarly, gingival inflammation contributes to the risk of spontaneous gingival bleeding, particularly in children with haematological malignancies.

Although profound thrombocytopenia is the most common reason for oral haemorrhage, other mechanisms such as disseminated intravascular coagulation may contribute to bleeding complications. Spontaneous oral bleeding can be managed well. Nonetheless, particularly in children oral bleeding can be a frightening experience.

Oral graft versus host disease. GvHD most commonly occurs in allogeneic HSCT recipients, although clinically similar lesions mimicking GvHD may also develop in autologous HSCT patients. The process is principally mediated via cytotoxic T-lymphocytes present in the graft that react against host tissue. Matching of patient and donor for histocompatibility is a primary means to reduce the risk. In allogenic HSCT, acute GvHD occurs between 14 and 100 days post-transplant; whereas chronic GvHD is defined as occurring after day 100. In most instances, oral GvHD occurs as a component of multi-organ involvement. While the frequency of GvHD is lower in paediatric patients than in adult populations, although the oral cavity can become involved with both acute and chronic GvHD (Majorana et al., 2000). The oral manifestations of acute and chronic GvHD are very similar: mucosal erythema with or without ulceration, mucosal atrophy and lichenoid changes, appearing as hyperkeratotic striae, papules, and plaques. In chronic oral GvHD lichenoid changes are more prominent. GvHD affecting the salivary glands causes dry mouth leading to increased mucosal injury, pain, and infection. Mucoceles may result from mucosal and ductal damage to minor salivary glands.

GvHD as well as its prophylaxis and treatment are immunosuppressive and contribute to infection risk. In addition, infections including dental and periodontal disease may cause an exacerbation of GvHD.

Late sequelae. Both chemotherapy and radiation to the head and neck can have significant effects on growth and development of dentofacial structures and the oral environment [reviewed by Sonis, 2004]. Radiation effects on the facial skeleton are most severe in children below the age of 5 years at the time of therapy and receiving radiation doses at or above 24 Gy. In the past, patients with ALL were treated with prophylactic craniospinal irradiation (dose between 18-24 Gy) to prevent central nervous system involvement. A study on long-term survivors found that approximately 50%-100% of these patients had
microcephaly (depending on their age at cancer diagnosis) and may also have mid-face hypoplasia [Sonis et al., 1990]. In addition to direct effects of irradiation to skull bone cells, diminished growth hormone production and toxicity to the growing brain (brain growth stimulates calvarium to expand) play a role. The same phenomenon may occur in young children receiving cranial radiation for brain tumours. Enucleation (removal of the eye) and/or radiotherapy for treatment of retinoblastoma also have profound effects on the growth of the maxilla and orbital bone structure, resulting in significant transversal malformation. Similarly, young children receiving radiation therapy for nasopharyngeal carcinoma and rhabdomyosarcoma in the head and neck region may develop severe facial malformation. In addition, mandibular growth can be affected if the radiation dose to condylar growth centres exceeds 18 Gy, and missing teeth have a negative impact on growth of the alveolar mandibular bone. Innovative techniques in the delivery of radiation such as the use of radiation modifiers and intensity-modulated radiation therapy may lessen these toxicities of radiation therapy in the future. In HSCT patients, craniofacial growth may also be affected by TBI. These children experience an overall decrease in length of both the maxilla and the mandible, but mandibular growth is particularly affected [Dahllof, 1998]. The notion that this is likely associated with diminished growth hormone production is supported by the finding that growth hormone therapy reduces mandibular growth disturbances [Forsberg et al., 2002].

Developing teeth exposed to radiation levels as low as 4 Gy may demonstrate significant defects that include tooth dwarfism, root underdevelopment (blunting and tapering), incomplete calcification, premature apical closure, delayed or arrested root development, agenesis, and lack of eruption [Rosenberg et al., 1987]. Chemotherapy given during dental development can result in similar abnormalities of the dentition (Fig. 3) [Nasman et al., 1994; Hollta et al., 2005].

Dental caries and periodontal disease. Sonis and coworkers [1995] found no increased caries risk in long-term survivors of ALL, whereas the risk to develop periodontal disease seemed increased, particularly in those who had received craniospinal radiation at a young age. Increased dental caries activity following cytotoxic therapy has been reported in children with active caries at the time of cancer diagnosis [Pajari et al., 2001]. The risk to develop dental caries and periodontal disease following HSCT also seems to be increased (Uderzo et al., 1997; Lucas et al., 1998), although Dahllof and co-workers [1997b] could not find evidence for a higher caries prevalence four years post-HSCT, despite decreased salivary flow and higher counts of cariogenic bacteria.

Other conditions. Bagesund et al. [2004] performed a study on subjective complaints including xerostomia in long-term surviving paediatric HSCT patients and identified a need for supportive care measures to relieve symptoms and prevent secondary complications. As noted above, radiation therapy, high-dose chemotherapy and HSCT are associated with an increased risk of a secondary malignancy including haematologic malignancies, and solid tumours, including epithelial malignancies (e.g. oral squamous cell carcinoma) [Curtis et al., 1997; Forrest et al., 2003].

In addition, it is important for the dentist to realise that childhood cancer treatment, particularly HSCT including TBI, may lead to a full range of adverse effects on general physical health [Sanders, 1990]. Permanent damage may have occurred to multiple organs such as the eyes, heart, lungs and kidneys. In addition, cancer therapies, particularly those including irradiation, may induce endocrine function abnormalities that may affect oral health.

**Oral management considerations**

**Assessment and management prior to cancer treatment.** Oral complications in paediatric cancer patients may be reduced when the oral bacterial load and pre-existent oral infection are reduced prior to cancer treatment. Oral evaluation and management of patients scheduled to undergo intensive chemotherapy, HSCT or head and neck radiation therapy should...
ORAL CONDITIONS IN CHILD CANCER

occur as early as possible. The overall goal is to eliminate or stabilize oral diseases (e.g. oral and dental infection) or conditions that could produce complications (e.g. sites that could become a nidus of infection such as impacted or mobile teeth, and trauma-inducing factors such as orthodontic appliances, sharp teeth, etc.) during or following cancer therapy. Obtaining a complete dental, periodontal and orthodontic record is advised as this may serve as a reference when therapy-induced oral complications develop.

Ideally, a specialized dental team that performs and coordinates oral care should be available in the cancer centre. It is often difficult to treat patients diagnosed with haematologic malignancies in an outpatient environment and detailed knowledge of the disease and its treatment as well as direct communication with the oncologist is important. The paediatric oncologist should clearly advise each child’s dentist about the oncology treatment plan, risk for cancer-therapy related complications, and available time to the onset of neutropenia, current medications and the patient’s medical status.

In patients planned to receive radiation therapy to the head and neck region, the dose of radiation and the planned fields need to be identified. In turn, the dental team should develop a plan for oral disease management and communicate this with the oncology team.

In patients with poor oral health the benefit of performing oral health care should be weighed against the potential risks for incomplete healing. Decisions should be based on the timing of therapy, the underlying systemic disease, and the potential risk of infectious complications if dental treatment is or is not performed. Presently there are no widely-accepted guidelines with respect to prophylactic antibiotic coverage prior to invasive dental procedures in immunocompromised cancer patients. In patients with a neutrophil count below 1000/mm³, antibiotic prophylaxis may be similar to endocarditis prophylaxis. Guidelines are not well supported for prophylaxis in patients with indwelling venous access lines. In addition, in profound thrombocytopenic patients, platelet infusions or administration of antifibrinolytic drugs before and during healing from invasive procedures may be necessary.

The oncology team should be informed if there is still oral disease present that may induce infectious complications during myelosuppression.

The patient and the parents should be informed about the oral complications that may develop during chemotherapy and the rationale for maintaining optimal oral hygiene and avoiding trauma. Oral hygiene instruction should be given geared to the age and individual needs of the patient. Tooth brushing can be safely performed with a soft toothbrush. To reduce bacterial overgrowth, the toothbrush should be rinsed well and be air-dried between uses. In addition, nutritional recommendations may be given; the frequency of intake of cariogenic foods and drinks should be limited and physically rough or abrasive foods should be avoided.

Oral care during cancer treatment. At the time of myelo- and immuno-suppressive therapy and following head and neck irradiation, it is important to provide basic oral care; keeping the oral tissues moist with bland rinses, reinforcing oral hygiene and avoiding trauma are important components of oral care protocols [Bonnaure-Mallet et al., 1998; Levy-Polack et al., 1998; Raber-Durlacher, 1999]. Considerations for Candida prophylaxis should be made.

In most cancer centres, the oncology nursing team plays a key role in providing and supervising oral care during hospitalization. The mouth should be inspected daily, preferably with a halogen light source, to detect oral complications at an early stage. Oral assessment tools including pain scales can be effective instruments to monitor the oral condition during cancer treatment and to identify the need for interventions. Myelosuppression per se is no contraindication for oral hygiene measures, although toothbrushes may act as a source of infection [Kennedy et al., 2003]. If the patient’s condition does not allow manipulation in the oral cavity, antimicrobial rinses containing chlorhexidine should be prescribed. The literature is conflicting about the efficacy of chlorhexidine to prevent or treat oral mucositis [Cheng et al., 2004; Rubenstein et al., 2004], but there is evidence for the effectiveness of this broad-spectrum antiseptic in inhibiting the accumulation of dental plaque [Addy, 1986]. In addition, chlorhexidine rinses are shown to be effective to reduce candidal colonisation when used in conjunction with systemic antifungal prophylaxis [Epstein et al., 2003; Barasch et al., 2004]. A prophylactic anti-herpetic regimen may benefit HSV seropositive patients receiving intensive chemotherapy because most seropositive patients will experience viral reactivation during myelosuppression [Epstein et al., 1996].

With respect to oral mucositis, adequate pain management is imperative and in patients with severe mucositis-induced pain, opioids are the agents of choice. Low-level laser therapy may be effective in preventing and ameliorating oral mucositis in patients receiving high-dose chemotherapy and radiation...
therapy, but requires expensive equipment. Unfortunately, no trials have been conducted in paediatric cancer patients.

If a neutropenic patient becomes febrile, it should be realised that besides mucositis, infections related to the dentition may be the cause, although signs of acute inflammation may be skewed in myelosuppressed patients.

Spontaneous oral bleeding associated with thrombocytopenia is usually managed with platelet transfusions; in case of gingival haemorrhage, manual compression of the tissues with gauze is often effective. In thrombocytopenic patients, topical application of agents to help with controlling bleeding can include vasoconstrictors, clot organising materials (thrombin, collagen products), fibrin glue, and agents to counteract clot breakdown (e.g. aminoacaproic acid). The goal of establishing good oral hygiene, reducing gingivitis, reduces the risk of oral bleeding from gingival sites.

In patients with hyposalivation daily fluoride application with neutral sodium fluoride may be indicated. When the masticatory muscles are in the irradiation field, physical therapy and exercises are indicated to prevent severe trismus.

**Dental care post-cancer treatment and recommendations in long-time survivors.** In patients who have been treated with chemotherapy and autologous HSCT dental treatment can take place without any specific precautions when the bone marrow and immune functions are restored. After allogeneic HSCT it takes approximately one year before immune functions are back to normal, and until recovered, surgical procedures and dental treatment that may result in aerosols with the risk of inhalation should be avoided. In addition, these patients may be treated with immunosuppressive agents (e.g. cyclosporine A and tacrolimus) to prevent graft rejection and GvHD. These drugs can induce gingival hyperplasia, particularly in patients with poor oral hygiene. Post-radiation osteonecrosis (ON) is a rare, but serious complication that may develop following high-dose radiation (dose >60 Gy). In such patients, invasive dental interventions should be conducted with the least minimal tissue manipulation as possible. One study recommends the prophylactic and therapeutic use of hyperbaric oxygen prior to invasive interventions or in established ON and radiation-induced soft tissue complications in children [Ashmala et al., 1996].

In the first few years following cancer therapy frequent dental check-ups are indicated, particularly in patients with enamel abnormalities and/or hyposalivation or in those who may be at risk for ON. Prevention regimens should be geared to the patient’s individual needs. If demineralization of teeth occurs and caries rate increases, a comprehensive prevention program including oral hygiene and diet instructions, fluoride, remineralisation, saliva stimulation (if possible), and chlorhexidine products may be used to reduce cariogenic flora. These products may be provided with increase contact time in custom made vinyl carriers. In patients with decreased salivary output fluoride applications are indicated [Epstein et al., 1996b]. In children who present with pseudomembranous or erythematous candidiasis topical therapy could be considered or systemic antifungals may be needed. The form of topical delivery, taste and texture and frequency of use required present special considerations in children. As compliance with topical applications may be limited, the use of systemic drugs may be considered, particularly for saliva stimulation and antifungals. Unfortunately, most products have not been studied in paediatric oncology patients, and thus evidence-based guidelines are lacking in children.

In patients who suffer from dentofacial growth and developmental disturbances, orthodontic therapy, maxillofacial surgery and implants may be indicated in order to restore function and aesthetics. These procedures require careful treatment planning by experienced dental surgeons.

For additional oral management protocols for cancer patients we refer to:

**Concluding remarks**

Paediatric dental specialists can play a role in early diagnosis of malignancies presenting in the head and neck area, in providing supportive care during cancer treatment and in the management of late oral sequelae of treatment. Pretreatment oral assessment and intervention followed by individualised oral care during and after cancer treatment may reduce the adverse impact of oral complications.

Providing oral supportive care in paediatric cancer patients requires an understanding of malignant disease and cancer therapy and its complications as well as close cooperation between multiple disciplines. Education in basic aspects of oncology specific oral care should be part of the curriculum of all health care providers who may encounter cancer patients in their clinical practice.
Studies on the pathogenesis of acute and chronic oral complications may provide a key to prevention and treatment. In addition, a better insight should be obtained in the epidemiology of these complications and in its risk factors. More clinical research specifically directed at paediatric oncology patients and including significant numbers of children should be performed in order to develop evidence-based recommendations and form a solid base for the recognition of the medical necessity of oral and dental supportive care. In addition, new treatment strategies in pediatric oncology warrant continuous adaptation of oral care regimens to the changing scope of oral complications.

Acknowledgements

The authors thank Dr. Andrei Barasch for helpful suggestions in the preparation of this review.

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