In Western countries, rising incidence and survival rates in childhood cancer have led to increased patient morbidity, including short- and long-term oral effects. Some acute oral complications occur three times more commonly in children than adults. This literature review sourced material from medical databases to discuss the acute and chronic oral complications of oncology treatment in children. The article explores caries, gingivitis, oral infections, and oral mucositis, as well as available tools for measuring their incidence, prevention, and treatment in children. Many tools and interventions appear to be available to prevent and treat oral complications of cancer treatment in children; however, they lack reliable and consistent research. Future research should use larger samples to report the incidence of oral complications, which would allow identification of children at increased risk. In addition, larger studies would provide baseline information to enable the construction of appropriate randomized clinical trials to test methods of prevention and proposed interventions for oral complications of cancer treatment in children.

At a Glance

- The mouth has been documented as the most common source of sepsis in immunosuppressed patients with cancer.
- Strategies for preventing and managing oral complications in adults have not been evaluated adequately in children.
- Implementation of a universally accepted standardized oral mucositis scale for pediatric patients is needed to improve patient care and advance clinical research.

Childhood cancer incidence is rising in Western countries, with 1 in 500–600 children affected prior to age 15 (Fadda, Campus, & Luglie, 2006). Survival rates in childhood cancer also are increasing (Wogelius et al., 2008), with long-term survival rates approaching 80% (National Cancer Institute [NCI], 2009; O’Leary, Krailo, Anderson, & Reaman, 2008). The recent improvement in treatment can be attributed largely to dose intensification and combination chemotherapy (Cheng, Molassiotis, & Chang, 2002). However, increased survival rates consequently result in patient morbidity (Gibson et al., 2006) and are accompanied by concerns of potential short- and long-term side effects (Wogelius et al., 2008). Therefore, medical treatment received by children with cancer is not aimed exclusively at treatment of the malignant disease but also involves preventing and managing the many possible complications of the treatment itself (Cabrerizo-Merino & Onate-Sanchez, 2005).

Acute oral complications such as mucositis, xerostomia, bleeding, and infections occur three times more commonly in children than in adults (Alberth et al., 2006). Such complications can interrupt treatment (Cabrerizo-Merino & Onate-Sanchez, 2005). According to the American Academy of Pediatric Dentistry (JAAPD), 2008, “The most frequently documented source of sepsis in the immunosuppressed cancer patient is the mouth” (p. 1). Oral mucositis, gingivitis, herpetic stomatitis, and candidiasis are potential sources of systemic infections in patients receiving cancer chemotherapy (Rojas de Morales et al., 2001).

Table 1 shows dentition in healthy children. The entire population exhibits considerable amounts of variation in dental development. If an oncology professional is concerned about the eruption timing or sequence of a patient’s dentition, a dental referral may be recommended for assessment. Dental lamina, the tissue from which teeth are derived, is evident from days 35–37 of embryonic life (Nery, Kraus, & Croup, 1970). Primary teeth begin calcification...
prior to birth, and calcification of permanent dentition commences with the first molar at about the time of birth (Cameron & Widmer, 2008). Dental development continues throughout childhood into adolescence; therefore, illness and medications throughout this time frame can be detrimental. Potential long-term and chronic effects of cancer treatment on the oral cavity in children include altered root development, enamel opacities, hypocalcification, periodontal issues, and higher caries rates (Rosenberg, 1990).

### Caries and Gingivitis

Figure 1 illustrates the structure of a healthy tooth. Poor oral hygiene demonstrated through the existence of caries and gingivitis during oncology treatment can strongly influence the onset of oral complications (Cabrero-Merino & Onate-Sanchez, 2005). Willershausen, Lenzner, Hagedorn, and Ernst (1998) investigated the incidence of gingivitis as part of a comparative study between pediatric patients hospitalized for cancer treatment and children hospitalized without cancer. The children with cancer had a lower level of oral hygiene and a significantly higher incidence of gingivitis (about 63%) compared to children without cancer (about 7%) (Willershausen et al., 1998).

Cancer and its treatments can be associated with mineralization disorders and impaired salivary secretions, which are known risk factors for dental caries (Wogelius et al., 2008). However, limited studies have looked at the incidence of dental caries in pediatric patients with cancer, and most that are available have small sample sizes and demonstrate conflicting results. A larger population-based study in Denmark concluded that children diagnosed with cancer prior to age 5 did not have increased rates of caries in permanent teeth at age 12 (Wogelius et al., 2008). Children diagnosed from ages 5–6 had an increase in severe caries at age 12, but the difference disappeared by age 15. The researchers concluded that cancer and cancer treatment during childhood were risk factors for caries, but the increased risk was short term and disappeared with long-term follow-up. The results supported those from other studies that had a longer follow-up term and also failed to demonstrate a relationship among cancer, cancer treatment, and an increased risk for caries. Studies with shorter or varied follow-up times tended to report a positive association between cancer and caries incidence (Wogelius et al., 2008).

### Oral Infections

#### Candida

Oral candidiasis is an acute complication that commonly occurs in children with leukemia because of altered cell-mediated immunity. Oral candidiasis also occurs frequently in patients receiving chemotherapy, particularly if they have severe neutropenia (Alberth et al., 2006; Gonzalez Gravina et al., 2007). The complication may lead to life-threatening systemic infection (Gonzalez Gravina et al., 2007). Candida albicans is the most common Candida species isolated. However, non-albicans species of Candida complicate oncology treatment, particularly

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Table 1. Median Age of Eruption of Teeth in Children

<table>
<thead>
<tr>
<th>TOOTH</th>
<th>AGE OF MAXILLA ERUPTION</th>
<th>AGE OF MANDIBLE ERUPTION</th>
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<tbody>
<tr>
<td></td>
<td>BOYS</td>
<td>GIRLS</td>
</tr>
<tr>
<td>DECIDUOUS DENTITION</td>
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<tr>
<td>Central incisor</td>
<td>9 months</td>
<td>9 months</td>
</tr>
<tr>
<td>Lateral incisor</td>
<td>1 year</td>
<td>1 year</td>
</tr>
<tr>
<td>Canine</td>
<td>1 year and 9 months</td>
<td>1 year and 9 months</td>
</tr>
<tr>
<td>First molar</td>
<td>1 year and 6 months</td>
<td>1 year and 4 months</td>
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<tr>
<td>Second molar</td>
<td>2 years and 7 months</td>
<td>2 years and 7 months</td>
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<tr>
<td>PERMANENT DENTITION</td>
<td></td>
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<tr>
<td>Central incisor</td>
<td>7 years and 4 months</td>
<td>7 years and 1 month</td>
</tr>
<tr>
<td>Lateral incisor</td>
<td>8 years and 7 months</td>
<td>8 years and 3 months</td>
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<tr>
<td>Canine</td>
<td>11 years and 8 months</td>
<td>11 years and 2 months</td>
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<tr>
<td>First premolar</td>
<td>11 years</td>
<td>10 years and 8 months</td>
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<tr>
<td>Second premolar</td>
<td>12 years and 1 month</td>
<td>11 years and 10 months</td>
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<tr>
<td>First molar</td>
<td>6 years and 8 months</td>
<td>6 years and 8 months</td>
</tr>
<tr>
<td>Second molar</td>
<td>12 years and 9 months</td>
<td>12 years and 5 months</td>
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</tbody>
</table>

as many are not susceptible to azole-type antifungals (Alberth et al., 2006). *C. albicans* is believed to be a noninvasive colonizer that rarely is implicated in systemic infections, whereas non-*albicans* species such as the more aggressive *C. tropicalis* are believed to be more likely to result in systemic infection (Anirudhan, Bakhshi, Xess, Broor, & Arya, 2008).

Alberth et al. (2006) found no association between type of malignancy and the presence of a positive fungal culture. Alberth et al. (2006) observed an initial *C. albicans* colonization which could be followed four to six days later by colonization of non-*albicans* species of *Candida* in patients with severe neutropenia. Certain agents that damage oral mucosa such as methotrexate, doxorubicin, cyclophosphamide, and vincristine allow for colonization of fungi, bacteria, and viruses (Gonzalez Gravina et al., 2007). A study of pediatric patients with mucositis found that fungal organisms were the most commonly isolated microorganisms in oral mucosal lesions, followed by bacteria (Anirudhan et al., 2008). Oropharyngeal colonization with *Candida* species can increase the risk for systemic infection, particularly during episodes of neutropenia if oral ulcers develop or broad spectrum antibiotics or steroids are in use (Alberth et al., 2006).

A study by Gonzalez Gravina et al. (2007) of 62 pediatric patients with cancer indicated that the highest incidence of candidiasis occurred in children aged 7–12 years. Clinical presentations predominantly were pseudomembranous, occurring most commonly on the tongue followed by the inside of the cheeks, soft palate, and lips. Of the positive cases identified, about 91% presented as painless lesions (Gonzalez Gravina et al., 2007). The finding indicates that the risk for systemic infection rather than pain may be the primary clinical concern of *Candida* infection during oncology treatment.

**Herpes Simplex Virus**

Although oral herpes simplex virus (HSV) infection in patients with cancer is not uncommon, investigations have concluded that HSV infection in this population is caused by virus reactivation rather than primary infection (Anirudhan et al., 2008; Carrega et al., 1994). A prospective cohort study by Ramphal et al. (2007) investigating the prevalence of HSV in pediatric patients with cancer with febrile neutropenia concluded that HSV was low in incidence and not related to prolonged fever. However, HSV was observed to be associated with prolonged mucositis and poorer responses to initial antimicrobial therapy (Ramphal et al., 2007).

**Mucositis**

Oral mucositis is the most frequent and severe complication of chemotherapy in children (Cheng et al., 2002) and is a devastating complication following radiotherapy treatment in patients with head and neck cancer (Cheng, Chang, & Yuen, 2004). Oral mucositis can lead to decline in clinical condition and quality of life through extreme pain, which may result in an inability to tolerate food or fluids and, in turn, cause dehydration, malnutrition, and possible electrolyte disturbances (Fadda et al., 2006; Gippsland Oncology Nurses Group [GONG], 2007). In addition, oral mucositis can inhibit a patient’s ability to talk, which can contribute to depression (GONG, 2007). Fatigue also is believed to be more common in cycles of chemotherapy complicated by mucositis (Elting et al., 2003). Fatigue is reported to be the most frequent symptom experienced by children and adolescents with cancer (Hockenberry, Hooke, Gregurich, & McCarthy, 2009). Most causes of fatigue in patients with cancer are unknown. However, weight loss and chronic pain, which can be related to oral mucositis, may result in fatigue in patients receiving therapy. Fatigue may be caused by the increased energy needed to repair damaged epithelial tissue (NCI, 2009). Oral mucositis also increases the risk for local and systemic infections with fungi, bacteria, and viruses because of the loss of integrity of the oral epithelium in an immunocompromised host (Cheng et al., 2002; Figliolia et al., 2008; GONG, 2007; Kowanko, Hodgkinson, Long, & Evans, 1998).

Severe oral mucositis is particularly serious in children because of the risk of airway compromise. A case report described the difficult airway management of a 16-year-old girl weighing 48 kg with severe oral mucositis that led to progressive airway compromise because of the formation of a pseudomembrane (Chaimberg & Cravero, 2004). Children are reported to require intubation for preservation of the upper airway more often than adults (Drew, Peters, & Rimell, 2000). Airway compromise from oral mucositis has an incidence of 2%–19% among all pediatric patients receiving bone marrow transplantation (Sonis et al., 2004). The presence of graft-versus-host disease also has been associated with an increased rate of intubation (Crawford & Petersen, 1992; Warwick, Mertens, Shu, Ramsay, & Neglia, 1998). Mucositis and blood in the airway are common causes of compromised airway (Drew et al., 2000). In addition, more than 90% of pediatric hematopoietic stem cell transfusion (HSCT) recipients with grade 3–4 mucositis have been reported to require feeding tubes for parenteral nutrition and opioid analgesics (Sonis et al., 2004).

Oral mucositis is a principal cause of pain for patients undergoing oncology treatment, with data showing that about 58% of pain in pediatric patients with cancer was secondary to treatment complications such as oral mucositis (Cheng, Molassiotis, Chang, Wai, & Cheung, 2001; Elliott et al., 1991; Walco, Sterling, Conte, &...
Engel, 1999). In addition, the relationship that can be observed between a high mucositis score and pain suggests that pain tends to worsen as mucositis becomes more severe (Cheng et al., 2002).

**Incidence:** Oral mucositis occurs in about 20%–40% of adult patients receiving chemotherapy and up to 50% of adult patients receiving chemotherapy and radiotherapy (GONG, 2007). Oral mucositis is more prevalent in children than in adults, with a reported incidence of about 65% in children (Cheng et al., 2002). However, the estimates of incidence vary greatly from 52%–80% (Cheng et al., 2004). Reliable data on oral mucositis incidence rates in the pediatric cancer population are scarce (Figliolia et al., 2008). Some attribute the higher incidence of oral mucositis in children to the higher mitotic index of their basal epithelial cell layer (Figliolia et al., 2008).

The chance of a pediatric patient with cancer experiencing oral mucositis during treatment has increased significantly as the use of high-dose and multiple chemotherapy agents in treating childhood cancer also has increased (Cheng et al., 2002). The treatment regimen, chemotherapy with or without radiotherapy, dosage, duration and sequence, type of malignancy, age, neutrophil count, and level of oral care all are believed to influence the incidence of mucositis (Cheng et al., 2004; Fadda et al., 2006). Severity of mucositis largely is related to the agent used. Methotrexate, fluorouracil, doxorubicin, paclitaxel, capecitabine, and etoposide are believed to be particularly stomatotoxic (Cheng et al., 2004; GONG, 2007). In addition, the risk of mucositis also increases with number of cycles of chemotherapy (Figliolia et al., 2008).

Hospitalization, supportive care, and pain control have economic consequences (Logan et al., 2007). Few articles in the literature have reported the financial implications of mucositis. Sonis et al. (2001) reported that additional days of fever, hospitalization, opioid usage, and parenteral nutrition among patients receiving HSCT with oral ulcers led to an increase in costs of $42,749 per patient. In addition, increased costs of $2,725 and $5,565 per cycle of grade 1–2 and grade 3–4 mucositis, respectively, have been reported (Elting et al., 2003). However, neither of the costs is specific to children, and additional investigation in this population is warranted.

Modifications of the treatment regimen to lower doses and longer recovery periods between doses remain the most effective methods for limiting the incidence and severity of mucositis. Therefore, mucositis remains a common primary dose-limiting factor (Cheng et al., 2002). Interruptions to treatment, dose reductions (Cheng et al., 2002), and potential cessation (Logan et al., 2007) can affect treatment prognosis. Patient survival, cure rates, and length of remission, therefore, can be affected directly (Cheng et al., 2002; Fadda et al., 2006).

**Signs and duration:** As mucositis develops, the oral epithelium alters to show mucosal erythema, which progresses to ulceration before a normal clinical appearance returns. However, the underlying mucosal environment remains altered (Logan et al., 2007). Lesions predominately appear in the nonkeratinized epithelium, such as on the cheeks, underside of the tongue, and floor of the mouth. In the most severe cases, the keratinized surfaces also can be involved (Cheng et al., 2002; Fadda et al., 2006). Oral mucositis lasts for about three weeks, beginning around days 3–5 and peaking 7–14 days after initiation of chemotherapy. In a study of 34 children, mucositis appeared around day 3, peaked on day 10, and started to resolve on day 14 (Cheng et al., 2004).

In the past, oral mucositis was considered to be inflammation of the mucosa of the mouth, which could range from redness to severe ulceration (Kowanko et al., 1998). To date, the pathobiology of mucositis is accepted to be much more complex, involving the epithelial tissues as well as damage to the subepithelial tissues of the mucosa (Sonis et al., 2004).

**Risk factors:** Conflicting evidence exists with regard to potential risk factors in addition to chemotherapy and radiotherapy for developing oral mucositis in the pediatric population. A retrospective case-control study of 337 children found that age and gender were not significant risk factors (Fadda et al., 2006). In addition, Figliolia et al. (2008) found in a study of 169 pediatric patients with acute lymphoblastic leukemia that patient age, gender, and leukocyte counts at diagnosis were not statistically correlated with occurrence of mucositis. However, Figliolia et al. (2008) noted a trend toward significance when looking at gender as a risk factor, with girls having an increased incidence (p = 0.08). The finding indicates that further research with larger sample sizes is needed. Other risk factors discussed in the literature include poor self-care ability, acutely ill condition, dehydration, and poor nutritional state. Additional risk factors suggested but not particularly relevant to the pediatric population include chronic alcohol and cigarette use and age older than 65 (GONG, 2007). Findings also suggest that some aspects of oral mucositis may be genetically predetermined (Sonis et al., 2004).

Despite the reported higher incidence of oral mucositis in children compared to adults, mucositis may still be underestimated in the pediatric population (Fadda et al., 2006). Therefore, some believe that oral mucositis should be systematically analyzed prospectively in specialist centers to allow for more effective patient care (Figliolia et al., 2008).

**Potential Late Complications**

Osteoradionecrosis remains a devastating complication of radiotherapy (Rosenberg, 1990) for children who receive more than 40 Gy in the jaw area (Paulino & Casillas, 2008). Osteoradionecrosis is not a common complication but frequently is noted following dental treatment such as extraction or surgery. The mandible is affected more commonly than the maxilla (Otmani, 2007; Paulino & Casillas, 2008).

Children who receive head and neck irradiation may have complete arrest of tooth and jaw development within the radiation field (Rosenberg, 1990). Mature ameloblasts have been permanently damaged by 10 Gy of radiation, halting tooth development from the time of irradiation (Kaste, Hopkins, & Jenkins, 1994; Minicucci, Lopes, & Crocci, 2003). As chemotherapy interferes with intracellular metabolism and the cell cycle, it may retard dental development. Therefore, dental anomalies are more common in patients treated for malignant diseases (Goho, 1993; Minicucci et al., 2003). A study that followed 40 children for two or more years after cancer treatment including HSCT demonstrated that almost all children examined had dental development disturbances, such as agenesis, short roots, and arrested root development (van der Pas-van Voskuilen et al., 2009).

The nature of the complications experienced by children will be influenced by their stage of development at the time of treatment and the treatment regimen prescribed (Cabrero-Merino,...
An oral mucositis scoring system should be objective, validated, and reproducible across all clinical situations and applications. The scoring system also needs to be sensitive enough to be effective consistently with different oncology treatment regimens. Minimal training should be needed to use the instrument, and it should have adequate intra- and inter-rater reliability. According to Sonis et al. (2004), “No scale established to date meets all of these criteria or is universally accepted” (p. 2002). The most relevant and commonly used scales for clinical management are those designed by NCI and WHO (Sonis et al., 2004) (see Table 2).

The National Cancer Institute Common Terminology Criteria (NCI-CTC) combines objective and functional aspects of a patient’s condition on a scale of 0–4 (Tomlinson, Judd, Hendershot, Maloney, & Sung, 2007). Functional items are included as they reflect limitations in activities related to oral mucositis, such as ability to eat, drink, and swallow. Difficulty in breathing is reported to be assessed only in the NCI-CTC scale (Tomlinson, Judd, et al., 2008).

The WHO oral mucositis scale is a simple instrument (Tomlinson et al., 2007) that uses a single scale from 0–4 based on functional abilities such as ability to eat and drink combined with the subjective symptoms of pain and objective signs of mucositis as observed by the examiner (Tomlinson et al., 2007; Tomlinson, Judd, et al., 2008). The WHO scale is widely used but requires assessment of the whole oral cavity, which can be challenging when children are very young and ill because of lack of access and cooperation (Tomlinson, Judd, et al., 2008).

With regard to the use of the WHO and NCI-CTC scales, functional scales can be problematic if analgesia is used (Tomlinson et al., 2007). Young children may refuse to eat for many reasons (e.g., nausea), and attribution of functional limitations versus other etiologies may not be possible. The inclusion of nutritional support in the NCI-CTC scale also is debatable as patients may receive parenteral nutrition for various reasons unrelated to mucositis (Tomlinson, Judd, et al., 2008).

Patient-reported outcomes are becoming more popular in clinical trials as they tend to capture the perspective of the patient for which the intervention is intended to benefit (Tomlinson, Isitt, et al., 2008). In addition, objective measures (such as WHO and

| Table 2. Common Scales for Management of Oral Mucositis Stages |
|-----------------|-----------------|-----------------|
| STAGE            | WORLD HEALTH ORGANIZATION | NATIONAL CANCER INSTITUTE |
| 1                | Soreness and erythema   | Painless ulcers; erythema or mild soreness in the absence of lesions |
| 2                | Erythema and ulcers; patient can eat solids. | Painful erythema, edema, or ulcers; patient is able to eat or swallow. |
| 3                | Ulcers; requires liquid diet only | Painful erythema, edema, or ulcers requiring IV hydration |
| 4                | Oral nourishment is not possible. | Severe ulceration; requires parenteral or enteral nutritional support or prophylactic intubation |

NCl-CTC) can be difficult to determine in pediatric populations as visualization of the entire oral cavity may not be possible (Tomlinson, Judd, et al., 2008). The version of the Oral Mucositis Daily Questionnaire called the Children’s International Mucositis Evaluation Scale is an example of a self-reporting tool. The issue with the use of this scale or one similar in the pediatric population is that the children may be too young to self-report; therefore, a proxy or parent reporter is needed (Tomlinson, Isitt, et al., 2008).

Assessment of Pain Secondary to Mucositis

Two arguments pertain to the inclusion of pain in oral mucositis assessments. Some argue that pain is one of the most distressing symptoms experienced by patients with oral mucositis, so the inclusion of a pain scale is essential (Epstein & Schubert, 2004; Tomlinson, Judd, et al., 2008). Others feel that because pain can be affected by the use of analgesia, investigators may underscore mucositis and, therefore, pain should not be included in the scales for research (Sonis et al., 2001; Tomlinson, Judd, et al., 2008).

Assessment of pain is particularly difficult in young children, and some professionals feel that the only clinical scale available is measuring the amount of opioid needed to make the child feel comfortable (Tomlinson, Gibson, et al., 2008). Oral mucositis pain intensity frequently is measured by asking parents to rate their child’s pain severity along either a 1-10 visual scale or the more children-friendly faces scale, such as the Children’s International Mucositis Evaluation Scale (Tomlinson et al., 2010). The faces scale was developed by Wong and Baker (1988) and is composed of six cartoon faces. This method of pain reporting is believed to be reliable and can be used on children as young as age 3 to enable self-reporting of symptoms (Cheng et al., 2002).

Prevention of Oral Complications

Successful management of oral complications during oncology treatment should begin with examination and implementation of prevention measures prior to commencement of treatment. AAPD (2008) recognizes that patient adherence is the key to maintaining a healthy oral cavity during cancer therapy. Patient education should include information such as the following. “Regular dental check-up examinations, oral microbial surveillance, and application of professional oral hygiene measures in children with cancer may decrease the incidence, duration, and severity of infectious complications” (Alberth et al., 2006, p. 240). “Proper oral care before, during, and after cancer therapy has been found to be effective in preventing and controlling oral complications” (Cho, Cheng, & Cheng, 2000, p. 203). Oral care helps to prevent tissue damage and reduce tissue irritation, bacterial plaque levels, and microbial load by decreasing colonization, leading to decreased gingival inflammation (Epstein & Schubert, 2004).

The severity and incidence of systemic infection secondary to chemotherapy may be reduced with the adoption of practices that reduce blood flow to oral mucosa, meaning that less of the toxic agent that is circulating systemically reaches the systemic circulation. Cryotherapy causes local vasoconstriction, which reduces blood flow to oral mucosa, meaning that less of the toxic agent that is circulating systemically reaches the systemic circulation. Cryotherapy involving rapid cooling of the oral cavity with ice chips is another prophylactic measure used with some chemotherapy agents. Cryotherapy causes local vasoconstriction, which reduces blood flow to oral mucosa, meaning that less of the toxic agent that is circulating systemically reaches the systemic circulation.

Prevention of Oral Mucositis

The literature has emphasized the need to prevent mucositis when possible. However, limited studies have examined preventing and reducing the incidence and severity of mucositis in children (Cheng et al., 2004). A study by Cheng et al. (2001) demonstrated that severity of oral mucositis and related pain were significantly lower in a group of pediatric patients with an oral care protocol including tooth brushing, 0.2% chlorhexidine mouth rinse, and 0.9% saline rinse compared to patients in the control group who did not receive information about the importance of oral care or receive the oral care protocol during treatment. Despite numerous recommendations, few experimental studies have assessed the effectiveness of different oral care protocols on reducing oral complications (Kowanko et al., 1998).

The use of chlorhexidine as a prophylaxis against chemotherapy- and radiotherapy-induced oral mucositis is seen commonly in the literature (Kowanko et al., 1998). Bland mouth rinses (salt and soda) are as effective as chlorhexidine and, therefore, are a more economical alternative for preventing oral mucositis (Rubenstein et al., 2004). In addition, MASCC does not recommend the use of chlorhexidine mouth rinse for the prevention of mucositis in patients with solid head and neck tumors who are undergoing radiotherapy (Keefe et al., 2007; Rubenstein et al., 2004).
the oral mucosa (Kowanko et al., 1998). If agents have a short half-life (such as 5-fluorouracil) and are administrated as a bolus injection, cryotherapy can reduce the dose reaching the oral mucous membranes, potentially minimizing the local cytotoxic effects of the drug in the oral cavity (Kowanko et al., 1998). Cryotherapy is not effective when continuous infusion treatment is being used (GONG, 2007; Kowanko et al., 1998), and patient compliance may be influenced by the uncomfortable sensation of having ice in the mouth (Keefe et al., 2007).

A systematic review by Worthington, Clarkson, and Eden (2007) concluded from studies suitable for meta-analysis that amifostine, Asian medicine, hydrolytic enzymes, and ice chips provided a significant difference in prevention or reduction of the severity of oral mucositis compared to placebo or no treatment. However, the strength of the evidence was variable and “well designed and conducted trials with sufficient numbers of participants to perform subgroup analyses by type of disease and chemotherapeutic agent” were needed (Worthington et al., 2007, p. 2).

Treatment of Oral Mucositis

The symptoms of oral mucositis must be treated effectively to reduce the severity of the associated pain and to avoid secondary local and systemic infections (Kowanko et al., 1998). With regard to treatment of oral mucositis, a Cochrane review concluded that “no clear pattern [is] emerging regarding the benefit or otherwise of antimicrobial use to manage mucositis” (Clarkson, Worthington, & Eden, 2007, p. 3). MASCC does not recommend the use of chlorhexidine to treat established standard-dose chemotherapy-induced oral mucositis (Keeffe et al., 2007; Rubenstein et al., 2004). Solutions containing alcohol may sting oral mucosa with established lesions (Rubenstein et al., 2004).

Cubukcu and Sevinir (2007) performed a clinical prospective study that looked at the effect of debridement of ulcers as treatment of oral mucositis in 40 children with severe mucositis randomly assigned to treatment or control groups. The results showed a significant reduction in the severity of oral mucositis in the debridement group as assessed by healing and decreased severity of oral mucositis (Cubukcu & Sevinir, 2007).

Benzydamine hydrochloride is a drug with anti-inflammatory, pain-relieving, fever-reducing, and antimicrobial actions that has been used to treat and prevent mucositis as a mouthwash (Cheng & Chang, 2003; Kowanko et al., 1998). Topical application of benzydamine has been subjected to randomized, blinded, controlled studies and has been shown to prevent mucositis and have pain-relieving and analgesic effects in adults receiving radiotherapy (Epstein & Schubert, 2004). Topical benzydamine is effective at improving signs and symptoms in radiation-induced mucositis in adults (Epstein et al., 2001), but additional research is needed to compare it with other agents and evaluate its effectiveness in chemotherapy-induced mucositis (Kowanko et al., 1998). Research focusing on the pediatric population has suggested that benzydamine is accepted as a rinse by children older than six years (Cheng, 2004), but larger trials are needed to determine its effectiveness in palliating symptoms of oral mucositis in children (Cheng & Chang, 2005).

Prevention of mucositis-related tissue damage is a central aspect of managing mucositis pain. The mucositis pain experience is multifactorial and is affected by the degree of tissue damage and emotional state of the patient, particularly anxiety, fear, or depression (Epstein & Schubert, 2004). The pain occurs for a limited duration of one to two weeks for chemotherapy recipients and as long as several months for radiotherapy recipients. Good oral care protocols and the use of topical agents can reduce the need for pain medication in patients with mucositis (Epstein & Schubert, 2004).

The oral mucosa is accessible and is suited to application of topical agents for pain management because of the intensity of its innervation and thinness of the epithelium barrier (Epstein & Schubert, 2004). Topical anesthetics are included in oral care protocols and numerous topical agents have been used, although few clinical trials have determined their relative effectiveness (Epstein & Schubert, 2004; Kowanko et al., 1998). Viscous solutions of lignogaine and xylocaine have been suggested in rinses for patients with severe pain symptoms from mucositis, although no evidence supports their use (Kowanko et al., 1998). An initial topical application of benzydamine is recommended for pain management (Epstein & Schubert, 2004). An agent available in the form of candy is capsaicin, the active ingredient in chilli peppers, which may desensitize neurons to provide temporary pain relief (Kowanko et al., 1998).

Although a number of treatments are available for oral mucositis, many interventions in clinical practice have not been evaluated adequately, and various combinations of agents are administered in different centers without evidence to support their use.

A systematic review of available therapies by the Joanna Briggs Institute found that “there is a bewildering number of interventions to choose from, but no high quality synthesis of the best research evidence for these interventions” (Kowanko et al., 1998, p. 1). A systematic review published by the Cochrane Library found “weak and unreliable evidence [moderate-high risk of bias] that allopurinol mouthwash, granulocyte macrophage stimulating factor, immunoglobulin, or human placental extract improve or eradicate mucositis” (Clarkson et al., 2007, p. 2). The same review concluded that no evidence suggested that patient-controlled analgesia was superior to continuous infusion in pain control, but less opiate was used per hour with patient-controlled analgesia and the duration of the pain was shorter (Clarkson et al., 2007). Only one of the 22 studies that were appropriate for this review included pediatric patients, demonstrating the lack of well-designed clinical trials in the pediatric population available in the literature.
Recommendations and Protocols

Willershausen et al. (1998) recommended “that for children with cancer and subject to aggressive therapy and/or long hospitalizations, beyond the general medical examination on hospital admission, a dental examination should be instituted” (p. 480). Strong support for the use of an oral care protocol is present in the literature and was emphasized by Cheng et al. (2004), who said, “Given the low cost and simplicity of routine oral care, oral hygiene protocols should be the standard intervention, with specific therapies to be developed” (p. 1209). Identification of potential multifactorial etiology of oral pain in patients with cancer also is needed. A multidisciplinary approach is recommended to assess the patient’s pain symptoms and address each component of the patient’s pain (Epstein & Schubert, 2004).

The Mucositis Study Group of MASCC and the International Society of Oral Oncology was created in 1998 to provide a multiprofessional approach to care, research, and education (Keefe, Peterson, & Schubert, 2006). Advancements since 1998 include the publication of guidelines for treating mucositis in 2004, which were updated in 2007 (Keefe et al., 2007). The guidelines, however, are not specific to pediatric patients.

No treatment or approach has been proven to be reliable and effective in studies of oral mucositis. Outcomes on children remain unknown for almost all available treatments (Cheng et al., 2004). Therefore, a need exists for improved risk assessment and continued research that examines all areas of oral mucositis (e.g., epidemiology, burden of illness, cost of care, prevention, treatment) in the pediatric population (Keefe et al., 2007).

Conclusion

This literature review suggests that an abundance of tools and interventions are available to measure and treat oral complications of cancer treatment in children. However, the tools and treatments lack reliable and consistent research to support their use. In addition, the literature lacks concrete information on the incidence of complications such as oral mucositis in children. The large variation evident in the literature highlights the need for the development of standardized tools to assess and report the oral health of children with cancer. Such efforts would allow for pooling of data and comparison of the various oral care protocols in use in different pediatric oncology centers. Construction of a database would permit more accurate comparisons in the future when clinical trials examine the outcomes of protocols and interventions for oral complications of oncology treatment in children.

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