

Oral care for children with leukaemia

SY Cho, AC Cheng, MCK Cheng

Objectives. To review the oral care regimens for children with acute leukaemia, and to present an easy-to-follow oral care protocol for those affected children.

Data sources. *Medline* and non-*Medline* search of the literature; local data; and personal experience.

Study selection. Articles containing supportive scientific evidence were selected.

Data extraction. Data were extracted and reviewed independently by the authors.

Data synthesis. Cancer is an uncommon disease in children, yet it is second only to accidents as a cause of death for children in many countries. Acute leukaemia is the most common type of malignancy encountered in children. The disease and its treatment can directly or indirectly affect the child's oral health and dental development. Any existing lesions that might have normally been dormant can also flare up and become life-threatening once the child is immunosuppressed. Proper oral care before, during, and after cancer therapy has been found to be effective in preventing and controlling such oral complications.

Conclusion. Proper oral care for children with leukaemia is critical. Long-term follow-up of these children is also necessary to monitor their dental and orofacial growth.

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Key words: Child; Leukemia/therapy; Mouthwashes; Oral hygiene/methods

Introduction

Cancer is an uncommon disease in children, yet it is second only to accidents as a cause of death for children in Hong Kong and many other countries.¹⁻⁴ In Hong Kong, around 150 new cases of cancer are reported each year in children younger than 15 years; approximately 40% of these cases are diagnosed in children younger than 5 years.⁴ The types of cancer seen in children are very different from those found in adults: leukaemia, lymphoma, and brain tumours are relatively more common in children.²⁻⁴ As in other countries, leukaemia constitutes approximately 30% of all childhood cancers and acute lymphoblastic leukaemia (ALL) is the most common type of malignancy encountered.²⁻⁴

Acute leukaemia is usually treated with chemotherapy. Human allogeneic bone marrow transplantation

with high-dose chemotherapy and total body irradiation is being increasingly used to treat patients experiencing a relapse of acute leukaemia—an event more common in patients with acute myeloblastic leukaemia (AML).^{2,5} Special precautions may be needed during some oral procedures to avoid or reduce the likelihood of serious undesirable complications. The treatment of leukaemia can directly or indirectly affect oral health and can result in higher morbidity and, occasionally, fatality. An additional consideration is the impact of the disease and its treatment on the developing dentition and orofacial growth in a child.

Oral findings of acute leukaemia

Initial signs and symptoms of leukaemia can appear in the mouth or neck. These oral presentations may lead the patient to seek dental care, or they may be noticed during a routine dental examination. Oral lesions are more commonly found in patients with AML; mucosal pallor, mucosal purpura, lymphadenopathy, gingival bleeding, and petechiae are typical manifestations.^{5,6} Gingival swelling is frequently found in patients with AML but is uncommon in patients with ALL.^{7,8} Other oral findings include tonsillar swelling, paraesthesiae, and signs of fungal infection. The dentist should be cautious if these signs are associated with intermittent fever, pallor,

Tuen Mun School Dental Clinic, Department of Health, 16 Tsun Wen Road, Tuen Mun, Hong Kong

SY Cho, MDS, FHKAM (Dental Surgery)

Dental Oncology Group, Ontario Cancer Institute, Princess Margaret Hospital, Toronto, Canada

AC Cheng, MS, FAMS

Department of Medicine and Therapeutics, Prince of Wales Hospital, Shatin, Hong Kong

MCK Cheng, MB, ChB

Correspondence to: Dr SY Cho

malaise, weakness, anorexia, and weight loss. The presence of a blood dyscrasia should be considered if the patient does not respond positively to routine dental treatment such as oral hygiene and periodontal work. When leukaemia is suspected, conservative care (eg giving antibiotics and analgesics as indicated) should be given rather than aggressive surgical intervention. Dental procedures that could trigger a bleeding episode and/or bacteraemia should be avoided. Appropriate referral and diagnostic blood tests should be performed simultaneously and a treatment plan should be finalised only after a definitive diagnosis has been confirmed. Many drugs that are used to treat leukaemia can also cause oral lesions; in addition, patients may have complications from bone marrow transplantation.⁵

Pretreatment dental care

The diagnosis of cancer often proves devastating for the families of affected children. Families tend to be concerned about the medical treatment that their child is receiving, and little time is spent on the patient’s oral care. Proper oral care, however, should not be overlooked, because untreated oral lesions are often painful and can greatly affect a child’s oral food intake. Most of the cases seen by dentists are referrals from hospital doctors. Dental screening of these patients so as to identify dental pathology is important, since any existing lesions that might normally lie dormant can flare up and become life-threatening once the child is immunosuppressed.⁹ Hence, proper oral care before, during, and after treatment for the cancer is very important.

A standard, easy-to-follow clinical protocol should be developed in each treatment centre. A sample protocol that we have used is summarised in Table 1. Panoramic and bite-wing radiographs are required. The dental findings and caries risk of the child should be estimated at the pretreatment screening. When dental treatment is indicated, careful discussion with the child’s paediatrician or oncologist is necessary to coordinate the timing of the treatment. As infection during neutropenia is the most common cause of death in oncology patients, all efforts should be made to minimise this risk.^{5,10} Chronic infections of the dental pulp and the periodontal tissues can develop into a source of significant systemic infection during periods of myelosuppression.^{9,11} Hence, the pulp treatment of primary teeth should be avoided in this patient group.^{2,12} The pulp treatment of permanent teeth in these patients is controversial.^{1,2,6,12} Despite the high success rates of root canal treatment in permanent teeth, the risk of a patient treatment failure with subsequent dental abscess formation cannot be ruled out. In our opinion, the potential risk of a patient having septicaemia during chemotherapy outweighs the benefits of conserving more teeth. Accordingly, all teeth with lesions extended to the pulp should be extracted prior to chemotherapy unless their removal is contra-indicated by other medical conditions. Extraction of such teeth is especially important in patients who will require total body irradiation.

Dental extractions should preferably be performed at least 10 to 14 days before the commencement of chemotherapy, so that epithelization of the extraction site has been completed prior to the initiation of

Table 1. Sample protocol of oral care for children with acute leukaemia

Disease phase	Treatment
Pre-chemotherapy	<ol style="list-style-type: none"> (1) Give thorough dental examination with panoramic and bite-wing radiographs (2) Extract teeth with poor/questionable prognosis (3) Temporarily dress all carious lesions (4) Brush teeth with fluoride paste twice daily (5) For children with high caries risk, use 0.12% chlorhexidine mouthwash twice daily
In-patient care	<ol style="list-style-type: none"> (1) Continue chlorhexidine mouthwash twice daily (2) Temporarily stop tooth-brushing if oral lesions are too painful (3) Give nystatin (100 000 units/mL) oral suspension four times daily if there are signs of oral candidiasis (4) Give topical acyclovir if there are signs of herpes simplex infection (5) Use artificial saliva and 5% sodium bicarbonate rinse in children with xerostomia
Remission	<ol style="list-style-type: none"> (1) Basic preventive dental care should include: <ul style="list-style-type: none"> • tooth-brushing with fluoride paste twice daily • fluoride rinse once daily • dental flossing once daily • dietary counselling and advice • recall at 1 to 6 months and topical fluoride treatment (2) Treat patient as normal if in full remission except for invasive procedures
Long-term management	Perform semi-annual recall to monitor dental and facial growth and development

Table 2. Necessary precautions prior to dental extraction in a paediatric oncology patient

Blood cell type	Peripheral blood count	Precaution
Platelets	>80 x 10 ⁹ /L <80 x 10 ⁹ /L	Give routine care Platelet transfusion needed
Neutrophils	>2 x 10 ⁹ /L <2 x 10 ⁹ /L	Give routine care Prophylactic antibiotics needed

chemotherapy.^{1,12} Thorough blood investigations must be carried out on the same day, before the extraction. A pre-extraction platelet transfusion is indicated if an abnormal platelet count is encountered. Pre-extraction antibiotic therapy is required if the neutrophil count is low (Table 2).^{1,2,5} All other carious lesions should be dressed with temporary fillings at this stage, and definite treatment should be delayed until the patient is in remission.

High-dose irradiation to the head and neck region has been shown to cause changes in the chemical composition of the saliva as well as a reduction in the rate and volume of salivary flow in adults.¹³⁻¹⁵ Radiation-induced xerostomia will also cause a shift in the oral microflora to a highly acidogenic and cariogenic population.¹⁶⁻¹⁸ Dental caries commonly affects the cervical areas of the dentition of irradiated patients. Studies of salivary secretion in children treated for malignant diseases are few. Although some chemotherapeutic agents are known to reduce salivary flow, their effects on salivary flow rates are much less severe than those caused by high-dose irradiation.^{10,19-21} It has been shown that a significantly greater proportion of children treated with total body irradiation or chemotherapy harbour high bacterial counts of mutans streptococci in comparison with the control children.¹⁹ Furthermore, more children in the treatment group exhibited a low saliva buffer capacity.¹⁹ Thus, to minimise the risk of development of radiation caries and dental complications, oral hygiene must be optimal and include good home-care and regular dental visits.^{1,22,23} Periodic dental radiographic imaging is needed to monitor caries risk.²⁴ Any carious lesions detected should be properly treated and restored.

For all patients, regardless of their caries risk, twice-daily tooth-brushing with a fluoridated toothpaste is mandatory.²⁵ In addition, daily rinsing with chlorhexidine digluconate is also recommended for children with a high caries risk.²⁶⁻²⁸ Use of 0.12% chlorhexidine mouthwash twice daily, has been found to effectively suppress the major pathogens present in the oral cavity.²⁹ In Hong Kong, both 0.2% and 0.12%

preparations are available commercially; the 0.2% preparation could be used after dilution to 0.12% with warm water. The use of warm water must be emphasised, as carious teeth can be very sensitive to cold water, and dilution of the mouthwash would make it less astringent and thus help increase compliance. In infants and very young children who are unable to manage the rinse-and-expectorate action, care-givers would need to be taught how to use the chlorhexidine as an oral swab. Children must be instructed to rinse their mouth thoroughly after brushing with toothpaste before using chlorhexidine rinse, as some of the ingredients in toothpaste can interfere with the action of chlorhexidine.³⁰

Daily use of a self-applied fluoride gel has been recommended for patients with xerostomia.³¹ The topical use of 0.4% stannous fluoride gel is known to be effective at preventing radiation caries.³² Consequently, its use has been recommended in children with a malignant tumour.² We have, however, found a low compliance of use of the gel in children, because many children dislike the metallic taste. The gel sometimes also causes mucosal irritation in patients with xerostomia. The daily use of 1% sodium fluoride gel in mouth-trays is also effective in preventing caries in these patients.³³ While this gel causes no irritation to the oral mucosa, it is less effective than 0.4% stannous fluoride gel in preventing root caries in patients with head and neck cancer.³⁴

In-patient care

Oral complications from chemotherapy are not uncommon. Acute manifestations that often develop include mucositis, gingival bleeding, xerostomia, secondary candidiasis, and herpes simplex and bacterial infections.^{10,21} Mucosal ulceration is the most frequent oral problem encountered and is associated with low neutrophil counts.^{10,21} The aim of oral management is to relieve symptoms as well as to prevent and treat any secondary infection.

The child may find the oral lesions so painful that tooth-brushing and talking become almost impossible. The use of chlorhexidine mouthwash is thus very important. A multi-agent mouthwash that combines topical steroid, antibiotic, an antifungal agent, and topical anaesthetic has been recommended for use by some authors,¹ but is now less commonly used, as chlorhexidine has most of its properties. This mouthwash has also been found to be effective in controlling mucositis and infection.³⁵ The frequent use of lignocaine (lidocaine) as a topical analgesic to treat mucositis

is not recommended, as rapid absorption into the bloodstream could occur through the oral lesions. Benzylamine hydrochloride has a good analgesic effect, but many children find its taste intolerable.

The clinical management of oral candidiasis in children consists principally of using antifungal agents. Nystatin suspension (100 000 units/mL) should be used four times daily, and the child should be asked to retain the suspension in the mouth for as long as possible before swallowing. Nystatin and chlorhexidine, however, should not be used simultaneously, because there is some evidence to suggest that each drug inhibits the other's action.³⁶ Hence, it is advisable to instruct the patient to allow a time gap between the use of the two agents to prevent any possible antagonism from occurring. As nystatin suspension could be cariogenic because of its sugar content, the maintenance of proper oral hygiene becomes more important when antifungal therapy is being given. When there is a fulminating infection, systemic antifungal agents are needed. Ketoconazole (one of the earlier drugs used) has been found to be associated with liver toxicity. The development of the safer drug, fluconazole, has greatly facilitated the treatment of oral candidiasis in this group of patients.^{1,37}

'Cold sore'-type herpes simplex lesions are often found in children undergoing chemotherapy; the use of topical acyclovir is usually effective. In cases of severe infection, however, the use of systemic acyclovir may be indicated and the paediatrician must be consulted before its use. For children who are affected with xerostomia, the saliva becomes more viscous and acidic, and artificial saliva could be prescribed to relieve the symptoms and help with deglutition. A 5% solution of sodium bicarbonate has also been recommended as an adequate oral cleansing agent; it helps to buffer oral acids and dissolve mucous.²³

The basic principle of management remains the same for children who have undergone bone marrow transplantation and total body irradiation. However, graft-versus-host disease may develop after the transplantation and the dentist must be able to detect oral signs of this reaction. Such signs includes mucosal desquamation and ulceration, lichenoid changes, and xerostomia.^{2,5}

Dental care during remission

Regular dental care is of no less importance during remission. Children in full remission can be treated as normal for most routine procedures; yet, thorough

blood investigations may still be needed if an invasive procedure is planned. Besides twice-daily brushing with fluoride toothpaste, a 0.05% solution of sodium fluoride as daily mouthwash should be prescribed to replace the chlorhexidine mouthwash.³⁸ The sodium fluoride solution can also be used as an oral swab if the child cannot manage the rinse-and-expectorate action. It should be remembered that the regular ingestion of excess fluoride can cause dental fluorosis in the developing child. A mouth-rinsing regimen involving the sequential use of chlorhexidine and sodium fluoride has been found to be effective for controlling root caries in patients receiving radiotherapy in the perioral region.³⁹ The regimen consists of twice-daily rinsing with 0.1% chlorhexidine before, during, and after radiotherapy. This is then followed with a daily rinse with 0.05% sodium fluoride. Nasman et al¹⁹ found that a preventive regimen combining the use of fluoride and chlorhexidine mouthwash is effective in controlling caries in children who have undergone bone marrow transplantation. Other basic preventive measures such as dental flossing, dietary control, and topical fluoride treatment can also be introduced at this stage. The child should be recalled at monthly intervals initially, to monitor their compliance to preventive procedures and to watch for new carious lesions.

Long-term effects of treatment-associated oral problems in dental development

Xerostomia caused by chemotherapy tends to resolve completely in children.²⁰ Meticulous oral care must continue, however, because of the many subclinical oral environmental changes that arise after antineoplastic therapy.^{19,20} Conflicting results have been reported concerning the caries profile of children who have been treated for malignant disease. Nunn et al⁴⁰ compared treated children with their siblings and found no difference in the dental caries rate, whereas others have reported an increased incidence of caries.^{41,42}

Young children who have been treated with chemotherapy during their most active stage of dental development do not seem to have their dental development significantly altered.⁴³ However, disturbances in enamel mineralisation are frequently found in these patients.^{19,43} In contrast, damage to developing teeth is a frequent complication of radiotherapy to the head and neck region. The damage includes enamel hypoplasia, arrested tooth development, abnormal tooth/root formation, and disturbance in jaw growth.^{19,44,45} Hence, all patients should be followed up closely until their growth and development are completed. Future dental treatment that may be complicated by the damage

includes orthodontic tooth movement, prosthetic abutment procedures, and endodontic procedures. Aesthetic restorations of the enamel defects are also often necessary.

Conclusion

Proper oral care in children with leukaemia is critical. An understanding of the nature of the disease and its treatment are an important part of total patient care. Pretreatment dental care aims to prevent oral complications during chemotherapy, whereas in-patient dental care involves treating oral infections and relieving acute oral symptoms that may complicate the cancer therapy. Dental care during remission should focus on maintaining the dental health of the affected child. Although this review concentrates mainly on the treatment of children with leukaemia, the principle of treatment should remain the same for children with other types of cancer.

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