Prevention and Treatment of Oral Complications

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Phase I, before initiation of cancer treatment (review of medical record and oral history, planning of preventive strategies and dental treatments); phase II, from initiation of chemo-radiotherapy to 30–45 days post-therapy (maintenance of oral hygiene, reinforcement of parent/patient education in oral care, prevention and treatment of complications derived from cancer treatment); phase III, from 1 year to lifetime (periodic check-ups, maintenance, and reinforcement of oral hygiene, dental treatments, symptomatic care of the effects of long-term cancer treatment). The use of standardised protocols can avoid or minimise oral cancer complications and the side effects of cancer therapies.

oral prophylaxis and oncology | oral hygiene and oncology | oral care in paediatric oncologic patients | dental management and oncology

1. Paediatric Oncology

1.1. Epidemiology

The incidence of childhood cancer is highest in North America, parts of South and Central America, Europe, and Australia with an age-standardised incidence rate of ≥ 15.4 per 100,000 person-years for those 0–19 years of age [1]. Despite therapeutic advances and the fact that childhood cancer is a rare disease, it is the leading cause of death from disease until 14 years of age in high-income countries [2].

The most frequent types of cancer in children are leukaemia (25–35%), predominantly acute leukaemia (acute lymphoblastic leukaemia (ALL) (78%) and acute myeloblastic leukaemia (16%)), central nervous system tumours (22.6%), lymphomas (15.6%), and neuroblastomas or sympathetic nervous system tumours (7.8%) [3].

The prognosis of childhood cancer has improved dramatically in recent years, reaching a worldwide 5-year survival rate of 84% in children aged 0–14 years. The rate is similar in most European countries, including Spain (78%), Italy and the UK (82%), Germany (84%), Austria (85.9%), and the USA (83%), but is higher than in Eastern Europe (60–77%) [3].

1.2. Clinical Signs and Symptoms

Initially, patients with leukaemia are asymptomatic but, as it progresses and bone marrow infiltration occurs, haematopoiesis fails and peripheral cytopenia occurs, leading to anaemic syndrome and B symptoms (fever without infection, weight loss, night sweats). Blastic infiltration of other organs results in hepatosplenomegaly, lymphadenopathy, bone pain, central nervous system infiltration, mediastinal mass due to thymus growth, testicular infiltration, and infiltration of the skin and gums, depending on the type of leukaemia [4]. In patients with ALL, oral manifestations include pallor of the mucous membranes, petechiae, gingival bleeding, oral ulcers, gingival hypertrophy, palpable lymph nodes, laryngeal pain, sore throat, mucositis, candidiasis, gingivitis, and periodontitis. Patients may develop infections and haemorrhages due to neutropenia, immunodeficiency, and thrombocytopenia [5][6].

Cancers in children have a higher potential for growth and development than in adults and both the disease and its treatment may seriously impair normal development [7].

1.3. Treatment

Deep genetic sequencing has offered an unprecedented vision of the biology of cancer and has resulted in huge advances in the treatment of leukaemia. With the advent of precision medicine, directed therapy is becoming increasingly applicable, with new chemotherapeutic agents focused on cancer-specific biology, including biological drugs, targeted therapy, monoclonal antibodies, anti-angiogenics, and chimeric antigen T-cell receptor immunotherapy. Despite these advances, surgical resection, chemotherapy, and radiotherapy remain the main therapies for childhood cancer [8].

Leukaemia therapy depends on factors such as the disease type and subtype, the risk factors, and the patient's age. In general, the treatment of choice is chemotherapy with or without coadjuvant treatments (radiotherapy, corticosteroids) and haematopoietic stem cell transplantation (HSCT) or bone marrow transplantation, which is generally carried out in acute cases and some chronic myeloid leukaemia cases [9].

Standard chemotherapy normally includes four well-defined therapeutic stages: induction therapy, preventive therapy or central nervous system prophylaxis, consolidation or intensification, and maintenance or continuation [6][10].

2. Oral Disease in Childhood Cancer

Oral complications may be due to the cancer itself or to the treatment received [10], and vary according to the age at diagnosis and the type of chemotherapy, the dose used, and the area of irradiation in the case of radiotherapy [11][12]. Oral complications are mostly associated with pre-existing factors (caries, gingivitis, and poor hygiene) that affect their initiation, increase, and persistence [7].

Childhood cancer patients may have many short- and long-term oral complications, which include specific oral tissue manifestations (alterations in the mucosa, salivary glands, muscle and bone, sensory alterations, alterations

in teeth and gums) and non-specific oral tissue manifestations (oral bleeding, opportunistic infections, secondary tumours, post-transplant lymphoproliferative disorders, dental anomalies, and craniofacial alterations) (Table 1).

Table 1. Oral complications in blood cancer patients and patients with bone marrow transplantation.

Category	Tissue	Oral Complication	Early Presentation	Late Presentation
Specific Tissue manifestations	Mucous membrane	Mucositis (approx. 100% children) [13][14][15][16].	+	+
		– Atrophy and burning. – Paleness (Anaemia). – Petechiae (22.6% children) [17]. – Ecchymosis (4.8% children) [17].	+	
		– Erosions and neutropenic ulcers (50% children) [17]. – Cracked lips (12.9% children) [17].	+	
		Lichenoid reactions, erythema, and ulcers (GVHD).		+
	Salivary glands	Pyogenic granuloma	+	
		Glandular hypofunction: Xerostomia (35.5% children) [17].	+	+
		Sialoadenitis	+	+
		Mucocele		+
	Musculoskeletal	Less elasticity, reducing the range of mobility and limiting the mouth opening (e.g., Scleroderma) (GVHD).		+
		Jaw osteonecrosis induced by therapy (osteoradionecrosis, or bisphosphonate-related osteonecrosis) [14].		+
		Temporomandibular disorders (eg. trismus).		+

Category	Tissue	Oral Complication	Early Presentation	Late Presentation
		– ATM pain (6.5% children) [14][17].		
	Sensory disoders	Dysgeusia/taste alteration [14].	+	+
		Neuropathies	+	+
		– Dental hypersensitivity – Oral pain (43.5% children) [17].		+
	Teeth and gums	– Dental mineralization and rampant caries [14][18]. – Dental abnormalities (short roots, tapering roots, enamel dysplasias, microdontia, tooth agenesis) [14][19].		
		– Gingival hypertrophy/hyperplasia [14].		+
		– Desquamative gingivitis (GVHD).		+
		– Acute periodontal infections (symptomatic). Gingivitis (38.7% children) [17]	+	+
		– Chronic pre-existing periodontal infections (asymptomatic)	+	+
Non specific Tissue manifestations		Oral bleeding (6–42% children) [8][14].	+	+
		Opportunistic infections: bacterial, viral and fungal. (herpes simplex infection: 9.7% children; candidiasis: 16.1% children) [14][15][17].	+	+

Category	Tissue	Oral Complication	Early Presentation	Late Presentation
		Secondary tumours (e.g., squamous cell carcinoma). (3.2% children) [20].	+	+
		Post-transplant lymphoproliferative disorders (lymphadenopathies of head and neck: 11.2% children) [17].	+	+
		Abnormalities of dental development and craniofacial alterations in paediatric patients. [21]	+	+

Note. GVHD: Graft versus host disease [Modification of table by Elad S, Raber-Durlacher J, Brennan MT, et al. 2015]. Early presentation: oral complications appear at the beginning of cancer treatment. Late presentation: oral complication appearing at the end of cancer treatment or after treatment.

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Institute Common Toxicity Criteria [25], the Children's International Mucositis Evaluation Scale (ChIMES) [22], the Oral Assessment Guide (OAG) [23], the modified Oral Assessment Guide (OAG) [24], the Oral Mucositis Assessment Scale [25] (and the Oral Mucositis Daily Questionnaire [26], and the Guidelines of the Children's Oncology Group oral-dental panel [27]. Some of these scales not only quantify changes in the integrity of the oral cavity but may also be useful in the early identification of complications that require prompt therapy to reduce morbidity in immunosuppressed patients and decrease the severity of oral changes before, during, and after chemotherapy [28].

Successful management of oral complications, including systemic infections of oral origin, should begin with the oral examination, the introduction of comprehensive oral hygiene measures, and definitive dental interventions prior to initiation of cancer therapy. The incorporation of a paediatric dentist in the multidisciplinary team in childhood cancer, and the establishment of standardised protocols based on prevention, and not just the treatment of the complications is, accordingly, necessary in order to ensure successful cancer treatment and the best quality of life.

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