

The Oral-Dental Findings of Patients Treated with Antineoplastic Treatments Targeting Non-Head and Neck Tumors in Childhood

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Abstract

Aim This study investigates oral complications in pediatric oncology patients undergoing antineoplastic treatments for non-head and neck tumors, with a focus on their impact on tooth development.

Material and method Twenty pediatric patients (aged 3 to 14) undergoing chemotherapy for non-head and neck tumors were examined clinically. Oral and perioral tissues were assessed, and specific complications were documented. Patient records were retrospectively reviewed to identify pre-existing oral issues.

Results The study revealed significant oral complications associated with antineoplastic treatments, including enamel defects (60%), gingivitis (60%), delayed apexification (55%), and mucositis (30%). Additional complications such as lymphadenopathy, delayed eruption, and herpes simplex infection were also observed.

Conclusion Antineoplastic treatments for non-head and neck tumors in pediatric patients can significantly affect tooth development, leading to various oral complications. Early detection and management of these complications are vital for treatment continuity and enhancing the quality of life for pediatric oncology patients.

Keywords Antineoplastic treatments, Chemotherapy effects, Childhood cancer, Oral complications, Tooth development

Introduction

Cancer is the second leading cause of death in children under the age of 14 (1,2). While the survival rate for childhood cancers was around 58% in the mid-1970s, advancements in multidisciplinary treatment approaches have significantly improved this rate to approximately 85% for children and 86% for teens (1-3). As we continue to make strides in multidisciplinary research, the role of dentists in diagnosing and treating oral manifestations in patients has become increasingly significant (4,5).

The complications of cancer chemotherapy are often more visibly apparent in the oral cavity than in other parts of the body (6). These complications can manifest as infection, bleeding, cytotoxicity, neurological symptoms of toxicity, and alterations in the color, nature, and continuity of the oral mucosa (6). Most of these reactions persist for an extended period even after the completion of treatment. The occurrence of these reactions varies based on the dosage of drugs, the combination of drugs, the duration of treatment, and individual patient characteristics (6-9).

Pediatric cancer patients often experience a range of oral complications directly related to chemotherapy. These complica-

tions include disturbances in tooth development, poorer oral hygiene, oral lesions, and hyposalivation. Additionally, there is an increased prevalence of dental caries compared to healthy children. These adverse effects can significantly impact the overall well-being of young patients undergoing cancer treatment (10). Recognizing and addressing these oral issues are crucial for maintaining their quality of life.

Given the high prevalence of dental and oral problems in pediatric oncology patients, a proactive approach to dental care is essential. Dentists play a vital role not only in pretreatment assessments but also in ongoing care during and after cancer therapy. By closely monitoring oral health, identifying early signs of complications, and providing timely interventions, dental professionals contribute significantly to the overall management of pediatric cancer patients. Collaborative efforts between oncologists and dentists can enhance the well-being of these young individuals (11,12).

Despite the prevalence of these complications, there is a limited number of studies that retrospectively and prospectively examine orodental complications in pediatric oncology patients (7-9). Therefore, investigating the incidence of oral problems in children undergoing chemotherapy for cancer is the objective of our study.

Material and Methods

Our study included 20 children aged between 3 and 14, who sought care at the Pediatric Oncology Department. The criteria for inclusion in this study were as follows: Tumor localization outside the head and neck region, Age ranging from 3 to 14 years,

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Scheduled chemotherapy, No application of radiotherapy to the head and neck region, Absence of any other systemic disease that could affect the teeth (such as diabetes type I).

In this study involving 20 patients, there were 9 cases of Rhabdomyosarcoma, 4 cases of Wilms Tumor (Nephroblastoma), 3 cases of Burkitt Lymphoma, 1 case of Osteosarcoma, and 3 cases of Ewing sarcoma.

The initial clinical examination encompassed an assessment of oral and perioral tissues. Extraorally, an inspection of submental, submandibular, cervical, and pre- and post-auricular lymph nodes was carried out, along with an evaluation of perioral skin. The intraoral examination involved assessing the condition of existing teeth, considering factors like luxations, color changes, and eruption timing. Additionally, examinations of the buccal mucosa, tongue, floor of the mouth, hard and soft palate, and gums were conducted. In cases where necessary, panoramic and periapical radiographs were taken. A retrospective review of forms completed during the patient's initial visit was performed to ascertain the presence of any oral issues at the time of the initial diagnosis.

Specific complications among pediatric oncology patients undergoing antineoplastic treatments for non-head and neck tumors were identified. These included a range of oral manifestations such as ulcerations, petechiae, mucositis, erythema, ecchymosis, painful dryness of the lips, oral mucosal pallor, lymphadenopathy, severe gingivitis, herpes simplex infection, candidiasis, sore throat, white patches on the tongue, delayed eruption of teeth, delayed apexification, taurodontism, enamel opacities, hypocalcifications, increased caries index, shortened and thin roots, hypoplasias, and root agenesis.

Results

In our study, we examined a cohort of 20 patients, aged between 3 and 14, consisting of 11 boys and 9 girls. The mean age within this group was 8.5 years. Various oral conditions were observed among pediatric oncology patients undergoing antineoplastic treatments for non-head and neck tumors. Enamel defects were prevalent, affecting 60% of the patients, alongside gingivitis and lymphadenopathy, also each presenting at a rate of 60%. Delayed apexification was noted in 55% of cases, followed by decreased enamel thickness at 40%. Mucositis was reported in 30% of patients, while enamel opacities and ulcerations were observed in 20% of cases each. Delayed eruption occurred in 15% of patients, while root agenesis, herpes simplex infection, and candidiasis were each documented in 10% of cases. Taurodontism was not observed in any of the patients in this cohort.

Due to thrombocytopenia-related complications in these patients, petechiae in the oral region were observed in 35% of cases. A pronounced intraoral ecchymosis developed in the 12th patient. Spontaneous bleeding occurred in the intraoral region, with the most common site being the gums. Along with bleeding, lip fissures, and, additionally, erythema, oral mucosal pallor, sore throat, and a coated tongue were observed in patients undergoing chemotherapy.

Discussion

Epidemiological Context and Treatment Advancements

Examining the broader context, the incidence of childhood cancer in Finland is reported at about 150 new cases annually. This positions cancer as the second most common cause of death among children under 14, following traffic accidents in the United States. The survival rates have witnessed a notable surge, primarily attributed to intensified multidisciplinary treatment protocols. Advanced chemotherapeutic agents play a pivotal role, not only in halting malignant cell growth but also in extending patients' lifespans, thereby enhancing their overall quality of life (10-12).

Antineoplastic Agents and Reproductive Cycle Dynamics

The effects of antineoplastic agents hinge on their ability to impede the metabolism or reproductive cycle of tumor cells (13). This cycle comprises distinct phases- G1, S, G2, and M- with cells entering from the G0 phase. The complexity arises from the varying selectivity of antineoplastic agents. Some are cycle-dependent, acting exclusively in specific mitotic phases, while others, like alkylating agents, operate in both reproductive cycles and resting phases (14,15). Alkylating agents work by adding an alkyl group to the guanine base of the DNA molecule, preventing the strands of the double helix from linking as they should. This causes breakage of the DNA strands, affecting the ability of the cancer cell to multiply (16).

Challenges in Chemotherapy and Oral Complications

An overarching challenge in antineoplastic treatments is the lack of selectivity between tumor and normal tissues (17), leading to complications, notably in the orodental region (18). Of particular concern are complications stemming from plant alkaloids (19), with vincristine alkaloids manifesting as severe side effects (20). As survival rates increase, addressing these orodental complications gains specific significance. A study by Ludwig et al. focuses deliberately on childhood tumors situated outside the head and neck region (21), excluding patients with primary head and neck tumors or recurrent cases.

Collaborative Care for Anticipating Complications

Mitigating complications, such as soft tissue discomfort and oral infections, becomes imperative during antineoplastic treatments (22). Collaboration between medical oncologists and dentists becomes a cornerstone in developing shared procedures integral to implementing the patient's oncological program (23). Stomatitis, a common side effect, was observed in our study, aligning with literature experiences and manifesting within varying timelines based on drug administration specifics (22,24).

Impact on Soft Tissues, Dental Structures; Hemorrhages, Dental Caries, and Structural Changes

Chemotherapy can indeed lead to a variety of oral complications, which can affect the patient's quality of life and the continuity of treatment as follows:

- **Mucosal Discomfort:** Chemotherapy can cause oral mucositis, a condition characterized by inflammation and ulceration of the mucous membranes in the mouth (25,26). This can lead to discomfort, pain, and difficulties in eating and speaking (25).
- **Pseudo-Toothache:** While specific information on pseudo-toothache related to chemotherapy is limited, it's known that chemotherapy can cause various oral and dental problems, including toothaches and increased sensitivity (27).
- **Altered Taste:** Changes in taste, also known as dysgeusia, are common during chemotherapy. Patients may experience a metallic or bitter taste, or other changes in their sense of taste (28,29).
- **Gingivitis:** Chemotherapy can lead to oral complications such as gingivitis, an inflammation of the gums. This can cause symptoms like swollen, red, or bleeding gums (30).
- **Mucositis:** This is a common side effect of chemotherapy, causing painful inflammation and ulceration of the mucous membranes lining the digestive tract (26,31).
- **Herpes Simplex:** Patients undergoing chemotherapy are at a higher risk of viral infections, including herpes simplex. This is due to the immunosuppressive effects of the treatment (32).
- **Ulcers in the Gingival Mucosa:** Ulcers can form on the gums as a result of chemotherapy-induced mucositis (33,34).

It's important for patients undergoing chemotherapy to maintain good oral hygiene and have regular dental check-ups to manage these potential side effects. If any oral complications arise, they should be addressed promptly to ensure the continuity of chemotherapy (35).

Oral Hemorrhages: Chemotherapy can cause thrombocytopenia, a condition characterized by low platelet counts, which can lead to bleeding issues, including oral hemorrhages. In our study, this was observed in a quarter of the patients (36,37).

Dental Caries: Despite care, dental caries were present in 60% of the patients at the onset and developed post-chemotherapy. This could be due to various factors, including changes in oral flora and decreased salivary flow caused by chemotherapy (38,39).

Structural Changes in Teeth: Chemotherapy can cause structural changes in the teeth, including enamel damage. Enamel hypoplasia (underdevelopment or incomplete development of the tooth enamel) and opacity were observed, which can have diagnostic value (40,41).

Dental Development Implications and Animal Studies Correlation

Chemotherapy has a multifaceted impact on dental development, leading to various changes in dental structures. These effects include delays in apexification, eruption, root agenesis, and thinning. Interestingly, taurodontism (an elongated pulp chamber) was not observed in this context. These alterations, particularly affecting enamel and dentin, are closely associated with specific drug combinations. The study underscores the importance of personalized interventions to address these dental complications. Furthermore, correlations with animal studies, especially those involving cyclophosphamide and doxorubicin, reinforce the findings and highlight the intricate effects of cytotoxic drugs on dental tissues (42,43).

Family Awareness and Comprehensive Care

Families play a crucial role in managing oral complications during chemotherapy. Specific recommendations include post-vomiting oral care and dietary considerations. Given the child's vulnerability to chronic fatigue, it is advisable to keep dental procedures brief. Additionally, healthcare providers should consider the impact of chemotherapy-induced photosensitivity on melanocytes, which may be compromised (44,45).

Conclusion

In conclusion, our study highlights the significant oral complications faced by pediatric oncology patients undergoing chemotherapy for non-head and neck tumors. From enamel defects to mucositis and delayed dental development, these complications underscore the need for proactive dental care within multidisciplinary treatment approaches.

Collaborative efforts between oncologists and dentists are important in early detection, timely intervention, and individualized dental care for pediatric cancer patients. Additionally, future research should focus on understanding the mechanisms behind chemotherapy-induced oral complications and developing effective preventive and therapeutic strategies to improve the quality of life and treatment outcomes for these vulnerable individuals.

Declarations

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