DENTAL TREATMENT OF PEDIATRIC ONCOLOGICAL PATIENTS

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ABSTRACT

In their work, dentists, especially those in general dental practice, encounter patients of various ages and with different health conditions. Undoubtedly, the pediatric population is not excluded in this context, and special attention is paid to oncological patients in this population.

Malignant diseases require a special approach in the field of dentistry, both through guidelines and preventive measures, as well as in cases where it is necessary to treat conditions or diseases resulting from oncology treatment or the disease itself.

Oncological treatment consequences are also visible in the oral cavity, which becomes extremely sensitive during the course of treatment. Children, as oncological patients, can quickly transition from a relatively "healthy state" to a state characterized by significant changes in the oral cavity, which are conditions that are extremely difficult for children to endure. These changes manifest as complications such as oral mucositis, xerostomia, opportunistic infections, dental hypersensitivity, developmental disorders of the jaw structures, and GvHD. For complications during and after chemotherapy, the treatment is symptomatic, involving the implementation of a treatment protocol with clearly defined procedures for each complication, ranging from preventive brushing to the application of medication.

Due to the increasing number of pediatric oncological patients, it is the dentist's task to understand the nature of malignant diseases, their basic characteristics, how to prevent the development of oral complications during and after oncological therapy, and how to treat any complications that may arise.

Keywords: oncological patients, chemotherapy, oral complications, preventive measures

Introduction

Advances in diagnostics and the application of new antineoplastic therapies have increased the expected survival of patients suffering from oncological diseases, which means that a doctor of dental medicine is more likely to meet oncological patients and provide them with dental treatment in various stages of oncological therapy. Cancer is a major public health problem in Bosnia and Herzegovina. Malignant tumors are the second leading cause of death after heart and blood vessel diseases.

It is estimated that around 400,000 children and young people (aged 0 to 19) get cancer worldwide each year. Most of these children live in low- and middle-income countries where treatment is often unavailable. As a result, between 15 and 45% of children with cancer survive in those countries, compared to more than 80% of survivors in high-income countries. This deep inequality threatens the achievement of health coverage and the realization of the political commitments of the United Nations Sustainable Development Agenda by 2030. Preventable childhood cancer deaths in low- and middle-income countries are the result of a lack of diagnosis, misdiagnosis or delayed diagnosis, barriers in accessing treatment, leaving treatment, higher relapse rates, etc.

According to the data on the five leading causes of death of the population from the Health Statistical Yearbook of the Federation of Bosnia and Herzegovina for the year 2022, malignant neoplasms (C00-C97) are the third leading cause of death in the 1–4, 5–9 and 15–19 age groups and the second leading cause of death in the 10–14 age group.

The causes of childhood cancer are quite different from those that affect adults. Several types of cancer are almost unique to children, and the forms of cancer most commonly seen in adults, including lung, breast, and stomach cancer, are very rare in children. It is believed that in most children born with a genetic predisposition to certain types of cancer, a trigger is needed for the manifestation of this disease. Research is trying to establish which factors trigger the development of cancer in childhood. The link between childhood cancer and ionizing radiation is well established. Some of the first evidence came from studies of children whose mothers underwent abdominal X-rays during pregnancy, a practice that is now avoided.

Over the past 20 years, it has been established that constant exposure to electromagnetic fields of certain frequencies increases the risk of childhood leukemia. The International Agency for Research on Cancer – IARC has classified electromagnetic radiation of extremely low-frequency electric and magnetic fields as possibly carcinogenic. There are concerns that exposure to electromagnetic radiation from mobile phones is harmful to health, prompting international agencies to call for precautions to limit their use.

Numerous studies have been devoted to the possible role of infections in the development of childhood cancer. Viruses are known to be involved in some types of human cancer, including Burkitt's lymphoma, Hodgkin's lymphoma, nasopharyngeal carcinoma (all associated with Epstein-Barr virus), liver cancer (associated with hepatitis B virus), and Kaposi's sarcoma (associated with HIV and HHV8). On the other hand, two different theories suggest that childhood leukemia may be the result of an abnormal response to a common infection, rather than the result of a specific virus.

The use of some medicines and drugs is associated with the occurrence of cancer in childhood. There are reports of possible carcinogenic effects of many drugs taken by mothers during pregnancy. A safe transplacental carcinogen is diethylstilbestrol (DES), a hormone given to pregnant women in some countries to prevent miscarriage. DES caused a specific type of cancer in girls and young women and has since been phased out. It is also known that some chemotherapy drugs carry the risk of causing secondary cancer.

According to the latest data from the Health Insurance Institute of the Federation of Bosnia and Herzegovina register, the number of newly diagnosed children ranges from 40 to 60, and even up to 100 per year. Considering these data, it is clear that dentists, especially those in general dental clinics, will encounter children who are oncological patients. Oncological therapy causes many complications in the oral cavity, and dentists must know ways to prevent and treat complications in the oral cavity.

Timely inclusion of dentists in the medical team will prevent the occurrence of complications with their knowledge and actions.

The purpose of this article is to present a modern approach to the dental treatment of pediatric oncological patients and their specificities and priorities. The article includes methods for preventing oral diseases and maintaining oral health during and after the completion of oncological therapy.

What is cancer?

Cancer is a common name for several related diseases. The common characteristic of all types of cancer is that the cells in the body begin to divide uncontrollably and spread to the surrounding tissues. Cancer cells differ from normal cells in several ways. One important difference is that cancer cells are less specialized than normal cells and do not have a function of their own. This allows them to constantly divide and ignore signals that normal cells respond to by stopping division or causing cell death. They are also able to evade the immune system and, in some cases, use it for growth. A tumor is a solid mass of tissue. It can be malignant or benign (Figure 1).

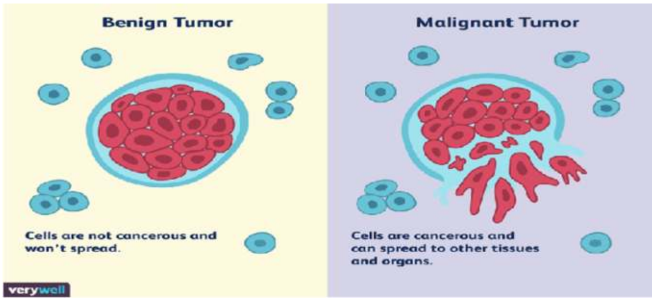

Figure 1

Cancer is a malignant tumor that can spread to the surrounding tissues but also to distant organs through the blood or lymphatic system. Then we call it a metastatic tumor and the process itself a metastasis. There are also non-cancerous cell changes, but they must be carefully monitored because they have a malignant alteration tendency. These are **hyperplasia, dysplasia, and carcinoma in situ**.

Genetics of cancer

Cancer is a genetic disease caused by **changes in the genes** that control cell growth and division. Such genetic changes can be hereditary or acquired. It is believed that only **5–10%** of cases are hereditary, while the rest are the result of external factors.

Types of genes that cause cancer

The genetic changes that contribute to cancer tend to affect three main types of genes—proto-oncogenes, tumor suppressor genes, and DNA repair genes. These changes are sometimes called "drivers" of cancer.

Proto-oncogenes are involved in normal cell growth and division. However, when these genes are altered in certain ways or are more active than normal, they can become cancer-causing genes (or oncogenes), allowing cells to grow and survive when they should not.

Tumor suppressor genes are also involved in the control of cell growth and division. Cells with certain alternations in tumor suppressor genes can divide in an uncontrolled manner.

DNA repair genes are involved in fixing damaged DNA. Cells with mutations in these genes tend to develop additional mutations in other genes and changes in their chromosomes, such as duplications and deletions of chromosome parts. Together, these mutations can cause cells to become cancerous. As scientists learned more about the molecular changes that lead to cancer, they discovered that certain mutations commonly occur in many types of cancer. Cancer treatments targeting gene mutations found in cancer are now available.

The most common types of cancer in children

Acute lymphoblastic leukemia is the most common childhood malignancy, and it usually occurs between the ages of 2 and 10. In acute lymphoblastic leukemia, immature blood cells are lymphocytes, white blood cells. Their role is to fight infection. For this reason, infections are not uncommon in children with this diagnosis (Figure 2).

Along with it, acute myeloid leukemia is also common. Symptoms that can occur in both forms are pale skin, bleeding, joint pain, general weakness, and weight loss. The disease progresses rapidly, and treatment should be initiated as soon as possible.

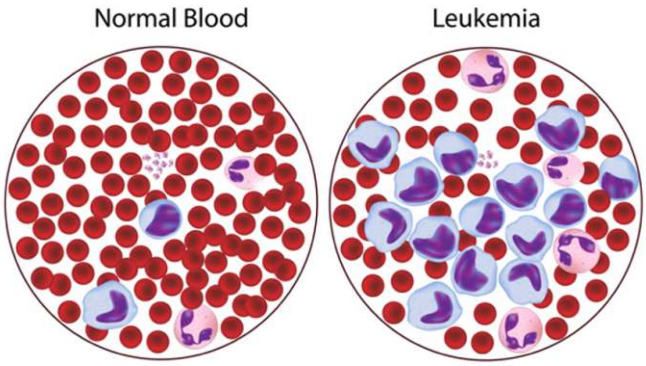

Figure 2

Malignant tumors of the brain and spinal cord

The second most common tumors in children are brain and spinal cord tumors. These are the most common solid tumors in children. There are several types of clinically distinct tumors. Symptoms depend on the location and size of the tumor, as well as the child's age. Some of the symptoms of brain tumors are headache, nausea, vomiting, drowsiness, dizziness, and vision problems. The symptoms of spinal cord tumors are back pain, weakness in the legs, and urinary hesitancy.

Non-Hodgkin's lymphoma

It differs from non-Hodgkin's lymphoma in adults. A more aggressive form occurs in children and requires more intensive treatment, but it responds better to treatment than in adults. The first symptoms in adults are enlarged lymph nodes. Anemia, weakness, rash, loss of appetite, and, occasionally, breathing difficulties occur in children.

Neuroblastoma

Neuroblastoma is a cancer of immature brain cells, and, in most cases, it starts in the adrenal glands. It occurs in young children, usually up to the age of five. It can cause a variety of symptoms, from abdominal swelling to fever.

Wilms' tumor

Wilms' tumor most often arises in one of the kidneys, rarely in both. In most cases, the tumor occurs in children up to the age of four and is extremely rare in older children and adults. Abdominal swelling, loss of appetite, nausea, and bone pain may occur.

Therapy for malignant diseases

There are several types of cancer treatment, and the choice depends on the type and location of the tumor, the patient's age, and general condition. Usually, it is not just one type of therapy, but a combination therapy is done to improve the effect of the treatment.

Surgery is the process by which a surgeon removes cancer from a patient's body. Surgery is performed on well-circumscribed solid tumors. When a tumor cannot be removed by surgery alone, surgical treatment is combined with other forms of therapy.

Chemotherapy and radiotherapy can be used both before and after surgery. Before surgery, they are used to reduce the tumor mass and make it easier to remove the tumor surgically, and after surgery, they are used to eliminate metastases if present.

Immunotherapy stimulates the normal immune system to defend against cancer cells by locating and destroying them.

Stem cell transplantation therapy is used mainly in patients with hematological tumors but also in those in whom chemo and radiotherapy did not work.

Dental treatment of pediatric oncological patients

Dental treatment of pediatric oncological patients focuses on two groups of patients. The first group includes patients undergoing therapy who develop oral complications during and after therapy. The second group includes children who have survived cancer and have dental and orofacial anomalies caused by the therapy itself. From the dental perspective, the most important component in oncology therapy is prevention before, during and after oncological therapy (Figure 3).

Figure 3

Preventive measures first include educating the patient and parents about the importance of oral hygiene to prevent and minimize oral complications during therapy.

A **clinical examination** includes inspection, palpation, percussion, tooth mobility testing, pulp vitality tests, and oral hygiene assessment.

The examination achieves the following:

- the risk of serious oral complications is reduced;

- existing infections that could otherwise cause serious systemic infections are diagnosed and remedied in time;

- oral cavity pain is prevented, reduced and eliminated,

- the patient is educated about oral hygiene during therapy;

- complications that could cause malnutrition are prevented;

- the chances of the patient successfully completing the planned therapy of the primary disease increase;

- the quality of life improves.

Dental approach and treatment during oncological therapy

The most important component in the course of oncological therapy is to preserve oral health by applying actions to prevent complications.

Preventive measures are:

- *self-examination* (enables detection of redness, swelling, sores)

- *intensive oral hygiene* (ultra-soft brushes, pastes with fluorides, chlorhexidine gauze, dental floss, adequate nutrition) and

- *oral care* (dry mouth prevention, rinsing with mouthwash or solution; H2O2, alcohol-based, or flavored mouthwashes are not recommended for rinsing).

Periodic check-ups without treatment (preferably once every 6 months), and more often in patients who develop chronic oral GvHD (**Graft Versus Host Disease**), xerostomia, or trismus. Orthodontic appliances and prostheses should only be worn if they do not cause any soreness or irritation of the mucous membrane and if hygiene is satisfactory. During oncological therapy, it is most important to carefully monitor the patient's oral health to enable the timely detection, prevention, and treatment of complications should they arise. When a dental procedure is necessary, it is necessary to consult with the patient's oncologist. Regular dental procedures are postponed until the end of therapy or are performed between cycles of chemotherapy.

Small carious lesions in children are treatable during therapy, with conservative methods, thanks to progress in the development of adhesive materials in dentistry. The materials of choice are glass ionomers and composites. All pits and fissures should be filled in order to prevent the formation of carious lesions. The method to prevent incipient carious lesions is the application of silver diamine fluoride. A side effect is black staining of the tooth surface, and this should be clearly emphasized to the parents and the patient before the actual application. Pediatric dentists have different opinions on the treatment of vital deciduous teeth with reversible pulpitis. Most dentists opt for extraction rather than vital pulpotomy in immunosuppressed patients to avoid later complications. There is a lack of evidence on the benefits of vital pulpotomy in immunosuppressed patients. Endodontic treatments on permanent teeth can be performed when indicated if the teeth can be restored. Endodontics must be performed 7 days before therapy initiation to allow enough time for the periapical tissue to heal.

CHEMOTHERAPY

During chemotherapy, it is vital to have a complete blood count (CBC) of the patient before any dental procedure. We ask the oncologist to do a CBC 24 hours before the dental procedure so that we can check the platelet count, neutrophil count, and clotting factors. Invasive procedures are postponed if the platelet count is under 75,000/mm3 and when the neutrophil count is under 1,000/mm3. The platelet count is not important only for extractions. There is also a risk of bleeding or hematoma formation in the application of local anesthetic injection. If the child has under 75,000/mm3 platelets, it is necessary to consult with an oncologist about the need for transfusion or hospitalization. If the patient has a fever and no other causes, the oral cavity should be examined for signs of oral infections. The usual oral symptoms of infection may be altered due to immunosuppression, and the dentist should keep this in mind. The most favorable time for dental procedures in children undergoing chemotherapy is 17–20 days after therapy or 2–3 days before the next cycle.

RADIOTHERAPY

During radiation, control examinations are performed every 7–14 days, i.e. every 10 fractions. It is important to ensure that the patient maintains oral hygiene at home, as well as in the hospital. We must regularly examine the oral mucosa for inflammation, infection, or bleeding. If necessary, we prescribe local antiseptics for rinsing the oral cavity. For pain relief, we can prescribe analgesics to the patient, and topically apply a local anesthetic. Removable orthodontic braces can be worn by patients as long as they can tolerate them and maintain oral hygiene. If the patient wears fixed orthodontic braces at the time of cancer diagnosis, it is recommended that the dental braces be removed, and orthodontic therapy can be continued two years after the end of radiation therapy. To relieve patients of the unpleasant symptoms of dry mouth, we recommend the following: drink water often (especially with meals), drink at least 1.5–2 liters of water or sugar-free liquids a day, suck on ice cubes, consume sugar-free chewing gum or candies, and use artificial saliva preparations if necessary (based on carboxymethyl-cellulose, glycerol). Follow-up examinations after radiotherapy are carried out every 4 to 8 weeks during the first 6 months.

Some side effects of radiotherapy are lifelong. These are xerostomia due to irreversible damage to the salivary glands, the risk of caries and the risk of osteoradionecrosis.

Dental approach after oncological therapy

After the completion of radiotherapy and resolution of acute complications, the patient should come for a dental check-up every 4 to 8 weeks during the first 6 months. Patients should continue to take care of oral hygiene, use splints with fluoride, and avoid cariogenic foods and drinks. Invasive procedures should be avoided in these patients. If they cannot be avoided, antibiotic prophylaxis is mandatory, and hyperbaric oxygen therapy can be considered before and after extractions.

Oral complications of oncological therapy

Oral mucositis is an inflammation of the mucous membrane of the oral cavity and can occur in mild, moderate, and severe forms (Figure 4).

Figure 4

In the mild form, only inflammation is present, without ulcerations. In the moderate form, there are ulcerations on the mucous membrane. In the severe form, there is severe pain and the inability of the patient to take food on his own. Mucositis increases the risk of oral and systemic bacterial, viral, and fungal infections. Oral mucositis develops in 40% of children receiving standard-dose chemotherapy and in 80% of children receiving radiation therapy for head and neck cancers. It also occurs in 75% of children undergoing bone marrow transplantation.

Oral infections are opportunistic infections that can occur in children undergoing therapy more often than in adults. The causes of secondary infections are the direct effects of drugs on the bone marrow and the consequent decrease in the number of white blood cells but also their cytotoxic effect on the cells of the oral epithelium. They can be bacterial, viral, and fungal. Candida albicans infection is most common. Clinically, we see scrapable white deposits in the mouth and inflamed red mucous membranes.

Xerostomia is a dry mouth caused by reduced saliva flow or its complete lack due to damage to the glandular cells. The diagnosis is based on the clinical picture and salivation tests. Some of the clinical symptoms are fissured tongue, cheilitis, glossitis, and dysphagia. Confirmation of the diagnosis is a measured unstimulated whole saliva flow rate of less than 0.2 mL/min. Saliva also changes its composition and becomes more mucoid because the serous glands are more sensitive to radiation.

Functional problems occur due to mucositis, dry mouth, trismus, and infections. Speech, feeding, and swallowing functions are impaired. Dry and chapped lips and angular cheilitis often occur as side effects of radiation and chemotherapy. The patient should lubricate the lips with glycerin- and petroleum jelly-based preparations. Natural moisturizers such as honey, coconut oil, olive oil, and aloe vera can also be used.

Neurotoxicity is a persistent, deep, sharp pain that is similar to a toothache, but the causative tooth does not exist. This complication is caused by antineoplastics from the group of vinca alkaloids, such as **vinblastine and vindesine**. The pain can be mistaken for trigeminal or facial neuralgia. To avoid diagnostic errors, it is necessary to know the side effects of the medicine the patient is receiving and to take X-rays of the teeth. Neuropathic pain is usually transient and disappears after the completion of chemotherapy.

Bleeding tendency occurs due to a reduced platelet count and clotting factors. Thrombocytopenia occurs due to the suppressive effect of high doses of radiation or antineoplastic drugs on the bone marrow. Symptoms that can occur in the oral cavity are submucosal hemorrhages, petechiae on the palate, ecchymoses, purpura of the lateral edge of the tongue, hemorrhagic bullae, and gingival bleeding caused by tooth brushing.

Radiation caries is characterized by accelerated enamel and dentin demineralization. It is associated with reduced salivation, which is an indirect consequence of radiation therapy. Radiation caries is a chronic side effect that occurs within three months from the initiation of therapy, and patients have a lifelong risk of developing this form of caries. The characteristic clinical finding is an initial caries lesion in the cervical part of teeth, most often incisors and canines, which progresses rapidly. It can appear in two other clinical forms, of which the more common one is the involvement of the entire buccal surface, followed by the lingual and palatal surfaces.

Trismus is caused by the loss of elasticity of nerve-muscle fibers. It results in limited mouth opening, speaking difficulties, and poor oral hygiene. Trismus is a chronic consequence of radiation and occurs 3–6 months after the end of therapy.

Osteoradionecrosis is the obliteration of blood vessels, damage to endothelial cells, and consequent ischemic bone necrosis. It occurs due to exposure to high doses of radiation and is the most dangerous side effect of radiation in the head and neck area. Clinical symptoms of osteoradionecrosis are discomfort and sensitivity in the affected area, bad taste in the mouth, paresthesia, fistulas, secondary infections causing osteomyelitis, and pathological fractures (Figure 5).

Figure 5

There is an exposed non-healing necrotic bone in the mouth. Microorganisms from the oral cavity can cause secondary infections of the damaged bone. The area is painful for the patient. The risk of developing osteoradionecrosis is lifelong and proportional to the radiation doses received.

Patients who have received doses of 50 Gy and above are at the highest risk. It occurs more often in the mandible due to the compact structure of the bone. Factors that increase the chance of osteoradionecrosis are tooth extractions, tumor localization, irradiated bone surface, total radiation dose, poor oral hygiene, tobacco and alcohol consumption, and uncontrolled diabetes.

The diagnosis is made by clinical examination and X-rays.

Oral complications of stem cell transplantation

Complications occur due to immunosuppression following stem cell transplantation. As many as 80% of patients develop oral complications. After allogeneic stem cell transplantation, patients can develop graft-versus-host disease (GvHD). In GvHD, the donated cells attack the patient's cells, which they recognize as foreign. A positive side effect is that these cells also attack the remaining tumor cells. GvHD can occur in acute and chronic forms. In 80% of cases, the oral cavity is affected by the chronic form of GvHD. Clinical symptoms in the mouth are reticulated white lesions on the mucosa of the cheeks and tongue, which are similar to lichen planus.

Challenges for the dentist when treating children in remission

Children who are treated for cancer at a later age develop craniofacial and dental anomalies as a result of their treatment. Dentists increasingly meet adolescents and young adults with these problems who have been cured of cancer thanks to advances in oncological treatment. The types of anomalies and their frequency depend on the type of cancer the patient had, the drugs used during treatment, and the patient's age at the time of diagnosis. The cranial base grows most in the first three years after birth, and radiation in this period causes the biggest problems. The midface grows and remodels throughout childhood and adolescence, along with alveolar bone growth and dentition. The biggest changes in the midface occur by the age of seven. The growth of the mandible follows the growth of the midface. Deciduous teeth develop from the fourth to the eighth week of intrauterine life, and the development of permanent teeth begins in the twelfth week of intrauterine life and ends with the development of the wisdom tooth crown. Radiation therapy affects odontoblastic mitotic activity, causing defects in the enamel and dentin. These defects include root resorption, incomplete calcification, premature root apical closure, and even lack of tooth eruption. Microdontia is a morphological anomaly of the size and shape of the teeth, usually occurring as a result of radiation. Cytostatic drugs negatively affect rapidly dividing ameloblasts and odontoblasts, especially between the first and fifth years of life. These drugs cause enamel discoloration, hypoplasia, and hypomineralization. They also cause dentin changes that are similar to enamel changes. The influence on the creation and division of ameloblasts also causes changes in root formation. Short, thin and fragile roots then form. Cytostatic drugs also cause hypodontia in up to 50% of children treated for Hodgkin's and non-Hodgkin's lymphoma. Cytostatics can also cause agenesis, a complete lack of teeth in the jaw, but in smaller percentages. If applied in early childhood, they prevent or slow down the formation of Hertwig's epithelial sheath, which causes taurodontism. The clinical appearance of these teeth is normal, but they have a shortened root and a large pulp chamber. All the mentioned anomalies cause later aesthetic, functional, and occlusal problems in patients.

Conclusion

A cancer diagnosis is difficult to accept at any age, especially in childhood. The diagnosis affects not only the child but also the parents. Children and parents often go through five stages of emotions during such a traumatic situation, so dentists must be prepared to deal with all the stages children and parents may find themselves in while in their office. Considering the severe symptoms occurring in the oral cavity as well, the dentist must prepare the patient and the parents for everything they can expect and make it as easy as possible for them. Patients will sometimes find it very difficult to cope with pain related to the oral cavity, which can cause additional stress. Children diagnosed with cancer who come to the dental office may not always be ready to cooperate. Their mood can change from hour to hour. Sometimes they may feel angry, sad, scared, anxious, or worried. In such situations, we must not force children to undergo the procedure, but we should talk to them, try to explain to them that they will feel better after the procedure, and, if necessary, postpone the procedure for another appointment. We can give parents advice on how to motivate and comfort their children at home. Dental anomalies that develop as side effects of treatment can also cause various psychological and emotional disturbances. The biggest problem is insecurity due to damaged aesthetics. In addition to the best possible dental rehabilitation, we must also provide the patient with psychological support and explain what can be expected from the therapy.

The main problem in the treatment of cancer patients is their lack of awareness of the complications that will occur in the oral cavity or the possibility of their prevention and alleviation. According to the National Head and Neck Cancer Audit data, only 8.5% of patients visited a dentist before starting cancer therapy. Patients who do not undergo a preventive dental examination develop serious oral complications that endanger their health. A pediatric dentist should be involved in therapy immediately after diagnosis. The oncologist should educate patients and parents about the importance of cleaning the oral cavity before therapy initiation, give them a recommendation for a preventive dental examination, and explain the importance of including dentists in the treatment team.

literature

1. Alajbeg I. Dentist in the Oncology Team for Head and Neck. In: Topić B. Interdisciplinarity in the Diagnosis and Therapy of Premalignant and Malignant Lesions of the Oral Mucosa: book 47. Sarajevo: ANUBiH CLXV; 2016. p. 151-61.
2. Topić B. Prevention and Treatment of Oral Complications of Radio(Chemo) Therapy in the Head and Neck Region. In: Topić B. Interdisciplinarity in the Diagnosis and Therapy of Premalignant and Malignant Lesions of the Oral Mucosa: book 47. Sarajevo: ANUBiH CLXV; 2016. p. 133-50.
3. Onkologija.net Platform [Internet]. What is radiotherapy ("radiation")? [cited 2021 Aug 18] Available from: https://www.onkologija.net/radioterapija
4. National Cancer Institute [Internet]. What is cancer? [cited 2024]. Available from: https://www.cancer.gov/ Oral Complications of Cancer Therapies (PDQ®)
5. Plivazdravlje.hr [Internet]. Leukemia [cited 2021 Aug 18]. Available from: https://www.plivazdravlje.hr/aktualno/clanak/26716/Leukemija.html
6. Hartnett E, Krainovic-Miller B. Preventive Dental Care: an educational program to integrate oral care into pediatric oncology. Clin J Oncol Nurs. 2017 Oct 1;21(5):611-616.
7. Amila Zukanović, Ph.D., specialist in preventive and pediatric dentistry, Damir Duratbegović, M.Sc., specialist in preventive and pediatric dentistry, Bulletin Heart for Children with Cancer, Prevention is Important, , 2016, Available from: www.srcezadjecu.ba
8. Institute for Public Health of the Federation of Bosnia and Herzegovina, February 15th International Day of Children with Cancer, Available from: www.zzjzfbih.ba/medunarodni-dan-djece-oboljele-od-raka-2024
9. Nabil S, Samman N. Risk factors for osteoradionecrosis after head and neck radiation: a systematic review. Oral Surg Oral Med Oral Pathol Oral Radiol. 2012;113(1):54-69.
10. 10. Treatment and Prevention of Oral Mucositis: A Literature Review.
11. Mohammad-Salar Hosseini, Sarvin Sanaie, Ata Mahmoodpoor, Saba Jabbari Beyrami Hossein Jabbari Beyrami, Shirin Fattahi, Farid Jahanshahlou, Mahdi Zarei, Alireza Rahimi Mamaghani and Mahshid Kuchaki Rafsanjan Cancer treatment-related xerostomia: basics, therapeutics, and future perspectives Available from: Hosseini et al. European Journal of Medical Research (2024) 29:571 https://doi.org/10.1186/s40001-024-02167-x
12. 1. Radiation caries, Available from: https://oralcancerfoundation.org › complications