Abstract

In the antineoplastic treatment the oral manifestations can be seen more intensely because radiotherapy and chemotherapy attack little differentiated cells or those with a high metabolism, affecting not only the blastic cells but also the normal ones. The main events are: mucositis, hyperplasia and gingival bleeding, opportunistic infections, radiation caries, xerostomia, trismus, osteoradionecrosis and taste alteration. Dentists must be aware of the oral manifestations in antineoplastic treatment to improve patients’ quality of life. When possible, patients should be examined before starting oral cavity treatment to remove infectious outbreaks. During treatment prophylactic measures can be taken such as strict control over oral hygiene, analgesic, antibiotic, and antiinflammatory administration when necessary, advising the patient to have a light alimentation.

Key-Words: leukemia; oral manifestations; antineoplastic agents.

Resumo

são. No tratamento antineoplásico as manifestações orais podem ser vistas mais intensamente, pois a radioterapia e a quimioterapia incidem nas células pouco diferenciadas, ou com alto metabolismo, atingindo não somente as células blásticas, mas também as normais. As principais manifestações são: mucosite, hiperplasia e hemorragia gengival, infecções fúngicas, virais e bacterianas, cárie de radiação, xerostomia, dermatite, trismo, osteorradionecrose, hiperтроfia dos nódulos linfáticos, palidez da mucosa, petéquias, eritema e alteração do paladar. O cirurgião-dentista deve ter consciência das manifestações bucais do tratamento antineoplásico para poder melhorar a sua qualidade de vida. Quando possível, o paciente deve ser analisado antes do início do tratamento para que a adequação da cavidade bucal e remoção dos focos infecciosos. Durante o tratamento podem ser adotadas medidas profiláticas como: controle rigoroso da
Introduction

Neoplasia is the second leading cause of death by disease in the world, and about 70% of patients undergo antineoplastic chemotherapy during the treatment\(^1\). Leukemia is among the most prevalent neoplasia, which represents between 30%-51% of that total\(^1\).-\(^7\).

Leukemia is characterized by uncontrolled production of immature white blood cells, causing a series of clinical and oral manifestations, which are important in disease diagnosis. Early detection of leukemia is very important because it provides a favorable prognosis\(^3\).-\(^8\).

Depending on the type, dosage and frequency of use of antineoplastic agents, severe oral complications can arise. In literature, about 40% of patients submitted to oncologic treatment have antineoplastic oral complications, such as mucositis, xerostomia, and fungal infections, viral or bacterial, among others\(^1\).-\(^9\).

As a health professional, the dentist should be able to handle not only dental alterations. He is responsible for the maintenance of health in the oral cavity and must also be attentive to the individual as a whole\(^7\).-\(^10\),\(^11\).

In addition to contributing to the disease diagnosis, the dentist’s great contribution is about the monitoring of antineoplastic treatment. An understanding of the pathogenesis of mouth acute infections in patients undergoing antineoplastic treatment is important to establish preventive strategies for these complications. Successful prevention, started prior to the treatment and maintained during myelosuppression, may reduce the morbimortality of these patients\(^10\).

Prevention and treatment of oral lesions resulting from antineoplastic treatment are essential since oral mucositis seriously interfere with the prognosis of patients, becoming them more susceptible to local and systemic infections, less tolerant to oral feeding. In addition, it interferes with the dosage and/or indication of drugs used in chemotherapy, prolonging the time of hospitalization and increasing costs. Many of the oral and systemic complications can be reduced with adequate oral hygiene guidance, adequacy of prior treatment, prevention and control of these children, which greatly improves these patients’ quality of life during treatment\(^11\).-\(^14\).

This second part of review of the literature is intended to clarify the features of leukemia, the main malignant disease, and help dentists by presenting not only the clinical and oral manifestations of the disease,
but also the alterations of antineoplastic treatment (chemotherapy and radiotherapy) in the oral cavity, as well as to provide some subsidies for the professionals to control these alterations and thus improve patient quality of life.

**Literature review**

Mucosal tissue has a protection function and is composed by an epithelium, which operates as a barrier through differentiation or maturation to produce layers with appropriate functional properties and constant replenishment of desquamated cells on the surface through the differentiation in the layers below. These cells have high cellular metabolism and are more susceptible to antineoplastic agents. When this barrier breaks up in some way, it is exposed to infection, inflammation, followed by painful and debilitating mucositis. However, if therapies that allow repair and regeneration are discontinued, the ability of rapid spread allows oral epithelium healing in 2 or 3 weeks. A small quantity of cells (stem cells) will divide more slowly and are less affected by radiotherapy and chemotherapy, being important for the epithelium repopulation after treatment damages¹⁵.

Oral complications can be classified as primary (resulting from the infiltration of malignant cells in the oral structures such as gum and bone infiltration), secondary (associated with thrombocytopenia and granulocytopenia as injuries associated with anemia, tendency to bleeding, susceptibility to infections, and ulcers), and tertiary (associated with myelosuppression and immunosuppressive therapy of direct or indirect cytotoxicity)¹⁶,¹⁷.

After the initiation of therapy there is an increase in prevalence of oral alterations, such as ulcerations, mucositis, taste decrease, skin desquamation, candidiasis, gingival bleeding, xerostomia, dysphasia, opportunistic infections, trismus¹⁸,²⁵, and late effects: vascular lesions, tissue atrophy, taste loss or change, fibrosis, edema, soft tissue necrosis, loss of teeth, salivary flow decrease, carious lesions, osteoradionecrosis, and condralonecrosis²³,²⁴.

Late effects of acute antineoplastic therapy cause discomfort to patients, hampering or limiting their normal activities, which affects the quality of life of individuals²⁴.

**Mucositis**

Mucositis is one of the most common side effects in antineoplastic treatments and can be defined as an inflammatory condition of the mucosa, which manifests itself as erythema, ulceration, bleeding, swelling, and pain³,¹¹,¹⁸,²⁶-³⁰.

The pain may cause problems with feeding, hydration and speech. The continuing difficulty with feeding because of pain can lead to weight loss, anorexia, cachexia and dehydration, affecting the patient’s quality of life³¹,³².
Thus, in many cases a treatment change or interruption can occur, which in turn leads to a decrease in the control of tumor growth and, consequently, the patient survival\textsuperscript{34}. According to the literature, approximately 11\% of cases of interruption and modification of the radiotherapy treatment occur due to the development of severe oral mucositis, requiring treatment replanning, and in some clinical situations, patient hospitalization\textsuperscript{32}.

Initial symptoms of mucositis include burning sensation, dry mouth and formication of lips. It occurs 5-7 days after initiation of therapy, due to a direct effect on the oral mucosa, and slowly disappears 2-4 weeks after the end of treatment\textsuperscript{34}.

The severity and duration of mucositis are directly related to the quality of preexistent oral health, treatment schedule, drugs used and occurrence of associated infections, such as patients with recurrent herpes simplex virus\textsuperscript{15,32}.

It is estimated that the incidence of mucositis varies between 40\% and 76\% for patients treated with conventional or high-concentration chemotherapy, respectively\textsuperscript{15}, and it can be observed in almost 100\% of patients undergoing head and neck cancer radiation therapy\textsuperscript{28,32}.

In the cases treated with radiotherapy, it is observed that the risk factors for the development of mucositis include location of the radiation field, preexistence of dental disease, poor oral hygiene, low production of saliva, compromised immune function, and local infection outbreaks\textsuperscript{35}. It is believed that patients receiving radiotherapy with concurrent chemotherapy are more likely to develop serious oral mucositis\textsuperscript{15}.

Another factor aggravating oral mucositis is the susceptibility to infection by micro-organisms normally present in the oral cavity which are opportunistic and invade the damaged tissue. Candida yeast colonization increase during radiotherapy\textsuperscript{32}.

With regard to age, young patients develop more severe mucositis than elderly people. However, the episodes of mucositis in young people require less time for a complete healing when compared to elderly patients. Moreover, patients with better stomatological conditions develop mucositis with less frequency and duration than those with poor oral hygiene and less frequent periods of odontological consultation\textsuperscript{15}.

It is important to note that when poor oral hygiene is observed, the action of viruses, fungi and opportunistic bacteria further deteriorates the situation. And as the patient is unable to adequately rinsing the oral cavity due to intense pain, a vicious circle is formed, which is very hard to break\textsuperscript{15}.

Thus, there is a wide variety of agents used in the prevention of mucositis, which seems to reflect research advancements in search for effective drugs, although further research still needs to be conducted\textsuperscript{15}.

Oral hygiene is the main prevention strategy because it reduces the growth of
microorganisms and the development of severe mucositis, allowing the elimination of infection factors. Reports indicate the need for instructions about diet and oral hygiene one week prior to the beginning of antineoplastic treatment. The instructions should include the correct use of dental floss; brushing with fluoridated toothpaste after meals; replacement of failed restorations; assessment of the functionality of prostheses and its sanitation, and restoring treatment.

Mouthwash is the most frequently mentioned agent in the studies, such as: 0.12% antiseptic chlorhexidine, sodium bicarbonate, which creates an alkaline environment, interfering with the bacterial multiplication and the establishment of candidiasis; however, research indicates the negative impact on the taste and uncomfortable feeling with its use; saline solution 0.9% is not irritating and does not alter saliva pH, and is economical and highly recommended; hydrogen peroxide, in spite of controversy, is still used, but causes irritation, damages granulation tissue, interrupts the normal flora of the oral cavity and can cause nausea due to its taste; magnesium and aluminum hydroxide suspensions are solutions that protect the mucosa, forming a layer with analgesic effect, minimizing acidity, however, they dry up oral mucosa, therefore, more research is needed; and mouthwash with nystatin for prevention of fungi are also recommended before starting treatment, three times a day for seven days; and 0.05% sodium fluoride (gel), daily. However, all mouthwash ingredients containing alcohol or phenol are counterindicated, since they cause mucosal desquamation and irritation.

With regard to the types of treatment available, it is important to emphasize that these are palliative and diverse, and involve prophylactic and therapeutic attempts to alleviate painful symptoms.

Prophylactic approaches include: awareness for the improvement of oral hygiene, avoid the use of spicy foods, use of growth factors, aluminum salts, cytokines, glutamine, cytoprotectors and antioxidants, and symptomatic approaches such as the use of camomile, betamethasone, benzidamide, acetylsalicylic acid, lidocaine, E polymyxine, lozenges, tobramycin, low-intensity laser, and criotherapy.

With regard to palliative treatments, the vast majority of studies indicate the use of mouthwash ingredients (these can be saline solution, bicarbonate, water, chlorhexidine and diluted hydrogen peroxide), epithelium protector medicines (aluminum hydroxide, magnesium hydroxide), topical anesthetics, systemic antibiotics and anti-inflammatory drugs.

It is noteworthy that oral rinse with 0.12% chlorhexidine gluconate is the most frequently indicated, but its use has controversy because it contains alcohol, and thus can dehydrate oral tissues, exacerbate
mucositis, besides being able to alter taste when used for a long period of time\textsuperscript{14}.

Studies suggest good results with the use of gel-based benzocaine and oral rinsing before meals; bicarbonate water (1 tablespoonful in 1 cup of water, three times a day for seven days)\textsuperscript{14,37,38}.

Other options that can be observed include: irrigation with saline solution to neutralize acidity, perform debridement, and dissolve secretions\textsuperscript{43}; sucralfate mouthwash which creates a protective barrier through its mechanism of action, the ionic connection to proteins in the ulceration site. Studies have identified its effectiveness in reducing mucositis severity and duration, with good results for patients experimenting pain, interruption of treatment, nutritional support, analgesia, and infection, being 1-3g the recommended dose, three to six times a day during antineoplastic treatment\textsuperscript{44}.

Also recommended are lidocaine 2%, carbamide peroxide 10% and urea peroxide 10%, mouthwash with vitamin E and nystatin\textsuperscript{45}. However, the use of hydrogen peroxide has been discouraged because of its mechanism of action previously described\textsuperscript{43}. Similarly, topical lidocaine, despite being a commonly used agent, has anesthetic effect for only 15-30 minutes, not always solving the problem\textsuperscript{34,44}.

A new therapeutic approach has indicated the use of low-intensity laser, which has proven to be capable of significantly alleviate pain and may also reduce the severity and duration of mucositis\textsuperscript{14,16}.

Laser treatment stimulates cellular activity, leading to the release of macrophage growth factors, proliferation of keratinocytes, population increase and degranulation of mast cells, and angiogenesis. These effects can lead to acceleration of wound healing processes, due in part to the reduction of acute inflammation duration, resulting in a quick repair, with analgesic and antiinflammatory properties\textsuperscript{34,44}.

Laser use eliminates the pain in the first application. It is believed that this happens because of the release of β-endorphin in the nerve endings of the ulcer, while it also promotes tissue biostimulation, facilitating a more rapid healing of ulceration\textsuperscript{46}.

According to literature, laser seems to be well tolerated by patients and has beneficial effects on mucositis, improving patient quality of life during oncologic treatment. But further controlled scientific studies with significant sampling are necessary for the development of protocols of this kind of treatment\textsuperscript{46}.

**Xerostomia**

Xerostomia appears to be one of the most frequent effects of radiotherapy in the head and neck area\textsuperscript{11,12,18,25,39}. It is characterized by a dysfunction of the salivary glands, when reduction or absence of salivary flow occurs. It occurs in around 53 percent of cases and could reach 100 percent\textsuperscript{11-13,25}.
Xerostomia occurs due to changes in the salivary glands, causing qualitative and quantitative changes in salivary flow (saliva becomes more viscous, with a high proportion of organic material and changes in color, from transparent to yellow) due to fibrosis induction by radiotherapy, fat degeneration, acinar degeneration, and necrosis of the salivary glands. This change acidifies the pH, and there is a change in bacterial flora from gram-positive to gram-negative \(^{11,12,18,26,36,39}\).

Xerostomia can be characterized as transitional during chemotherapy (being reverted in 48 hours) or severe, progressive or permanent in cases of radiotherapy (reversal may occur within 4 to 12 months after therapy) \(^{18,29,47}\).

According to Lima et al. (2004) \(^{49}\), who evaluated the flow speed and salivary pH after radiotherapy in the head and neck area, at the end of treatment and up to six months later, no patient in that study showed salivary flow speed within the normal range of values, suggesting that there is a direct relationship between the dose of irradiation and the extent of glandular changes \(^{25,29}\).

Xerostomia causes damage in oral physiology including difficulty with chewing, swallowing, speech, and a prevalence increase of infections such as candidiasis, periodontal disease and caries \(^{12,18,26,36,39}\). Moreover, there is also taste and appetite loss, as well as nausea, vomiting, and painful symptoms. These factors together predispose patients to adopt cariogenic food habits. Thus, the framework of hypofunction or permanent loss of salivary flow may result in a rapid progression of dental caries, periodontal disease, candidiasis, dysgeusia and nutritional deficiency \(^{3,49}\).

The proposed treatment for xerostomia has been the use of artificial salivas based on carboxymethylcellulose, stimulation of remaining saliva, meticulous oral hygiene and fluoride topical application \(^{14}\). More recently, the use of pilocarpine has been suggested, which is a cholinergic parasympathomimetic agent being used to stimulate salivary flow \(^{29}\).

Given the significant changes in salivary pH values \(^{32}\), dental monitoring is of paramount importance to minimize the risk of caries and dental erosion \(^{18,26,36,39}\).

**Osteorradionecrosis**

Osteorradionecrosis (ORN) is one of the most severe and serious oral complications of radiotherapy for head and neck cancer \(^{18,23,36,49,50}\).

Radiation reduces the potential for tissue vascularization, which creates hypoxic and hypovascular conditions, putting at risk cellular activity, collagen formation and the capacity for wound healing. Altered vessels induce blood flow decrease, thus reducing nutrients and defense cells. Without the necessary nutrients and defense the entire maxillary and mandibular bone structure suffers degeneration, characterized as a bone ischemic necrosis \(^{23,49,50}\).

At the time of diagnosis, ORN may involve bone structure either superficially or...
deeply. Furthermore, it may be a gradual process with slow or rapid change, possibly leading to a pathological fracture\textsuperscript{31}.

This process is usually associated with signs and symptoms such as intra- or extra-oral fistula, trismus, pain, difficulty chewing, pathological fracture, local infection, and drainage of purulent secretion\textsuperscript{23,49}.

Predisposing factors include poor oral hygiene, periodontal disease, alveolodental abscess, extensive caries, anatomical location of the tumor, radiotherapy dose increase, and alveolodental surgery during radiotherapy or in post-operative period. Alcohol and tobacco habits irritate the oral mucosa and may also increase the risk of ORN\textsuperscript{50}.

Regardless pathophysiology of the disease, it should be established that cruel procedures such as exodontias or periodontal surgery are counter-indicated, since they may be risk factors for tissue decomposition and ORN\textsuperscript{4}.

Oral conditions of individuals under cancer treatment always trend to aggravate. The initially inflamed mucosa is aggravated by hyposalivation. Xerostomia facilitates the proliferation of \textit{Lactobacillus sp} and \textit{Streptococcus mutans} to prevent saliva buffering capacity. The difficulty of saliva production leads the individual to change eating habits. In general, food becomes viscous and rich in carbohydrates. Since the individual is not able to rinse oral cavity properly due to intense pain, a vicious circle is formed which is very difficult to be broken. As a consequence, besides taste loss, the patient is unable and unwilling to eat properly, becoming increasingly frail. These factors provide an ideal environment for the development of carious lesions and periodontal disease, predisposing to ORN\textsuperscript{51}.

Some authors argue that despite the improvement in oral care prior radiotherapy, ORN incidence has not declined significantly in recent years, on the contrary, it has increased by 1-30 percent. Meanwhile, other authors report that the introduction of preventive oral hygiene and thorough dental assessment before and after irradiation, improvement of radiotherapy techniques, establishment of a reliable diagnosing, and adoption of the best therapeutic practices resulted in a decreased ORN incidence\textsuperscript{51}.

Treatment is still a challenge and initially it occurs in a conservative way through wound debridement and cleaning with surgical antimicrobial solutions, through antibioticotherapy and minor surgery. In cases of refractory to conservative treatment, hyperbaric oxygen therapy (HBO) should be indicated, associated or not with surgery\textsuperscript{23,49}.

The oxygen administered in controlled doses and pressure provokes oxygen tension growth in the affected area, vascular neoformation, increase in the number of cells, cellular activity increase, and collagenase increase, besides being bacteriostatic and bactericidal. These measures provide appropriate means for healing the tissue damaged by radiation\textsuperscript{23,49}.
Alternative techniques such as BMPs (morphogenetic proteins) that induce bone differentiation have been studied and show to be promising\textsuperscript{51}.

Recently, low intensity laser radiation has presented good results for bone fracture and bone neoformation. It also works as a bio-stimulator in osteoblasts and as bio-modulator of mesenchymal undifferentiated cells in osteoblasts and osteocytes, but it still needs further studies\textsuperscript{51}.

**Candidiasis**

Candidiasis is one of the most common fungal opportunistic infections and contributing factors include myelosuppression, impairment of the salivary flow and trauma to the mucosa, inadequate oral hygiene, malnutrition, debilitating physical condition, and mucositis injuries\textsuperscript{3,8,11,39}. Clinically, it is characterized by the presence of white plaques in the oral mucosa, tongue and palate, caused by *Candida albicans* fungi, eventually resulting from the aggressive effects of chemotherapy or radiotherapy\textsuperscript{51}.

It can be treated through topic and/or systemic medication. Topic medication most commonly used is nystatin and its action depends directly on the time of contact with the tissues. The systemic use of fluconazole also has proven effective in antifungal therapy. But when comparing the effectiveness between topical and systemic drugs, no significant difference is found\textsuperscript{4,16}. If left untreated, candidiasis can progress to a systemic infection\textsuperscript{51}.

**Gingival bleeding**

Spontaneous bleeding or from traumatic brushing occurs because of platelet reduction. It is most commonly associated with chemotherapy, with severity depending on the degree of thrombocytopenia and immunosuppression\textsuperscript{18,27,39}.

Oral hygiene in these cases it is of fundamental importance, since when it is inadequate or absent, gingival bleeding is exacerbated, which enables the severity of the clinical status\textsuperscript{25,29}.

**Dysgeusia**

It is characterized by taste changes and is resulting from direct radiation damage to gustatory buds as well as changes in salivary flow, with 50\% reduction in the perception of bitter and sour tastes\textsuperscript{18,26}. Taste loss is transitional and partial or total recovery may occur between 2-12 months after radiotherapy. It can be fixed with zinc supplementation\textsuperscript{11,30}.

**Trismus**

It is the limitation of mouth opening as a result of edema, cellular destruction and fibrosis of muscle tissue induced by radiation, making it difficult to maintain patient’s proper oral hygiene. The degree of restriction depends on the radiation dose, tumor location, and radiation distribution\textsuperscript{11,18}.
The treatment should include exercises to stimulate mouth opening and closing, concomitantly with moist heat before and after the exercises, as well as administration of antiinflammatory medication, and muscle relaxers\textsuperscript{11}.

**Carious lesions**

Taste changes combined with mouth dryness provoke dietary changes, leading patients to consume soft food with cariogenic potential. In addition, mouth rinsing difficulty because of the oral cavity sensitivity favors the growth of cariogenic bacterial flora and the consequent emergence of new carious lesions\textsuperscript{18,25}.

Thus, carious lesion is not a direct result of a healthy tooth structure affected by radiotherapy or chemotherapy, but a direct and secondary result of salivary gland hypofunction, dietary and oral microflora changes, and a precarious oral hygiene\textsuperscript{18,25,26,36,39}. It appears that both chemotherapy and radiotherapy cause sequels during the oral antineoplastic treatment; however, they are related to dietary habits and inadequate oral hygiene\textsuperscript{25}.

Dentists should encourage patient’s commitment to topical fluoride use, dietary restrictions and regular appointments. The use of antibiotics can help eliminate the infection and the patient should be reassessed periodically every 3 months\textsuperscript{4,14}.

**Infections**

In patients with myelosuppression arising from chemotherapy, fungal, viral, and bacterial infections can occur\textsuperscript{18,27,39}.

A complex interaction of factors contribute to the etiology of infections, including pre-existing oral diseases, loss of the oral mucosa integrity, impairment of the immune system, xerostomy and uncontrolled proliferation of oral and/or opportunistic microbiota. These factors are capable of causing serious infections that, besides compromising the quality of life and interfering in the protocols of antineoplastic treatment, can pose risk to the patients’ life\textsuperscript{15,27}.

A common oral infection which may occur is caused by herpes simplex virus, associated with chemotherapy and bone marrow transplant. There may be a primary infection or, most commonly, the activation of infection latent form during periods of immunosuppression and intensive chemotherapy\textsuperscript{14}.

Intra herpetic injuries are often seen on the palate, grouped as lesions that may ulcer up quickly. Depending on the degree of bone marrow suppression, erythema can occur. Other oral viral infections that pose risk to cancer patient include varicella-zoster and cytomegalovirus\textsuperscript{14}.

Bacterial infections are derived from a secondary involvement of the ulcerated mucosa due to the therapy, and may become a source of cellulite and/or septicemia\textsuperscript{14}.
The role of dentists and oral surgeons

Dentists and oral surgeons play an important role in diagnosing oral manifestations related to antineoplastic treatment and should monitor the processing of applications, providing a better quality of life, since lesions resulting from cancer treatment considerably aggravate the patient clinical condition and the risk of infection\textsuperscript{4,11,14,26}.

Ideally, dental treatment should start before antineoplastic treatment to minimize morbidity and improve the general health of patients during therapy. In such cases, prevention becomes critical, since oral lesions resulting from the oral treatment considerably aggravate the clinical condition and the risk of infection, and even hamper the dental treatment when necessary\textsuperscript{11,29}.

However, there is some difficulty in prior dental treatment, due to the short interval of time between disease diagnosis and initiation of antineoplastic treatment. Often the disease is in advanced stages or with clinical manifestations, which hampers dental treatment. It would be interesting that dentists and cancer multidisciplinary team attending the patient work together, so that the initial dental assessment can be carried out adequately\textsuperscript{15}.

The development of a treatment plan, besides being appropriate for each individual’s condition, aims to eliminate possible sources of infection\textsuperscript{15,46}. Thus, dental treatment should start after a clinical and radiographic evaluation\textsuperscript{11}. There are different approaches described in the literature\textsuperscript{14,35,36,39,51}, but generally the following should be prioritized: removal of infected areas through exodontias, endodontic treatment and oral care; dental prophylaxis; topical applications of fluoride 0.5 or 1.23%; antiseptic mouthwash, and periodic control.

Any dental program should be focused mainly on education and awareness regarding the patient's oral health\textsuperscript{51}.

It should be emphasized that dentists should orient their patients about oral care and hygiene (use of fluoridated toothpaste, dental floss, and dental soft brush) throughout cancer treatment and post-treatment maintenance\textsuperscript{15}, since some oral complications such as osteoradionecrosis and trismus present risk of relapse\textsuperscript{4}.

With regard to diet, dentists should inform the patient which foods should be avoided, such as rough, thick, hot and spicy food, as well as those that irritate or burn the oral mucosa, such as citrus juices and alcoholic beverages\textsuperscript{11,14,35}. On the other hand, cold foods and liquids should be suggested, since they are well tolerated and, frequently, bring a sense of relief\textsuperscript{14}.

When it comes to child patients, studies indicate that a large number of parents and guardians received little or no explanation about oral changes that occur during antineoplastic treatment. Thus, it is believed that the presence of a dentist as a member of the oncology team can reduce the morbidity
and mortality related to these complications. In addition, the dentist can provide guidance and establish a more frequent and intense hygiene control which will contribute to reducing mucositis rate, carious lesions, etc\(^4\).

Thus, preventive measures should be taken to alleviate the side effects of antineoplastic therapy, through the provision of information on cancer treatment. Also, guiding measures to alleviate discomfort and support to reduce anxiety and depression should be provided\(^1\)\(^5\)\(^24\).

It is important to be aware that patients and their families are in a very delicate moment of their lives, requiring great dedication and support from all those involved in their treatment, and everything possible must be done for the patients to feel protected and confident\(^16\).

**Conclusion**

Through this literature review it can be concluded that dentists should be concerned about patients’ general health, being attentive to fatigue, low and constant fever, malaise, anorexia and diffuse infection, and mainly to oral manifestations such as gingival bleeding and hyperplasia, as well as viral, fungal or bacterial infection.

Patients already diagnosed and under treatment can present oral manifestations such as mucositis, gingival hyperplasia, infections (viral, bacterial or fungal), spontaneous bleeding, radiation caries, xerostomia, dermatitis, trismus, osteoradionecrosis, lymph-node hypertrophy, mucosal pallor, petechiae, erythema, and taste dysfunction.

Dentists should improve patients’ mouth conditions, thus increasing their quality of life through an appropriate protocol which should possibly include oral cavity evaluation and adequacy before starting antineoplastic treatment, strict control of oral hygiene, antiseptic mouthwash, analgesic, antibiotic, and antiinflammatory administration when necessary.

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