

UPDATE REGARDING ORAL AND PERIODONTAL CARE FOR THE ONCOLOGY PATIENT DURING CHEMOTHERAPY. A REVIEW.

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Abstract

Oral infections and periodontal disease may be exacerbated during chemotherapy and represent an important risk due to the neutropenia that many of the patients develop during treatment. The main objectives of oral care during immunosuppression periods are maintaining the oral health status, evaluating and treating any side effects that may occur during chemotherapy and patient education regarding the importance of maintaining good oral hygiene in minimalizing the risk of oral complications and discomfort during the chemotherapy treatment. The aim of this study is to revise the means of treatment and prevention of the adverse effects of chemotherapy in oncology patients.

Keywords: *chemotherapy, oral side effects, mucositis, dysgeusia, xerostomia, treatment, prevention*

Introduction

An important factor of chemotherapy is the mucotoxicity that a large number of chemotherapy agents have.

The intensity of toxicity depends on a series of variables that may influence the degree of oral mucosa destruction like the type of anti-neoplastic agent used, therapeutic regime, treatment duration and dose intensity [1]. Among the most frequent side effects within the oral cavity are mucositis, infections (bacterial, fungal or viral), dental and neurological alterations, dysgeusia, hiposalialia or xerostomia, haemorrhage and osteonecrosis [2]. Periodontal disease is an infectious affliction that manifests through progressive loss of tissues that form dental

support and which, in the absence of treatment, it may lead to toothloss. After caries, periodontal disease is one of the most prevalent global diseases and have a profound effect on public oral health [3,4]. The microlesions and ulcerations of the periodontal tissue can be entry gateways for bacteria situated in periodontal pockets, allowing them to enter the bloodstream. Furthermore, the local inflammatory state is a reservoir of endotoxins and proinflammatory mediators that will affect the entire organism. The odontal and periodontal infection prevalence during chemotherapy was recently reported to be 5.4% [5]. On the other hand, Vozza et al. have stated in their study that the prevalence of periodontal disease in cancer

patients that were soon to be treated with chemotherapy was 35.2% at the moment of establishing the oncological diagnostic and that periodontal treatment had favorable effects on hygiene and periodontal parameters during chemotherapy [6]. During chemotherapy, monitoring the oral health of patients has proved to be very important because of the multiple changes that may occur. The modification of the hematological status can be observed, for example, in the gingival tissues during anemia when the color of tissues turns pale or during thrombocytopenia when the tissues can gain an erythematous aspect [7]. Once neutropenia occurs or has a high chance of occurrence, all interventional maneuvers like periodontal probing or scaling and root planning should be avoided which is why a thorough oral evaluation and treatment prior to chemotherapy is very important. It has been cited that periodontal disease, even when it is not manifested through obvious clinical signs, can be a potential inflammation source for chemotherapy patients suffering from neutropenia fever [8].

Guidelines in treating oral side effects of chemotherapy

The main objectives of oral care during immunosuppression periods are maintaining a good oral health status, treating the side effects that negatively impact the chemotherapy treatment and the patients quality of life and inform and educate the patients regarding the importance of a correctly performed oral hygiene and its effect on minimizing the oral complications and discomfort that may occur during chemotherapy. As a general consensus, oral therapy should be avoided

during immunosuppression periods. However, in the event of emergencies, these should be discussed with the oncology medic in order to opt for the best solution for the patient that will most likely involve the administration of analgesics or antibiotics until the general status will allow treatment [9].

Infections. During neutropenia the inflammation signs might be diminished, thus stressing the importance of careful monitoring of the oral cavity and early diagnostic and treatment of bacterial, fungal and viral infections [10]. Prophylactic medication should be administered immediately, however it is recommended to perform microbiology tests in order to administer specific antibiotics in accordance to the testing and achieve better results with fewer antibiotic treatment side effects in the chemotherapy patient [11].

Fungal infections. According to Lalla et al., the prevalence of fungal infections during cancer treatment is approximately 7.5% before treatment, 40% during and 30% after treatment [12]. Even though some authors consider that there is insufficient data in the scientific literature to recommend or contraindicate the use of antifungal agents in the treatment of oral candidiasis in chemotherapy patients [13], there are others that support several means of treating oral fungal infections. It is, however, recommended that the dental practitioner reduce the morbidity and acts to prevent potential systemic infections. The topical application of antifungal medication is quoted multiple times due to their reduced risk of side effects and drug interactions, but it seems their degree of efficiency is variable [14]. The American Society of infectious diseases recommends

the use of clotrimazole and nystatin as first line medicine in the treatment of oropharyngeal candidosis [15]. There are instances, however, when the use of these solid form drugs is not possible due to low salivary flux or presence of oral mucositis in which cases the alternative would be the use of nystatin oral rinses [16]. Another option remains the systemic administration of antifungal medication like fluconazol 100-200 mg per day for 14 days which can be used as a means of moderate or severe infection management. In cases resistant to fluconazol, the prescribed drug should be itraconazol capsules (200mg/day for 2-4 weeks) or itraconazol oral rinse (for 2 weeks) [12]. Another secondary option is posaconazol [15]. In refractory cases of infection, it is recommended to use stronger wide spectrum drugs like voriconazole, caspofungin and amphotericin B, taking into account, however, the higher chance of side effects that they may have (high photosensitivity, risk of skin cancer, high fever) [17].

Viral infections. The herpes simplex virus has a high prevalence in the general population and, thus, in most cases, the herpetic infection is related to an activation of the latent form of the virus. The scientific literature suggests that the immunosuppression consecutive to chemotherapy is the main factor of occurrence for this infection, reaching up to 40% prevalence [18]. Furthermore, it seems that a reactivation of the herpesvirus and the cascade of inflammatory mediators increases periodontal pathogenic bacteria as well [19]. Neutropenia patients have a 50% increased risk of developing a herpetic infection [20]. Presently, the most used anti-viral medication is acyclovir and valacyclovir that have proven to be

efficient in the prevention and treatment of herpetic infections [21]. Used in a prophylactic manner, these two medications should be administered as follows: acyclovir 200-800 mg, three times a day or valacyclovir 500mg twice a day [22]. During chemotherapy, acyclovir may also be administered intravenously 5 mg/kg every 8 hours or orally 300-400 mg, three to five times a day. Valacyclovir can only be administered orally 500-1000 mg twice a day. An alternative to the two medications mentioned is famcyclovir and in case of resistance to treatment, foscarnet (phosphonomethanoic acid) should be administered via intravenous infusion of at least 60 minutes, 40-60 mg/kg for 14-21 days [23].

Haemorrhage. Oral bleeding may occur after developing thrombocytopenia, coagulation factor disturbance or destruction of vascular integrity. These events are best addressed through local management, such as antifibrinolytic rinses, hemostatic sponge applications, local pressure on the affected tissues or systemically via transfusions or aminocaproic acid administration [24].

Hiposialia and xerostomia. Oral adverse effects like hiposialia and xerostomia are fairly frequent in patients undergoing chemotherapy. These reactions can be ameliorated by using chewing gums or sugar-free sucking tablets, special toothpastes for dry mouth syndrome, saliva substitutes, frequent ingestion of water, alcohol-free oral rinses [25] or hydrating oral substances. Some authors highly recommend the use of fluoride rinses and gel applications [26]. In the case of patients suffering from xerostomia the main recommendation is frequent ingestion of small quantities of water every 10

minutes and maintaining ice chips intraorally in order to improve the comfort of the patient.

Moreover, artificial saliva sprays can be used like Xerotin, Moi-Stir, Salivart, Xero-Lube, Saliva Orthana and oral hydration gels like Biotene Oral Balance [27]. The lubrication of lips is also advised by using compounds containing lanoline or petrolium. Certain foods should be avoided, like coffee, tea, beverages containing coffee because they have the potential to further dehydrate the oral mucosas. Stimulating salivary gland activity and saliva production can be achieved by using saliva stimulation tablets and medications containing pilocarpine. Patients are encouraged to use xilitol or sorbitol based chewing gums for both saliva production stimulation and caries protection [28].

Mucositis. One of the most cited adverse reactions to chemotherapy is mucositis. Presently, there is no specific medication proven to successfully eliminate the lesions in mucositis [29]. However, the painful symptoms and oral discomfort can be managed with the aim to improve the quality of life level of the patient. In the case of chemotherapy induced mucositis, most of the attention is directed towards pain management and encouraging a correct nutrition [30]. One of the cited strategies in pain management refers to the use of oral rinses containing diphenhydramine, viscous lidocaine, bismuth, subsalicylate and corticosteroids [31] that seem to reduce pain levels and allow the ingestion of food with more ease. In the case of severely painful mucositis, strong analgesic substances may be used like opioids [32].

Alternatively, recent studies have investigated the potential of newer therapeutic interventions that refer to the efficiency of growth factors and cytokines in the prevention of severe mucositis and, respectively, reducing the duration of the lesions. One of these substances is palifermin, a human keratinocyte growth factor that seems promising in reducing mucositis grade 3 and 4. It has been proven that palifermin reduces the duration of mucositis lesions, thus reducing parenteral feeding and increasing the scores for physical and functional wellbeing of the body [33]. It also seems that palifermin plays an important role in the prevention of mucositis [34]. It does, however, present some side effects of its own like taste alteration [35].

Other means of prevention, management and treatment of the lesions in mucositis is applying ice chips (orally every 30 minutes in order to prevent the development of ulcerous lesions), laser therapy and the use of a compound containing L-glutamine and leptine that have a positive impact on the appearance of mucositis [36, 37]. The rationale behind the application of ice chips intraorally is that due to the local vasoconstriction, the release of chemotherapy in the epithelium mucosa is reduced [38].

Dysgeusia. It is estimated that between 50% and 75% of chemotherapy, radiotherapy or combined treatment patients suffer taste alterations [39]. A lower degree of dysgeusia is generally well tolerated, however more severe forms can lead to loss of appetite, a reduction of calorie intake, weight loss and alters the nutritional status of the patient [40]. The administration of zinc supplements seem to have a positive outcome on patient

suffering from dysgeusia [41]. Although results may vary, it seems that zinc may be an important structural element in proteins responsible for the regulation of taste bud pores [27]. Another supplement that seems to have had a beneficial impact on patient with dysgeusia is vitamin D [42]. Diet counseling also seems to help with long term taste alterations and improve results concerning chemotherapy patients [43]. The morbidity and mortality of head and neck squamous-cell carcinoma (HNSCC) have high values even to this day, regardless of how complex the cancer treatment is. Thus, the aim of this study was to further understand the aetiology, risk factors and interactions between the risk factors in order to develop new views on the cancerous treatment, to complement the therapy used presently and to

understand the impact these afflictions have on the quality of life of patients. [44]

Conclusions

The oral adverse effects of chemotherapy are multiple and frequently affect the patients systemic, psychological status and overall quality of life. The most frequent oral side effects during chemotherapy are bacterial/fungal/viral infections, hemorrhage, hyposialia, xerostomia, mucositis and dysgeusia and there are multiple ways to ameliorate their symptoms. It is important to address the oral events that occur in an interdisciplinary manner in order to achieve pain management, prevention and a beneficial outcome of chemotherapy treatment.

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