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Review and Meta-analysis

Treatment Options for Cancer Patients Suffering from Oral Mucositis

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More than 75% of those receiving chemotherapy will experience oral mucositis, which is a major problem for both patients and carers. Lesions form in the digestive tract when chemotherapy drugs attack the rapidly dividing cells there. Tissue alterations might range from being completely painless to so severe as to cause bleeding, prevent oral intake, and need narcotic pain medications. Chemotherapy treatment is often postponed when oral mucositis is present. To better clearly categorise the symptoms linked with this condition, many assessment scores have been devised. Very few pharmaceutical therapies for oral mucositis, either to prevent its onset or to alleviate its symptoms, have been approved. Given the advancements in other areas of supportive care for chemotherapy patients, research into oral mucositis should be prioritised. This review will provide the management of oral mucositis in patients with cancer.

Introduction

Oral mucositis is characterised by the presence of ulcerative and erythematous lesions of the oral mucosa in cancer patients undergoing chemotherapy and/or radiation treatment to the oral cavity. Oral mucositis lesions are frequently excruciatingly painful, affect nutrition and oral hygiene, and raise the risk of local and systemic infection. Mucositis can also affect other regions of the gastrointestinal system; for instance, diarrhoea can be a symptom of gastrointestinal (GI) mucositis [1]. Thus, mucositis is a serious and potentially dose-limiting side effect of cancer treatment. In extreme situations, oral mucositis can increase mortality by about 40 per cent [2]. Oral mucositis can be a major issue for cancer patients, since it may demand parenteral nourishment, might lead to infection, and causes the patient pain and discomfort. Oral mucositis is currently gaining increasing attention and emphasis as a result of advances in pharmaceutical treatments used to treat other adverse effects, such as nausea and vomiting.

Pathophysiology

Chemotherapy and radiation-induced toxicity target rapidly proliferating cells preferentially; hence, the oral mucosa is very sensitive to chemotherapy-induced damage. Oral and gastrointestinal mucosa inflammation can result in painful ulcerations, infections, and the inability to eat, drink, or swallow. Chewing is more likely to produce cuts or scratches in patients taking these therapies. This mucosa is one of the body’s defences against microbial invasion that is compromised by its disruption [3]. The open sores in the mouth and weaker defences against external invaders created by chemotherapy-induced mucositis foster the growth of bacteria. Mucositis has been linked to the use of fluorouracil (5- FU), doxorubicin, etoposide, and methotrexate as chemotherapeutic agents.

Oral mucositis develops 3 to 10 days following the beginning of chemotherapy and can last for three weeks. It has been demonstrated that its peak occurs between 7 and 14 days, after which it steadily resolves unless it is worsened by infection [4]. Mucositis improvement appears to coincide with neutrophil recovery. Although several regimens have been explored to prevent and treat none has emerged as the therapy of choice.

Epidemiology of Oral Mucositis

Oral mucositis is a serious issue for people taking chemotherapy for tumours. 51% of 599 patients undergoing chemotherapy for solid tumours or lymphoma got oral and/or GI mucositis, according to the research [5]. Oral mucositis occurred in 22% of 1236 chemotherapy cycles, gastrointestinal mucositis in 7% of cycles, and both oral and gastrointestinal mucositis in 8% of cycles [6,7]. Even more, individuals who undergo high-dose chemotherapy before hematopoietic cell transplantation (about 75–80%) suffer clinically severe oral mucositis [8]. Patients receiving radiation therapy for head and neck cancer generally get a daily dosage of roughly 200 cGy, five days per week, for 5–7 weeks. Almost all of these individuals will develop oral mucositis to some degree. In recent studies, 29–66% of patients undergoing radiation treatment for head and neck cancer developed severe oral mucositis [9]. The incidence of oral mucositis was particularly high in 1) patients with primary tumours in the oral cavity, oropharynx, or nasopharynx, 2) those who also received concomitant chemotherapy, 3) those who received a total dose greater than 5000 cGy, and 4) those who were treated with altered fractionation radiation schedules (e.g., more than one radiation treatment per day).

Clinical Significance of Oral Mucositis

Oral mucositis can be quite painful and has a substantial impact on nutritional patterns, oral hygiene, and quality of life. Oral mucositis has been identified as the single most disabling consequence of transplantation in individuals undergoing high-dose chemotherapy before hematopoietic cell transplantation. In times of severe immunosuppression, infections linked with oral mucositis lesions can induce life-threatening systemic sepsis [10]. Oral mucositis ranging from moderate to severe has been associated with systemic infection and transplant-related death. In patients with hematologic malignancies receiving allogeneic hematopoietic cell transplantation, increased severity of oral mucositis was associated with an increased number of days requiring total parenteral nutrition and parenteral narcotic therapy, an increased number of days with fever, the incidence of significant infection, an increased length of hospital stay, and an increase in total inpatient charges.

In patients undergoing chemotherapy for cancer or lymphoma, the incidence of infection during cycles with mucositis was greater than double that during cycles without mucositis and was directly related to the degree of mucositis. Infection-related mortality was also more prevalent throughout oral and GI mucositis cycles [11]. Moreover, the average length of hospitalisation for treatment cycles with mucositis was much greater. Notably, a decrease in the next chemotherapy dosage was twice as prevalent after cycles with mucositis compared to cycles without mucositis. Thus, mucositis can be a dose-limiting complication of chemotherapy for cancer with a direct impact on patient survival. Due to mucositis discomfort, the majority of patients undergoing radiation therapy for head and neck cancer are unable to continue eating by mouth and receive nourishment through a gastrostomy tube or intravenous line [12].

It has been shown that individuals with oral mucositis are substantially more likely to have severe discomfort and weight loss of at least 5 per cent. In one research, roughly 16% of head-and-neck cancer patients undergoing radiation therapy were hospitalised owing to mucositis. In addition, 11% of patients undergoing radiation therapy for head and neck cancer experienced unanticipated interruptions in treatment owing to severe mucositis [13]. Thus, oral mucositis is a prominent dose-limiting hazard of head and neck radiation treatment.

Management of Oral Mucositis

Until recently, oral mucositis was mostly treated with palliative care; however, tailored treatment strategies are currently being explored. For the prevention and treatment of oral mucositis, a wide range of non-pharmacological and pharmacological treatments have been employed [14]. There is

currently no gold standard since there are no evidence-based recommendations.

Management of Pain Control

Pain is the major symptom of oral mucositis. This discomfort greatly impacts dietary intake, oral hygiene, and quality of life. Consequently, the control of mucositis discomfort is a crucial aspect of any mucositis therapeutic approach. Numerous clinics employ saline mouth rinses, ice chips, and topical mouth rinses with anaesthetics such as 2% viscous lidocaine [15]. Equal amounts of lidocaine, diphenhydramine, plus a soothering covering agent like Maalox or Kaopectate may be used with the lidocaine. These topical anaesthetics may give temporary relief [16]. Other topical mucosal adherent treatments that are not anaesthetics but are believed to alleviate pain by creating a protective covering over ulcerated mucosa are also available. Of them, sucralfate has been examined the most. Due to the lack of consistent outcomes, no recommendation has been given for the use of sucralfate in chemotherapy-induced oral mucositis. Most patients with severe mucositis require systemic analgesics, frequently including opioids, for acceptable pain control, in addition to topical medications.

Management of Bleeding

In individuals who are thrombocytopenic owing to high-dose chemotherapy (e.g., recipients of hematopoietic cell transplants), oral mucositis ulcerations may cause bleeding. Generally, topical haemostatic treatments, such as fibrin glue or gelatin sponge, can be used to stop intraoral haemorrhage. Patients whose platelet counts fall below 20,000 need to have a platelet transfusion due to the risk of spontaneous internal bleeding, which can have severe effects, particularly in the central nervous system [17].

Oral Decontamination

In this demographic, oral decontamination may result in considerable benefits. First, it has been postulated that microbial colonisation of oral mucositis lesions exacerbates the severity of oral mucositis; hence, decontamination may aid in reducing mucositis. Multiple studies have shown that maintaining proper oral hygiene helps lessen the severity of oral mucositis. Patients who have received hematopoietic cell transplantation and who develop oral mucositis are three times more likely than patients without mucositis to have bacteraemia, resulting in longer hospital admissions. Therefore, oral cleansing may minimise mucositis, hence decreasing bacteraemia. Additionally, oral cleansing helps prevent oral cavity infections caused by opportunistic bacteria [18]. Consequently, a second role of oral cleaning is to lower the risk of systemic sepsis caused by resident oral and/or opportunistic infections. This is especially true for immunocompromised people undergoing chemotherapy. The risk of systemic sepsis from oral mucositis has not been well examined, however, one research revealed that an intensive oral care programme reduced the incidence of oral mucositis but not the proportion of patients with proven septicaemia. Patients who get just radiation treatment are less likely to acquire oral sepsis.

Nutritional Support

Pain associated with severe oral mucositis can significantly impair nutritional intake. Additionally, taste alterations might develop as a result of chemotherapy and/or radiation treatment. The dietary intake and weight must be monitored by a dietician or other expert in collaboration with family carers [19]. When oral mucositis is present, a soft diet and liquid dietary supplements are more easily tolerated than a conventional diet. In patients who are anticipated to develop severe mucositis, a gastrostomy tube is occasionally put prophylactically, but the frequency of this practice

varies substantially from centre to centre.

Discussion

Mucositis prevention should be a priority for all healthcare practitioners. Before beginning chemotherapy, all newly diagnosed cancer patients should undergo an oral checkup, including a baseline assessment of their teeth and gums. Oral exams should ideally involve a dental team and the patient. The frequency of these exams should be dictated by the toxicity of the drug and the patient's oral state at baseline. Patients with poor oral hygiene are at greater risk for oral mucositis; thus, brushing and flossing skills should be examined, and a thorough dental history should be obtained. Patients should be taught to use fluoride toothpaste after each meal and before bed, as well as floss once per day. The tongue needs to be cleansed carefully using a toothbrush or tongue scraper. Chlorhexidine gluconate mouthwash (0.12% or 0.2%) has been found to reduce the severity and duration of oral mucositis in patients undergoing severe chemotherapy. In the majority of studies, a chlorhexidine mouth rinse was administered twice daily in addition to a 0.9% saline rinse in the morning, before bed, and after each meal [20]. Similar to the WHO analgesic ladder, a step- by-step strategy should be utilised for treating the pain associated with oral mucositis. Recent practice recommendations advocate patient-controlled opioid analgesia for the management of oral mucositis-related discomfort in patients undergoing hematopoietic stem cell transplantation. Clinicians should approach analgesic therapy with a focus on providing acceptable pain management for the patient. There may be no correlation between the dose of pain medication and the severity of mucositis [21]. Oral rinses, topical anaesthetics (lidocaine, benzocaine), combination mouthwashes, and maybe mucosal surface protectants such as hydroxypropyl cellulose gels or sucralfate solutions should be the starting point of the stepwise approach. When these drugs fail to offer significant pain relief, a progression to systemic analgesics is necessary. The method of administration, dosage and management of opioid-related adverse effects should be individualised for each patient.

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In conclusion, oral mucositis is a clinically significant and occasionally dose-limiting side effect of cancer treatment. Lesions caused by mucositis can be unpleasant, damage nutrition and quality of life, and have a substantial cost burden. Oral mucositis has multiple and complex aetiology. This article examines the morbidity, economic effect, pathophysiology, and clinical progression of mucositis. The majority of the current therapeutic care for oral mucositis focuses on palliative interventions such as pain control, nutritional assistance, and maintenance of excellent oral hygiene. Nonetheless, numerous potential therapeutic options for the treatment of oral mucositis are at various phases of clinical development.

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