BRIEF REVIEW

Oral Mucositis: understanding the pathology and management

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Abstract

Oral Mucositis is a common complication of cancer therapy which may limit the completion of treatment and affect the quality of life of the patient. As we have come to understand its pathogenesis new developments in its management and prevention have allowed us minimize this side effect. Hippokratia 2012; 16 (3): 215-216

Key Words: Oral, mucositis, radiotherapy , chemotherapy, cancer

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Introduction

Oral mucositis is a common complication of radiotherapy to the head and neck region, chemotherapy and the combination of the two such as seen in conditioning regiments for homologous stem cell transplantation (HSCT). It is often a dose limiting toxicity prohibiting the patient from receiving optimal therapy. It is characterized by oral erythema, ulceration and pain and can predispose to septicemia in the case of neutropenic patients[1,2]. On a molecular pathology level mucositis is characterized as having five phases: initiation, upregulation with messenger generation, signaling and amplification, ulceration and inflammation and finally healing[3]. This condition affects the quality of life and nutritional state of the patient who may require hospitalization thus increasing health care costs. The prevention and management of mucositis involves many agents and modalities that include basic oral care protocols, antinflamatories, biologic response modifiers, cytoprotectants and cryotherapy

Discussion

Chemotherapy induced stomatitis is typically less severe and usually lasts 3-12 days while radiotherapy induced stomatitis can last up to 3-12 weeks[4]. In head and neck cases combination chemoradiation shortens the onset and increases the severity and duration of this condition. In the case of radiotherapy to areas such as head and neck mucositis occurs in 80% of cases in some form or another[5]. The incidence varies with location of the tumor with patients receiving treatment for laryngeal and hypopharyngeal cancer faring better than oropharynx. In addition to the cumulative dose, hyperfractionated schedules and combination chemoradiation also increase toxicity[6-8].

Pathogenesis

There are five steps in the pathogenesis of oral mucositis. The first is the initiation phase which involves the initial injury to cells by radiotherapy and chemotherapy either by direct DNA damage or more commonly indirectly via reactive oxygen species. This leads to a series of enzyme and transcription factor activation which eventually leads to upregulation of genes coding for inflammatory cytokines such as TNF-α, IL-1β and IL-6 which target the submucosa and basal epithelium resulting in tissue damage. The resulting inflammation and tissue damage leads to ulceration and subsequent bacterial colonization further feeding a vicious cycle of inflammatory cytokine mediated damage. The final healing phase involves signaling via the extracellular matrix resulting in epithelial proliferation and epithialization reastablishing the mucosal barrier.

Treatment

Oral care is of outmost importance in the prevention of mucositis[9]. This includes the regular brushing of teeth with a soft bristle brush and rinsing with non-alcoholic mouthwash such as a combination of saline and baking soda. It is also recommended that a dental exam and any dental work such as tooth extractions be done before therapy[10].

Anti-inflammatories also play a role in the management of stomatitis; this may involve simple washes with chamomile tea which has antinflamatory properties[11,12]. The use of benzydamine which has multiple modes of action including antinflammatory, antimicrobial analgesic and cytoprotectant actions has been evaluated in small head and neck trials involving treatment with radiation and has been proven to have significant effect[12].

Antibiotics and antifungals such as in the form of chewable pastilles are an option to reduce oral microflora resulting in infection[12,13].

The use of biologic response modifiers was initially investigated with the use of GM-CSF as a possible treatment but failed to show sufficient evidence to warrant its use[12]. More recently the biologic response modifier palifermin a human recombinant keratinocyte growth factor has been shown to reduce the duration and severity of mucositis in patients undergoing chemotherapy and radiotherapy for hematologic malignancies[14]. This drug has gained FDA approval for patients undergoing HSCT. There is however some evidence of it being effective in other aetiologies of mucositis[15], such cancers of the head and neck and in chemotherapy regiments using 5FU and leukovorin although cost remains an issue. As with all growth factors, an issue still remains of whether these substances promote tumor growth. Actually, there is no clear evidence of this phenomenon from current literature and in recent studies the overall survival between patients receiving palifermin and control subjects is the same. However, further studies on this drug are required[16,17].

In the case of cytoprotectants, the most extensively studied is amifostine which acts as a scavenger of free oxygen radicals. It has gained approval for the prevention of xerostomia in head and neck cancer radiotherapy but studies show it has a role in mucositis prevention as well[18,19].

Cryotherapy is a simple procedure most commonly used before the administration of 5-FU bolus[2]. The procedure involves giving the patient ice chips to chew 30 minutes before administration of the drug. This leads to vasoconstriction preventing the drug from reaching the oral mucosa.

Conclusion

Understanding of the pathobiology of oral mucositis has allowed us to target the various steps in the process to prevent and minimize it occurrence. Examples are prevention of infection through good oral hygiene, oral rinses and antibiotic pastilles, prevention of free radical damage via cytoprotectants, targeting the inflammatory process via antinflamatories and promoting re-epithiliazation via biologic response modifiers. All these modalities serve to promote the completion of radiotherapy and chemotherapy regimes by preventing this dose limiting toxicity.

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