

Advancing the Assessment and Treatment of Mucositis

Etiology and Impact of Oral Mucositis

Mucositis is the inflammation of the mucosal tissue, which could be anywhere in the gastrointestinal (GI) system. Susan L. Beck, PhD, APRN, AOCN®, FAAN, explained that oral mucositis involves the oral and oropharyngeal tissues. Historically, this has been called stomatitis, but stomatitis and oral mucositis really mean the same thing, she said.

“Oral mucositis is a dose-limiting side effect of cancer therapy,” Beck said. “That is one of the reasons it is so important that we address oral mucositis.”

Beck reported that 40% of patients receiving standard dose chemotherapy develop mucositis (Rosenthal, Karthaus, & Ganser, 2000). As many as 60% of patients on high-risk protocols develop it. In addition, patients undergoing bone marrow transplant—who often have total body irradiation—have much higher rates of incidence (75%–90%) (Kostler, Hejna, Wenzel, & Zielinski, 2001).

“Virtually every patient undergoing head and neck irradiation will develop oral mucositis,” Beck said. “It has become a barrier to treatment intensification.”

Beck listed several risk factors for oral mucositis (Kostler et al., 2001). Patient-

related factors include age (very young and very old may be at greater risk for developing mucositis), poor baseline oral hygiene, hyposalivation or increased viscosity of saliva, ill-fitting dentures, and hematologic malignancy.

Several risk factors are related to specific treatment regimens as well. For example, stomatotoxic chemotherapeutic agents (methotrexate, 5-fluorouracil [5-FU], taxanes, docetaxel), prolonged or repetitive (versus bolus) administration of a drug, high cumulative radiation doses, and high numbers of cycles and intensity of chemotherapy are associated with higher risk for developing mucositis. Patients with head and neck cancers receiving concomitant chemoradiation therapy and bone marrow transplant or stem cell transplant recipients also face higher risks.

Severe mucositis leads to increased fever and infection, increased use of total parenteral nutrition and opioids, and a fourfold increase in mortality risk. Beck said that hospital charges were almost \$43,000 higher in patients with ulcerative mucositis (Elting et al., 2004). In addition, severe oral mucositis may result in dose reductions and dose delays of chemotherapy, increased fatigue, and bleeding.

Direct mucositis is the effect of the drug or treatment directly on the mucosa. Indirect mucositis also can occur as a result of neutropenia that makes the host susceptible to bacterial or viral infection.

“An oral ulcer is a wound,” Beck explained, reviewing the phases of wound healing (inflammation, tissue generation, tissue remodeling). Growth

Oral mucositis is inflammation of the mucosal oral and oropharyngeal tissues. It is a troubling and difficult side effect of cancer treatment. This program discussed the biology of oral mucositis and its effect on cancer therapy outcomes. Speakers covered the treatment goals for patients with oral mucositis and reviewed treatment options and related nursing implications.

factors and mucosal protectants are important parts of wound healing. Having a moisture-protective barrier over a wound promotes healing. The recruitment of macrophages and growth factor secretion could be important in promoting healing as well.

Several tools for measuring oral mucositis are available. Beck described the Oral Mucositis Assessment Scale, the National Cancer Institute’s (NCI’s) Common Toxicity Criteria, and Telephone-Link Care, an NCI-funded symptom management study. These tools provide the clinician with information that, when combined with a patient’s signs and symptoms, will provide a full picture of the extent of oral mucositis.

Impact on Quality of Life and Costs

“If you take a single symptom and look at the impact it has on somebody’s overall multidimensional quality of life, the worse the symptom is, the greater the impact it has on quality of life,” said David Cella, PhD. Mucositis affects pain, swallowing, and the ability to eat and drink to sustain nutritional balance. A complex mouth care regimen requires extra time. Mucositis also affects the ability to talk, communicate, and “engage in social intercourse. . . a vital part of people’s lives,” Cella said.

Cella described a retrospective chart review of 599 patients with myelosuppression who received 1,236 cycles of chemotherapy (Elting et al., 2004). Results showed that oral mucositis increased the infection rate by 32% and hospitalization by two days. GI mucositis increased bleeding by 5%, infection by 37%, and hospitalization by eight days. Oral

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mucositis also increased the resources devoted to patients in the terms of professional time, outpatient support, prescription medications, and hospitalizations. The average total cost was \$19,000 (in today's dollars) (Peterman et al., 2001).

Cella shared information from a study conducted at his institution in which patients were asked to rate their mouth pain using a 0–10 scale. Researchers found that subjective and objective ratings peaked at around two weeks, and pain tracked directly with “objective” measures of mucositis severity, supporting the conclusion that “when it comes to mucositis severity, perhaps the patient knows best,” Cella concluded (Cella et al., 2003).

Advancing Assessment and Treatment

Oral mucositis typically starts with asymptomatic redness or erythema. As it progresses, patients have slightly painful white patches within the mouth that develop into more acutely painful lesions. Patients then may complain of burning and increased sensitivity to hot and spicy foods. As it progresses, an isolated lesion becomes confluent lesions, resulting in severe pain and impaired function.

“Mucositis occurs as a continuum,” said Pat Kramer, RN, MSN, AOCN®, who explained the importance of having an assessment on record, so changes can be identified. “The goal is to be proactive with intervention so we can optimize and improve the patient’s outcome, particularly in terms of pain and functional ability,” Kramer said. Assessment can be performed by the healthcare team and by patients and caregivers. Assessments must be frequent enough to identify changes but not be so frequent that they increase patient and caregiver burden.

Kramer said that a good place to start is by asking patients about feelings of dry mouth and inability to eat, swallow, and maintain oral nutrition. Assessment must include subjective complaints, objective findings, and the impact on the patient’s functional ability to eat, speak, and maintain nutrition and quality of life. She noted that the patient’s inability to eat may be a function of inadequate pain relief more than a measure of severe mucositis. “Pain and functional ability go hand in hand,” she said.

Kramer said that many nurses report that they have not been trained to do a

Pathobiology of Oral Mucositis

- **Phase 1—Initiation:** radiation or chemotherapy do direct damage to the cells, tissues, and vessels. Reactive oxygen species (ROS) generated within cells.
- **Phase 2—Upregulation and message generation:** chemotherapy, radiation therapy, and ROS activate NF- κ B. NF- κ B upregulates many genes, including proinflammatory cytokines. Tissue injury, cell death, and angiogenesis occur.
- **Phase 3—Amplification:** a vicious cycle begins. TNF- α leads to more production of NF- κ B. Epithelial cells in mucosa start to thin. Substructures become inflamed. Entire system amplifies.
- **Phase 4—Ulceration:** endotoxins activate the macrophages, more production of proinflammatory cytokines. The patient experiences pain, inflammation, and the risk of infection or sepsis.

thorough oral examination. She suggested partnering with a mentor who is experienced in oral examination. During the oral examination, look for changes in color, changes in moisture levels, the quality of the saliva, the overall cleanliness of the mouth, the presence of any ulcerations or lesions, and any interruption in the integrity of the oral mucosa. In addition, check for dry, cracked, or chapped lips, and evaluate the quality of speech and voice. Kramer said that the areas of the mouth that are most vulnerable to oral mucositis include the buccal mucosa, the ventral parts of the tongue, under the tongue and the lips, and the soft palate.

Kramer emphasized the importance of educating patients about good oral care, which includes the following.

- Brush and floss two to four times daily for 90 seconds with a soft-bristled toothbrush and fluoridated paste.
- Rinse the mouth with normal saline, salt and bicarbonate rinses, sterile water, or a bland, nonalcoholic rinse.
- Use a lip lubricant.
- Add a topical fluoride gel or rinse to patients’ therapies if they are receiving head and neck or whole brain radiation or have significant xerostomia.

“Magic mouthwash” is commonly used to aid in relieving pain from oral mucositis. Kramer reported on a clinical study comparing pain relief and overall pain scores associated with salt and bicarbonate alone, chlorhexidine, magic mouthwash with lidocaine, diphenhydramine, and Maalox® (Novartis Consumer Health, Parsippany, NJ) (Dodd et al., 2000). Because severity and duration of mucositis was no different in any of the three arms, the researchers concluded that salt and

bicarbonate should be recommended.

Kramer said that ice chips should be avoided because they cause vasoconstriction. Clinical trials have supported cryotherapy as a preventive measure during bolus infusion of 5-FU; however, cryotherapy is not effective for continuing infusions.

In chemoprevention trials, beta carotene was shown to produce regression of precancerous lesions (oral leukoplakia) of the oral cavity (Lodi, Sardella, Bez, Demarosi, & Carrassi, 2002). Other antioxidant therapies include amifostine; chlorhexidine; growth factors, including human keratinocyte growth factor; benzydamine; L-glutamine, which is undergoing phase III testing; and Gelclair®

(OSI Pharmaceuticals, Melville, NY), a bioadherent gel that has been found to be effective for rapid and durable pain relief (Innocenti, Moscatelli, & Lopez, 2002).

Gelclair works by forming an adherent barrier and shielding exposed or sensitized nerves. Kramer shared results from a pilot study of Gelclair that demonstrated a 92% reduction in mean pain scores five to seven hours after initial treatment (Innocenti et al., 2002).

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