COMMENTARY

Evidence-Based Management of Oral Mucositis

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As well described in the clinical review by Brown and Gupta[1] in this issue of *JCO Oncology Practice*, oral mucositis is a common toxicity of cancer therapy. The morbidity of oral mucositis includes pain, nutritional compromise, and infection risk, which potentially result in breaks or dose reductions in cancer therapy. Historically, management was focused mainly on pain control and nutritional support. However, evidence-based clinical practice guidelines for oral and GI mucositis were recently updated. They include recommendations (on the basis of level I or II evidence) and suggestions (on the basis of lower levels of evidence). These guidelines are developed by the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology.[2]

For oral mucositis in patients receiving systemic chemotherapy, the guidelines include:

- Recommendations for oral cryotherapy in patients receiving bolus fluorouracil and high-dose melphalan[3]
- A recommendation for intravenous keratinocyte growth factor-1 in patients with hematologic cancer receiving high-dose chemotherapy for autologous hematopoietic stem-cell transplantation (HSCT)[4]
- A recommendation for intra-oral low-level laser therapy in patients receiving high-dose chemotherapy for HSCT.[5]

For oral mucositis in patients receiving head and neck radiation therapy (H&N RT), the guidelines include:

- Recommendations for intra-oral low-level laser therapy in patients receiving H&N RT with or without concurrent chemotherapy[5]
- A suggestion for benzydamine mouthwash in patients receiving H&N RT with concurrent chemotherapy[6]
- A recommendation for benzydamine mouthwash in patients receiving moderate-dose H&N RT (< 50 Gy)[6]
- A suggestion for oral glutamine in patients receiving H&N RT with concurrent chemotherapy.[7]

The guidelines also include a suggestion for the use of oral care protocols in all these populations. Because of inadequate evidence, no guideline was possible related to professional oral care for mucositis prevention. However, an expert opinion from the panel states that dental evaluation and treatment as indicated before cancer therapy are desirable to reduce the patient's risk for local and systemic infections from odontogenic sources. Similarly, no evidence-based guideline was possible related to commonly used saline and sodium bicarbonate rinses. However, the expert opinion states that these are inert bland rinses that increase oral clearance, which may be helpful for maintaining oral hygiene and improving patient comfort.[8]

A number of proprietary mucoadhesive topical coating agents are marketed for oral mucositis. Because of inadequate or conflicting evidence, no guideline was possible related to any of these agents. However, evidence supported recommendations against the use of generic topical sucralfate, which is a coating agent, in the aforementioned populations because of lack of efficacy.[9] Similarly, no guideline was possible related to the use of marketed supersaturated calcium phosphate rinses in any population because of inadequate or conflicting evidence.[7]

More recently, stomatitis has also been reported secondary to targeted agents for cancer but with different clinical features from oral mucositis secondary to conventional chemotherapy or H&N RT.[10] Ulcerative stomatitis secondary to mammalian target of rapamycin (mTOR) inhibitors has a clinical appearance similar to aphthous stomatitis (canker sores). Oral ulcerations have also been reported secondary to anti–epidermal growth factor receptor agents, including the tyrosine kinase inhibitors afatinib and dacomatinib, which appear as limited and superficial ulcers that may be aphthous-like. The SWISH trial demonstrated that prophylactic use of dexamethasone mouthwash significantly reduces the incidence and severity of stomatitis in patients receiving the mTOR inhibitor everolimus for breast cancer (compared with historical control patients).[11] Topical, intralesional, or systemic steroids are currently used for the management of ulcerative stomatitis secondary to targeted agents on the basis of the limited body of evidence and expert opinion.

In contrast, stomatitis secondary to sunitinib and sorafenib has been typically reported as oral sensitivity/burning with no clinical signs. Nonulcerated oral lichenoid or hyperkeratotic lesions have been reported with imatinib, vemurafenib, and dabrafenib and less commonly with immune checkpoint agents. Such lesions are usually asymptomatic and may not require specific management.[10]

Evidence-based management of oral mucositis can significantly improve the patient's quality of life and facilitate adherence to recommended cancer therapy regimens. As the motto of MASCC states, supportive care makes excellent cancer care possible.

ASSOCIATED CONTENT

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