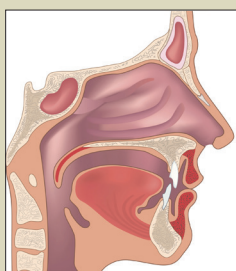


Evidence-Based Interventions for Cancer Treatment–Related Mucositis: Putting Evidence Into Practice

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Mucositis is an inflammatory process that can involve the mucosal epithelial cells from the mouth to the rectum. Historically, mucositis and stomatitis were used interchangeably, but momentum has increased toward more specific terminology since the 2000s. *Stomatitis* refers to inflammatory diseases of the mouth, including the mucosa, dentition, periapices, and periodontium, whereas *mucositis* refers more globally to an inflammatory process involving the mucous membranes of the oral cavity and the gastrointestinal tract. In addition, differentiation is needed regarding mucositis involving the oral cavity and the remainder of the gastrointestinal tract that require use of a scope-type device for close examination. As a result, oral cavity mucositis has been the focus of the majority of the studies reported to date. The mucous membranes beyond the oral cavity are more challenging to view, so the mouth has been presented as revealing potential changes in the gastrointestinal tract. However, because of the variation in morphology, function of different locations, and risks associated with procedures to validate that speculation, evidence is limited. The purpose of this article is to review evidence-based interventions for mucositis, particularly in the oral cavity, and provide clinicians with guidelines for nursing interventions.

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Advances in the pharmacologic and supportive therapy management of cancer treatment-related bone marrow suppression, nausea and vomiting, and neutropenia-related infections have enabled dose escalation of many treatment protocols. However, mucositis is now seen with increased frequency and has evolved into a dose-limiting side effect of treatment. As a result, prevention and management of this side effect have become more relevant for cancer treatment success.

Once believed to involve a simple linear process, mucositis is now seen as a complex process involving many different factors, including the inflammatory process, cellular apoptosis,

cytokines, cytotoxicity of treatments, and micro-organisms in the oral cavity. Sonis (2004) developed a proposed theoretical model to facilitate understanding of the complex process. When the inflammation progresses to a breakdown in the protective mucosal barrier, the micro-organisms normally present in the oral cavity and throughout the gastrointestinal tract are able to enter the bloodstream and cause potentially life-threatening infections that require strategic intervention. In addition to the risk of infections, mucositis causes pain, restricts oral intake, and contributes to malnutrition, interruption of treatment, and increased hospitalizations. The incremental costs of mucositis are usually associated with hospital stays, but

the costs more than double when mucositis is severe (Carlotto, Hogsett, Maiorini, Razulis, & Sonis, 2013).

Patients receiving chemotherapy, epidermal growth factor receptor inhibitors, tyrosine kinase inhibitors, and/or radiation to the head and neck are susceptible to the development of oral mucositis. Mucositis occurs in about 40% of patients after standard doses of chemotherapy, and in as many as 100% of patients receiving high-dose chemotherapy or combination chemotherapy and radiation for head and neck cancer (Gibson et al., 2013). Risks for mucositis include patient- and treatment-related factors (Barasch & Peterson, 2003). Patient-focused factors include poor nutrition, age (children and older adults), neutropenia, poor oral hygiene, genetic factors, impaired salivary function, and use of alcohol and tobacco. Treatment-focused risk factors include specific chemotherapy agents, chemotherapy dose and administration schedule (high doses and stem cell transplantation), combination radiation and chemotherapy, radiation for head and neck cancer, and concomitant medications.

One of the reasons for the wide variation in documented incidence of mucositis is inconsistent use of valid and reliable instruments for the assessment of oral cavity changes. In addition, the severity of mucositis can range from mild erythema

to severe ulcerations and bleeding. Visible changes associated with mucositis include erythema, ulceration, and pseudomembrane formation. Patients with membrane changes experience varying degrees of pain and changes in function including difficulty speaking and swallowing. As a result, patients focus on the symptoms that affect quality of life rather than the risk of life-threatening infection that is of concern to healthcare professionals. The increased length of hospitalization and costs attributed to mucositis are primarily related to pharmacologic management of the infections associated with mucositis and altered ability to maintain oral nutrition. To improve patient outcomes, the goals of nursing care are to prevent membrane breakdown, maintain the ability to eat, and treat or prevent pain.

This article builds on the earlier work by Oncology Nursing Society (ONS) Putting Evidence Into Practice (PEP[®]) mucositis teams (Eaton & Tipton, 2009; Harris, Eilers, Harriman, Cashavelly, & Maxwell, 2008; Johnson, Henry, Saca-Hazboun, & Samuel-Blalock, 2014). The span of the work attests to the commitment of oncology nurses to make a difference in patient outcomes through evidence-based practice and the ongoing challenge of mucositis in cancer care.

TABLE 1. Mucositis Interventions: Recommended for Practice

| Agent | Findings | Studies Reviewed |
|---------------------------------|---|--|
| Cryotherapy | Topical application: ice water, ice cubes, ice chips, or ice lollipops during chemotherapy infusion Reduced symptoms, incidence, severity, and pain associated with mucositis for patients receiving chemotherapy agents with a short half-life | Aisa et al., 2005; Karagözoglu & Filiz Ulusoy, 2005; Katranci et al., 2012; Kwong, 2004; Lilleby et al., 2006; Migliorati et al., 2006; Mori et al., 2006, 2008; Nikoletti et al., 2005; Papadeas et al., 2007; Peterson et al., 2010; Salvador et al., 2012; Svanberg et al., 2010; Vokurka, Bystricka, et al., 2011; Worthington et al., 2011 |
| Low-level laser therapy | Historically has shown mixed results in individual studies in children and adults; however, the majority of recent studies demonstrated a benefit. Systematic reviews showed effectiveness. A meta-analysis showed significant high effect sizes for reducing prevalence, severity, pain, and duration of mucositis. Current European Society for Medical Oncology guidelines recommended low-level laser treatment prior to hematopoietic stem cell transplantation. Most research has been restricted to patients with head and neck cancer and those undergoing transplantation. | Antunes et al., 2008, 2013; Arbabi-Kalati et al., 2013; Arora et al., 2008; Bjordal et al., 2011; Carvalho et al., 2011; Cauwels & Martens, 2011; Clarkson et al., 2010; Cruz et al., 2007; Cunha et al., 2012; de Castro et al., 2013; Figueiredo et al., 2013; Gautam, Fernandes, Vidyasagar, & Maiya, 2012; Gautam, Fernandes, Vidyasagar, Maiya, et al., 2012; Genot-Klastersky et al., 2008; Gouvêa de Lima et al., 2012; Jaguar et al., 2007; Khouri et al., 2009; Kuhn et al., 2009; Lima et al., 2010; Maiya et al., 2006; Migliorati et al., 2006, 2013; Nes & Posso, 2005; Peterson et al., 2010; Qutob et al., 2013; Schubert et al., 2007; Simões et al., 2009; Worthington et al., 2011; Zanin et al., 2010 |
| Oral care protocols | To provide consistent frequent oral hygiene, prophylactic mouth rinses, and routine assessment for early detection Decreased the incidence, duration, and severity of mucositis Structure and components of oral care are important. | Bhatt et al., 2010; Caplinger et al., 2010; Cheng et al., 2001; Dodd et al., 2000; Hogan, 2009; Kwong, 2004; McGuire et al., 2013; Peterson et al., 2011; Qutob et al., 2013; Shih et al., 2002; Yamagata et al., 2012 |
| Palifermin | Effective preventive IV treatment for patients receiving high-dose chemotherapy | Blijlevens et al., 2013; Henke et al., 2011; Langner et al., 2008; Le et al., 2011; Nasilowska-Adamska et al., 2007; Niscola et al., 2009; Peterson et al., 2010; Raber-Durlacher et al., 2013; Rosen et al., 2006; Schmidt et al., 2008; Shea et al., 2007; Sonis, 2009; Spielberger et al., 2004; Stokman et al., 2006; Vadhan-Raj et al., 2010; von Bültz-inglöwen et al., 2006 |
| Sodium bicarbonate mouth rinses | Shown to be effective in systematic reviews | Potting et al., 2006; Shih et al., 2002 |

TABLE 2. Mucositis Interventions: Likely to Be Effective

| Agent | Findings | Studies Reviewed |
|---|---|---|
| Benzylamine rinses ^a | Rinses have lowered severity and pain of mucositis. A systematic review reported inconsistent results in comparison to chlorhexadine. European Society for Medical Oncology guidelines recommended a benzylamine oral rinse for patients with head and neck cancer. Multinational Association of Supportive Care in Cancer guidelines recommended use in patients with head and neck cancer receiving radiation therapy without chemotherapy. | Epstein et al., 2001, 2008; Kazemian et al., 2009; Kwong, 2004; Nicolatou-Galitis et al., 2013b; Peterson et al., 2011; Petit et al., 2014; Roopashri et al., 2011; Shih et al., 2002 |
| Lactobacillus lozenges | Reduced incidence of oral mucositis compared to placebo in patients with head and neck cancer receiving chemotherapy and radiation therapy | Sharma et al., 2012 |
| Prophylactic chlorhexidine mouth rinses | Reduced incidence and pain associated with oral mucositis in three of five individual studies Two systematic reviews reported moderate support for prophylactic use. Chlorhexidine is not recommended as treatment for existing mucositis. | Cheng et al., 2001, 2004; Dodd et al., 2000; Donnelly et al., 2003; Pitten et al., 2003; Qutob et al., 2013; Sorensen et al., 2008 |

^a Benzylamine is not approved by the U.S. Food and Drug Administration for use in the United States.

Methods

Search Strategy

The literature search for relevant articles indexed in PubMed and CINAHL[®] was conducted by a research librarian at ONS. Search terms selected were consistent with prior searches for earlier PEP mucositis teams. PubMed was searched for *Mucositis[ti]* OR *Mucositis[majr]* OR “oral complication*” and CINAHL was searched for (MM “Mucositis” OR MM “Stomatitis” OR TI *Mucositis* OR TI *stomatitis* OR “oral complication*”) AND (cancer OR neoplasms OR oncolog* OR chemotherap*). The articles had to include patients with cancer and be published in English from May 1, 2008 to December 31, 2013. The search yielded 635 PubMed citations and 338 CINAHL citations. The abstracts were reviewed based on the following inclusion criteria: (a) studies were full research reports, systematic reviews, guidelines, or meta-analyses; (b) studies had to report on the results of measurement of oral mucositis; (c) studies examined an intervention aimed at affecting the problem of oral mucositis; and (d) the study samples included patients with cancer. Studies were excluded if they included grey literature, were descriptive, or reported intervention effects on the pain of mucositis but not the actual incidence or severity of the symptom mucositis itself. The screening of abstracts identified 138 articles for full article review. After removal of duplicates and studies that did not meet inclusion criteria and the addition of manuscripts retrieved in other topics meeting topic specific criteria, 100 publications were identified for team member review. Four additional studies were identified through an ongoing alert from the ONS research librarian. As a result, 104 publications were added to the prior ONS PEP mucositis work. Because the methods used for the PEP reviews presented in this supplement were consistent across the evidence-based practice teams, the detail of that content is available in Johnson (2014).

Evidence

New research in mucositis is plentiful, particularly related to novel agents with many derived from natural sources. The bulk

of those agents are classified as effectiveness not established because of inadequate research, study design flaws, and conflicting or unconfirmed results. The evidence was challenging to categorize because clinical measurement of mucositis was inconsistent across trials and the validity and reliability of the measurement was not always addressed by the study authors.

Recommended for practice: This category includes interventions for which effectiveness has been demonstrated by strong evidence from rigorously designed studies, meta-analyses, or systematic reviews and for which expectation of harm is small compared with the benefits. In previous reviews, only oral care protocols were recommended. However, additional therapies now included in this category are cryotherapy, low-level laser therapy, oral care protocols, palifermin, and sodium bicarbonate mouth rinses (see Table 1).

Likely to be effective: These interventions include evidence from a single rigorously conducted controlled trial, consistent evidence from well-designed controlled trials using small samples, evidence from meta-analyses or systematic reviews using small samples, or evidence from guidelines developed from evidence and supported by expert opinion. New recommendations in this category include prophylactic chlorhexidine, benzylamine, and lactobacillus lozenges (see Table 2).

Effectiveness not established: This category includes interventions for which data are insufficient or lack adequate quality. Numerous topical and systemic pharmacologic and nonpharmacologic interventions have been studied for efficacy in the prevention and management of oral mucositis or management of associated pain. Evidence for the interventions is limited because of inconsistent research results, small studies, and study designs. As a result, this category includes the greatest number of agents (see Table 3).

Effectiveness unlikely: These are interventions for which lack of effectiveness has been demonstrated by negative evidence from a single rigorously conducted controlled trial, consistent negative evidence from well-designed controlled trials using small samples, small samples within meta-analysis or systematic reviews, or ineffective guidelines developed by consensus

TABLE 3. Mucositis Interventions: Effectiveness Not Established

| Agent | Remarks | Studies Reviewed |
|--|---|--|
| Allopurinol mouthwash | Three systematic reviews showed no benefit. One research evidence summary | Kwong, 2004; Panahi et al., 2010; Stokman et al., 2006; Worthington et al., 2004 |
| Aloe vera | One phase II study with patients undergoing RT | Su et al., 2004 |
| Amifostine IV | Seven studies A systematic review showed conflicting results, but associated guidelines suggest use of amifostine. | Antonadou et al., 2002; Buentzel et al., 2006; Gibson et al., 2013; Hwang et al., 2004; Jantunen et al., 2002; Lorusso et al., 2003; Nicolatou-Galitis et al., 2013a; Spencer et al., 2005; Thieblemont et al., 2002 |
| ATL-104 | One RCT Plant extract, used as an oral rinse | Hunter et al., 2009 |
| Bethanechol mouth rinse | One systematic review One randomized phase III prospective trial among patients with HNC | Jensen et al., 2013; Jham et al., 2009 |
| Calcium phosphate (Caphosol® mouth rinse) | Two systematic reviews Three small studies in adult patients One small study in pediatric patients | Lambrecht et al., 2013; Markiewicz et al., 2012; Papas et al., 2003; Quinn, 2013; Raphael et al., 2014; Stokman et al., 2012 |
| Calendula officinalis mouthwash | Perennial herb in the daisy family One small RCT | Babae et al., 2013 |
| Camellia and wheat extract tincture or cream | Sinesis leaf extract derived from green tea One small RCT | Carulli et al., 2013 |
| Colchicine mouthwash | Extracted from autumn crocus One RCT | Garavito et al., 2008 |
| Colony-stimulating factors (mouth rinses) | Two systematic reviews A meta-analysis showed possible benefit but weak evidence. | Cawford et al., 1999; Clarkson et al., 2010; Dazzi et al., 2003; Hejna et al., 2001; Hong et al., 2009; Kim et al., 2013; Mantovani et al., 2003; McAleese et al., 2006; Nicolatou-Galitis et al., 2001; Qutob et al., 2013; Rossi et al., 2003; Ryu et al., 2007; Sprinzl et al., 2001; Valcarcel et al., 2002; Worthington et al., 2011; Wu et al., 2009 |
| Epithelial growth factor recombinant epithelial growth factors | Given systemically for prophylaxis Oral spray | |
| Doxepin mouthwash | Tricyclic antidepressant One open-label study | Epstein et al., 2008 |
| Fluoride chewing gum | One RCT | Gandemer et al., 2007 |
| Flurbiprofen tooth patch | Patch containing 15 mg flurbiprofen One study with historic controls | Stokman et al., 2005 |
| Folinic acid | Given systemically after high-dose methotrexate | Sugita et al., 2012 |
| Glutamine (oral) | Four RCTs One retrospective study | Blijlevens et al., 2005; Cerchiatti et al., 2006; Peterson et al., 2006; Vidal-Casariago et al., 2013; Ward et al., 2009 |
| Hangeshashinto (TA) | A traditional Japanese medicine | Kono et al., 2010 |
| Herbal medicine | A systematic review of 18 studies among patients treated with a single herb | Meyer-Hamme et al., 2013 |
| High-dose laser therapy | Small study in pediatric population | Chermetz et al., 2013 |
| Honey (TA) | Studies included children with low-grade symptoms. Studies in adults showed mixed results and had numerous design limitations. | Abdulrhan et al., 2012; Bardy et al., 2012; Hawley et al., 2014; Jayachandran & Balaji, 2012; Maiti et al., 2012; Motallebnejad et al., 2008; Rashad et al., 2009; Song et al., 2012; Worthington et al., 2011; Yarom et al., 2013 |
| Human intestinal trefoil factor (TA) | Peptide found in mucosal goblet cells One phase II study | Peterson et al., 2009 |
| Hyaluronic acid or sodium hyaluronate oral spray | Mixed small studies and one expert review | Barber et al., 2007; Buchsel & Murphy, 2008; Colella et al., 2010; Vokurka, Skardova, et al., 2011 |

(Continued on the next page)

HNC—head and neck cancer; RCT—randomized, controlled trial; RT—radiation therapy; SCT—stem cell transplantation; TA—topical application

TABLE 3. Mucositis Interventions: Effectiveness Not Established (Continued)

| Agent | Remarks | Studies Reviewed |
|---|--|--|
| Indigowood root (gargle) | Chinese herb Small control trial | You et al., 2009 |
| Infrared phototherapy | Use of near infrared wavelength light One study in SCT with melphalan | Hodgson et al., 2011 |
| Irsogladine maleate (oral) | Synthetic drug with antiviral activity One study with patients with HNC | Nomura et al., 2013 |
| Manuka and kanuka (TA) | Plant-derived essential oils with antibacterial, antifungal, anti-inflammatory, and essential analgesic actions Small feasibility study | Maddocks-Jennings et al., 2009 |
| Misoprostol | One review recommended against use in RT for patients with HNC. Two additional studies | Lalla et al., 2012; Nicolatou-Galitis et al., 2013b; Veness et al., 2006 |
| Payayor (herbal medicine) | Small herb cultivated in southeast Asia Used in combination with benzydamine | Jensen et al., 2013; Putwatana et al., 2009 |
| Phenylbutarate mouthwash | Gene modulator approved for urea cycle disorder Small RCT | Yen et al., 2012 |
| Pilocarpine | Cholinergic agonist Two small studies | Awidi et al., 2001; Jensen et al., 2013; Lockhart et al., 2005 |
| Povidone iodine (TA) | Studies with mixed result | Madan et al., 2008; Vokurka et al., 2005; Yoneda et al., 2007 |
| Professional oral care | Two individual studies | Kashiwazaki et al., 2011; Yoneda et al., 2007 |
| Propolis (topical bee glue) | Resin-like material made by bees to coat inside of hive Small pediatric study | Abdulrman et al., 2012; Tomazevic & Jazbec, 2013 |
| Pycnogenol (topical pine bark extract) | Topical use of pine bark extract Pediatric, single-blind RCT | Khurana et al., 2013 |
| Repifermin (keratinocyte growth factor) | Keratinocyte growth factor 2, administered via IV Small study in SCT | Freytes et al., 2004 |
| Rhodiolo algida (herbal solution taken by mouth) | Tibetan plant; Chinese medicine to nourish qi Control trial not specific to mucositis | Loo et al., 2010 |
| Salivary stimulation with a mechanical chewing device | Electrical salivary stimulation Small study in SCT | Jensen et al., 2013; Pimenta Amaral et al., 2012 |
| Samital mouth rinse | Combination of three botanic drug extracts (vaccinium myrtillus, macleaya cordad, and Echinacea angustifolia root) Small control trial | Bertoglio et al., 2013; Pawar et al., 2013 |
| Selenium | One RCT in allogeneic transplantation | Jahangard-Rafsanjani et al., 2013 |
| Tetracaine for pain management | Tetracaine gel combined with other agents Small trial in patients with HNC undergoing RT | Alterio et al., 2006 |
| Triclosan mouth rinses | Antibacterial agent for periodontal therapy Small RCT | Satheeshkumar et al., 2010 |
| Turmeric | One RCT for patients with HNC undergoing RT | Rao et al., 2013 |
| Visible light therapy | Broad band visible light therapy Small RCT in SCT | Elad et al., 2011 |
| Vitamin E (TA) | Two systematic reviews and two studies in pediatric patients | Clarkson et al., 2010; Khurana et al., 2013; Sung et al., 2007; Yarom et al., 2013 |
| Zinc or zinc supplements | One systematic review and seven individual studies | Arbabi-Kalati et al., 2012; Ertekin et al., 2004; Lin et al., 2006, 2010; Mansouri et al., 2011; Mehdipour et al., 2011; Sangthawan et al., 2013; Yarom et al., 2013 |

HNC—head and neck cancer; RCT—randomized, controlled trial; RT—radiation therapy; SCT—stem cell transplantation; TA—topical application

or expert opinion. Three agents are in this classification. One of these agents, Traumeel S, consists of multiple homeopathic substances that are expected to have effects on wound healing and inflammation. This compound was studied for its effect on oral mucositis. Other agents previously included and remaining in this category are iseganan and Wobe-Mugos E. Studies with the agents failed to produce statistically significant results (see Table 4). Misoprostol, an agent previously classified in this category, has been moved to effectiveness not established.

Not recommended for practice: Interventions in this category are those for which lack of effectiveness or harmfulness has been demonstrated by strong evidence from rigorously conducted studies, meta-analyses, or systematic reviews or interventions for which the costs, burdens, or harms associated with the intervention exceed anticipated benefit. Two agents remain in this category: chlorhexidine (nonprophylactic) and sucralfate. The concerns with both agents for treatment of mucositis is related to rinse-induced discomfort and taste. The recommendation is supported by other systematic reviews (Kwong, 2004; Shih, Miaskowski, Dodd, Stotts, & MacPhail, 2002; von Bültzingslöwen et al., 2006) (see Table 5).

Other Agents

The extensive volume of literature available regarding treatment and prevention of mucositis presents a challenge for systemic reviews of evidence. In addition to interventions categorized for this article, many others have been trialed and reported in various journals and venues. When systematic reviews are included in a process such as is reported here, multiple agents may have been involved. For the most part, the agents are not included if the researchers concluded that they were not able to make a recommendation. The numerous nonpharmacologic agents used in different settings throughout the world also present a challenge because reviewers were not always able to ascertain the details of the mixtures used. In addition, nonpharmacologic interventions have not always received the same scrutiny prior to use.

Agents that provide a protective barrier are an example of another type of intervention (e.g., Episil[®], Gelclair, MuGard[™]). Typically, that type of agent is regarded as a device, which undergoes a different review process prior to approval for use. As a result, the studies reported may not have the same scientific rigor required for randomized clinical trials. In addition, the literature is not always clear regarding whether the primary

outcome for a given study is pain management or mucositis management.

Implications for Practice

This comprehensive review of mucositis literature examined pharmacologic and nonpharmacologic interventions. Although only a limited number of interventions met the criteria for recommended for practice, they can provide clinicians with a basis for improved outcomes. Nurses are frequently acknowledged as the professionals spending the greatest amount of time with patients. The reality is that nurses in the clinical setting are facing an ever-increasing number of challenges and are expected to do more with less; therefore, nursing interventions such as basic oral care once seen as routine in acute care settings are becoming much less routine. That change in practice and the shift of the majority of cancer care to the outpatient setting have contributed to inconsistency in the promotion of oral care protocols that may be seen as too basic. This review adds support to the use of oral care protocols as the foundation for mucositis prevention and treatment. Nurses have a primary role to relay that importance to patients and families and to provide instruction regarding agents to avoid, particularly those containing alcohol, which has long been stated in the literature. In addition, nurses should recommend the use of sodium bicarbonate mouth rinses as an essential component of the routine oral care protocol.

Although indications for cryotherapy are restricted to potentially mucotoxic agents with a short half-life being administered over a relatively short time period, the intervention is low cost and evidence-based nursing practice. Individuals with cancerous lesions in their oral cavity would not be candidates for the intervention because the vasoconstriction induced by the cooling has the potential to limit exposure of the cancer cells to effective antineoplastic doses. In addition, cryotherapy is not indicated for individuals receiving oxaliplatin because of problems with exposure to cold, including pain, sensitivity, chest tightness, and laryngospasm.

The two remaining recommended interventions fall within interprofessional care. Low-level laser therapy requires the necessary equipment and trained personnel, so it is not available in all treatment centers. Variations in terminology and dose related to the use of lasers and other forms of light therapy for mucositis must be considered. The second intervention, palifermin, has

TABLE 4. Mucositis Interventions: Effectiveness Unlikely

| Agent | Findings | Studies Reviewed |
|----------------------|--|--|
| Iseganan (a peptide) | Did not improve mucositis compared to placebo | Giles et al., 2004; Saunders et al., 2013; Trotti et al., 2004 |
| Traumeel S | Consists of multiple homeopathic substances that are expected to have effects on wound healing and inflammation Showed no benefit in adults or children | Sencer et al., 2012; Steinmann et al., 2012 |
| Wobe-Mugos E | Mixture of proteolytic enzymes Associated with an increase in mucositis incidence and duration in one small study | Dorr & Herrmann, 2007 |

TABLE 5. Mucositis Interventions: Not Recommended for Practice

| Agent | Findings | Studies Reviewed |
|---------------------------------|--|---|
| Chlorhexidine (nonprophylactic) | Did not improve existing mucositis and is not recommended in guidelines or systematic reviews for adults or children | Nashwan, 2011; Niscola et al., 2009; Peterson et al., 2010; Potting et al., 2006; Shih et al., 2002; Worthington et al., 2011 |
| Sucralfate | Did not improve oral mucositis | Castagna et al., 2001; Dodd et al., 2003; Etiz et al., 2000; Nottage et al., 2003; Qutob et al., 2013; Saunders et al., 2013 |

been approved by the U.S. Food and Drug Administration for patients with hematologic malignancies who receive high doses of chemotherapy and radiation therapy followed by stem cell rescue. Palifermin requires a prescription, and, because of its expense, has not been universally adopted. As a result, further work is needed to identify those to treat with palifermin.

Nurses regularly involved in direct patient care have difficulty staying adequately abreast of the literature on a topic such as mucositis, particularly when their practice is not restricted to the management of one symptom. Therefore, ongoing reviews are at the core to advancing evidence-based practice. Nurses would benefit from ready availability of a simplified version of the tables in the current article to guide practice. With current advances in technology, this could be available electronically and updated regularly. Such a table would also facilitate knowledge regarding the current status of agents that have been identified as unlikely to be effective and/or not recommended for practice. At this time, the number of agents in the categories remains limited, which would facilitate easy review.

Knowledge of resources for accessing the available reports of evidence summaries and how to evaluate new publications will assist nurses in remaining up-to-date regarding changes in the literature. Participation in professional organizations such as ONS and the Multinational Association of Supportive Care in Cancer (MASCC) also provides nurses with support to improve patient outcomes. Initial review of the recommendations from these two organizations may trigger questions regarding inconsistencies. The important component to consider when comparing any other guidelines is to be aware of the criteria used when evaluating individual references and for classification of the levels of evidence once the review content is synthesized. Some of the difference is because ONS is focused on nursing and primarily addresses care in North America, whereas MASCC is multinational and more multidisciplinary in approach. That further explains the stronger focus on dental interventions in the MASCC guidelines as compared to ONS clinical teams, which do not incorporate dental services.

Nurses can contribute to the evidence guiding future practice by participating in research studies. When the resources and opportunities to participate are not available, nurses still can play a key role in improving patient outcomes through performance improvement activities at the local level or perhaps with other institutions. Participation will necessitate the use of valid and reliable assessment tools.

Assessment is the essential initial step for nurses to truly make a difference. Unfortunately, this process is inconsistent at best and often uses instruments that lack essential validity and reliability (see Table 6 in Harris et al., 2008). The more common assessment

instruments, such as the Common Terminology Criteria for Adverse Events, version 4.0 (U.S. Department of Health and Human Services, 2010), and the World Health Organization's (1979) scale, focus on grading mucositis and are used in clinical trials, whereas some instruments, such as the Oral Mucositis Assessment Scale (Sonis et al., 1999), focus on mucous membranes with quantifiable function and objective or subjective measures, and other instruments, such as the Oral Assessment Guide (Eilers, Berger, & Petersen, 1988), address overall changes in the oral cavity but do not grade the mucositis. Awareness of the divergent basis has implications for nursing. Although pain is a common component of the mucositis experience, retaining the pain assessment as a separate element is rational because the rating is dependent on adequacy of treatment, not just the severity of mucositis. Regardless of the mucositis assessment method chosen, the critical aspect involved is that all healthcare providers in an institution should be trained to rate the characteristics in a similar manner and cross-checked to ensure accuracy between assessors.

A baseline assessment is needed to focus on risk factors and the initial status of the oral cavity. Given that one of the identified risk factors for mucositis is cancer treatment, increased understanding is needed about the severity of the risk with a given treatment. Knowing the emetogenicity of cancer treatments, including combination protocols, guides treatment plans, but practice would also benefit from increased awareness of the mucotoxicity of therapies. That information could then enable nursing to establish electronic flags to accompany cancer treatment order sets. The flags could include the need to conduct assessments, which would be followed by evidence-based interventions. Such practice is dependent on adequate evidence that tends to be available, but that will need to be updated regularly.

As is commonly seen in research reports and reviews of evidence, research on mucositis remains limited. The bulk of the literature consists of small studies, nonrandomized designs, and a lack of valid and reliable instruments. Another concern is lack of clarity if the intent of the intervention was prevention or treatment of mucositis. Each concern needs to be addressed with a higher level of science in future work. Although not included in the results section of this review, the population treated and details of the intervention protocol are important to note. Readers are encouraged to refer to the original studies to determine the level of detail available for the studies reported in the current article.

Future Recommendations

The work reported has strengths, particularly in the volume reviewed and the number of nurses involved in the ONS PEP

Patient Education: Mouth Care During Cancer Treatment

The mouth, also called the oral cavity, is often the site of changes from cancer and cancer treatment. These changes can vary from minimal to severe and painful.

One of these changes is called “mucositis” (mu – ko – si – tis). The term *mucositis* means an inflammation of the mucous membranes. It can occur in the mouth and the rest of the gastrointestinal tract. This includes your esophagus, stomach, bowel, and rectum. You may see or feel changes. These changes can include the following.

- Deep or raspy voice: may be like when you have a sore throat or loss of your voice
- Pain when you swallow: may be mild to severe
- Dry or cracked lips: may include bleeding
- Coated and or shiny tongue: may blister or crack
- Altered taste in your mouth and as you eat
- Thick or rope-like saliva and/or loss of saliva
- Reddened tender mouth: may have no sores or open sores with bleeding
- Swollen gums or bleeding

You may have some but not all of these changes. Also, how intense each of the changes is may vary.

What You Can Do to Make a Difference

Care of your mouth is important during cancer treatment. It can help to prevent and treat problems.

Good mouth care includes:

1. Brush your teeth at least two times per day.
 - a. Brush all tooth surfaces for at least 90 seconds using a soft toothbrush.
 - b. Allow your toothbrush to dry before storing.
2. Continue to floss your teeth at least daily. Speak with your nurse if you have not been doing this.
3. Rinse your mouth at least four times per day.
 - a. Use a bland, alcohol-free rinse.
 - b. You may use a mixture of a little salt and baking soda in a cup of warm water for your rinse.

- c. Rinse your mouth more often (every two hours while awake) if you have sores or other problems.

4. Keep your lips moist using a lip moisturizer of your choice. Avoid petroleum-based products or products that cause your lips to burn or feel dry. Select a moisturizing lip balm available “over the counter” through your local pharmacy.
5. Avoid tobacco, alcohol, and irritating foods (hot, rough, acidic, or spicy).

If you develop problems:

- Tell your doctor or nurse.
- Continue to brush your teeth with a soft toothbrush if you can.
- Use a soft foam toothette to clean the entire inside of your mouth. Dip these in the salt and baking soda mixture.
- Take your pain medications as ordered by your doctor.

When to call your doctor or nurse:

- If you have symptoms of an infection such as fever, chills, or white patches in your mouth
- If you develop new or more severe mouth pain
- If you are not able to eat or drink
- Before you go to the dentist or have dental work done

A limited number of other treatments may be available, so check with your doctor or nurse. Always check with them before using any “natural” or other product you can purchase without a specific order.

Note. Full Oncology Nursing Society Putting Evidence Into Practice information for this topic and description of the categories of evidence are located at www.ons.org/practice-resources/pep/mucositis. Users should refer to this resource for full dosages, references, and other essential information about the evidence.

Implications for Practice

- ▶ Assess for oral mucositis with a valid and reliable instrument as an initial step for prevention and management.
- ▶ Develop evidence-based oral care protocols as the foundation for cancer-related mucositis care.
- ▶ Teach oral cavity self-management techniques for mucositis to patients and family members.

review for mucositis. However, improvement is needed. Evidence-based practice encourages nurses to evaluate their processes, which can also guide the PEP process. How can nurses build on past reviews and continue to refine the process used? How should nurses decide when to include miscellaneous agents individually to allow building on the information with future work? How do nurses decide when an intervention that was not found to have adequate evidence should move into an archive rather than remain on an evidence table with an outdated reference? Clinicians need to become critical consumers of attempts to promote the use of specific interventions or new products. Requiring a review of the evidence would serve clinicians and patients. As quality-improvement advocates, clinicians have a responsibility to identify areas of concern and question why established evidence is not being followed. In addition, researchers need to create well-designed studies with valid and reliable instruments, a clear purpose, intervention rigor, and an adequate sample. Finally, those results must be published and shared to pursue excellence as a profession.

Conclusion

Mucositis is a complex process involving the mucosal membranes of the oral cavity. Further knowledge regarding the process will continue to drive the identification of new potential treatments and the reevaluation of others. This update of the evidence for the prevention and management of mucositis provides essential information to guide nursing care of individuals experiencing this potentially life-threatening side effect. The guidelines are not intended to be static in nature, and they should not be blindly followed for every patient. Evidence-based practice must be seen as a process requiring ongoing diligence and review of the literature as well as the appropriateness for application with specific patients. Evidence-based interventions are critical for optimal prevention and management of mucositis. Similarly, the process used for PEP should continually be refined to allow for the provision of meaningful information to clinicians.

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