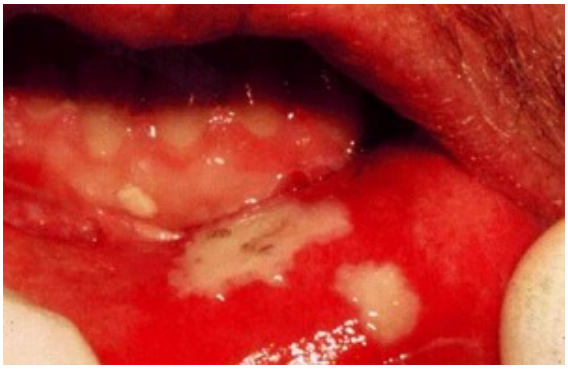
Mucositis: New therapies for an old complication?



Mucositis is commonly seen in high dose chemotherapy protocols for hematologic malignancies (ie conditioning or induction regimens for leukemia), or aggressive chemo-radiation for head and neck cancers. It is a term physicians use to describe a wide range of oral complications related to cancer treatment.This may include redness, pain, ulceration, swelling and surface lesions (pseudomembrane, hyperkeratosis, lichenoid lesions). The World Health Organization has proposed a grading scale for mucositis:

Grade 0= no change
Grade 1= soreness
Grade 2= erythema (redness), ulcers, can eat solids
Grade 3= ulcers, requires a liquid diet
Grade 4= severe ulcers prohibiting oral intake

Preventive strategies for mucositis include mouthwashes (Peridex, saline, sodium bicarbonate), ice (i.e. ice chips prior to infusion), and good oral hygiene.

There are various strategies to treat mucositis. Certain drugs are direct cytoprotectants. They work either by a barrier method on the mucosa, or by preventing inflammation. An age old treatment is sucralfate which is an aluminum salt which works by creating a protective barrier at the ulcer site. Another commonly used treatment often goes by the name of “Magic Mouthwash”. Magic Mouthwash is a rinse that patients are asked to use 4-6 times a day and is a component of various ingredients. The components often include a local anesthetic (e.g.,viscous lidocaine), an anti-inflammatory (e.g., hydrocortisone, or benadryl), a local antibiotic (e.g.,tetracycline or nystatin), and an antacid (e.g., Maalox). The goal is to reduce inflammation and provide a local anesthetic.

Another agent is called Gelclair. Gelclair works by adhering to the oral surface to create a protective barrier. It is also a rinse that is administered up to 3 x a day.

Another strategy is via vitamins and anti-oxidants. Vitamin E applied topically may speed the resolution of mucositis. Beta carotene may help in severe mucositis. Azelastine is a drug which suppresses reactive oxygen, and stabilizes cell membranes. In one small trial of 63 patients undergoing chemotherapy and radiation by Osaki and colleagues, they found that there was a

reduction in severe mucositis (grade 3 and 4).

There are other miscellaneous methods as well. For example, a relatively easy treatment is cryotherapy, which sounds fancy, but is bascially ice or popsicles before, during and after infusions. The mechanism of actions is likely via constriction of blood vessels to the mucosa.

Growth factors such as neupogen have had conflicting results with regards to control of mucositis. There is some thought that these growth factors may delay the onset of mucositis , but overall they had minimal effect on overall duration and severity.

A new strategy is via Kepivance (palifermin), which is a recombinant human keratinocyte growth factor. A double blind study conducted in 212 patients with hematologic cancers found that palifermin administered for three days before high dose therapy (radiation + chemotherapy) reduced the rate of grade 4 stomatitis, soreness and pain, and narcotic use, and TPN.

The mainstay of therapy, however, for difficult mucositis pain, is opioid therapy. Morphine mouthwash has been shown in studies to be more effective for pain reduction than a standard “magic mouthwash” (example here). For patients who are hospitalized delivery via IV pumps are often the most effective way to get appropriate pain medication. In the outpatient setting, using a multidisciplinary team well versed in opioid management may be the best way to get adequate control of mucositis pain.

The treatment of mucositis is still evolving. There are age old and simple therapies with good evidence such as cyrotherapy (ice), as well as new and exciting agents (Kepivance). Each individual, however, is different, and there are many factors (both clinical and treatment related) that need to be assessed prior to recommending therapies. In most cases evaluation and treatment of mucositis requires a detailed assessment from someone directly involved who can actually examine a patient.

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