Background

Oral mucositis, is a common, debilitating complication of cancer chemotherapy and head and neck radiotherapy. It results from systemic effects of cytotoxic chemotherapy and from the local effects of the oral mucosa. Oral mucositis presents as inflammation of the mucosa of the mouth that ranges from redness to severe ulceration. Symptoms vary from pain and discomfort to inability to tolerate food or fluids. Oral mucositis may be so severe as to delay treatment thereby compromising therapy. It is therefore important to prevent and manage this adverse effect.

This document aims to advise prescribers in the prescribing of mouthcare for patients to prevent and treat mucositis and to manage symptoms associated with this condition.

Table 1. Scales for assessment of oral mucositis.

<table>
<thead>
<tr>
<th>NCI Scale</th>
<th>WHO Grading Scale</th>
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</thead>
<tbody>
<tr>
<td>Grade 0</td>
<td>None</td>
</tr>
<tr>
<td>Grade 1</td>
<td>Soreness +/- erythema, no ulceration</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Erythema, ulcers. Patients can swallow solid diet</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Ulcers, extensive erythema. Patients cannot swallow solid diet</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Oral mucositis to the extent that alimentation is not possible</td>
</tr>
</tbody>
</table>

Prophylaxis of Mucositis

There have been a large number of studies performed in the prevention of mucositis in patients receiving cancer treatment. The patient should ensure they maintain good oral hygiene. They should be advised to clean their teeth twice daily using fluoride toothpaste and a soft bristle tooth brush. Worthington et al [1] performed a systematic review of prevention of mucositis in patients receiving chemotherapy and radiotherapy. Sutherland et al [2] performed a similar review in patients receiving radiotherapy to the head and neck region only. There was no clear evidence that prophylaxis mouthwashes prevented oral mucositis. The alcohol content in chlorhexidine mouthwash may cause pain and discomfort to patients that are receiving radiotherapy to the head and neck region and to those with mucositis.

The reviews found that benzydamine 0.15% (Difflam®) mouthwash may potentially be of benefit in the prevention of oral mucositis. Benzydamine 0.15% (Difflam®) is not recommended for patients having concurrent radiotherapy to the head and neck as the alcohol in the agent may cause the patient discomfort.
Caphosol® is a supersaturated calcium phosphate rinse indicated as an adjunct to good oral care in the prevention of mucositis. The systematic review performed by Worthington et al.[1] found that Caphosol® showed some benefit in preventing or reducing the severity of mucositis associated with cancer treatment.

The use of Caphosol® in the prevention of mucositis is restricted to the following high risk patient groups:

1. Head and neck cancer patients undergoing chemotherapy and radiotherapy who have suffered grade 3 and above mucositis on previous cycles
2. Sarcoma patients undergoing chemotherapy who have suffered grade 2 and above mucositis on previous cycles and/or had their treatment delayed due to mucositis
3. Haematology patients receiving high dose melphalan or any full intensity allogeneic stem cell transplant

The dose of Caphosol® is 30mls QDS (15mls of phosphate solution mixed with 15mls of calcium solution) started at the onset of treatment.

**Summary**
- All patients receiving chemotherapy and radiotherapy should be given advice on good oral hygiene.
- It is **not** advised to use routine prophylaxis mouthwashes such as chlorhexidine 0.2% (Corsodyl®) in chemotherapy and radiotherapy patients.
- Patients receiving intensive chemotherapy regimens may be prescribed Difflam® mouthwash PRN to take home to provide pain relief if they do develop mucositis.
- The use of Caphosol® is restricted to high risk patients as specified above.

**Prophylaxis of Infections**

Many studies have addressed the prevention and treatment of candidiasis in cancer patients. The UKCCSG[3] have reviewed the evidence for using antifungal prophylaxis. It was found that partially absorbed or fully absorbed antifungals were effective at preventing fungal infections.

Nystatin and Amphotericin lozenges are not absorbed through the GI tract and were found to be ineffective at preventing fungal infections.

High risk patients as described in the North London Antifungal Policy may be given antifungal prophylaxis.

High risk patients include
- Patients receiving high dose fludarabine or cytarabine regimens.
- Adult patients receiving chemotherapy for ALL
- AML patients receiving chemotherapy
- Patients receiving an allogenic transplant

**Summary**
- It is **not** advised that routine antifungal prophylaxis is given to chemotherapy and radiotherapy patients.
- The North London Antifungal Policy (revised February 07) describes groups of patients at high risk of fungal infections these patients should be given systemic antifungals as advised in the policy, either itraconazole liquid (200mg bd) or Ambisome® (1mg/kg), if the patient is receiving vincristine.

**Mucositis Treatment**

Several interventions have been thought to be effective at enhancing the healing of mucositis. To date nothing has demonstrated to be effective in randomised controlled studies. Clarkson et al.[4] performed a systematic review of interventions for treating oral mucositis and concluded there was no reliable evidence that any intervention improved or eradicated mucositis. Sucralfate is thought to enhance the healing of ulcers although this has yet to be proven. A step wise approach with systemic pain relief should be used. NSAID’s should be avoided in many cancer patients as their treatment may consist of nephrotoxic agents. Haematology patients should not be prescribed NSAIDs due to likelihood of low platelets at some stage during treatment. Local mouthwashes may also help in the treatment of pain.
Table 2. Local treatments for oral mucositis pain relief.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Directions</th>
<th>Uses and special instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; line - Difflam® Mouthwash</td>
<td>10mls QDS. Use as a mouthwash. Do not swallow.</td>
<td>Local anaesthetic. May reduce pain. Not recommended for patients having concurrent radiotherapy to the head and neck.</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; Line - Difflam® Spray</td>
<td>One to two sprays every 1.5 - 3 hours. However usually used QDS.</td>
<td>Local anaesthetic. May be useful if patient has soreness at the back of the mouth. Not recommended for patients having concurrent radiotherapy to the head and neck.</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; Line - Lidocaine 2% Mouthwash</td>
<td>Lidocaine 4% 5mls mixed with 5mls water and used as a mouthwash QDS.</td>
<td>Local anaesthetic. Can make eating less painful if used before mealtimes.</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; Line - Aspirin mouthwash</td>
<td>300mg tablet dissolved in water. Used as a mouthwash QDS. Do not swallow.</td>
<td>Local pain relief of oral mucositis. Not to be used in haematology patients and with caution in patients receiving nephrotoxic agents.</td>
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</tbody>
</table>

Table 3. Systemic treatments for oral mucositis pain relief.

<table>
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</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; Line - Paracetamol</td>
<td>1g QDS</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; line pain relief (liquid/soluble available if patient has PEG tube)</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; Line - Codeine</td>
<td>8mg QDS 30mg QDS</td>
<td>Addition to paracetamol (15mg/5ml liquid available) Co-codamol 30/500 is non-formulary. Co-codamol 8/500 available as dispersible tablet.</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; Line - Tramadol</td>
<td>50-100mg QDS</td>
<td>In addition to paracetamol. Available as dispersible tablet.</td>
</tr>
<tr>
<td>4&lt;sup&gt;th&lt;/sup&gt; Line - Morphine Sulphate 10mg/5ml solution</td>
<td>Start at 5-10mg when required to determine daily dose required. Either convert to a long acting opiate preparation or use regularly if required.</td>
<td>Use with Paracetamol. Convert Tramadol/codeine to morphine sulphate immediate release to reduce pill burden. Oramorph® contains alcohol which may cause discomfort on use</td>
</tr>
</tbody>
</table>

- Sucralfate mouthwash 1g/5ml (5mls QDS) may be used for the treatment of mucositis. The patient should rinse around the mouth then swallow.
- A combination of pain control may be used –local and systemic see tables 1 and 2.
- Diclofenac is usually NOT recommended.

**Xerostomia**

The UKCCSG looked at 2 large systematic reviews in patients with xerostomia or salivary gland damage. It was found that there was strong evidence for using pilocarpine (5mg tds) for treatment of symptomatic xerostomia caused by radiation in adult patients.

**Summary**

- Regular water sips should be used.
- A trial of Pilocarpine 5mg tds with or immediately after meals may be prescribed for patients with a dry mouth, as a consequence of radiotherapy to the head and neck region. Some patients may not tolerate the drug and in this case the drug should be discontinued.
- Sodium chloride 0.9% mouthwash may cause further discomfort and should be avoided.
- Artificial saliva (glandosane®) may be sprayed onto the oral/pharyngeal mucosa as required.

**Excessive saliva and thick mucous**

Very little information was found in this area. Drugs that dry secretions include hyoscine hydrobromide and glycopyrrolate. The administration routes may not be desirable as they are administered parenterally. Hyoscine patches are another alternative.

Some patients experience thick mucous and sodium bicarbonate may be used in these patients.
Summary

- Hyoscine patches 1mg behind the ear can be used every 72 hours.
- Sodium bicarbonate powder can be used for thick mucous. One flat teaspoon should be dissolved in a little water (5-10mls) and rinsed around the mouth. This **should not be** swallowed.

References


