

Wessex Paediatric Oncology Supportive Care Guidelines: Management of Mucositis

Scope

This guideline applies to all paediatric oncology patients in the region. It does not apply to neonates on neonatal units.

Purpose

Children receiving treatment at the Southampton Paediatric Oncology Principal Treatment Centre (PTC) have open access to the designated Paediatric Oncology Ward at either the PTC or their Paediatric Oncology Shared Care Unit (POSCU) Hospital. Their parents/carers will be in possession of contact details for these wards and have been instructed to contact them for any medical problems that arise while they are receiving treatment. These Guidelines are intended for the use of the medical teams at the PTC or POSCU. If one of the Paediatric Oncology patients presents to a medical service outside of the PTC or POSCU, please contact the medical teams at the PTC or POSCU for advice.

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Contents

1.1 Introduction	3
1.2 Prevention of mucositis and oral care at the time of diagnosis	3
1.3 Oral Hygiene During and Between Treatment Courses	4
Table 1. Oral assessment Guide	4
1.4 Grade 1-2 mucositis.....	5
1.5 Grade 2 mucositis.....	5
1.6 Grade 3 mucositis and above	5
1.7.4 Salivary gland dysfunction	6
Table 2. Medications useful for mucositis prevention and treatment.	7
1.7.5 Other Agents used in mouth care – limited evidence to support their use.	8
1.8 Neutropenic enterocolitis.....	8
References & Further Reading	8

1.1 Introduction

Mucositis describes inflammation of the oral mucosa resulting from chemotherapeutic drugs or local radiotherapy causing direct injury to the mucosa. Complications frequently develop during and following treatment. The oral mucosa consists of rapidly dividing cells that are susceptible to the damaging effects of cytotoxic therapy. It initially starts as erythema, progressing through to frank ulceration and necrosis as the severity of mucositis increases. It is commonly a dose limiting toxicity for cytotoxic agents and is a particular problem with **high dose methotrexate, high dose cytarabine, melphalan, doxorubicin, actinomycin and amsacrine**. Treatment induced leucopenia will contribute to the development of mucositis and delay healing. Mucositis may increase the risk of systemic bacterial, fungal or viral infection.

1.1.2 Factors that increase the risk of mucositis include

- Poor oral hygiene and pre existing mouth damage
- Mucositis with previous cycle of treatment
- Previous gastritis
- Impaired immune status

1.1.3 Common Terminology Criteria for Adverse Events (CTCAE) version 4, grading of oral mucositis and WHO scale for oral mucositis

Grade 0	Normal mucosa, no symptoms
Grade 1	Asymptomatic/mild symptoms: erythema of the mucosa, normal diet: Intervention not required
Grade 2	Moderate pain, not interfering with oral intake: patchy ulcerations Modified diet not indicated.
Grade 3	Severe pain, interfering with oral intake: confluent ulcerations, bleeding with minor trauma
Grade 4	Life threatening consequences, urgent intervention indicated. Tissue necrosis, significant spontaneous bleeding
Grade 5	Death

1.2 Prevention of mucositis and oral care at the time of diagnosis

All patients should be reviewed by their dentist as early as possible in their treatment to identify any potential problems, and should be regularly reviewed (every 3-4 months) throughout their treatment. There should be good communication between the cancer team and dental provider.

All patients should be advised on the need for good oral hygiene:

- Brush teeth at least twice a day, aim for 4 times with a fluoride toothpaste (containing 1000 ppm fluoride \pm 10%)
- The toothbrush should be for the sole use of the child and changed every month or following an episode of oral infection. If the mouth is sore use a soft toothbrush with a small head.
- Additional aids such as flossing and fluoride supplements should only be used with advice from dental team.
- For babies without teeth parents should clean the mouth with oral sponges moistened with water.
- When it is not possible to brush teeth, the mouth should be cleaned with oral sponges as a temporary measure – these should be moistened with water or diluted chlorhexidine.
- Sugary drinks should be restricted to mealtimes where possible.

- Written advice for patients and parents is in Parent Held Oncology Record.
- Parents should check young children's mouths regularly – how frequently depends on stage of treatment, but should be increased if any problems occur.

1.3 Oral Hygiene During and Between Treatment Courses

During inpatient treatment (or outpatient if any problems) use Oral Assessment Guide (OAG) score. **OAG score > 8 means increased risk of oral complications.** An appropriate pain assessment tool should also be used with OAG > 8 to judge effectiveness of interventions.

Table 1. Oral assessment Guide

Category	Method	1	2	3
Teeth	Observe appearance	Normal, clean, no debris	Plaque or debris in localised area	Plaque or debris generalised along gum line
Voice	Talk with patient	Normal	Deeper, raspy	Painful, difficult
Swallow	Ask patient to swallow	Normal	Difficulty in swallowing	Unable to swallow, pooling, dribbling of secretions
Lips	Observe appearance	Smooth, pink, moist	Dry/cracked	Ulcerated, bleeding
Tongue	Observe appearance	Pink, moist, papillae visible	Coated/loss of papillae, Candida	Ulcerated, sloughing, cracked
Saliva	Observe appearance	Watery	Excess amounts of drooling	Thick, ropy or absent
Mucous membranes	Observe appearance	Pink, moist	Reddened/coated	Ulcerated, sloughing, ± bleeding
Gingiva	Observe appearance	Pink, moist, stippled	Oedematous/ smooth	Spontaneous bleeding

Oral assessment guide – adapted from Eilers

1.4 Grade 1-2 mucositis

- In older children, consider regular normal saline or water mouthwashes 5-10ml QDS. Encourage vigorous rinsing using a 'ballooning and sucking' motion of the cheeks for at least 30 seconds; this action removes loose debris from the teeth.
- Younger children may not tolerate the taste of saline mouthwash, consider using chlorhexidine mouthwash 5-10ml QDS. In paediatric chemotherapy patients there is no reliable evidence to show that chlorhexidine is superior to saline or water mouthwashes.
- Teething gel (if not contraindicated) can be applied to mouth ulcers.
- Regular analgesia; opioid analgesia with morphine NCA/PCA may be necessary.
- **Benzydamine** (Difflam®) can be considered to improve local analgesia within the oral cavity and pharynx; this can be particularly beneficial if given before eating, however there is little evidence to support its use. Please see table for dosing.
- Closely monitor nutritional status and hydration and consider hospital admission for symptom management if mucositis worsening or patient not able to maintain oral intake.

1.5 Grade 2 mucositis

In addition to the measures Caphosol may be considered:

- **Caphosol** (supersaturated calcium phosphate mouth rinse) has been useful in prevention of mucositis in adults at high risk of developing mucositis, but not yet extensively tested in children. Used 4 x daily, starting day before chemotherapy, can be increased to 10 x daily if develop mucositis. Rinse in mouth for 1 minute. Defer eating or drinking until 15 minutes after.
- **Folinic acid mouthwash** could be considered for treatment of mucositis following high dose methotrexate therapy.

1.6 Grade 3 mucositis and above

- The patient should be admitted to hospital and commence IV fluids.
- Assess for oral infection, repeat mouth swabs for microscopy, sensitivity and culture and virology.
- Discuss with senior regarding appropriateness of enteral or parenteral feeding and patient to be reviewed by dietician.
- Consider reducing dose of chemotherapy/radiotherapy for next cycle.
- Continue mouthwashes and analgesia.

1.7 Management of oral infections

1.7.1 Bacterial Infections

For anaerobic bacterial infection, treat with oral or IV metronidazole depending upon severity. See table for dosing recommendations

1.7.2 Fungal infections

Fungal infection i.e. Oral candidiasis may lead to systemic infection. Mucositis, xerostomia and poor oral hygiene may increase a patient's risk of developing oral candidiasis. Oral candida should be treated with oral fluconazole , dosing recommendations are found in table. Consider prophylaxis at times of neutropenia for patients with recurrent oral candidiasis.

1.7.3 Viral infection- Herpes simplex infection.

Asymptomatic carriage of the herpes simplex virus (HSV) is extremely common. Immunosuppression is one of many factors which can activate the virus, leading to pain and blistering on the lips and in the mouth.

Oral Herpes Simplex

Lesions should be treated with oral aciclovir (as long as can tolerate and absorb) for 5 days: IV aciclovir can be considered for those who are unable to swallow or tolerate oral.

Primary prophylaxis is only given following myeloablative treatment. Consider prophylaxis during times of cytopenia if recurrent oral herpes. Dosing recommendations are in table

Monitor renal function and base the dose on ideal body weight for height if the child is obese.

1.7.4 Salivary gland dysfunction

This can be caused by both chemotherapy and radiotherapy. Cytotoxic drugs can alter the flow and composition of saliva causing xerostomia (a sensation of dryness in the mouth). Both salivary gland damage and xerostomia impact upon the patient's quality of life, causing oral discomfort, taste disturbances, difficulty in chewing and swallowing and speech problems. In addition they lead to an increased risk of oral infections. Long term effects of salivary gland damage include dental caries.

Consider using frequent sips of water, saliva stimulants, artificial saliva, chewing sugar free gum.

Table 2. Medications useful for mucositis prevention and treatment.

Drug	Route	Age	Dose
Benzydamine 0.15% mouthwash	Topical	13-17 years	15ml every 1.5-3hrs as required
Benzydamine 0.15% oromucosal spray	Topical	1 month – 5 years	1 spray/4kg body weight (max. 4 sprays) every 1.5-3hrs
		6-11yrs	4 sprays every 1.5-3 hrs
		12-17yrs	4-8 sprays every 1.5-3 hrs
Antibiotics			
Metronidazole	PO	1 month	7.5mg/kg every 12 hrs
		2 months- 11 yrs	7.5mg/kg (max. 400mg) TDS
		12-17 yrs	400mg TDS
	IV	1 month	15mg/kg as a single loading dose followed after 8hrs by 7.5mg/kg TDS
		2 months-17yrs	7.5mg/kg (max. 500mg) TDS
Antifungal			
Fluconazole treatment	PO	1 month – 11yrs	3-6mg/kg on day 1, then 3mg/kg/day (max. 100 mg) for 7-14 days, (14-30 days if oesophagitis)
		12-17 years	50mg daily for 7-14 days, (14-30 days if oesophagitis). Increase dose to 100mg daily only for unusually difficult infections.
Fluconazole prophylaxis (for oral candidiasis)	PO	1 month-17yrs	3mg/kg/day (max. 100mg)
Antiviral			
Aciclovir treatment doses	PO	1 – 23 months	200mg x 5 daily
		2yr -17yrs	400 mg x 5 daily
	IV	1-3 months	20mg/kg TDS
		3months -11 yrs	500mg/m ² TDS
		12-17 yrs	10mg/kg TDS
Aciclovir prophylaxis	PO	1 – 23months	100-200 mg QDS
		2 -17 yrs	200 - 400 mg QDS
Miscellaneous			
Sucralfate	Oral	1 month – 1 yr	250mg 4-6 times daily.
		2-11 yrs	500mg 4-6 times daily
		12- 14 yrs	1g 4-6 times daily
		15-17 yrs	2g twice daily or 1g 4 times daily

1.7.5 Other Agents used in mouth care – limited evidence to support their use.

Sucralfate may relieve pain short term by coating mucosa. Not recommended for routine use but some patients find sucralfate helpful. Suspension (1g in 5 ml) is more palatable than tablets (dispersible). If swallowed, follow dosing recommendations in table, if swished and spat out, sucralfate can be used when required.

Use with caution in renal failure.

Can reduce bioavailability of other drugs – check interaction and drug timings.

Gelclair

May be useful to reduce oral pain post chemotherapy. Some Pharmacy departments are experiencing difficulty obtaining Gelclair, as it is not approved on the formulary. It may be possible to obtain Gelclair locally or from an outside pharmacy.

1.8 Neutropenic enterocolitis

Neutropenic enterocolitis also known as typhilitis is a life threatening complication of chemotherapy. It is characterised by fever and abdominal pain and other presenting symptoms can include abdominal distension, nausea and vomiting and diarrhoea. Typhilitis often occurs 10-14 days after initiation of cytotoxic chemotherapy. The pathogenesis of typhilitis is poorly understood, but is thought to be caused by mucosal injury by cytotoxic drugs, neutropenia and impaired host defence to intestinal organisms. Diagnosis can be made with ultrasound, showing bowel wall thickening, a fluid filled dilated cecum, a right lower quadrant inflammatory mass and pericecal soft tissues.

Conservative management consists of bowel rest, TPN and broad-spectrum antibiotics therapy. *C. Difficile* antibiotic cover should be considered.

References & Further Reading

- UKCCSG – PONF Mouth Care Group; “Mouth Care for Children and Young People with Cancer: Evidence-based Guidelines” (Version 1.0 February 2006).
- Lalla RV et al. Management of oral mucositis in Patients with Cancer. *Dent Clin North Am* (2008) 52(1), 61-viii
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