Mucositis management in children and young people receiving chemotherapy

NHS University Hospitals of Leicester NHS Trust

Trust Ref: E2/2021

Introduction and Who this Standard Operating Procedure applies to

This CYPICS network guideline has been developed by clinicians from Nottingham Children's Oncology Unit with consultation across the network including from the Leicester Royal Infirmary and has been ratified by the Leicester Children's Hospital guideline process.

This guideline applies to all children and young people under the age of 19 years who are receiving chemotherapy for malignant disease

UHL local Paediatric Oncology specialists are:

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Mucositis

	Title of Guideline (must include the word "Guideline" (not protocol, policy, procedure etc)	**Guideline for the management of mucositis in children and young people receiving chemotherapy**
	Contact Name and Job Title (author)	Colin Ward, Lead Pharmacist, EM CYPICS Dani Jones, CYPICS Clinical Educator
	Directorate & Speciality	Division: Family Health, Speciality: Paediatric Haematology and Oncology
	Date of submission	July 2023
	Date on which guideline must be reviewed	March 2023July 2026
	Explicit definition of patient group to which it applies	This guideline applies to all children and young people under the age of 19 years who are receiving chemotherapy for malignant disease.
	Abstract	This guideline describes the principles and management of Mucositis in children and young adults receiving chemotherapy.

	Key Words	Children: Young People: chemotherapy: mucositis
	Statement of the evidence base of the guideline – has the guideline been peer reviewed by colleagues?	
1a	meta analysis of randomised controlled trials	
2a	at least one well-designed controlled study without randomisation	See references
2b	at least one other type of well-designed quasi-experimental study	
3	well –designed non-experimental descriptive studies (ie comparative / correlation and case studies)	
4	expert committee reports or opinions and / or clinical experiences of respected authorities	
5	recommended best practise based on the clinical experience of the guideline developer	
	Consultation Process	All paediatric haematology and oncology consultants, lead nurse, pharmacists, clinical educator, ward managers
	Target audience	All clinical staff working in paediatric haematology and oncology to include doctors, nurses and pharmacists.
	This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date.	

Document Control

Document Amendment Record

Issue Status	Version	Issue Date	Lead Author	Description
Final/Draft	V1		1995	Original document
	V2		Bev Harwood	
	V3	Aug 2013	Adam Henderson Clare Fosbrook	
	V4	Aug 2016	Anneka Sareen	Updated NCI CTCAE grading Addition of Episil
	V5	March 2020	Ghazala Javid Dani Jones	Review of references Inclusion of CCLG guideline Treatment guide amended to sit in line with CTCAE grading Inclusion of monitoring observations during admission to hospital and de-escalation plans if relevant

				Review of drug doses Updated NCI Common Terminology Criteria for Adverse Events (CTCAE) Version 5 2017 Inclusion of Daily mouth assessment.
	V6	July 2023	Colin Ward, Dani Jones	1. Minor correction of spellings 2. Update of references 3. Removal of reference to folinic acid mouthwash to treat methotrexate induced mucositis, lack of evidence to support intervention
	V7	September 2023	Colin Ward, Dani Jones	1. Rewording of swabs for grade 4 mucositis

General Notes:

This guideline is part of the CYPICS* documentation.

*Children's and Young Peoples Integrated Cancer Service

Statement of Compliance with Child Health Guidelines SOP

This guideline refers to activities of only one specific team and consultation has taken place with relevant members of that team. Therefore this version has not been circulated for wider review.

Dr Jennifer Turnbull& Dr Emma Ross Clinical Leads CYPICS
July 2023

Introduction

Mucositis refers to mucosal damage secondary to cancer therapy occurring in the oral cavity; pharyngeal, laryngeal, and oesophageal regions; and other areas of the gastrointestinal tract. Oral mucositis presents as erythema and/or ulceration of the oral mucosa. In addition, the pharyngeal, laryngeal, and oesophageal mucosa are also at risk for mucositis. It is typically very painful, requiring opioid analgesics, and impairs nutritional intake and quality of life.[i]

Oral mucositis secondary to cancer therapy is an acute inflammation of the oral mucosa in response to systemic oncology therapy and/or radiation to fields involving the oral cavity. The clinical presentation ranges from a general erythematous oral mucosa to erosive lesions and overt ulceration. Lesions are often very painful, may compromise nutrition and oral hygiene, and can increase the risk of local and systemic infection. Furthermore, severe oral mucositis may necessitate an undesirable dose-reduction and/or a break in cancer therapy. Therefore, mucositis is a highly significant complication of cancer therapy, with a potential impact on patient prognosis.

Depending on its severity, severe oral mucositis can become a disabling condition, as it hinders nutrition, requires the administration of powerful analgesics, increases the length of hospital stay and treatment costs, and above all, impairs the quality of life of patients. The prevalence of chemotherapy induced oral mucositis has been shown to range from 16.7-91.5% of patients (mean incidence 53.6%), depending upon treatment type, while severe oral mucositis accounted for the 15.8% (0.0–35.2%) among selected studies.[ii]

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

The National Cancer Institute Common Toxicity Criteria of Adverse Events (NCI CTCAE 2017) grades mucositis according to its severity based on clinical examination findings and functional/symptom assessment (see below).

NCI Common Terminology Criteria for Adverse Events (CTCAE) Version 5[iii]

Grade	Description
Grade 0 (none)	None
Grade 1 (mild)	Painless ulcers, erythema, or mild soreness in the absence of lesions
Grade 2 (moderate)	Painful erythema, oedema, or ulcers but eating or swallowing possible
Grade 3 (severe)	Painful erythema, oedema, or ulcers requiring intravenous hydration
Grade 4 (life-threatening)	Severe ulceration or requiring parenteral or enteral nutritional support or prophylactic intubation
Grade 5 (death)	Death related to toxicity

Prevention of mucositis

Patients can be directed to the Macmillan Cancer website (www.macmillan.org.uk) or Children's Cancer and Leukaemia Group (CCLG) (www.cclg.org.uk) where there is advice about 'dry mouth' and 'sore mouth'. A visit to the dentist or dental hygienist before chemotherapy starts is advised to ensure that any oral hygiene issues have been addressed. By treating dental disease early, the risk of oral infections during cancer treatment may be reduced. Patients are encouraged to visit the dentist regularly throughout treatment.

Prevention is based on good oral hygiene, use of mouthwashes and simple analgesia. Ideally the aim is to reduce the risk of severe mucositis developing during chemotherapy. The following advice has been taken from both the Macmillan and CCLG websites (accessed June 2023).[iv,v]

- All patients should be advised on the need for good oral hygiene
- Patients should brush their teeth regularly using a soft toothbrush and fluoride toothpaste after each meal and at bedtime. Toothbrushes should be replaced at least every 3 months to minimise infection risk.
- For children up to the age of 6 years, parents / carers should be instructed on how to brush their child's teeth.
- For babies without teeth and children where it is not possible to brush teeth, parents / carers should be instructed on how to clean the mouth with sterile gauze (pick adequate size) moistened with water
- If brushing of the teeth becomes too painful patients should use fluoride toothpaste or gel applied to the teeth with a finger to maintain good oral hygiene.
- Emphasis should be made on the need to restrict sugary food and drink to meal times.
- Additional aids, such as flossing and fluoride supplements should only be prescribed according to risk assessment by a member of the dental team.

Assessment of mouth

The patients mouth should be assessed on admission and at least daily thereafter until symptoms start to reduce and de-escalation of treatment is in place.

Mouth Care Assessment Tool

Category	Method of Assessment	1	2	3
Swallow	Ask the child to swallow or observe the swallowing process. Ask the patient if there are any notable changes	Normal Without difficulty	Difficulty swallowing	Unable to swallow at all
Lips and corner of mouth	Observe the appearance of tissue	Normal, Smooth, pink and moist	Dry cracked and swollen	Ulcerated and bleeding
Tongue	Observe the appearance of the tongue using a pen torch to illuminate the oral cavity	Firm without fissures (cracking or splitting) prominent papilla, pink	Coated or loss of papillae with a shiny appearance with or	Ulcerated, sloughing or cracked

		and moist	without redness and/or oral candida	
Saliva	Observe consistency and quality of saliva	Normal Thin and watery		
Mucous membrane	Observe the appearance of tissue using a pen torch to illuminate the oral cavity	Normal Pink and moist	Excess amount of saliva, drooling	Thick ropey or absent
Gingiva (Gums)	Observe the appearance of tissue using a pen torch to illuminate the oral cavity	Normal Pink or coral with stipples (dotted) surface. Gum margins tight and well defined, no swelling	Oedematous with or without redness, smooth	Spontaneous bleeding
Teeth (if no teeth score 1)	Observe the appearance of tissue using a pen torch to illuminate the oral cavity	Normal Clean with no debris	Plaque or debris in localised areas	Plaque or debris generalised along gum line
Voice	Talk and listen to the child. Ask the parent if there are any notable changes	Normal tone and quality when talking or crying	Deeper or raspy	Difficult to talk, cry or not talking at all

Gibson, F. and Soames. (2008) *Mouth care: Cancer in children and young people*

Scoring following assessment
Total score of 8 is equal to Grade 1-2 of CTCAE treatment
Total score 9-16 is equal to Grade 2 of CTCAE treatment
Total score of 16+ is equal to Grade 3 of CTCAE treatment

Treatment of mucositis[vi]

Check if there is any evidence of infection – if infection is present see section below on oral infection.

Assess severity of mucositis and treat accordingly.

Grade 0-1 mucositis
See table above, for mild symptoms intervention not indicated

Grade 2 mucositis

- Mouth assessment daily as per assessment tool

- In older children, consider regular normal saline or water mouthwashes 5-10ml QDS. It is important to 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.
- In younger children who do not tolerate the taste of the saline mouthwash, consider using chlorhexidine mouthwash 5-10ml QDS. In paediatric chemotherapy patients there is no reliable evidence to show that chlorhexidine mouthwash is superior to saline or water mouthwashes.
- Apply teething gel PRN to mouth ulcers, if not contra-indicated
- Regular opioid analgesia may be necessary.
- Consider adding benzydamine 0.15% mouthwash dose as per BNFc every 1.5-3 hours before meals to improve local analgesia within the oral cavity and pharynx to aid eating. For those unable to use the mouthwash, benzydamine spray dose as per BNFc every 1.5 to 3 hourly can also be used.
- Closely monitor nutritional status and hydration and consider hospital admission for symptom management if mucositis worsening or patient not able to maintain oral intake
- Review the need for de-escalation once symptoms start to reduce

Grade 3 mucositis

- Mouth assessment daily as per assessment tool
- Gelclair: 1 sachet up to TDS from the onset of symptoms until resolution. Gelclair forms a bio protective barrier that adheres to the oropharyngeal mucosa and covers exposed nerve endings and reduces pain. Take 30-60 minutes before eating. Dissolve 1 sachet in 40ml water, Use the mouth wash straight away and gargle for 1 minute or longer. Until the tongue and the inside of the mouth is well coated. Once gargled then spit out. The gel can be applied undiluted directly to ulcers.
- Caphosol effervescent tablets: Drop one tablet in 50ml of water. Allow the tablet to dissolve and settle. Rinse with half the solution for 1 min. Then repeat with the left over solution for a further minute. This tablet can be prescribed four to ten times daily
- Episil oral liquid: 1 – 3 pumps up to three times daily on to the affected areas of the mucosa from the onset of symptoms until resolution. Episil adheres to the oral mucosa and forms a protective film that acts as a mechanical barrier to provide pain relief. This can be used when needed
- Regular opioid analgesia may be necessary, morphine NCA / PCA may need to be considered
- Review oral intake and consider referral to dietician for nutritional management
- Review the need for de-escalation once symptoms start to reduce

Grade 4 mucositis

- Mouth assessment daily as per assessment tool. Monitor patients observations for signs of infection
- Discuss whether to stop chemotherapy and/or radiotherapy with a registrar or consultant
- Commence intravenous fluids
- Assess for oral infection as the patient is at high risk
- Take mouth swabs for microscopy, sensitivity and culture and virology, if cultures positive see section below on oral infection
- Discuss with a senior regarding appropriateness of enteral or parenteral feeding and patient to be reviewed by dietician
- Consider reducing dose of chemotherapy/radiotherapy for next cycle

- Regular analgesia; opioid analgesia with morphine NCA / PCA may be necessary
- Review the need for de-escalation once symptoms start to reduce

Treatment of confirmed oral infection

- Continue mouthwashes, analgesia and observations as above
- Metronidazole 7.5mg/kg TDS, orally or Intravenous for anaerobic bacterial infections for 5 days then review

Fungal infection - Candidiasis:

- There is no evidence to support the use of topical antifungal agents such as nystatin suspension for the treatment of oral candidiasis
- Use systemic therapy: fluconazole 3mg/kg daily orally for 5 days then review following discussion with consultant. **Care when azoles are prescribed especially if vincristine, vinblastine or vinorelbine are due**. Stop azoles 48 hours before, on the day and 48 hours after vinca alkaloids. As per patient protocol, refer to protocol
- Seek microbiology advice if antifungals not working
- Consider prophylactic antifungals if underlying clinical concerns (risk of candidiasis) discuss with microbiologist and consultant
- If oral candidiasis episodes are severe or recurrent then prophylactic antifungal (fluconazole 3mg/kg daily orally) may be considered for the next chemotherapy cycles. Please discuss with the consultant
- For resistant oral candidiasis seek advice from microbiology

Viral Infection - Herpes simplex infection:

- Mild and non-progressing lesions on the lip should be treated with topical aciclovir, applied five times daily
- Progressing and severe lesions on the lip should be treated with oral aciclovir
- Aciclovir dosing:
  PO: (for 5 days (longer if new lesions appear during treatment or if healing incomplete).

1 month-23 months	200mg 5 times daily
2-17 years	400mg 5 times daily

  IV: if unable to swallow/severe

1-3 months	20mg/kg every 8 hours
3 months-11 years	500mg/m^2 every 8 hours
12-17 years	10mg/kg every 8 hours

- Monitor renal function and base the dose on ideal body weight for height if the child is obese.
- Consider prophylactic antivirals in repeated herpes infection

UHL Education and Training

None

References

[vi] Lalla, R.V., Bowen, J., Barasch, A., Elting, L., Epstein, J., Keefe, D.M., McGuire, D.B., Migliorati, C., Nicolatou-Galitis, O., Peterson, D.E., Raber-Durlacher, J.E., Sonis, S.T., Elad, S. and (2014), MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. Cancer, 120: 1453-1461. https://doi.org/10.1002/cncr.28592

[vi] Docimo, R., Anastasio, M. D., & Bensi, C. (2022). Chemotherapy-induced oral mucositis in children and adolescents: a systematic review. European archives of paediatric dentistry: official journal of the European Academy of Paediatric Dentistry, 23(4), 501–511. https://doi.org/10.1007/s40368-022-00727-5

[vi] Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0; Published: November 27, 2017 (Accessed June 2023)

[vi] Macmillan Cancer Support – Mouth Problems (Accessed June 2023)

[vi] Children's Cancer and Leukaemia Group (CCLG) – Mucositis and mouth care (Accessed June 2023)

[vi] British National Formulary for Children (Accessed June 2023)

Key Words

Children, Young People, Chemotherapy, CYPICS

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
SOP Lead (Name and Title) Emma Ross; Consultant Paediatric Oncologist	**Executive Lead** **Chief Medical Officer**

Details of Changes made during review:

1. Minor correction of spellings
2. Update of references

Removal of reference to folinic acid mouthwash to treat methotrexate induced mucositis, lack of evidence to support intervention

Grade 4 mucositis swabbing advice amended from repeat to take.