CHILDREN'S ONCOLOGY GROUP

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Guideline for the Prevention of Oral and Oropharyngeal Mucositis

COG Supportive Care Endorsed Guidelines

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The "Clinical practice guideline for the prevention of oral and oropharyngeal mucositis in pediatric cancer and hematopoietic stem cell transplant patients: 2021 update" developed by the Pediatric Oncology Group of Ontario (POGO) was endorsed by the COG Supportive Care Guideline Committee in December 2021.

The source clinical practice guideline is published (Patel P, et al. Clinical practice guideline for the prevention of oral and oropharyngeal mucositis in pediatric cancer and hematopoietic stem cell transplant patients: 2021 update. Eur J Cancer 2021; 154: 92-101.) and is available at: https://www.sciencedirect.com/science/article/pii/S095980492100321X

The purpose of the source clinical practice guideline was to update the 2015 clinical practice guideline for mucositis prevention in pediatric cancer and HSCT patients. The recommendations of the source clinical practice guideline are presented below.

Summary of Recommendations for the Prevention of Oral and Oropharyngeal Mucositis

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
What prophylactic interventions are effective at preventing or reducing the severity of oral and oropharyngeal mucositis in pediatric patients (0 to 18 years) receiving treatment for cancer or undergoing HSCT?	
1. Use cryotherapy for older, cooperative pediatric patients receiving treatment for cancer or undergoing HSCT who will receive short infusions of melphalan or 5-fluorouracil. ***Remarks:*** The panel valued the absence of documented adverse effects, low costs and consistent benefits associated with cryotherapy. The duration of melphalan and 5-fluorouracil administration in the included trials was 30 min or less where infusion duration was described. The panel did not believe that cryotherapy would be feasible for chemotherapy administrations longer than 1 h.	Strong recommendation High-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
2. Consider using cryotherapy for older, cooperative pediatric patients receiving treatment for cancer or undergoing HSCT who will receive short infusions of chemotherapy associated with mucositis other than melphalan or 5-fluorouracil. ***Remarks:*** The panel hypothesized that the efficacy of cryotherapy is likely generalizable to chemotherapy other than melphalan and 5-fluorouracil. However, the indirectness of the data lowered the panel's certainty and resulted in a conditional recommendation. It is important to counsel families and patients that mucositis may develop even with diligent cryotherapy use, and the efficacy of cryotherapy may vary depending on the chemotherapy regimen administered.	Conditional recommendation Moderate-quality evidence
3. Do not administer palifermin routinely to pediatric patients with cancer receiving treatment for cancer or undergoing HSCT. ***Remarks:*** While the panel acknowledged the significant reduction in severe mucositis associated with palifermin, the observed effect size was relatively modest. Based on its known short-term adverse effects, its potential for long-term negative effects on cancer outcomes, high costs and restricted availability, the panel made a strong recommendation against its routine use.	Strong recommendation High-quality evidence
4. Use intraoral photobiomodulation therapy in the red light spectrum (620–750 nm) for pediatric patients undergoing autologous or allogeneic HSCT and for pediatric patients who will receive radiotherapy for head and neck carcinoma. ***Remarks:*** The panel valued the consistent benefits of photobiomodulation therapy and data regarding feasibility in pediatric patients. The ability to deliver photobiomodulation therapy requires specialized equipment, training and protective eyewear for the patient and those in attendance. The panel believed these requirements to be acceptable given the magnitude of benefit and the restricted patient populations included in the recommendation based on direct data. The ability to deliver photobiomodulation therapy to very young children requires assistance and support from family members and may not always be successful.	Strong recommendation High-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
5. Consider using intraoral photobiomodulation therapy in the red light spectrum (620–750 nm) for pediatric patients who will receive radiotherapy for head and neck cancers other than carcinoma. ***Remarks:*** Although direct data were not available, the panel hypothesized that the efficacy of photobiomodulation therapy for head and neck carcinoma patients receiving radiotherapy is likely generalizable to pediatric patients who will receive radiotherapy for other head and neck cancers such as rhabdomyosarcoma. However, the indirectness of the data lowered the panel's certainty and resulted in a conditional recommendation.	Conditional recommendation Moderate-quality evidence
6. Do not administer GCSFs to pediatric patients receiving treatment for cancer or undergoing HSCT for the purpose of mucositis prevention. ***Remarks***: While the panel recognized that patients receive GCSFs for other indications including shortening the duration of neutropenia, the absence of benefit, adverse effects and costs led the panel to make a strong recommendation against its use for the purpose of mucositis prevention.	Strong recommendation High-quality evidence

*see Appendix 1

HSCT: hematopoietic stem cell transplant; GCSFs: granulocyte colony-stimulating factors

Appendix 1: GRADE

Strength of Recommendations:

Strong Recommendation	When using GRADE, panels make strong recommendations when they are confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.
Weak or Conditional Recommendation	Weak or conditional recommendations indicate that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is less confident.

Strength of Recommendation Determinants:

Factor	Comment
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Certainty in evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Costs (resource allocation)	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted

Certainty in Evidence or Quality of Evidence

High Certainty/Quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate Certainty/Quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low Certainty/Quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very Low Certainty/Quality	Any estimate of effect is very uncertain

Guyatt, G.H., et al., *GRADE: an emerging consensus on rating quality of evidence and strength of recommendations.* BMJ, 2008; 336: 924-926.
Guyatt, G.H., et al., *GRADE: going from evidence to recommendations.* BMJ, 2008; 336: 1049-1051.