

Guideline for the Prevention of Oral and Oro-pharyngeal Mucositis in Children Receiving Treatment for Cancer or Undergoing Hematopoietic Stem Cell Transplantation

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On Behalf of:

The POGO Mucositis Prevention Panel

Preaching to the Choir



Oral Mucositis is Important in Pediatric Cancer/HSCT



- Pain
- Inability to eat and drink
- Hydration, TPN
- Provides a portal of entry for bacteria
- Dose limiting toxicity
- QoL
- Economic burden

In 2014, POGO Supportive Care Panel recognized the need for a mucositis prevention CPG

Approach

- Multidisciplinary panel including Oncologists, Nursing, Pharmacist and Dentist
- >130 RCTs mucositis prevention in adult and pediatric cancer
- Interventions effective in adult populations likely to have a similar effect in children

Evaluate both adult and pediatric literature with emphasis on appraisal of pediatric studies

Finding the Evidence:

- Recommended/suggested by MASCC/ISOO for prevention of oral mucositis
- Evidence of benefit in Cochrane systematic review

Cryotherapy

Low level laser therapy (LLLT)

Keratinocyte growth factor (KGF)

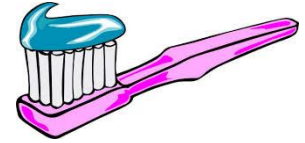
Additional reviews restricted to pediatric patients

- All RCTs of any intervention to prevent oral mucositis
- Any primary study type of KGF use

Good Practice Statements

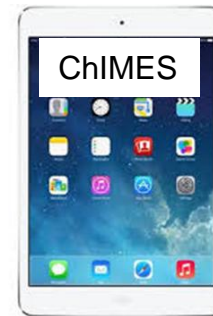
1. Good oral hygiene important in all children

- Regular tooth brushing
- Dental evaluation and treatment



2. Need for mucositis screening and measurement

- Several valid instruments



LLLT

- Low level light or LED – most 630-670 nm – applied daily (5 days/week) to oral mucosa
- No thermal generation
- Internal or external
- Widely used in Brazil



Recommendation 1.2: We suggest that LLLT may be offered to cooperative children receiving **chemotherapy or HSCT** conditioning with regimens associated with a high rate of mucositis.

Weak Recommendation, High Quality Evidence

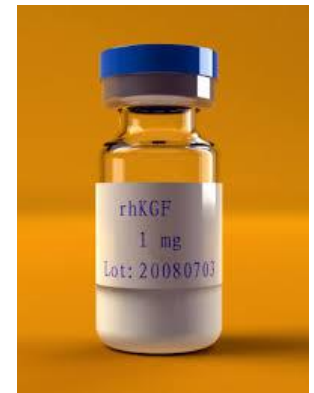
Remarks:

- High value – possibly effective intervention, low risk harm
- Weak recommendation – feasibility, specialized equipment
- Ideal treatment parameters and cost-effectiveness unknown

Keratinocyte growth factor

- Epithelial growth factor - 28-kD, heparin binding member of the family of fibroblast growth factors
- Palifermin - recombinant human KGF
- 11 RCTs, 1,470 patients
- 9/11 reported a benefit of KGF

- 4 non-randomized Pediatric trials – all HSCT
 - Allogeneic – 3
 - Autologous – 1



Recommendation 1.3: We suggest that KGF may be offered to children receiving **HSCT** conditioning with regimens associated with a high rate of severe mucositis.

Weak Recommendation, High Quality Evidence

Remarks:

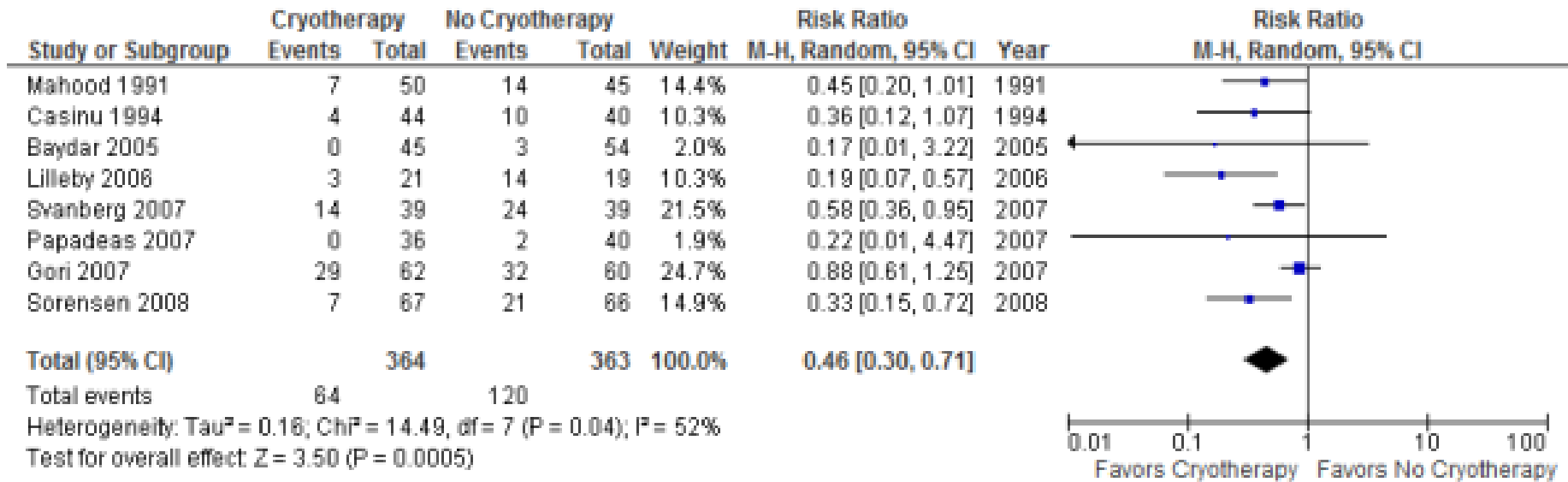
- High value – evidence efficacy adult trials
- Weak recommendation – indirectness, particularly potential for harm in pediatric cancers and costs

Oral Cryotherapy

- Placing ice cubes or ice chips in the mouth and continually replenishing fresh ice during the period of cytotoxic treatment (typically 30 to 60 minutes)
- Effect presumed to be related to vasoconstriction and reduced delivery of chemotherapy to mucosa
- 14 RCTs, 1,301 patients
- 12/14 RCTs reported benefit
- Only 1 with Children



RCTs of Cryotherapy vs No Cryotherapy for Reduction Severe Oral Mucositis



RR 0.46
 95% CI 0.30 to 0.71
 P=0.0005

Recommendation 1.1: We suggest that cryotherapy may be offered to cooperative children receiving chemotherapy or HSCT conditioning with regimens associated with a high rate of mucositis.

Weak Recommendation, Moderate Quality Evidence

Remarks:

- High value – possibly effective intervention, low risk harm
- Weak recommendation – indirectness, limitations study design
- Regimens appropriate for cryotherapy restricted to agents with a short infusion time and short half-life

Implications for Practice

- Cryotherapy or as a short infusion
- Flavoured ice or likely to be more palatable
- Challenge identifier
 - a) Have sign
 - b) Have drugfeasible



is administered
or 'freezies' are
to children

therapy



Where MIGHT Cryotherapy Help

- Short infusion anthracycline infusions
 - ALL Induction/Delayed Intensification
 - AML Induction
 - Sarcoma Regimens (Ewings, Non-Rhabdo)
 - Hodgkin Disease
- ‘Capizzi’ Methotrexate Regimens
- MOST outpatient chemo regimens

When cryotherapy is NOT feasible

- High Dose Methotrexate
 - Burkitt Lymphoma
 - High Risk ALL/LL
- Continuous infusion anthracycline
 - Neuroblastoma
 - Osteosarcoma
- Transplant Regimens

Need more/better options and evidence!

Conclusions

- Mucositis routine care should include good oral hygiene, monitoring and dental evaluation
- Consider cryotherapy implementation
- Future work should look to consider feasibility of LLLT in Ontario and safety of KGF in Pediatric malignancy
- <http://www.pogo.ca/healthcare/practiceguidelines/>
- (Or Google “POGO Practice Guidelines”)

For Full Guideline:

- Sung L, Robinson P, Treister N, Baggott T, Gibson P, Tissing W, Wiernikowski J, Brinklow J, Dupuis LL: Guideline for the prevention of oral and oropharyngeal mucositis in children receiving treatment for cancer or undergoing haematopoietic stem cell transplantation. *BMJ Supportive and Palliative Care* 2015: Early view: Mar 27, 2015
- Open access:
<http://spcare.bmj.com/content/early/2015/10/01/bmjspcare-2014-000804.full.pdf+html>

