Oral Cryotherapy for Prevention of Chemotherapy-Induced Oral Mucositis in Oncology Patients

Emily Huber
UNC Lineberger-Lauterborn-Piver Oncology Nursing Fellow
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• Definitions – Oral Mucositis & Oral Cryotherapy
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Research Question - **PICO**

In adult oncology patients receiving chemotherapy treatment(s), how does oral cryotherapy compare to standard care (either saline mouth rinse or no treatment) in prevention of chemotherapy-induced oral mucositis?

- **Population** – Oncology patients receiving chemotherapy that induces oral mucositis (Bolus 5FU and Melphalan)
- **Intervention** – Oral cryotherapy (ice chips, ice-cold water, popsicles) during treatment
- **Compared to** – Standard care (saline mouth rinse or no treatment)
- **Outcome** – Reduced incidence and severity of oral mucositis
The Burden of Oral Mucositis (OM)

- A common complication secondary to cancer treatment
- Patients may experience...
  - severe pain
  - Less able to eat or drink → dehydration and malnutrition
  - Increased risk for infection due to open sores in the oral mucosa
- Consequently, this may interrupt therapy, cause pain, increase the length of hospitalization, increase the use of antibiotics and narcotics, and increase the overall cost of treatment for patients.

(Lalla et al., 2008)
The Burden of Oral Mucositis

Figure 4 | World Health Organization's Oral Toxicity Scale. Republished with the permission of Dr. Patrick Stiff, Loyola University Medical Center, Maywood, IL, USA.
The first signs of mucositis usually begin with a feeling of mucosal irritation about 3-4 days after chemotherapy which is accompanied by ulcer development. The lesions usually heal within 2-4 weeks of the last dose of chemo (Lalla et al., 2008).

In a prospective study involving 298 patients treated with chemotherapy for solid tumors (Shankar et al., 2017):
- 40% of patients developed → WHO grade 1 (mild)
- 5% of patients developed → WHO grade 2 (moderate)
- 1% of patients developed → WHO grades 3–4 (severe)
Oral Cryotherapy

- Mouth cooling using cold consumables
  - Ice chips
  - Ice cold water
  - Popsicles
  - Cold mouthpieces

(Riley et al., 2015, p. 1846)
Cochrane Oral Health Group conducted a systematic review to determine whether oral cryotherapy (ice, ice-cold water, ice cream or ice lollies/popsicles) during chemotherapy can help prevent oral mucositis in patients receiving treatment.

- 14 RCT from 1991-2015
- 1316 randomized participants were to receive oral cryotherapy versus standard care (either saline mouth rinses or no treatment)
  - Patients receiving 5FU (bolus)
    - Received cryotherapy 5 minutes prior to treatment and continuing for 30 minutes
  - Patients receiving Melphalan
    - Received cryotherapy for longer periods of time (as long as 7 hours)

(Riley et al., 2015, p. 1846)
Key Results: **Patients Receiving 5FU (bolus)**

- Oral cryotherapy leads to large reductions in oral mucositis of all severities

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<thead>
<tr>
<th>Outcomes</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Oral Mucositis -any grade severity</td>
<td>Oral cryotherapy reduced the risk of developing oral mucositis by <strong>39%</strong></td>
</tr>
<tr>
<td>Oral Mucositis -moderate + severe</td>
<td>Oral cryotherapy reduced the risk of developing moderate to severe oral mucositis by <strong>48%</strong></td>
</tr>
<tr>
<td>Oral mucositis -severe</td>
<td>Oral cryotherapy reduced the risk of severe oral mucositis by <strong>60%</strong></td>
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(Riley et al., 2015, p. 1846)
Key Results: Patients Receiving Melphalan

- Oral cryotherapy reduce oral mucositis incidence and severity in adults receiving high-dose melphalan before bone marrow transplant but confidence intervals were wide.

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<tr>
<td>Oral Mucositis - any grade severity</td>
<td>41% reduction in the risk of developing oral mucositis [Confidence Interval or CI 1%-65%]</td>
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<tr>
<td>Oral Mucositis - moderate + severe</td>
<td>57% reduction in the risk of developing moderate to severe oral mucositis [CI 9%-83%]</td>
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<tr>
<td>Oral mucositis - severe</td>
<td>Oral cryotherapy reduced the risk of developing severe oral mucositis by 62%</td>
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(Riley et al., 2015, p. 1846)
The panel recommends…

- the use of intra-oral PBM therapy using low-level laser therapy for the prevention of OM in adult patients receiving RT and CT for H&N cancer (LOE I)
- that 30 minutes of oral cryotherapy be used to prevent OM in patients receiving bolus 5FU chemotherapy (LOE II)
- that recombinant human Keratinocyte Growth Factor-1 be used to prevent OM in patients receiving high-dose CT and RT, followed by stem cell transplant, for a hematological malignancy (LOE II).
- that low-level laser therapy be used to prevent OM in patients receiving stem cell transplant conditioned with high-dose CT, with or without RT (LOE II).

(Multinational Association of Supportive Care in Cancer, 2019)
The panel suggests...

- the use of benzydamine mouthwash for the prevention of OM among H&N cancer patients receiving RT-CT (LOE III)
- the use of oral glutamine in H&N cancer patients undergoing RT-C (LOE III)
- that oral care protocols be used to prevent oral mucositis in all age groups and across all cancer treatment modalities (LOE III)
- that oral cryotherapy be used to prevent oral mucositis in patients receiving high-dose melphalan, with or without total body irradiation, as conditioning for hematopoietic stem cell transplantation (LOE III)
Benefits of Oral Cryotherapy

• Safe with very low rates of minor side effects such as, headaches, chills, numbness/taste disturbance, and tooth pain (Riley et al., 2015, p. 1846)
• Easily accessible (Riley et al., 2015, p. 1846)
• Cost-effective (Riley et al., 2015, p. 1846)
• Reduced incidence and severity of oral mucositis leading to…
  • Decreased need for fluids and supplemental nutrition (Svanberg et al., 2010, p. 2148)
  • Decreased incidence of interruptions to cancer treatment (Svanberg et al., 2007, p. 1157)
  • Decreased use of opioid analgesics and antibiotics (Svanberg et al., 2007, p. 1157)
Special Thanks

- Bob and Sylvia Lauterborn
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- Claire Gillet and Susie Mason
References


