Oral health is an important component of individual health, and any alteration will reflect directly on quality of life (Eilers & Milloin, 2011). Therefore, different oral care protocols and strategies were established for patients with cancer to prevent and minimize oral mucositis. Oral cryotherapy is one of the recent modalities used to prevent and manage oral mucositis. Oral cryotherapy significantly minimizes the incidence and severity of oral mucositis and decreases secondary oral mucositis complications. Using oral cryotherapy concurrently with a regular oral care protocol can improve its efficacy for preventing and managing oral mucositis. Additional studies should be conducted to create standard oral cryotherapy protocols.

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Key words: cryotherapy; oral cryotherapy; myeloablative; bone marrow transplantation; hematopoietic stem cell transplantation; oral mucositis; prevention

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Oral mucositis is a distressing toxic effect of cancer therapy and one of the major side effects of the myeloablative conditioning used to prepare patients for bone marrow transplantation (BMT). Oral cryotherapy is one of the recent modalities used to prevent and manage oral mucositis. The purpose of this review is to clarify the cryotherapy effect on oral mucositis severity among patients receiving myeloablative conditioning followed by BMT. A literature search was performed using six different electronic databases: CINAHL®, MEDLINE®, Nursing Ovid, PubMed, Springer, and Science Direct. Six articles were deemed relevant and included in this review. Oral mucositis increases mortality rate, length of hospital stay, opioid use, and the need for parenteral nutrition usage. It also decreases patient’s quality of life and his or her desire to complete treatment. However, oral cryotherapy significantly minimizes the incidence and severity of oral mucositis and decreases secondary oral mucositis complications. Using oral cryotherapy concurrently with a regular oral care protocol can improve its efficacy for preventing and managing oral mucositis. Additional studies should be conducted to create standard oral cryotherapy protocols.
TABLE 1. Article Review: Cryotherapy Effect on Oral Mucositis Severity

<table>
<thead>
<tr>
<th>Study and Design</th>
<th>Purpose</th>
<th>Sample and Variables</th>
<th>Treatment</th>
<th>LOE</th>
<th>Result</th>
<th>Cryotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gori et al., 2007</td>
<td>To assess the effect of oral cryotherapy during administration of MTX followed by myeloablative conditioning</td>
<td>Experimental: n = 62 Control: n = 60 Independent: cryotherapy Dependent: oral mucositis</td>
<td>MTX (given as GVHD prophylaxis)</td>
<td>II</td>
<td>No difference was observed between groups regarding mucositis grade or duration.</td>
<td>One hour starting at the time of MTX infusion</td>
</tr>
<tr>
<td>Mori et al., 2008</td>
<td>To assess whether removing the excreted cytarabine in the saliva by intensive mouth rinse during high-dose cytarabine infusion could reduce the incidence of oral mucositis</td>
<td>Experimental: n = 50 Control: n = 35 Independent: mouth rinse Dependent: oral mucositis</td>
<td>TBI six fraction for 3 days plus cytarabine (3 g/m² every 12 hours) for 4 days</td>
<td>III</td>
<td>Mouth rinse during and shortly after high-dose cytarabine infusion could be an effective measure in reducing the incidence of moderate to severe oral mucositis cased by high-dose cytarabine.</td>
<td>Patients were instructed to rinse their mouths using ice-cold water every 10 minutes, starting simultaneously with the two-hour cytarabine infusion and continuing for one hour postinfusion.</td>
</tr>
<tr>
<td>Salvador et al., 2012</td>
<td>To assess the effectiveness of oral cryotherapy plus oral care to reduce oral mucositis</td>
<td>Experimental: n = 23 Control: n = 23 Independent: oral cryotherapy Dependent: oral mucositis</td>
<td>Melphalan (200 mg/m²) once</td>
<td>II</td>
<td>The oral mucositis for the experimental group was significantly lower than the control group.</td>
<td>60 minutes</td>
</tr>
<tr>
<td>Svanberg et al., 2007</td>
<td>To investigate if oral cryotherapy could delay or alleviate the development of mucositis, reducing the number of days with IV opioids among patients receiving myeloablative therapy before BMT</td>
<td>Experimental: n = 39 Control: n = 39 Independent: oral cryotherapy Dependent: oral mucositis, opioid use</td>
<td>BEAM²; BEAC³; high-dose melphalan; busulfan, cyclophosphamide, and TBI; fludarabine plus busulfan</td>
<td>II</td>
<td>Experimental group showed significantly lower total opioid doses, and less severe oral mucositis compared with the control group.</td>
<td>Sucking ice chips or rinsing oral cavity with cooled water to maintain a cold oral cavity during chemotherapy infusion</td>
</tr>
<tr>
<td>Svanberg et al., 2010</td>
<td>To investigate if oral cryotherapy during myeloablative therapy may influence frequency and severity of mucositis, nutritional status, and infection rate after BMT</td>
<td>Experimental: n = 39 Control: n = 39 Independent: oral cryotherapy Dependent: oral mucositis grade, nutritional status, infection rate, days of hospitalization and parenteral nutrition</td>
<td>BEAM²; BEAC³; high-dose melphalan; busulfan, cyclophosphamide, and TBI; fludarabine plus busulfan</td>
<td>II</td>
<td>Oral mucositis severity, length of hospital stay, and use of parenteral nutrition was significantly lower in the experimental group compared with the control group.</td>
<td>Sucking ice chips or rinsing oral cavity with cooled water to maintain a cold oral cavity during chemotherapy infusion</td>
</tr>
<tr>
<td>Vokurka et al., 2011</td>
<td>To focus on the risk factors and the effect of cryotherapy on oral mucositis in patients after BEAM² conditioning for autologous BMT</td>
<td>Experimental: n = 36 Control: n = 30 Independent: oral cryotherapy Dependent: oral mucositis, severity</td>
<td>Melphalan (200 mg/m²) once or BEAM²</td>
<td>III</td>
<td>Oral mucositis and oral mucositis severity were significantly lower in the experimental group compared with the control group.</td>
<td>Started five minutes before melphalan administration, and continued for 15 minutes during drug infusion and 15 minutes postinfusion</td>
</tr>
</tbody>
</table>

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A high-dose chemotherapy using carmustine (300 mg/m² once), etoposide (100 mg/m² every 12 hours for 4 days), cytarabine (200 mg/m² every 12 hours for 4 days), and melphalan (140 mg/m² once)  
A high-dose chemotherapy using carmustine (300 mg/m² once), etoposide (200 mg/m² every 12 hours for 4 days), cytarabine (200 mg/m² every 12 hours for 4 days), and cyclophosphamide (35 mg/kg every 12 hours for 4 days)  
BMT—bone marrow transplantation; GVHD—graft-versus-host disease; LOE—levels of evidence; MTX—methotrexate; RCT—randomized, controlled trial; TBI—total-body irradiation
Methodology

The current study’s authors carried out a comprehensive search of literature published from January 2007 to October 2012. Six electronic databases were searched, including CINAHL®, MEDLINE®, Nursing Ovid, PubMed, Springer, and Science Direct. The key words used to search in the different databases included cryotherapy, oral cryotherapy, myeloablative, bone marrow transplant, hematopoietic stem cell transplant, oral mucositis, and prevent oral mucositis. Inclusion criteria for the review included English-language articles that detailed myeloablative conditioning followed by BMT (either allogeneic or autologous), and used cryotherapy for oral care before, during, and after chemotherapy infusion time.

The relevant articles were evaluated according to the levels of evidence criteria developed by LoBiondo-Wood and Haber (2006). Six relevant articles were selected for this review: four randomized, controlled trials (RCTs) and two quasi-experimental studies (see Table 1). The sample size in all studies ranged from 46–126. In all of the RCTs, the samples were divided into the experimental and control groups. A middle-range theory, the symptom management theory, will be used to guide this review (Smith & Liehr, 2008).

Results

About 75%–99% of patients receiving BMT with or without total-body irradiation experience oral mucositis (Qutob, Gue, Revesz, Logan, & Keefe, 2012). This complication may increase morbidity and mortality for patients undergoing BMT, as well as the risk for infections, opioid use, need for parenteral nutrition, and length of hospital stay (Svanberg et al., 2007). Therefore, oral care is a critical management for patients undergoing BMT (Epstein, Raber-Drulacher, Wilkins, Chavarria, & Myint, 2009).

Svanberg et al. (2007) conducted a study to investigate if the oral cryotherapy could delay or alleviate the development of mucositis, reducing the number of days with IV opioid among patients undergoing BMT who received myeloablative conditioning before BMT. The main goal was to maintain a cold oral cavity. The experimental group showed significantly lower mucositis severity and opioid use compared with the control group.

In 2007, Gori et al. conducted a study in Italy to assess the effect of oral cryotherapy during the administration of methotrexate after myeloablative conditioning as a prophylaxis regimen for graft-versus-host disease. The sample in this study (N = 122) was divided into experimental and control groups (Gori et al., 2007). Oral cryotherapy was applied as ice, and preparation started at the time of methotrexate infusion and lasted for one hour. The World Health Organization (1979) Oral Mucositis Scale was used to evaluate oral mucositis. No differences were observed between the groups regarding oral mucositis severity and duration.

In 2008, Mori et al. assessed the efficacy of a mouth rinse, using ice-cold water to prevent oral mucositis in 85 patients receiving high-dose cytarabine for allogeneic hematopoietic stem cell transplantation. Oral mucositis severity was significantly lower in the experimental group compared with the control group.

In addition, Svanberg et al. (2010) investigated whether oral cryotherapy during myeloablative conditioning influenced the frequency and severity of oral mucositis, the infection rate, and nutritional status in patients undergoing BMT. Length of hospital stay, severity of oral mucositis, and need for parenteral nutrition was significantly lower in the experimental group compared with the control group. However, the infection rate between both groups remained unchanged (Svanberg et al., 2010). In 2011, Vokurka et al. focused on the risk factors and the effect of cryotherapy in oral mucositis. They focused on the patients who received high-dose melphalan or BEAM conditioning (carmustine, etoposide, cytarabine, and melphalan) before an autologous BMT. The result showed significantly lower oral mucositis incidence and severity. Salvador et al. (2012) investigated the effect of cryotherapy on oral mucositis. The study recruited 48 patients who were scheduled for autologous BMT. The experimental group showed significantly lower oral mucositis severity and pain, which was associated with better food intake compared to the control group.

Conclusion

Oral mucositis is a major side effect for patients undergoing BMT. Oral mucositis increases the mortality rate among patients receiving myeloablative conditioning, as well as prolongs hospitalization and increases the need for parenteral and opioid usage. However, the use of oral cryotherapy before, during, and after the chemotherapy infusion reduced oral mucositis incidence, severity, and pain, thereby improving patients’ quality of life and minimizing the life-threatening secondary complications of oral mucositis.

Recommendations for Future Study

Additional studies should be conducted to create a standard oral cryotherapy protocol. Oral cryotherapy may be useful to other patients receiving chemoradiotherapy as a cancer treatment, but this needs to be further explored. Healthcare providers should be educated regarding cryotherapy benefits and patient application.

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References


