Oral Mucositis in Adults & Children: What is the State of the Art?

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Oral mucositis has many faces…
Consequences of Oral Mucositis
Impact on Quality of Life (QoL): Adults

- They believed that mucositis was something inevitable that they would have to endure and that it would improve or resolve as soon as their blood counts came up.

Descriptions of participants:
- A mouth so dry it could be described as “growing oral fur”
- Living with foul breath
- Being able to eat only “mushy” baby food
- Needing to retrain oneself to eat
- Feeling anxiety at mealtimes that swallowed food would not “go down”
- Discovering that some things, such as fruit juice, “sear” the throat
- Becoming socially isolated as a result of the sheer discomfort of mucositis and its effects

- Mouth sores were selected as the single most debilitating side effect (42%) (Bellm et al., 2000; Borbasi et al., 2002)
Impact on Quality of Life (QoL): Children

OM in children affects not only the patients but also their families!

Children:
- Pain is described as the worst symptom of OM: throat ulcers were the worst
- Turmoil of emotions: unhappiness, anger, crying, psychological distress (eating and speaking problems) → tension between children and parents
- «Not being able to eat is the worst suffering»

Parents
- Parents experienced increased psychological distress, which corresponded with a steady decline in the oral function of their children
- Very distressed by the eating difficulties of their children
- Oral care is stressful

(Cheng, 2009)
Impact of Symptoms on QoL in pediatric and adolescent patients

Symptoms reported in pediatric and adolescent patients were related to:

- Eating (82.4%)
- Swallowing (78.9%)
- Drinking (75.4%)
- Sleeping (71.9%)
- Talking (43.9%)

Swallowing and Sleeping had the strongest standardized coefficients, suggesting, that among all five symptoms, swallowing and sleeping affected the patients’ quality of life most.

(Cheng et al., 2012)
Definition

Oral Mucositis:
- Describes inflammation of oral mucosa resulting from chemotherapeutic agents or ionizing radiation
- Typically manifests as erythema or ulcerations
- May be exacerbated by local factors

Stomatitis:
- Refers to any inflammatory condition of oral tissue, including mucosa, dentition/periapices, and periodontium
- Includes infections of oral tissues as well as mucositis

(NCI, 2014)
Incidence

**Children**
- 52 – 80% (Cheng et al., 2004)
- 46% in ALL (Figliolia et al., 2008)

Pediatric and adolescent patients have a higher proliferating fraction of basal cells than adults, and they may therefore be at increased risk of OM

(Sonis & Clark, 1991)

**Adults**
- 20 – 40% Conventional chemotherapy
- 80% in patients with high-dose chemotherapy
- 100% in patients receiving head and neck radiation therapy

(Jones et al., 2006; Vera-Llonch et al., 2006; Vera-Llonch et al., 2007)
Pathobiology of mucositis

(Sonis, 2004)
Duration of Oral Mucositis

Chemotherapy

• The early clinical sign of mucositis is erythema presenting about 4–5 days following chemotherapy infusion
• Seven to 10 days after chemotherapy ulcers develop
• Chemotherapy-induced mucositis lasts approximately 1 week and generally heals spontaneously by 21 days after
• Average length of severe OM is 5.5 +/- 3.4 days (adults) and 6.3 +/- 4 days (pediatric and adolescent patients)

(Scully, Sonis & Diz, 2006; Blijlevens et al., 2008; Cheng et al., 2011)
Constellation of symptoms in mucositis

Keefe at al., 2007
MASCC/ISOO Guideline: Oral Mucositis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Recommendation</th>
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</thead>
<tbody>
<tr>
<td>Recombinant human Keratinocyte Growth Factor-1 (Palifermin) 3 days prior to conditioning treatment and for 3 days posttransplant in SCT</td>
<td>Recommendation in favor of an intervention</td>
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<tr>
<td>Low level laser therapy (LLLT) in SCT</td>
<td>Recommendation in favor of an intervention</td>
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<tr>
<td>Patient-Controlled analgesia with morphine to treat pain in patients with SCT</td>
<td>Recommendation in favor of an intervention</td>
</tr>
<tr>
<td>Oral care protocols (Basic oral care) in all age groups and across all cancer treatment modalities</td>
<td>Suggestion in favor of an intervention</td>
</tr>
<tr>
<td>Transdermal fentanyl to treat pain</td>
<td>Suggestion in favor of an intervention</td>
</tr>
<tr>
<td>0.5% Doxepin (Aponal®, Sinquan®) mouthwash to treat pain</td>
<td>Suggestion in favor of an intervention</td>
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<tr>
<td>Chlorhexidine mouthwash</td>
<td>Suggestions against an intervention</td>
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<tr>
<td>Granulocyte macrophage colony-stimulating factor (GM-CSF) mouthwash</td>
<td>Suggestions against an intervention</td>
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<tr>
<td>Systemic Pentoxifylline (Trental ®) administered orally</td>
<td>Suggestions against an intervention</td>
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<tr>
<td>Systemic Pilocarpine (Salagen®) administered orally</td>
<td>Suggestions against an intervention</td>
</tr>
<tr>
<td>Sucralfate (Ulcogant®) mouthwash</td>
<td>Recommendation against an intervention</td>
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<tr>
<td>Intravenous glutamine</td>
<td>Recommendation against an intervention</td>
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</tbody>
</table>

Due to inadequate and/or conflicting evidence, no guideline was possible in relation to:

**Agents of natural origin**: Vitamin A and E, honey, aloe vera, chamomile, chinese herbals, indigowood root, manuka and kanuka oils

**Antimicrobials, anesthetics, analgesics**: Acyclovir, Clarithromycin, Nystatin, Povidone-Iodine, Capsaicin, Methadone, Ketamine, Gabepentin, Cocaine, Fluconazole

(Lalla et al., 2014)
State-of-the-art interventions

- Risk-factors
- Oral assessment
- Prophylaxis prior to admission
- Prevention of OM
- Management of OM and oral complications
Patient-related risk factors

**Adults**
- Female sex
- Comorbidities
- BMI > 25
- Malnutrition
- Genetic polymorphisms
- Systemic disease (e.g. Addisons Disease)
- Poor oral health and hygiene
- Tobacco and alcohol use

**Children**
- Lower body weight prior to therapy
- Hematological malignancies
- Neutropenia prior to therapy
- High serum creatinine
- Blood group 0
- High anxiety level
- Poor oral health and hygiene

(Jones et al., 2008; Blijvens et al., 2008; Vera-Llonch et al., 2007; Cheng et al., 2011; Lalla & Keefe, 2011; Otmani et al., 2008; Otmani et al., 2011; Brennan Tyler, 2011)
Treatment-related risk factors

**Adults**
- Conditioning with Total Body Irradiation (TBI) and Cyclophosphamide
- Melphalan and Carmustine dose per kilogramm of body weight
- Graft versus Host-Disease (GvHD) prophylaxis with Methotrexat
- Unrelated donor

**Children**
- Antimetabolic drugs (Methotrexat)
- Prior OM

(Jones et al., 2008; Blijvens et al., 2008; Vera-Llonch et al., 2007; Cheng et al., 2011; Lalla & Keefe, 2011)
Assessment of Oral Mucositis

(WHO, 1979)

- Objective
- Functional
- Symptomatic

(Sonis et al., 2004)
Prophylaxis
Oral Hygiene prior to admission
Basic oral care

- Ongoing oral assessment using validated staging tool
- Verbal and written instruction and patient education
- Toothbrushing with fluoride toothpaste
- Flossing (Cave: Platelets!)
- Mouth rinses: Water, saline, (sodium bicarbonate)
- No tobacco and alcohol use
- Avoid hot, abrasive, sharp or hard foods
- Use water-based moisturizers to protect lips
- Maintain adequate hydration

(Rubenstein et al., 2004; Harris et al., 2007; Cheng, 2009; Brennan Tyler, 2011; Lalla et al., 2014; )
Oral Mucositis – treatment in the future?

Caphosol®: supersaturated calcium and phosphate rinse

Papas et al., 2003: 95 Patients (allogeneic and autologous), prospective RCT, double-blind

Wasko-Grabowska et al, 2011: 32 patients (hematologic malignancies), 24 patients in the retrospective control group

Markiewicz et al., 2012: 40 Patients (allogeneic), RCT, not blinded

Kröner, Aerts, Schanz, Meyer & Spirig (in process): 72 patients (allogeneic), prospective RCT, not blinded
References


References


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References


Thank you!

Questions?