Evidence-Based Guidelines for the Management of Oral Side-Effects of Cancer

Family Practice Oncology Network CME Day

Saturday, November 24, 2018

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Disclosures

None
Where it all began...
Problem Statement #1

Late stage diagnosis remains a problem for a significant percentage of oral and oropharyngeal cancers in BC, resulting in poor 5-year survival rates.
Oral Cancers in BC

- 42% were diagnosed in an advanced stage
## Five Year Survival Rates

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>All Cancers</td>
<td>50%</td>
<td>54%</td>
<td>66%</td>
</tr>
<tr>
<td>Prostate</td>
<td>69%</td>
<td>76%</td>
<td>99%</td>
</tr>
<tr>
<td>Thyroid</td>
<td>93%</td>
<td>94%</td>
<td>97%</td>
</tr>
<tr>
<td>Breast</td>
<td>75%</td>
<td>79%</td>
<td>89%</td>
</tr>
<tr>
<td>Hodgkin's Disease</td>
<td>74%</td>
<td>79%</td>
<td>86%</td>
</tr>
<tr>
<td>Larynx</td>
<td>67%</td>
<td>66%</td>
<td>64%</td>
</tr>
<tr>
<td>Oral</td>
<td>53%</td>
<td>55%</td>
<td>60%</td>
</tr>
<tr>
<td>Colon</td>
<td>52%</td>
<td>59%</td>
<td>65%</td>
</tr>
<tr>
<td>Non-Hodgkins lymphoma</td>
<td>48%</td>
<td>53%</td>
<td>65%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>35%</td>
<td>42%</td>
<td>51%</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>26%</td>
<td>29%</td>
<td>35%</td>
</tr>
<tr>
<td>Lung</td>
<td>13%</td>
<td>13%</td>
<td>16%</td>
</tr>
</tbody>
</table>
Problem Statement #2

• Many cancer patients (H&N and others) are referred to Oral Oncology @ BC Cancer prior to initiating cancer care.

• Once cancer therapy is complete, we refer the patient back to their community-based dentist for ongoing care.

• Dentists report that they lack the knowledge to competently and safely treat cancer patients in their practice; the same can be said of physicians.
Even Worse...
Oral Cancer Risk Factors
Recent Changes in Epidemiology

young non-smokers
non-drinkers
## Changes in Cancer Incidence 2004-2008 (United States)

<table>
<thead>
<tr>
<th>Year</th>
<th>all cancers</th>
<th>HNC</th>
<th>tongue</th>
<th>pharynx</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>1,368,030</td>
<td>28,260</td>
<td>7,320</td>
<td>8,250</td>
</tr>
<tr>
<td>2005</td>
<td>1,372,910</td>
<td>29,370</td>
<td>7,660</td>
<td>8,590</td>
</tr>
<tr>
<td>2006</td>
<td>1,399,790</td>
<td>30,990</td>
<td>9,040</td>
<td>8,950</td>
</tr>
<tr>
<td>2007</td>
<td>1,444,920</td>
<td>34,360</td>
<td>9,800</td>
<td>11,800</td>
</tr>
<tr>
<td>2008</td>
<td>1,437,180</td>
<td>35,310</td>
<td>10,140</td>
<td>12,410</td>
</tr>
<tr>
<td>total</td>
<td>7,022,830</td>
<td>158,290</td>
<td>43,960</td>
<td>50,000</td>
</tr>
</tbody>
</table>

### 5-year Change

<table>
<thead>
<tr>
<th>Year</th>
<th>all cancers</th>
<th>HNC</th>
<th>tongue</th>
<th>pharynx</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-year</td>
<td>69,150</td>
<td>7,050</td>
<td>2,820</td>
<td>4,160</td>
</tr>
<tr>
<td>%</td>
<td>5.1%</td>
<td>24.9%</td>
<td>38.5%</td>
<td>50.4%</td>
</tr>
</tbody>
</table>
Oral Cancer and HPV
Quality of Life and Oral Function Following Radiotherapy for H&N Cancer

What Are Patients Telling Us?


Survey mailed to > 100 patients > 6 months post-treatment at the BC Cancer; 65 respondents

- Difficulty Chewing: 43%
- Dry Mouth: 92%
- Taste Change: 75%
- Difficulty Swallowing: 63%
- Increase in Dental Decay: 38%
- Problems with Dentures: 48%
Summary of RT/CT Effects

- Mucositis
- Xerostomia
- Dental Decay / Oral Pain
  - Infections (fungal, viral, bacterial)
  - Bone Necrosis (ORN or MRONJ)
    - Dysgeusia / Dysphagia
      - Trismus
    - Oral GVHD
Xerostomia
“Radiation Caries”
Fungal Infections

(note: clinical presentation can vary)
Viral Infections
Osteoradionecrosis (ORN)
Osteochemonecrosis (MRONJ)
15 Gy # - Day 0 – 28 (rat model)
## Prevalence of Oral Complications

<table>
<thead>
<tr>
<th>Oral complication</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CT only = 56.3%</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>RT only = 66.5%</td>
</tr>
<tr>
<td></td>
<td>Combined CT and RT = 76%</td>
</tr>
</tbody>
</table>

MASCC/ISOO Oral Care Study Group
Systematic Reviews. Support Care Cancer 2010;18 (8)
Dysphagia (altered swallowing)

- Persistent dysphagia reported in up to 50% of head-and-neck CRT patients (defined by need for instrumental swallowing assessment – MBS, FEES)

- Patients may lose oropharyngeal swallow integrity 2\textdegree\ XRT or surgery-induced fibrosis (tongue ROM, decreased glottic closure, decreased cricopharyngeal relaxation, etc)

- Risk for aspiration-related complications....fear of eating, social isolation, depression....

- Aggravated by inability to masticate, lubricate or mobilize food bolus
Trismus

- Occasionally seen in patients whose RT field includes the TMJ and muscles of mastication.
- Treatment includes passive stretching of muscles / physio.
- May need to reduce vertical dimension.
**Prevalence of Oral Complications**

<table>
<thead>
<tr>
<th>Oral complication</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional RT</td>
<td>25.4%</td>
</tr>
<tr>
<td>Trismus</td>
<td>IMRT = 5%</td>
</tr>
<tr>
<td>Combined RT and CT</td>
<td>30.7%</td>
</tr>
</tbody>
</table>

MASCC/ISOO Oral Care Study Group
Systematic Reviews. Support Care Cancer 2010;18 (8)
Oral GVHD
(pre-malignant potential?)
Proposed Solution

With our centralized cancer care model in British Columbia, we have a tremendous opportunity to develop a comprehensive educational and communication strategy for BC dentists and physicians to address these two issues.
Education and Communication Strategy

- Undergraduate Curriculum Teaching
- Guiding Principles Document
- Evidence-Based Guidelines for Symptom Management
- Early Detection Guidelines
Training the Clinicians of the Future
Undergraduate Curriculum UBC

- Provided for first time in Fall 2017 to 3rd Year Dental Students @ UBC Faculty of Dentistry

- Twelve 2-hour Oncology lecture series with focus on managing cancer patients in general practice
Evidence-Based Guidelines

Based on the work of the Oral Care Study Group of MASCC/ISOO

Extensive literature review of 9 most common oral side-effects of cancer therapy, including:

- Xerostomia/Salivary Gland Hypofunction
- Oral Mucositis
- Dysgeusia
- Trismus
- Fungal Infections
- Viral Infections
- Oral Graft-vs-Host Disease (GVHD)
- Osteoradionecrosis (ORN)
- Medication-Related Osteonecrosis of the Jaw (MRONJ)
MASCC/ISOO Clinical Practice Guidelines for 9 Most Common Oral Complications in Cancer Therapy (JSCC)

Systematic Review of **Basic Oral Care** for the Management of Oral Mucositis in Cancer Patients  
*Mc Guire DB et al. 2014*

Systematic Review of Miscellaneous Agents for the Management of **Oral Mucositis** in Cancer Patients  
*Jarvis V et al. 2014*

Systematic Review of **Dental Disease** in patients undergoing cancer therapy  
*Hong, CHL et al. 2010*

Systematic review of **Dysgeusia** induced by cancer therapies  
*Hovan A, et al. 2010*

A systematic review of **Trismus** induced by cancer therapies in Head and Neck Cancer Patients  
*Bensadoun RJ et al. 2010*

Systematic review of **Oral Fungal Infections** in patients receiving cancer therapy  
*Lalla RV et al. 2010*

A systematic review of **Viral Infections** associated with oral involvement in cancer patients: a spotlight on Herpesviridea  
*Elad S et al. 2010*

**Osteoradionecrosis** in cancer patients: the evidence base for treatment  
*Peterson DE et al 2010*

A systematic review of **Salivary Gland Hypofunction and Xerostomia** induced by cancer therapies  
*Jensen SB et al. 2010*
Methodology

• Search based on pre-defined inclusion/exclusion criteria and key search words (Pub Med, Medline, OVID)

• Each article reviewed by 2 reviewers

• Guidelines based on level of evidence (I-V)

• 3 possible guideline determinations: **Recommendation** (based on Level I or II evidence), **Suggestion** (level III-V evidence) or **No Guideline Possible** (either little or no evidence or lack of consensus on interpretation of existing evidence)
Levels of Evidence

**TABLE 1. Criteria for Each Level of Evidence**

<table>
<thead>
<tr>
<th>Level</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence obtained from meta-analysis of multiple, well-designed, controlled studies; randomized trials with low false-positive and false-negative errors (high power).</td>
</tr>
<tr>
<td>II</td>
<td>Evidence obtained from at least 1 well-designed experimental study; randomized trials with high false-positive and/or false-negative errors (low power).</td>
</tr>
<tr>
<td>III</td>
<td>Evidence obtained from well-designed, quasi-experimental studies such as nonrandomized, controlled single-group, pretest-posttest comparison, cohort, time, or matched case-control series.</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence obtained from well-designed, nonexperimental studies, such as comparative and correlational descriptive and case studies.</td>
</tr>
<tr>
<td>V</td>
<td>Evidence obtained from case reports and clinical examples.</td>
</tr>
</tbody>
</table>
Mucositis – 8 Sections

GI Mucositis (1 section)

Oral Mucositis (7 Sections)

1. Basic Oral Care
2. Growth Factors/Cytokines
3. Anti-Inflammatories
4. Antimicrobials, Coating Agents, Anesthetics and Analgesics
5. Laser and Other Light Therapies
6. Cryotherapy
7. Natural and Miscellaneous Agents
Mucositis Systematic Review

8,279 papers identified by search

1,032 retrieved for detailed evaluation based on titles and abstracts

570 qualified for final inclusion/double reviews

16 new recommendations/suggestions for/against therapies bringing total to 32 (22 Oral; 10 GI)
Oral Mucositis

Recommendations In Favour of an Intervention

1. The panel recommends that 30 min of oral cryotherapy be used to prevent oral mucositis in patients receiving bolus 5-FU chemotherapy.

2. The panel recommends that palifermin be used to prevent oral mucositis in patients receiving high dose chemotherapy and TBI followed by autologous SCT.

3. The panel recommends that low-level laser therapy be used to prevent oral mucositis in patients receiving HSCT conditioned with high-dose chemotherapy with or without TBI.

4. The panel recommends that patient-controlled analgesia with morphine be used to treat pain due to oral mucositis in patients undergoing HSCT.

5. The panel recommends that benzydamine mouthwash be used to prevent oral mucositis in patients with head and neck cancer receiving moderate dose radiation therapy (up to 50 Gy) without concomitant chemotherapy.

More recently updated to include patients receiving high-dose radiation therapy (up to 70 Gy).
Other Results of Interest

• Use of prophylactic HBO therapy for the prevention of ORN in patients requiring post-RT dental extractions
  
  **Level of Evidence III; No guideline possible (inconsistent findings)**

• Use of zinc supplements for the prevention or management of cancer-related dysgeusia
  
  **Level of Evidence III; No guideline possible (inconsistent findings)**

• Use of oral pilocarpine following radiation therapy in head and neck cancer patients for improvement of xerostomia
  
  **Level II evidence to support the use; however, the improvement in salivary gland hypofunction may be limited**

  • Etc
Oral Care Manual

BC Cancer
Oral Oncology – Dentistry

March 2018
Guiding Principles Document (part of Oral Care Manual)

Answering FAQs commonly asked by dentists/physicians when treating cancer patients in their practice:

• Timing of elective procedures relative to chemo?
• Antibiotic Coverage with central or peripheral lines?
  • Blood Values of Relevance to Dental Work?
• Implants/Dental Extractions in Irradiated Jaws?
• Prosthesis care (obturators, dentures, etc)?
  • What Is/Isn’t Covered for Patients?
    • Chemo Brain, etc
3 Key Components

At the request of the College of Dental Surgeons of British Columbia, this guideline has been written by a working group of the BC Oral Cancer Prevention Program, which is a multidisciplinary team composed of clinicians and scientists from the BC Cancer Agency.

This guideline is intended to provide guidance about the appropriate use of oral cancer screening techniques and to help dentists make informed decisions about screening for oral cancer in practice. It should be used to facilitate clinical decision-making.

Due to the importance of ongoing research related to oral cancer screening, this guideline will be updated on a regular basis with multidisciplinary input.

- Oral cancer is a common cancer of global concern. It is known to be a devastating disease of tremendous consequence to the individual, to family and to society.
- This year 3,200 people will be diagnosed with oral or pharyngeal cancer in Canada. Of these, it is estimated that about 2,700 (84 per cent) could potentially be detected by a dentist.
- The five-year survival rate is approximately 62 per cent.
- Early detection has the potential to significantly reduce oral cancer deaths and morbidity.

- Known risk factors include tobacco and alcohol consumption, together responsible for about 75 per cent of oral cancers in developed countries.
- Most oral premalignant lesions and cancers should be detectable at the time of a comprehensive oral examination.
- These lesions often present as a white patch or, less frequently, a red patch. Progression from premalignant lesions to cancer usually occurs over years.

Guideline for the Early Detection of Oral and Oropharyngeal Cancer in British Columbia 2018

At the request of the College of Dental Surgeons of British Columbia, this guideline has been written...
Endorsements

✓ BC Cancer

✓ College of Dental Surgeons of B.C.

✓ B.C. Dental Association

✓ Family Practice Oncology Network
Roll-Out

• UBC Undergraduate Curriculum - In place

• Oral Care Manual – Pacific Dental Conference March, 2018

• Early Detection Guideline Update – November 2018

  • Website/ SHOP Launch – Early 2019

• ASCO Adoption of Guidelines (MRONJ, Mucositis)
Measuring Success

Website Hits

External (vs Internal) Consults

Tracking Adverse Outcomes
Looking Ahead
Planning for Long Term Success
Thank You