HOT SPOT

The Newsletter of the Rapid Response Radiotherapy Program of the Odette Cancer Centre





Volume 12, Issue 3, August 2010

Editorial

By Cyril Danjoux, MD, FRCP(C), Associate Professor, University of Toronto

This issue of **Hot Spot** contains many interesting articles by our expert panel, as well as some highlights of the achievements at the Odette Cancer Centre (OCC).

Dr. May Tsao is the recipient of the 2009–2010 University of Toronto Department of Radiation Oncology award for Excellence in Post-graduate Medical Education. Ms. Lori Holden (Vice-Chair of Rapid Response Radiotherapy Program (RRRP)/Bone Metastases Site Group, also an Assistant Professor at the University of Toronto) is a Schulich Award Winner for Nursing & Clinical Excellence. This award recognizes and celebrates the exceptional staff and students at Sunnybrook Health Sciences Centre who continually go above and beyond their usual role to exemplify hospital values. At the 2010 Annual Hospice Palliative Care Conference, RRRP was awarded "Outstanding Leadership Award" by the Ontario Palliative Care Association. We welcome our new fellow to the RRRP team-Dr. Kristopher Dennis!

In this issue, Mr. Matthew Mendonca headlines the very successful University of Waterloo co-op program at the OCC. The article by Ms. Florencia Jon provides those of us who were unable to attend the 2010 Annual Hospice Palliative Care Conference with an overview of this conference.

Physicians often approach end-of-life discussions rationally, as a choice between medical treatment versus treatment withdrawal. However, treatment withdrawal often implies giving up, abandonment, not giving the doctor a chance to do his or her job, and not caring. Dr. Monica Branigan's article discusses the challenges to humane end-of-life treatment conversations.

A remarkable story has been gaining momentum over the past few years. It is the story of the growing cadre of individuals who have been diagnosed and treated successfully for cancer. Dr. Margaret Fitch reports on the new trend in survivorship care.

Anxiety is equivalent to the engine warning light in our car. It is our complex

signal system indicating danger and that we must take action. This enables us to run faster, jump higher, be stronger, breathe harder, and pump enough blood through our bodies—miraculously all within mere seconds. Dr. Eileen La Croix's article discusses panic in cancer patients.

A patient's inability to swallow medication is a complex phenomenon. The impact that dysphagia has on a cancer patient's ability to take medication is underappreciated. The article by Dr. Carlo DeAngelis provides practical advice on "Dysphagia and pill taking in the oncology setting."

Dr. Ewa Szumacher continues to provide the latest list on continuing medical education. The educational insert on "Breakthrough cancer pain: Assessment and management challenges" is well written by Dr. Larry Librach.

We hope you enjoy reading this summer edition of **Hot Spot**!

Humane end-of-life treatment conversations

By Monica Branigan, MD, MHSc(Bioethics)

In our work with patients living with life-limiting illness, health care professionals often need to have difficult conversations. We need to engage in advanced care planning. When a patient, predictably, becomes too ill to make decisions for his or her care, health care professionals need to know who will be making decisions and what the patient would want. For some patients and families, this exercise is a welcome expression of autonomy. For many others, however, this exercise is experienced as a burden. The challenge then becomes: how can we have these conversations in a humane, compassionate way?

I believe these conversations are challenging for three main reasons. First of all, many physicians, nurses, patients and families are death avoidant. Speaking about the end of life may initially cause some anxiety and distress. Not making plans, however, is almost guaranteed to ensure distress among providers and patients when death comes. Planning for that which *can* be controlled is a way of reducing anxiety.

Two decision-making tools support these conversations. The Joint Centre for Bioethics "Living Will" (University of Toronto, 2008) is available for use by fami-

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New trend: Survivorship care

By Margaret Fitch, RN, PhD

A remarkable story has been gaining momentum over the past few years. It is the story of the growing cadre of individuals who have been diagnosed and treated successfully for cancer. The five-year survival rate for individuals diagnosed with cancer is 62% (NCIC, 2010). At present, there are more than one million individuals in Canada who can be considered survivors.

This large cohort of survivors is beginning to help us understand the challenges these individuals continue to face. Because of their cancer and its treatment, a significant number experience late and long-term effects. In essence, although the disease may be gone, the illness impact continues. For some, the situation is chronic in nature.

The after-effects faced by cancer survivors can be grouped into four categories: symptoms of distress, problems related to sleep difficulties and persistent fatigue, existential and spiritual issues, and persistent underlying biological changes that may result in increased risk for other diseases or cancer recurrence (Carlson & Speca, 2007).

Symptoms of distress. Many survivors report experiencing distress to a greater or lesser degree. It can be most acute at the end of treatment, as the individual transitions into survivorship care. Although it may lessen over time, various life events and reminders of the cancer experience can trigger an escalation. The current standard of practice supports the idea of screening for distress (as the sixth vital sign) at every fol-

low-up visit much as one would assess other vital signs. The results of such a screen can be the basis for conversation with the survivor and tailoring subsequent interventions.

Sleep and fatigue. Both sleep disturbances and fatigue are common experiences for cancer survivors. Each can reach a point where the individual feels quite debilitated by their impact. Although both may be difficulties for individuals, some studies have found sleep disturbances to be independent from fatigue levels (Lavidor, Weller, & Babkoff, 2003). Both of these issues ought to be assessed and interventions offered prior to difficulties resulting in crisis.

Existential and spiritual issues. A cancer experience typically brings with it a heightened awareness of mortality and death. It is often a trigger for life transition (e.g., changes in work, relationships, volunteer commitments) to those who survive. Perceived effective life transition can lend to post-traumatic growth (PTG) for individuals.

PTG is receiving increased attention and is defined as the discovery or process of searching for benefits or positive implications for the cancer experience and related life changes. Survivors may benefit by attending specifically designed survivorship transition programs to aid in exploring the potential for benefit funding and well-being.

Biological consequences. Cancer survivors are reported to have higher incidences of lung and heart disease, obesity, and pain syndromes (Keating, Nørredam, Landrum, Huskamp, &

Meara, 2005). As well, they are more likely than the general population to report being in fair or poor health and have limitations in work and functionality (Yabroff, Lawrence, Clauser, Davis, & Brown, 2004). In particular, cardiovascular health is an important consideration for cancer survivors and close monitoring of this parameter is important. Sometimes the evidence of treatment-induced damage may not emerge until years later.

Implication for practice: Survivorship care plans

Although the survivorship group is diverse with different prognosis depending on many factors, a common goal for all is to maintain the best quality of life, with a healthy longevity and survival. Each person needs to have his or her own plan for moving in this direction.

An emerging practice is the creation of a survivorship care plan for each patient at the end of treatment. This plan has six major components:

- Basic Information and Treatment Summary
- 2. Follow-up Surveillance Plan
- 3. Coping and Adjustment Guidelines
- 4. Healthy Living Guidelines
- 5. Resources and Activities for Survivors
- 6. Care Team Members

Best practice calls for this survivorship care plan to be discussed with the patient at the end of treatment and a written copy pro-

Humane end-of-life treatment conversations

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lies and is a Canadian document. Aging with Dignity (2010) has also created "Five Wishes". This guides patients and families through five important wishes:

- 1. The person I want to make care decisions for me when I can't
- 2. The kind of medical treatment I want or don't want
- 3. How comfortable I want to be
- 4. How I want people to treat me
- 5. What I want my loved ones to know.

A second challenge is how we approach these discussions. Physicians often approach these discussions rationally and frame them as a choice between medical treatment versus treatment withdrawal. However, when framed in this manner, treatment withdrawal is a negative choice that often implies giving up, abandonment, not giving the doctor a chance to do his or her job, and not caring (Ambuel, 2002). Thus, patients may view decisions symbolically—care or no care, rather than rationally.

Physicians can reframe the doctorpatient dialogue about end-of-life treatment by starting a conversation with the patient focused on the question "How can we help you live well?" Bernard Hammes suggests that the goal of the living well interview is to elicit the patient's perspective regarding how they want to spend their remaining time. Treatment decisions are then discussed within this broader context of patient goals and hopes rather than narrowly focused on resuscitation preferences.

Additional support for eliciting patient goals comes from David E. Weissman (Weissman, Quill & Arnold, 2010). He believes that many patients align around three major goals or values:

- 1. time
- 2. independence/function
- 3. quality/comfort.

In addition to these broad goals, we also need to consider unique individual patient goals:

- What are you hoping for now?
- What is important to you?
- What do you need to accomplish?
- Who do you need to see in the time that is left?

Treatment decisions can then be framed in terms of their likelihood in achieving these goals, rather than presenting numbers such as likelihood of survival, that may not have meaning to individual patients.

The final major challenge in these discussions is that death is a negotiated event. If patients and families have made treatment choices that vary dramatically from the standard of care, this may serve as a source of conflict with health care providers. These important discussions need to involve physicians and nurses so that goals of the patient align with goals that are possible. Given that what is possible changes over time, these conversations, although challenging, need to occur as a process, rather than as a single event.

Certainly these conversations are challenging. We tend to forget, however, that they may be of tremendous benefit in reducing fear and uncertainty. We do have resources to help us (Center to Advance Palliative Care, 2010). Just last week, the daughter of a dying woman presented me with her mother's copy of the Living Will. She said, "I feel so fortunate to know what my mother wanted and to be able to respect her wishes."

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vided to the individual. The plan can then be used as a guide by the survivor and his/her primary care and community providers.

Significant effort has occurred in the United States regarding the use of survivorship care plans, but their implementation in Canada is just beginning. Clearly, if survivors are to take charge of their lives, beginning with an informed plan is important.

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Dysphagia and pill-taking in the oncology setting

By Carlo DeAngelis, PharmD, Clinical Pharmacy Coordinator—Oncology, Department of Pharmacy, Odette Cancer Centre, Sunnybrook Health Sciences Centre

Dysphagia is a common problem in the oncology setting with many causes ranging from disease- (cancers of the oral cavity, esophagus, stomach, etc.) to treatment-related (oral mucositis, esophagitis, nausea, vomiting, etc.). Optimizing oral pharmacological therapy in a patient with dysphagia poses many challenges. In addition, inappropriate administration of oral medications (e.g. crushing of sustained release formulations) to overcome swallowing difficulties can put the patient at risk for serious side effects (Cornish, 2005; Jackson, Little, Kung, et al., 2008). It is critical that these patients be identified so that a review of their prescribed medication regimen can be performed to assess appropriateness of dosage forms, and strategies being used by the patient and/or caregiver to overcome the swallowing difficulties so as to be able to suggest alternative dosage forms to optimize pharmacological benefit, reduce the occurrence of side effects and ensure adherence to the prescribed therapy. Despite these realizations, the literature regarding the prevalence of and medication swallowing problems in cancer patients is limited.

A patient's inability to swallow medication is a complex phenomenon. Dysphagia can be classified as being either oropharyngeal (difficulty initiating swallowing or moving oral contents from the mouth to the upper esophagus), or esophageal (inability to transfer food from the esophagus to the stomach) in origin or, alternatively, as either structural or functional in origin (Gasiorowska & Fass, 2009). From the perspective of the ability to ingest medication to result is the same, but the strategies to overcome medication-swallowing difficulty may be different depending on the underlying cause. A common strategy to overcome medication swallowing problems is to resort to the use of medications in liquid form, but this my not resolve the problem if the patient has difficulty swallowing liquids. Under certain circumstances, crushing of solid oral dosage forms is also not appropriate. Crushing enteric coated or sustained release formulations may reduce the pharmacological effect of the mediation or produce enhanced and potentially life-threatening consequences respectively (Cornish, 2005; Jackson, Little, Kung, et al., 2008).

When assessing the medication regimen of a patient with dysphagia, the following considerations need to be taken into account:

- Is the patient taking medication formulations that are enteric coated or have altered release characteristics
- Are there liquid formulation alternatives to the medications the patient has been prescribed

- Is the consistency of the liquid formulation alternative to the patient's medication consistent with their ability to swallow fluids
- If it is possible to crush or open the capsule the oral solid dosage form, does crushing the tablet or opening the capsule expose the patient or caregiver to a potentially dangerous substances (e.g., antineoplastic agent)
- Is the patient taking medications that may worsen or contribute to the swallowing problem (e.g. medications with anticholinergic side effects reduce saliva production making it difficult to "wet" food or the tablet/capsule in preparation for swallowing)
- Are there medications that can be discontinued without putting the patient at risk for adverse outcomes?

In developing a medication-taking plan for a patient with dysphagia keep in mind the following:

- Will the patient or caregiver be able to carry out the plan
- Provide clear unambiguous instructions for pill crushing or capsule opening procedures
- Mix the powder from the crushed tablet or capsule in a liquid or food with a consistency appropriate for the patient's swallowing abilities
- Communicate your recommendations to all members of the patient's health care team
- Consider the use of alternative routes of administration (transdermal or parenteral) when appropriate.

The impact that dysphagia has on a cancer patient's ability to take medication is under-appreciated and, often, the patient or caregiver is left to devise solutions, which may or may not put the patient at risk for therapeutic failure or experiencing an adverse event. While the strategies used to help patients with dysphagia take their medications must be individualized, members of the cancer patient's health care team must become more vigilant to medication swallowing problems and devise standardized approaches to assessing medication delivery in this group of patients.

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2010 Annual Hospice Palliative Care Conference

By Florencia Jon, MRT(T), Research Radiation Therapist, Rapid Response Radiotherapy Program and Bone Metastases Site Group, Sunnybrook Odette Cancer Centre

It was another huge success for our program at the second Annual Hospice Palliative Care Conference on April 19–21 this year. Not only did we have as many as 15 posters and oral presentations showcased at the conference; RRRP was also selected by the Ontario Palliative Care Association for a special "Outstanding Leadership Award" for our contribution in clinical services, education and research.

The presentations and posters selected to present at the conference included:

- A multidisciplinary bone metastases clinic at Sunnybrook Odette Cancer Centre: A review of the experience from 2006–2008.
- A survey to assess patients' awareness and interest in hypnosis for cancer pain and distressing procedure.
- 3. International cross-cultural field validation of an EORTC questionnaire module for patients with bone metastases (EORTC QLQ-BM22): A preliminary analysis.

- Organization for research and treatment of cancer brain module (EORTC-QLQ-BN20+) for assessing quality of life in patients with brain metastases—a preliminary analysis of Canadian centres
- Projected referral for health care services in outpatient palliative radiotherapy clinic.
- Evaluation of a daily diary for assessing the prevalence of radiation-induced emesis (RIE): A pilot study in progress.
- 7. Predictive models of survival for patients with advanced cancer.
- 8. Predictive factors anxiety and depression in metastatic cancer patients.
- Response to palliative radiation of bone metastases associated with improved BM22 and C15 symptoms and quality of life.
- Initial BN20+2 and C15 symptom and quality of life scores in patients with brain metastases.
- 11. Pain relief for mechanical and tumourrelated factors from spinal metastases:

- Can we predict who will respond to palliative radiotherapy?
- 12. Radiation treatment of bone metastases—Biased or evidence-based?
- Assessing baseline quality of life in patients with bone metastases using the European Organization for Research and Treatment of Cancer Bone Metastases Module (EORTC QLQ-BM22).
- 14. Patient expectation and understanding of palliative radiotherapy treatment at the RRRP: A quantitative survey.
- Pattern of radiation-induced nausea and vomiting in a palliative radiotherapy clinic.

The conference provided all health care professionals an opportunity to unite and share their visions and practices within the end-of-life care settings. With the theme of "One Vision, One Voice", everyone had the chance to convene, network and share best practices in all areas related to hospice care. We look forward to showcasing more presentations and posters in next year's conference.

Panic in cancer patients: "Fight-or-Flight"

By Eileen Louise La Croix, MSc, MD, FRCPC, Psychiatrist, Psycho-Oncology Clinic, Patient and Family Support Program, Odette Cancer Centre

Anxiety is equivalent to the engine warning light in our car. It is our complex signal system indicating danger and that we must take action. Think of primitive man suddenly seeing a lion baring its teeth and running towards him. Neurologically, he first determines the danger through processing in the prefrontal cortex and insula of the brain. An immediate neurochemical signal is sent to release the normally inhibited amygdala. The message ultimately reaches the sympathetic nervous system causing release of adrenaline. This enables him to run faster, jump higher, be stronger, breathe harder, and pump enough blood through his body-miraculously all within mere seconds.

Anxiety is normal and adaptive. The "fight-or-flight" response has historically helped to ensure our survival. For reasons that may be hereditary, biological, stress related, childhood or lifestyle related, our fear system can become over-sensitized. We begin to react in our minds and bodies as if there was a lion coming at us when there is no danger at all. Researchers believe this is the result of insufficient inhibition of the amygdala in the case of panic attacks.

Anxiety can be extremely disabling when it is intense, lasts longer than expected, or occurs frequently. Cancer patients may present with any number of anxiety-related symptoms ranging from uncontrollable worry, agitation, restlessness, palpitations, insomnia, intractable nausea, obsessions, compulsions, flashbacks, nightmares, avoidance, missed appointments, or specific phobias (e.g., blood, needles, MRI, radiation therapy machines, chemotherapy suite).

Management

Severe anxiety in the oncology clinic setting is extremely frightening for patients, staff, and family. Patients may appear out of control or inconsolable. Optimal care includes prompt recognition and treatment. Assessing patient safety and understanding the multiple possible sources of the anxiety is necessary. First-line management includes psychological support through use of cognitive behavioural and/or exploratory supportive techniques. Patients tend to experience catastrophic thoughts during an anxiety attack. They may think they are having a heart attack, stroke, or are about to die. Calmly correcting faulty self-talk through

direct reassurance is important. A benzodiazepine such as lorazepam 0.5 mg to 1 mg given sublingually is often needed in combination with the psychological support when the anxiety is severe.

Box breathing

One useful behavioural technique is box breathing. Patients with high sympathetic arousal experience shortness of breath, which may result in hyperventilation syndrome. Hyperventilation is self-promulgating, as it decreases the carbon dioxide levels in the blood, increases alkalinity and prevents oxygen transport to the brain and body. Box breathing serves as a reminder that our breathing has four parts: inhalation, a breath pause, exhalation, and another breath pause. The four parts should be equal in time like the four sides of a box. Guiding a patient to control their breathing through tracing the box across the top (inhalation—abdominal), down the right side (breath pause), across the bottom (exhalation—abdominal), and then back up (breath pause) can be an effective treatment of hyperventilation due to psychological

SUNNY SIDE UP

By Matthew Mendonca

Six Years of Unsurpassed Success at the RRRP!

Rapid Response Radiotherapy Program (RRRP). When the name first blipped on the Waterloo co-op radar, they were offering two co-op positions to students in the spring term of 2004. One job was even labelled "Summer Co-op Student". Six years later, the RRRP has become the ultimate hotspot for health research, filling dozens of jobs with Waterloo students.

So what's all the buzz? The RRRP, located at Sunnybrook Health Sciences Centre, is an internationally ranked research-intensive program. Its cutting-edge studies (and the co-op students who help conduct them) are often hot topics in the medical academic community.

The RRRP is renowned for its focus on palliation.

Here at Waterloo, however, the RRRP is regarded as the mecca of successful co-op students. The experience it provides is unlike any other.

Credit: sun

Take a look at the success of Sunnybrook's RRRP, a team of physicians and researchers at the Odette Cancer Centre joined by several Waterloo students each term. The RRRP, along with the Odette Pharmacy Team and the Palliative Care Consult Team (PCCT), are continually making headlines and breakthroughs in the medical community. Just look at the number of times a Waterloo student has been professionally published!

Odette Cancer Centre

Many of the Waterloo co-op students who walk through the doors of Sunnybrook have taken a specific interest in cancer research. The RRRP provides palliative care to relieve the symptoms of patients with advanced cancer. This research team has been the host to more than 15 talented Waterloo co-op students in the past few years. Since 2005, a member of the RRRP has won Waterloo's Student of the Year Award every year. In addition, the Odette Pharmacy Team and the PCCT have grown to include formidable Waterloo co-op students as a part of their lineup.

SE/M

Co-op Students of the Year

2005 2006 2007 2008 2009

Nicole Bradley (AHS)

therapy or surgery.

Amanda Hird (AHS)

Roseanna Presutti (AHS)

Kristin Harris (AHS)

Amanda Hird (AHS)

Between past and present RRRP co-op students, they share...

115

papers published in medical journals

oral presentations delivered 60

56

poster presentations

published book chapters 23

5

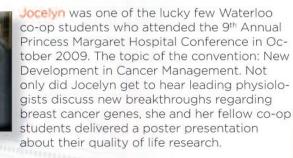
consecutive years of winning the Marion J. Todd Award* (2006 - 2010)

*Award from Faculty of AHS; presented to a female student with high academic success and exceptional experience with health related research

WHAT ARE THEY WORKING ON?

Janet Nguyen and Jocelyn Pang are Waterloo's most recent RRRP coop students. Here's some of the interesting work these talented students completed on their co-op terms.

Janet and the RRRP team investigated the possible use of hypnosis in treating cancer pain. Literature and studies on the subject are scarce, so Janet implemented a survey to find out how many patients are even aware of hypnosis for pain treatment. Knowing that over 50% of cancer patients have pain that goes untreated, the RRRP is exploring various methods of treating pain before resorting to radio-



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Continuing Medical Education 2010

By Ewa Szumacher, MD, MEd, FRCP(C)

Continuing Medical Education (CME) can update health care professionals on the latest advances for modifications to their clinical practice. At the request of the CME organizers, Hot Spot will list the national and international CME activities in palliative medicine that are of interest to our readers. Please forward details of the CME activities to: Ewa.Szumacher@sunnybrook.ca

- September 23–24, 2010
 19th Annual Provincial Conference: The Changing Landscape of Palliative Care, Winnipeg, MB, Canada http://www.manitobahospice.mb.ca
- October 5–8, 2010

 18th International Congress on Palliative Care, Montreal, QC, Canada
 http://www.palliativecare.ca/en/index.html
- October 7–9, 2010
 6th Annual Chicago Supportive
 Oncology Conference, Chicago, IL
 http://www.supportiveoncology.net/chicago2010/index.html
- October 14–17, 2010
 The Canadian Association of General Practitioners in Oncology Annual Meeting: Recent Advances in Oncology Care, Halifax, Canada http://www.agora-event.com/cagpo/
- October 20–22, 2010

 "The Future of Bereavement Care:
 Honouring Stories and Embracing
 Needs"—Bereavement Ontario Network,
 Orillia, ON
 http://www.bereavementontario
 network.ca/confer.html
- October 26, 2010
 8th Annual Palliative Care Conference: Managing Pain in Elders—Challenges and Choices, New York, NY http://www.jewishhome.org/who-we-are/jewish-home-lifecare-news/eighth-annual-palliative-care-conference
- October 28–30, 2010
 10th Annual Princess Margaret
 Hospital Conference: Translating
 Scientific Advances into Clinical
 Practice, Toronto, ON
 http://www.pmhconference.ca/
- October 28–31, 2010
 2010 Canadian Hospice Palliative Care Conference: Changing the National Perspective on Hospice Palliative Care, Ottawa, ON http://conference.chpca.net/chpca/reghome.nsf/pages/registration

- October 29–31, 2010
 14th World Society of Pain
 Clinicians Congress (WSPC) 2010:
 From Ancient to Modern Pain
 Medicine, Beijing, China
 http://www.ccwspc.org/
- October 31-November 4, 2010
 ASTRO's 52 Annual Meeting
 "Gathering Evidence, Proving Value",
 San Diego, CA
 http://www.astro.org/Meetings/
 AnnualMeetings/
- November 3–5, 2010
 Passport to Palliative Care: Journeys and Destinations, Centre for Education and Research on Health and Aging (CERHA) Lakehead University, Thunder Bay, ON http://cerah.lakeheadu.ca/events/
 ?display=events&eventid=131
- November 8–10, 2010
 7th Global Conference—
 Making Sense of: Dying and Death:
 Care, Dying and the End of Life,
 Prague, Czech Republic
 http://www.inter-disciplinary.net/
 probing-the-boundaries/
 making-sense-of/dying-and-death/
 details/
- November 11–14, 2010
 The First International Multidisciplinary Forum on Palliative Care, Budapest, Hungary http://www.imfpc.org/
- November 18–20, 2010
 Excellence in Oncology,
 Athens, Greece
 http://www.excellence-in-oncology.org/
- November 26–27, 2010
 2nd Conference on Positive Aging:
 An Interdisciplinary Team Approach for Health Professionals, Vancouver, BC, Canada
 http://www.interprofessional.ubc.ca/Positive_Aging_2010.html
- April 29–May 1, 2011
 6th World Congress of the World
 Institute of Pain (WIP), Seoul, Korea
 http://www2.kenes.com/wip/Pages/
 Home.aspx
- May 19–21, 2011
 30th Annual Scientific Meeting of the American Pain Society, Austin, TX http://www.ampainsoc.org/meeting/annual_11/

The newsletter of the Rapid Response Radiotherapy Program of the Odette Cancer Centre is published through the support of: Abbott Laboratories, Ltd **AstraZeneca** AstraZeneca 2 **AMGEN**® **Amgen** Boehringer Ingelheim **Boehringer Ingelheim** Celgene GlaxoSmithKline **Kyphon Novartis Ortho Biotech** Pharmascience PURDUE **Purdue Pharma** Roche Roche) Sanofi Aventis sanofi aventis Valeant Canada VALEANT

Vol. 12, Issue 3, August 2010

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Produced by Pappin Communications, Pembroke, Ontario www.pappin.com

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Breakthrough cancer pain: Assessment and management challenges

By S. Lawrence Librach, MD, CCFP, FCFP, Director, Temmy Latner Centre for Palliative Care



Introduction

Cancer pain is a common phenomenon in oncology practice with more than 70% of patients with advanced cancer having moderate to severe pain. Many of these patients, 40% to 80%, will have what is called breakthrough pain. Breakthrough pain (BTP) is a transient exacerbation of pain experienced by a patient who had relatively stable and adequately controlled baseline pain. This phenomenon of BTP has been discussed for many years, but the pathophysiology and neurophysiology of this type of pain has yet to be determined and the management has been very empirical. Recent attention has been focused on BTP and newer approaches to management have an evidence base that was lacking in the past. In this article, the classification of BTP, its components and a best practices approach to management will be discussed.

Classification and characteristics of BTP

There is no consensus on the classification of BTP. As interest in BTP has increased, new terminologies have been proposed including intermittent or episodic pain. There are components, though, which are common in all terminologies or classifications:

- a) Any baseline pain should be under stable and "good" control.
- b) End-of-dose failure, which is pain that consistently occurs before the scheduled around-the-clock dose, usually indicates an inadequate analgesic dose. This is not seen as BTP by most authors.
- c) Incident pain is intermittent but predictable pain related to a specific precipitant, which may be voluntary

- (e.g., after movement, as with bone metastases) or involuntary (e.g., with cough or sneeze). Incident pain may occur with or, more infrequently, without a background of continuous pain or prescribed around-the-clock analgesics. Incident pain typically is quick in onset.
- d) Spontaneous BTP may occur without any precipitating factor with any type of cancer pain. It may be inflammatory, visceral or neuropathic in origin and there is no clear evidence why this type of pain occurs in the face of stable, normally well controlled pain.
 Spontaneous pain may be rapid in onset, but often builds slowly to a crescendo.
- e) Generally, BTP is short in duration lasting a few seconds (e.g., lancinating neuropathic pain) to minutes (e.g., bone pain on movement), but some spontaneous pains may last for hours.

Impact of BTP

BTP has been associated with:

- Poor overall pain control with higher levels of baseline pain and peak pain
- Decreased satisfaction with overall pain management (e.g., 78% of patients with chronic pain satisfied with treatment versus 25% of patients with BTP)
- Multiple physical (e.g., insomnia), psychological (e.g., anxiety, depression) and social (e.g., isolation) complications
- Significant functional impairment
- A significant negative effect on quality of life
- Increased health care costs.

Therefore effective assessment and management of BTP can be very important to patients and their families.

Assessment of BTP

Assessment of BTP depends on careful questioning of the patient. There are a number of clinical assessment tools that have been developed that assist in asking questions to determine the type of BTP. When considering BTP, the following questions should be asked of the patient:

- 1) How well is the baseline pain controlled? Poorly controlled pain is not BTP.
- 2) Is there a specific time in the taking of around the clock analysesics when pain appears "spontaneously? This question may indicate end-of-dose failure.
- 3) Is the pain related to any voluntary or involuntary (e.g., coughing) movement?
- 4) What is the temporal nature of the pain: how quickly does it come on, how quickly does it resolve, how many times in an hour/day/week.
- 5) What is the severity of the pain?
- 6) What do you do to relieve the pain? How many extra doses of analgesics are you taking? Are you missing doses of analgesics and why?
- 7) Are there any other symptoms such as nausea that are associated with the intermittent pain?
- 8) How does the BTP impact your function and your quality of life?

A physical examination is important, as usual, to find bony tender points, changes in palpable masses or new problems such as evidence of bowel obstruction.

A review of imaging or ordering of new imaging may be required.

Management of BTP

The evidence base for the management of BTP in cancer is increasing, but there are still some basic principles that must be considered in managing this type of pain:

- a) Educate the patient and family and other care providers about the nature of BTP and its treatment.
- b) Ensure that baseline pain is correctly managed.
- c) Involve the patient and family in monitoring the outcomes of the treatment of BTP.
- d) Always consider adjuvant modalities to aid in the management of BTP.
- e) Consult cancer pain or palliative care specialists as necessary.

Non-pharmacological approaches

a) Chemotherapy and radiotherapy

There is no clear evidence that chemotherapy can produce immediate help for BTP. Analgesics should be used while awaiting the response to chemotherapy. Radiotherapy, on the other hand, may be the most effective treatment for baseline pain and associated incident BTP from bone metastases.

b) Physical and occupational therapy

Seeking the advice of physical and occupational therapists may be helpful to help control incident pain. Specific splints and braces and mobility aids may help these patients. As well, these therapists can instruct patients and families on the best ways to move to avoid precipitating BTP. Techniques such as TENS, massage, and visualization may also be helpful in some patients as adjuvant techniques.

c) Surgery

Orthopedic surgeons should be consulted, as necessary, for the possible surgical management of incident bone pain. Bowel or duct obstruction causing BTP may require the intervention of surgical oncologists.

Breakthrough cancer pain: Assessment and management challenges

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d) Interventional anesthesia and neurosurgical approaches

Anesthetic approaches (e.g., nerve block, chemical neurolysis, intrathecal infusions) and surgical interventions (e.g., cordotomy) are generally considered after all other approaches have failed.

Pharmacological approaches

a) Adjuvant analgesics

For lancinating neuropathic BTP, the usual neuropathic adjuvants such as the antidepressant and anticonvulsant adjuvants should be prescribed. NSAIDs may be helpful on occasion in managing bone pain, but there is little evidence for efficacy in managing incident pain. Bisphosphonates have no proven efficacy in managing BTP.

b) Immediate release opioids

The mainstay of treatment of BTP until recently has been the immediate release opioids such as morphine, oxycodone and hydromorphone. The main drawback to oral IR opioids is the 30 to 60 minutes it takes for onset of the analgesic effects. For patients with spontaneous BTP, if

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they can take these IR opioids as the pain is beginning to get stronger, they may be able to reduce the BTP considerably. For voluntary incident pain, IR opioids can be taken prophylactically before movement, although this is often impractical and is not very effective. Using intravenous or subcutaneous IR opioids like morphine or hydromorphone may be more effective, but increases the complexity and costs of treatment.

c) Transmucosal fentanyl

In Canada, we will see, in the near future, the introduction of several different formulations of oral and nasal transmucosal fentanyl for the management of BTP. These preparations make use of the excellent potency and lipophylic properties of fentanyl that enable it to cross mucous membranes unlike other opioids. In Canada, palliative care specialists have been using the parenteral form of fentanyl applied to oral membranes, but this method presents difficulties with administration and dose titration. These new formulations are generally easier to administer and titrate.

All the formulations share common characteristics:

- Rapid onset, usually within 10 to 15 minutes to effective pain control and a T₁₆ of three to six hours.
- 2) All avoid first pass metabolism of fentanyl.
- 3) Easy administration and preference by patients over the oral IR opioid route.
- 4) Similar adverse effects as all opioids.
- 5) Not to be used in opioid naïve patients.
- 6) Metabolism through the cytochrome P450 process and, therefore, the possibility of interaction with drugs using the same route of metabolism.

- 7) All have the possibility of abuse and diversion like all opioids.
- 8) All should be used by prescribers experienced in prescribing opioids. They all require careful titration and monitoring.

Formulations of Transmucosal Fentanyl

Oral transmucosal fentanyl citrate lozenge

Sublingual fentanyl tablet

Fentanyl buccal tablet

Bioerodible mucoadhesive buccal film

Intranasal fentanyl

i) Oral transmucosal fentanyl lozenges

(OTFC) have been available in the U.S. and in Europe for some time for BTP.
OTFC produced greater analgesic effect, increased global satisfaction and more rapid onset of action than usual rescue medication or placebo. It has been proved safe and effective for long-term use. There is evidence that OTFC can significantly reduce visits to emergency and rates of hospital admission.
However, this preparation is not likely to be introduced in Canada because of Health Canada's concerns about safety of this lollipop-like formulation.

ii) Fentanyl buccal tablets (FBT)

FBTs are of two types. One utilizes effervescent reaction that is accompanied by transient change in pH to facilitate tablet dissolving and enhanced absorption of un-ionized fentanyl across buccal mucosa and with increased early systemic uptake of fentanyl.

Doses should be reduced by 30% compared with dose of OTFC. Another type of tablet adheres to the oral mucosa where it slowly releases fentanyl. Both of these are currently under review by Health Canada.

iii) Bioerodible mucoadhesive buccal film (FBSF)

This film is applied to the oral mucosa where it slowly dissolves releasing fentanyl through the mucosa. This is the only formulation currently approved in Canada. It has greater bioavailability than OTFC and a higher C_{max} . Time to first detectable plasma concentration eight to 11 min with T_{max} in the range of 40 minutes to 57 minutes. Experience so far is limited, but studies have shown efficacy and good patient acceptance.

iv) Intranasal fentanyl (INF)

INF can only be given in small volumes of <200 mcL at a time, as a nasal spray, in order to avoid runoff into the pharynx because of the relatively small surface area of the nasal mucosa. It is rapidly absorbed into systemic circulation from highly vascularized and extensively perfused nasal mucosa, avoiding first-pass metabolism. INF has been shown to be safe, effective and well tolerated in regulatory studies. It is under review by Health Canada.

Summary

BTP is an important source of suffering for cancer patients who have pain with considerable impact on quality of life. Effective assessment and a multimodal approach can be effective. The new transmucosal fentanyl products may represent an important step in managing BTP effectively.