PUTTING EVIDENCE INTO PRACTICE: IMPROVING ONCOLOGY PATIENT OUTCOMES

Pharmacologic and Nonpharmacologic Interventions for Pain

Introduction

A variety of treatments such as chemotherapy, radiation therapy, and other approaches to shrink tumors are known to result in pain reduction. This resource does not consider these approaches for cancer-related pain management. It is also well recognized that opioids are a mainstay of pain management for both nociceptive and neuropathic pain. Simple opioid use is not fully considered in this synthesis of evidence except where there are uses that are innovative compared to current guidelines, differing time-release formulations, varied administration routes, or pain management involving drug combinations with various coanalgesics in addition to opioids.

This update of the 2009 ONS PEP resource for cancer-related pain is also intended to begin to integrate nonpharmacologic interventions and pharmacologic interventions. Nonpharmacologic approaches summarized here include evidence from systematic reviews or meta-analyses from January 2000 to April 2011 and other relevant evidence sources from April 2008 to April 2011. The search strategy and criteria for inclusion are shown in the Appendix.

The PEP project team of nurse scientists and clinicians categorized individual interventions based on the decision rules shown in Figure 1.

Problem

Cancer-related pain is a complex problem that negatively impacts quality of life. Its causes are related to the disease and its progression, treatment, and mechanisms unrelated to cancer or its treatment. Cancer-related pain is acute or chronic and may also be further defined as breakthrough or intractable.

- **Acute pain** is typically related to diagnostic procedures and cancer treatment and is generally defined as lasting three months or less. The most common types of acute pain related to treatment are postoperative pain and oral mucositis (Miaskowski et
### Recommended for Practice

*Interventions for which effectiveness has been demonstrated by strong evidence from rigorously designed studies, meta-analyses, or systematic reviews and for which expectation of harms is small compared with the benefits*

- Supportive evidence from at least two well-conducted randomized controlled trials that were performed at more than one institutional site and that included a sample size of at least 100 participants
- Evidence from a meta-analysis or systematic review of research studies that incorporated quality ratings in the analysis and included a total of 100 patients or more in its estimate of effect size and confidence intervals
- Recommendations from a panel of experts that derive from an explicit literature search strategy and include thorough analysis, quality rating, and synthesis of the evidence

### Likely to Be Effective

*Interventions for which the evidence is less well-established than for those listed under Recommended for Practice*

- Supportive evidence from a single well-conducted randomized controlled trial that included fewer than 100 patients or was conducted at one or more institutions
- Evidence from a meta-analysis or systematic review that incorporated quality ratings in the analysis and included fewer than 100 patients or had no estimates of effect size and confidence intervals
- Evidence from a synthetic review of randomized trials that incorporated quality ratings in the analysis
- Guidelines developed largely by consensus/expert opinion rather than primarily based on the evidence and published by a panel of experts that are not supported by synthesis and quality rating of the evidence

### Benefits Balanced With Harms

*Interventions for which clinicians and patients should weigh the beneficial and harmful effects according to individual circumstances and priorities*

- Supportive evidence from one or more randomized trials, meta-analyses, or systematic reviews but where the intervention may be associated, in certain patient populations, with adverse effects that produce or potentially produce mortality, significant morbidity, functional disability, hospitalization, or excess length of stay

### Effectiveness Not Established

*Interventions for which there are currently insufficient data or data of inadequate quality*

- Supportive evidence from a well-conducted case control study
- Supportive evidence from a poorly controlled or uncontrolled study
- Evidence from randomized clinical trials with one or more major or three or more minor methodologic flaws that could invalidate the results
- Evidence from nonexperimental studies with high potential for bias (such as case series with comparison to historical controls); evidence from case series or case reports
- Conflicting evidence but where the preponderance of the evidence is in support of the recommendation or meta-analysis showing a trend that did not reach statistical significance

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Figure 1. PEP Decision Rules for Summative Evaluation of Evidence (Continued)

Effectiveness Unlikely

*Interventions for which lack of effectiveness is less well-established than for those listed under Not Recommended for Practice*
- Evidence from a single well-conducted randomized trial with at least 100 participants or conducted at more than one site and which showed no benefit for the intervention
- Evidence from a well-conducted case control study, a poorly controlled or uncontrolled study, a randomized trial with major methodologic flaws, or an observational study (e.g., case series with historical controls) that showed no benefit and a prominent and unacceptable pattern of adverse events and serious toxicities (CTCAE grade III/IV)

Not Recommended for Practice

*Interventions for which ineffectiveness or harmfulness has been demonstrated by clear evidence, or the cost or burden necessary for the intervention exceeds anticipated benefit*
- Evidence from two or more well-conducted randomized trials with at least 100 participants or conducted at more than one site and which showed no benefit for the intervention and excessive costs or burden expected
- Evidence from a single well-conducted trial that showed a prominent and unacceptable pattern of adverse events and serious toxicities (CTCAE grade III/IV)
- Evidence from a meta-analysis or systematic review of research studies that incorporated quality ratings in the analysis, included a total of 100 patients or more in its estimate of effect size, and confidence intervals with demonstrated lack of benefit or prominent and unacceptable toxicities
- Intervention discouraged from use by a panel of experts in the related subject, after conducting a systematic examination, quality rating, and synthesis of the available evidence

CTCAE—National Cancer Institute Cancer Therapy Evaluation Program Common Terminology Criteria for Adverse Events


al., 2005). Acute pain in patients with cancer may also be due to arthralgia or myalgia as side effects of some chemotherapy drugs and biologic therapy.

- **Chronic pain** persists for three months or more. The most frequent cause of cancer-related chronic pain is bone metastasis (Miaskowski, 2010). Chronic pain may also be a result of cancer treatment including surgery, chemotherapy, and radiation therapy.
- **Breakthrough pain** may occur when pain is fairly well controlled. It is sudden, brief, and may occur at rest or related to activity or a change of position in a patient who has chronic pain and is receiving opioids (Fitzgibbon & Loeser, 2010).
- **Intractable pain** or **refractory pain** occurs when pain cannot be adequately controlled despite aggressive measures (Fitzgibbon & Loeser, 2010).

The etiology of pain is classified as nociceptive, neuropathic, or both. Nociceptive pain is caused by tissue damage and inflammation (Fitzgibbon & Loeser, 2010). Neuropathic pain results from damage to the peripheral or central nervous system (Challapalli, Tremont-Lukas, McNicol, Lau, & Carr, 2005). Common neuropathic pain
syndromes include chemotherapy-related peripheral neuropathic pain and iatrogenic neuralgias that occur after surgery, such as mastectomy, amputation, or thoracotomy. Post-radiation myelopathy is a central neuropathic pain syndrome that patients with cancer experience (Curry & Fausel, 2007).

Cancer-related pain rarely occurs in isolation of other symptoms. Individuals with cancer-related pain may experience fatigue, sleep disturbance, depression, and loss of appetite (Fitzgibbon & Loeser, 2010; Gaston-Johannson, Fall-Dickson, Bakos, & Kennedy, 1999; Miaskowski & Lee, 1999). Pain, fatigue, and depression have been identified as a symptom cluster in individuals with cancer. To be classified as a cluster, symptoms must be related to one another and occur concurrently. This symptom cluster may be related through a common underlying pathophysiologic mechanism such as systemic inflammation (Fallon, Colvin, & Laird, 2010).

Cancer-related pain is highly subjective and unique to each individual experiencing it. It is a multidimensional phenomenon consisting of six dimensions—physiologic, sensory, affective, cognitive, behavioral, and sociocultural (McGuire, 1995). These dimensions are useful as a framework for the assessment, management, and study of cancer-related pain. A multimodal approach to managing pain is critical to achieving optimal patient outcomes.

Incidence

The prevalence of cancer-related pain has been estimated to be 44%–73% in patients receiving cancer treatment and 58%–69% in patients with advanced disease (van den Beuken-van Everdingen et al., 2007). Patients with all types of cancer experience pain. Patients with head and neck cancer tend to have the highest prevalence of pain. Breakthrough pain occurs frequently in patients with cancer and has been found to range from 19%–95% (Mercadante et al., 2002; Zeppetella & Ribeiro, 2003). The wide variability in prevalence is related to different definitions for breakthrough pain used by cancer pain researchers.

Prevention

Acute pain in patients undergoing procedures and cancer treatment is prevented through accurate assessment and adequate analgesia and anesthesia prior to and during the procedure or treatment. Post-procedural and post-treatment pain can be prevented or managed appropriately with continuous assessment, reassessment, and regular analgesic medication administration. Chronic cancer pain may be controlled through early aggressive pain management as emerging evidence indicates (Maltoni et al., 2005; Tessaro et al., 2010). Assessment of pain severity and occurrence of breakthrough episodes is key to determining the most effective standard medication dosing and overall symptom management in order to prevent increased pain and breakthrough episodes.

Palliative Care

Palliative care provides relief of pain and other distressing symptoms without curing the underlying disease (World Health Organization, n.d.). Its goal is to
improve the quality of life of patients and families who face an incurable disease. A team approach is used to provide support from diagnosis to end of life. Adequate pain assessment and treatment is fundamental to the delivery of effective palliative care.

**Survivorship Issues**

Improved cancer treatment has led to increasing life expectancy and cure rates in many cancer types. The prevalence of chronic pain in long-term cancer survivors has not been studied as well as pain in patients receiving cancer treatment or with advanced disease (Burton, Fanciullo, & Beasley, 2007). A recent systematic review found the prevalence of pain in cancer survivors to be 30% (van den Beuken-van Everdingen et al., 2007). Most chronic pain in cancer survivors is a result of cancer treatment. Successful pain management is essential to optimizing quality of life and functionality in cancer survivors. The same approaches used in patients with chronic pain apply to cancer survivors; however, the therapeutic focus shifts to a management and adaptive coping strategy rather than finding a cure for the pain (Burton et al., 2007). The possibility of a significant pain exacerbation being related to a recurrence of cancer is a problem that is unique to cancer survivors; thus, careful attention to the patient’s emotional and psychological state is needed (Gonzales, Elliot, Portenoy, & Foley, 1991).

**Assessment**

Pain assessment and management are oncology nursing priorities. High-quality pain management begins with a careful patient assessment. Screening for the presence of pain is followed by a comprehensive assessment when pain is present. Pain location, intensity, duration, frequency, quality, and modulating factors are components of a pain assessment (Fitzgibbon & Loeser, 2010).

Self-report is the gold standard for pain assessment (Chang, Hagen, & Lee, 2007). Unidimensional pain scales provide measurement of one dimension of pain. Pain intensity may be measured with scales such as numeric rating scales, verbal rating scales, Likert scales, and visual analog scales. A visual analog scale is simply a 100 mm line with an anchor of “no pain” at the low end, and an anchor of “as bad as it could be” at the 100 mm mark. For the visual analog scale, pain greater than 30 mm out of 100 mm is generally clinically significant (Collins, Moore, & McQuay, 1997).

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