The Management of Pain in Patients With Cancer

Presented by Robert A. Swarm, MD

Abstract

More than 30% of patients with cancer report chronic pain, which is an indication of both the frequency of cancer-related pain and the failure to optimally manage it. Although access to opioid analgesics has greatly improved over the past 25 years, much remains to be done for patients experiencing severe pain. Opioids are far from ideal analgesics, noted Dr. Robert A. Swarm at the recent NCCN 18th Annual Conference. Universal screening for cancer pain is part of the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Adult Cancer Pain. This is not a one-time effort but should be part of management throughout the cancer care continuum. (JNCCN 2013;11:702–704)

“A bad death is a medical emergency,” said Robert A. Swarm, MD, during a presentation at the recent NCCN 18th Annual Conference, quoting Dame Cicely Saunders, the mother of the hospice movement. Dr. Swarm is Professor of Anesthesiology and Chief of Pain Management at Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine and Chair of the NCCN Panel on Adult Cancer Pain.

The key current goals for controlling cancer pain are to 1) fully integrate symptom control into comprehensive cancer care, which includes prevention, detection, and treatment; 2) develop and implement disease- and site-specific cancer pain management protocols; and 3) provide pain management care paths for cancer survivors, 30% to 40% of whom are left with chronic cancer-related pain.

Too often, Dr. Swarm said, “We wait for patients to present with pain at a magnitude of 8 or 9 on a 10-point scale. We don’t have care paths in place to help us identify patients at risk for that severe pain and to implement therapies in a prospective way. We need to respond to poor symptom control with urgency, but the goal is to avoid the emergency and treat according to a consistent care path.” Pain management must be a priority, and this will require clearly defined medical leadership in this area, he added.

The WHO Analgesic Ladder and NCCN Guidelines

Since the WHO published its 3-tiered analgesic ladder in 1986, opioid access for cancer care has improved worldwide. By 2010, the global average opioid consumption (by morphine equivalence) was approximately 70 mg/person (700 mg/person in the United States), a dramatic uptick from about 3 mg per person before the WHO’s intervention—though in some developing countries opioid use still remains less than 0.01 to 0.1 mg per person per year.

Current NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) “go much further” than the WHO Analgesic Ladder, he noted. The NCCN Guidelines mandate universal screening for pain in all patients at each contact. Patients who report pain must undergo a comprehensive pain assessment to determine pain etiology, pathophysiology and severity, and the patient’s goals for function and comfort (Figure 1). “The patient’s own report of pain, the subjective experience, is what is important,” Dr. Swarm emphasized.

The prescription of analgesics is stratified according to whether patients are opioid-naive, opioid-tolerant, or have pain related to painful events and procedures. The
Comprehensive Pain Assessment

- Patient’s self report of pain is the standard of care.
- Pain experience – evaluated, defined
  ➤ Characteristics, impact
  ➤ Efficacy of prior treatment
  ➤ Consequence, impact of pain, pain Rx
- Psychosocial impact, needs assessment
  ➤ Patient, family
- Medical history

Figure 1  The main points of the comprehensive pain assessment. For the full comprehensive assessment, visit the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Adult Cancer Pain, available on NCCN.org.

“ongoing care” portion of the NCCN Guidelines reinforces the management goals from diagnosis throughout survivorship; if goals are not being met, the assessment is performed again, new treatment options are sought, and consultation with palliative care or pain specialists is considered.

Risk Factors for Poor Pain Control

A landmark study in 1994 identified a number of factors that predict for “negative pain management,” including physician’s underestimation of pain, underlying pain not cancer-related, good performance status, racial minority, age 70 or above, and female gender.1 Fisch et al2 recently reviewed contemporary oncologic pain management in a prospective observational study involving 3123 outpatients from 38 oncology institutions. They found that adequate pain treatment was most often associated with the following characteristics:

- Non-Hispanic white race
- Treatment at sites with more than 60% non-Hispanic white patients
- Poor performance status (ECOG ≥ 2)
- Advanced cancer with ongoing treatment
- Physician attributed pain to cancer
- Physician judged pain to be patient’s worst symptom

They further found that 67% of patients reported pain or analgesic use, confirming a high prevalence of pain in cancer patients. Of those with pain or pain treatment, 67% rated pain control as acceptable but 33% rated it as inadequate. At the initial evaluation, physicians ranked pain as the patient’s worst symptom in 22%. Further, 19% of patients rated their pain as moderate to severe, and 41% of these individuals had no prescription for opioids. Of patients reporting severe pain, 20% had no prescription for any analgesic. Even in modern oncologic practice in the United States, cancer pain continues to be undertreated in a significant number of cases.

Barriers to Pain Management

Barriers to pain management occur within patient, physician, disease/treatment, and health care system domains. A reluctance to communicate about pain is seen among patients and physicians alike, as are misconceptions about treatment, such as fears of opioid addiction, side effects, and diversion. A lack of education is a factor, as is underuse of available treatments.

Access to care, especially to affordable medication (Figure 2), is a healthcare system problem, as is a burdensome reimbursement process and complex regulatory system. Progressive disease and neuropathic pain hamper effective pain control as well.

Concerns about drug abuse and overdose led to the FDA’s Risk Evaluation and Mitigation Strategies (REMS) programs. REMS programs are in place for transmucosal fentanyl formulations and are being implemented for long-acting, extended-release opioids. They are likely to change the standard of care for the prescribing of analgesics, according to Dr. Swarm. “Buckle your seatbelt for prescribing opioids. We need to improve safety in our prescribing of these necessary medications, but we must do so in a way that does not unduly limit access to them for essential pain control. REMS programs are likely to have a significant impact on new drug development,” he predicted.

The Challenges of Treating Cancer Pain

Chronic cancer pain, reported by 30% to 40% of patients, is not simply long-lasting acute pain but a neuroanatomic disease that has nociceptive, neuropathic, affective, cognitive, and behavioral components. Opioid analgesics are the best available medications when this pain is severe, but they are not ideal, Dr. Swarm said.

Opioids provide only incomplete analgesia for neuropathic pain (especially mechanosialodynia, such as pain associated with light touch, as may be seen after shingles or other nerve injury, severe somatic pain (bony fractures, wound debridement), and episodic pain. A ceiling effect occurs at high-dose opioid (eg, intravenous morphine ≥ 100 mg/hour in some patients). For these patients, all their opioid receptors
appear to be occupied at this dose; pain actually may be worsened by increasing the dose.

The adverse events of opioid use are well known, but tolerance-induced hyperalgesia and the potential for opioid-induced oncogenesis are recent concerns. The latter is thought to be possible through immunosuppression, stimulation of angiogenesis, and possibly direct opioid stimulation of tumor cells, which might promote tumor proliferation and migration.3 Although demonstrated in animal models, the clinical significance of opioid-induced oncogenesis in humans is uncertain, Dr. Swarm said.

Tolerance-induced hyperalgesia, however, has become a clinical concern that is “modifying the enthusiasm for opioids,” he added. Hyperalgesia involves pain sensitization and facilitation due to receptor modification, alteration of gene regulation, and excitotoxicity of spinal (inhibitory) neurons, and it is fairly common with daily opioid use. New research suggests that epigenetics (environmentally-induced alterations in gene transcription) may be an underlying mechanism. Pain-specific gene demethylation, with its subsequent increase in gene transcription, appears to be involved in facilitation of pain signal transmission after injury and inflammation.4 Opioid receptor DNA methylation, associated with chronic opioid administration, correlates with opioid tolerance and increased chronic pain in experimental studies.5

Management of hyperalgesia is challenging. Strategies include minimizing and rotating opioids, treating with non-opioid analgesics, involving a multidisciplinary pain management team, and using interventional pain management therapies.

Cancer Pain Management in 2013

The International Association for the Study of Pain issued the Declaration of Montreal6 in 2010 that called for recognition of the following:

- The right of all people to have access to pain management without discrimination,
- The right of people in pain to acknowledgment of their pain and to be informed about how it can be assessed and managed, and
- The right of all people with pain to have access to appropriate assessment and treatment of the pain by adequately trained health care professionals.

To this end, broadening the scope of treatments beyond systemic analgesics is necessary. Disease-specific treatments that also incorporate psychological, behavioral, and rehabilitation services are especially important for cancer survivors. Additionally, anesthetic and interventional treatments, including neurosurgical approaches, have a role in some cases of otherwise intractable pain. Palliative care should be incorporated into cancer treatment at the start of the cancer continuum.

Fortunately for patients, pain control is becoming a priority for health care systems as part of the HCAHPS program (Hospital Consumer Assessment of Healthcare Providers and Systems). HCAHPS includes consistent pain control among the measures of patient satisfaction that help determine value-based purchasing. “Hospitals only get credit when patients report good pain control and indicate their health care providers did all they could to control the pain.”

In addition, for accreditation in 2015 by the American College of Surgeons, cancer centers must incorporate universal distress screening (which includes pain) for all cancer patients. Screening tools are already available in the NCCN Guidelines.

**References**