

11. CANCER PAIN AND PALLIATION

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While supportive care was not one of the original clinical areas selected for the development of quality indicators, the Oncology and HIV Panel felt that this was a significant omission. Based upon the panel's recommendations, the staff drafted four indicators for cancer pain management and the treatment of vomiting. The panel accepted two indicators for pain management and one indicator for the prevention of chemotherapy-induced emesis. The core references for this chapter include a chapter on cancer pain in the textbook *Supportive Care* (Cherny, 1998), the AHCPR (Jacox et al., 1994) and ASCO (1992) clinical practice guidelines for the management of cancer pain, and the National Cancer Institute (1997) statement on the management nausea and vomiting from CancerNet PDQ Information for Health Care Professionals.

CANCER PAIN

Importance

Cancer is diagnosed in over 1 million Americans each year. Approximately 8 million Americans either currently have cancer or have a history of cancer (Jacox et al., 1994). The prevalence of pain in patients newly diagnosed with cancer is approximately 30 percent. In patients with advanced disease, the prevalence of pain approaches 80 percent (Cherny, 1998). Among cancer patients with pain, 40 to 50 percent report it to be moderate to severe and an additional 25 to 30 percent describe it as very severe (Jacox et al., 1994).

Diagnosis

Cancer pain is frequently undertreated and the most important reason for this is inadequate assessment (Jacox et al., 1994; Cherny, 1998.). Studies have shown that the most important predictor of inadequate pain relief is a discrepancy between the patient's and physician's evaluation of the severity of the pain (Cherny, 1998; Jacox et al., 1994). For this reason, the AHCPR Guideline makes this recommendation: "Health professionals should ask about pain, and the patient's self-report should be the primary source of assessment" (Jacox et al., 1994).

Initial pain assessment should include a description of its character and intensity (Cherny, 1998; Jacox et al., 1994; ASCO 1992). Pain rating scales can be useful adjuncts to patient's qualitative description of the pain and are recommended in the AHCPR and ASCO guidelines (Jacox et al., 1994; ASCO, 1992). In addition, a complete physical exam, as well as appropriate diagnostic tests, should be performed to attempt to localize the pain and determine its cause (Cherny, 1998; Jacox et al., 1994; ASCO, 1992).

Pain associated with cancer can have many etiologies. Acute pain may be the result of diagnostic or therapeutic procedures, anticancer therapies (such as the intravenous infusion of chemotherapy), infections, or paraneoplastic complications (such as thromboses). Most chronic cancer pain is caused by the local effects of the tumor on bones or nerves. Bone metastases are the most common cause of chronic pain in cancer patients (Cherny, 1998).

Based upon these guidelines and the advice of our expert panel, we proposed, and the panel accepted, a quality indicator that requires an assessment of cancer pain at least once every six months for all patients with cancer metastatic to bone (Jacox et al., 1994; ASCO 1992) (Indicator 1). While all cancer patients should be vigilantly evaluated for pain on an ongoing basis, this indicator is limited to patients with metastases to bone since this well-defined group has the highest prevalence of cancer pain. Furthermore, in the absence of published guidelines on the frequency of pain assessment, we have selected every six months as a *minimum* requirement.

Treatment

Cancer pain can be controlled in approximately 90 percent of patients with standard analgesic therapy (Jacox et al., 1994). The World Health Organization has developed a well-validated and widely accepted analgesic ladder for the effective titration of pain medications in cancer patients (WHO, 1996; Berger et al., 1998; Jacox et al., 1994; ASCO 1992). This analgesic ladder has three steps. The first step, for mild pain, is a non-steroidal analgesic medication (NSAID). For moderate pain, or pain that does not respond to step one, the clinician should move to step two: a weak opioid, such as codeine or hydrocodone, in combination with an NSAID. Patients with severe pain, or pain that is not relieved by the step two approach, should be treated with step three medications: strong opioid drugs such as morphine, hydromorphone, methadone, or fentanyl. The opioid doses

should be increased as needed to control pain. Based on the WHO approach, and AHCPR and ASCO guidelines, we proposed an indicator requiring that cancer patients whose pain is uncontrolled be offered a change in pain management within 24 hours of the pain complaint (Jacox et al., 1994; ASCO 1992) (Indicator 2). The panel accepted this indicator.

Palliative radiation therapy is an important adjuvant to the pharmacological treatment of pain. Radiation therapy is indicated in the treatment of symptomatic metastases where tumor infiltration has caused pain, compression, bleeding or obstruction (Jacox et al., 1994; Cherny, 1998). The treatment of bony metastases with localized radiation therapy results in at least partial relief of symptoms in over 70 percent of patients (Jacox et al., 1994; Berger et al., 1998). However, the effectiveness and durability of radiation therapy in producing pain relief is dependent upon the location of the tumor as well as the type (some tumors are less radiosensitive.) In addition to external beam radiation, systemic radioisotopes, such as Strontium-89, are also available. Systemic radioisotopes provide an attractive alternative for patients with widely disseminated bone metastases (Jacox et al., 1994; Berger et al., 1998). The AHCPR Guideline recommends that non-invasive pharmacologic analgesic therapies be attempted prior to the more invasive approach required with radiation therapy. The Oncology and HIV Expert Panel considered a quality indicator specifying that patients with painful bony metastases, who are unresponsive to or intolerant of narcotic analgesia, should be offered radiation therapy or Strontium-89 within one week (Indicator 3). This indicator was dropped by the panel due to low validity and feasibility scores.

CHEMOTHERAPY ASSOCIATED EMESIS

Importance

Prevention and treatment of nausea and vomiting in cancer patients is of paramount importance as the symptom can lead to serious metabolic derangements, deterioration of physical and mental well-being, decreased functional status, and withdrawal from potentially curative treatment. (National Cancer Institute, 1997) Five different emesis syndromes have been identified and described in patients receiving chemotherapy:

1. *Acute chemotherapy-induced emesis* is defined as nausea and vomiting that occurs within the 24-hour period immediately following chemotherapy administration.
2. *Delayed emesis* begins after the first 24-hours following chemotherapy.
3. *Anticipatory emesis* is a behaviorally conditioned response that occurs prior to subsequent chemotherapy in response to a stimulus (such as the nurse starting the intravenous line.)
4. *Breakthrough emesis* is vomiting that occurs on the day of chemotherapy in spite of appropriate prophylaxis.
5. *Refractory emesis* is vomiting that occurs despite optimal antiemetic treatment in previous course (Cherny, 1998).

The most important factor in determining whether a patient experiences nausea and vomiting with chemotherapy is the emetogenicity of the chemotherapy (Hasketh et al., 1997; National Cancer Institute, 1997; Cherny, 1998). Chemotherapy agents are classified according to their emetogenic potential, based upon the percentage of patients who will experience emesis with that drug administered as a single agent (Hasketh et al., 1997; National Cancer Institute, 1997; Cherny, 1998). In addition, the potential for emesis with most chemotherapy agents increases with increasing dose and can often be worsened when it is given in combination with other agents (Hasketh et al., 1997).

Treatment

There are many drugs available to treat chemotherapy associated emesis, including prochlorperazine, metoclopramide, lorazepam, and steroids. However, the use of highly selective antagonists of the type 3 serotonin receptor has had the greatest impact on controlling symptoms from highly emetogenic chemotherapy. In randomized controlled trials, the serotonin antagonists have demonstrated equal or superior efficacy to high dose metoclopramide, with fewer side effects, for acute chemotherapy-induced emesis (National Cancer Institute, 1997; Cherny, 1998). However, studies of serotonin antagonists for the treatment of delayed chemotherapy-induced emesis have not shown them to have an advantage over conventional therapies (National Cancer Institute, 1997; Cherny, 1998). The FDA indication for intravenous preparations of serotonin antagonist anti-emetics is limited to the prophylaxis of

chemotherapy-induced emesis in the setting of highly emetogenic chemotherapy (National Cancer Institute, 1997).

Consistent with the literature, we proposed a quality indicator requiring that all patients receiving highly or severely emetogenic chemotherapy (see Table 11.1) be offered concurrent type 3 selective serotonin antagonist anti-emetic therapy (Indicator 4).

Table 11.1
Severely and Highly Emetogenic Chemotherapy Agents

| Severely Emetogenic Agents | Highly Emetogenic Agents |
|---|---|
| Carmustine (>250 mg/m ²) | Carboplatin |
| Cisplatin (>50 mg/m ²) | Carmustine (<250 mg/m ²) |
| Cyclophosphamide (>1500 mg/m ²) | Cisplatin (<50 mg/m ²) |
| Dacarbazine | Cyclophosphamide |
| Mechlorethamine | (>700 mg/m ² and <1500 mg/m ²) |
| Streptozocin | Cytarabine (>1g/m ²) |
| | Doxorubicin (>60 mg/m ²) |
| | Methotrexate (>1000 mg/m ²) |
| | Procarbazine |

Source: Adapted from Heskath et al., 1997

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RECOMMENDED QUALITY INDICATORS FOR CANCER PAIN AND PALLIATION

The following indicators apply to men and women age 18 and older.

| Indicator | Quality of Evidence | Literature | Benefits | Comments |
|--|---------------------|---------------------------------|--------------------------|--|
| Diagnosis | | | | |
| 1. Patients with metastatic cancer to bone should have the presence or absence of pain noted at least every 6 months. | II-2, III | Jacox et al., 1994; ASCO, 1992 | Improve pain management. | While all cancer patients should have their pain addressed, we have limited this quality indicator to patients with bony metastases since this is the group with the highest prevalence of pain. |
| Treatment | | | | |
| 2. Cancer patients whose pain is uncontrolled should be offered a change in pain management within 24 hours of the pain complaint. | III | Jacox et al., 1994; ASCO, 1992 | Reduce pain. | Cancer pain can be controlled in 90% of patients with standard analgesic therapy. |
| 3. Patients with painful bony metastases, who are noted to be unresponsive to or intolerant of narcotic analgesia, should be offered one of the following within one week of the notation of pain: <ul style="list-style-type: none"> • Radiation therapy to the sites of pain; • radioactive strontium therapy. | II-1, II-2, III | Jacox et al., 1994 | Reduce pain. | 70% of patients with painful bony metastases will have at least partial relief of symptoms with radiation therapy. |
| 4. Patients receiving emetogenic chemotherapy should be offered concurrent potent antiemetic therapy (e.g. 5HT blockade). ¹ | I, III, III | National Cancer Institute, 1997 | Reduce emesis. | In RCTs, serotonin antagonists have demonstrated superior efficacy to metoclopramide. |

Definitions and Examples

¹ Potent antiemetic therapy: Ondansetron (Zofran), granisetron (Kytrel), dolasetron mesylate, tropisetron, batanopride.

Quality of Evidence Codes

- I Randomized Controlled Trial (RCT)
- II-1 Nonrandomized controlled trials
- II-2 Cohort or case analysis
- II-3 Multiple time series
- III Opinions or descriptive studies