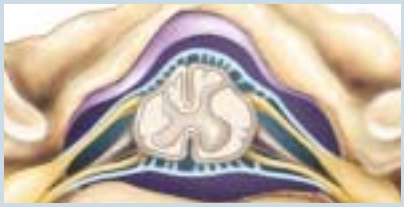
abstract



Cancer pain is a significant problem in older adults. Management in this population is made more challenging by issues such as comorbid conditions and age-related alterations in drug disposition. The first step is to perform a multidimensional assessment in order to identify the various factors that may influence the perception and expression of pain. The second step is to apply a process of targeted interventions, which optimizes the use of pharmacological and non-pharmacological therapies and takes into consideration the unique characteristics of the older patient.

Key words: *cancer pain, pain assessment, opioids, adjuvant analgesics.*

Management of Cancer Pain in the Older Adult

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Introduction

Cancer is the leading cause of death in Canada, and pain is one of its most frequent and feared manifestations. The topic of cancer pain in the older adult warrants attention for a number of reasons:

- According to 2003 statistics, 44% of new cancer cases and 59% of cancer deaths in Canada occurred in people aged 70 years or older;[1]
- Older cancer patients are at higher risk for inadequate treatment of pain;[2,3]
- The assessment and treatment of cancer pain in older adults may be complicated by factors such as cognitive impairment, multiple comorbid conditions and increased vulnerability to adverse effects of medications.

The purpose of this article is to provide a practical overview of the management of cancer pain, highlighting issues of particular concern in older adults.

Assessment

Pain as a Multidimensional Construct

The pain experience is a process consisting of nociception, perception and expression. Pain is only measurable at the point of expression. However, it is crucial to recognize that the pain experience may be modulated by many factors at each step. The assumption that 100% of a patient's pain expression is due to nociception may lead to an inappropriate reliance on antinociceptive measures. Rather, by identifying the multiple contributors to a pain complaint, an individualized and targeted plan of management may be developed.[4] The components of a multidimensional pain assessment are reviewed here.

Etiology

Most pain in cancer patients is secondary to direct tumour involvement. However, a disproportionate number of older patients also experience cancer treatment-related pain, such as chemotherapy-induced painful neuropathy.[5] In addition, the prevalence of painful comorbidities, such as osteoarthritis, is significantly higher among older adults.[6] The management of chronic non-cancer pain differs in some respects from that of cancer pain.[7]

Mechanism

Pain may be generated by either stimulation of pain-sensitive receptors (i.e., nociceptive pain, including both visceral and somatic pain) or injury to central or peripheral neural structures (i.e., neuropathic pain). The latter type is often more challenging to control.[8] Identification of the pain mechanism through clinical assessment and correlation with investigations allows for appropriate selection of adjuvant analgesic drugs.

Intensity

Various validated tools are available for the assessment of pain intensity, including visual analogue scales, numerical scales and categorical scales. Regular use of a tool improves caregiver recognition of pain[9] and assists in the evaluation of the outcome of analgesic interventions. In choosing a tool, individual functional deficits should be taken into consideration (e.g., avoiding visual analogue scales in a visually impaired patient). A further

Table 1: Non-pharmacological Approaches in Cancer Pain Management

Radiotherapy
Systemic antineoplastic therapy (e.g.,hormonal therapy, chemotherapy)
Invasive techniques (e.g., epidural/ intrathecal opioid therapy, nerve blocks, orthopedic surgery, neurosurgery)
Psychotherapy
Physical therapy
Occupational therapy
Transcutaneous electrical nerve stimulation (TENS)

useful indicator of pain intensity is the degree to which it interferes with sleep and activities.

Incident Pain

This syndrome refers to the situation in which background pain is well controlled, but the patient experiences episodes of severe pain, usually of sudden onset with a predictable trigger.[10] Incident pain is often more difficult to treat, as attempts to control the episodes by titration of opioids may result in an overmedicated state between episodes. Alternative strategies such as non-opioid adjuvant analgesics and non-pharmacological interventions may be required.

Cognitive Failure

Delirium is a common complication of advanced cancer.[11] Older adults are particularly vulnerable to the development of delirium and, moreover, may have a pre-existing dementia. The presence of cognitive failure complicates the assessment of pain, as the patient's report of pain may not be accurate, associated agitation may be misinterpreted as pain, and the patient's expression of pain may be disinhibited.[12] If cognitive failure is not recognized and the pain complaint is treated with excessive analgesics, the cognitive failure may be aggravated. Routine use of a screening tool such as the Folstein Mini-mental State Examination[13] improves detection of cognitive failure.[14] Although some older patients with mild-to-moderate cognitive impairment may be able to reliably report their pain,[15] ongoing reassessment of the pain complaint is advisable, especially if analgesic therapy does not result in improvement of the pain complaint or causes toxicity. When the pain complaint is not reliable, other indicators such as level of consciousness and function may need to be taken into account (e.g., a patient who is somnolent or who mobilizes easily is less likely to be experiencing severe pain).

Addiction

Addiction is a commonly feared but extremely rare complication of opioid therapy. However, patients who have a prior history of alcohol or drug abuse have a poorer prognosis for achieving good pain control.[8] They may have a tendency to use opioids to cope with psychosocial-spiritual distress, leading to dose escalation and toxicity. Recognition of addiction is essential, so that appropriate supportive interventions may be undertaken. Unfortunately, addiction is underdiagnosed, and therefore routine use of a screening tool such as the CAGE questionnaire is advised.[16]

Somatization

Somatization, which is the manifestation of psychosocial-spiritual distress in physical symptoms, is another poor prognostic factor for achieving good pain control.[8] If unrecognized, patients may inappropriately receive increasing doses of analgesics, leading to toxicity while the underlying problem remains unaddressed. There is no simple way to detect somatization, as patients may not necessarily have insight into the relationship between their psychosocial-spiritual distress and pain. Ultimately, somatization remains a diagnosis of exclusion in patients with difficult-to-control pain.

Other Symptoms

Pain is only one of many symptoms that

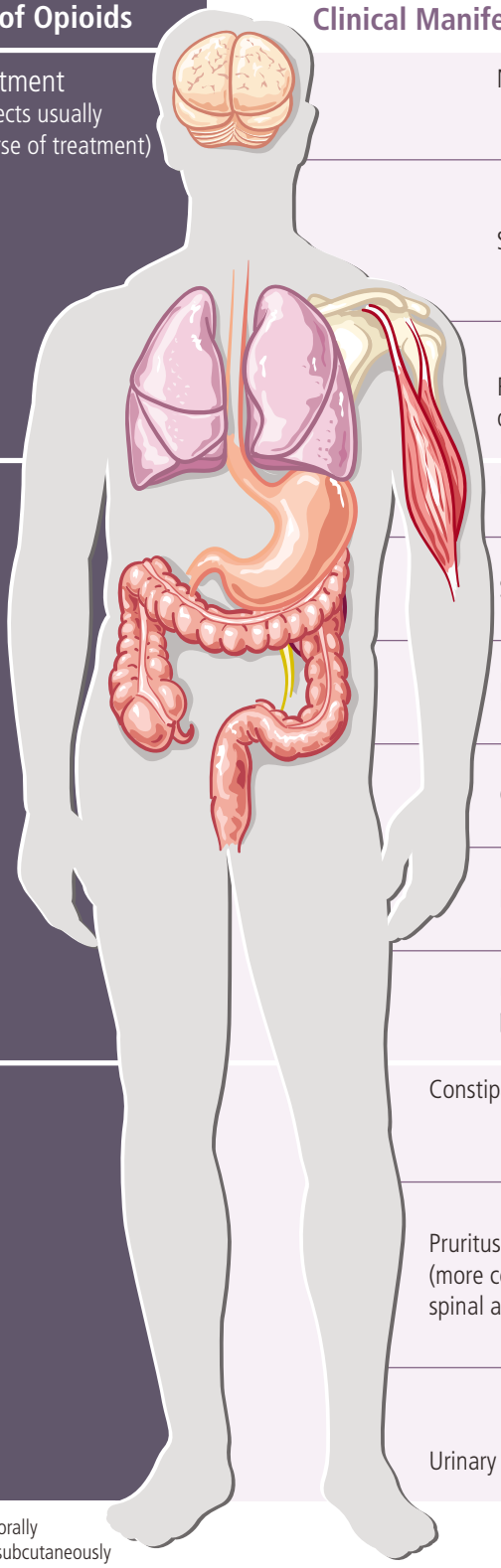
Table 2: Opioid Agonists in the Management of Cancer Pain in Older Adults

Drug	Oral Equivalent Dose	PO:SC/IV Ratio	Precautions and Suggestions
Codeine	150mg	2:1	When total daily dose exceeds 240–360mg, switch to morphine
Morphine	15mg	2:1	– "Start low and go slow"
Oxycodone	10mg	N/A	– Around the clock, plus breakthrough analgesic doses every hour as needed
Hydromorphone	3mg	2:1	– Short-acting for titration, long-acting for maintenance
Methadone	1.5mg*	N/A	– May consider a longer interval between regularly scheduled doses (e.g., short-acting every 6 hours instead of every 4 hours)
Fentanyl TTS**	Use chart supplied by manufacturer	Use chart supplied by manufacturer	

*High variability exists
**TTS: transdermal therapeutic system

Adverse Effects of Opioids

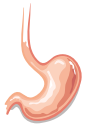
	Clinical Manifestations	Mechanism
Early phase of treatment (tolerance to these effects usually develops over the course of treatment)	Nausea	Gastroparesis Chemoreceptor trigger zone stimulation
	Sedation	Central nervous system depressant actions
	Respiratory depression	Depression of medullary respiratory centre neurons
Late phase of treatment	Myoclonus	Possible role of metabolite accumulation
	Seizures	
	Hallucinations	
	Confusion	
	Hyperalgesia	
	Non-cardiogenic pulmonary edema	Possible arterial and venous dilation at high doses
All phases of treatment	Constipation	Decreased gastrointestinal motility
	Pruritus (more common with spinal administration)	Not clearly understood
	Urinary retention	Increased smooth muscle tone



bid: twice daily
tid: three times daily
qid: four times daily
q4h: every 4 hours

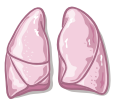
PO: orally
SC: subcutaneously
IV: intravenously

Interventions

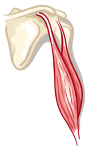


- Metoclopramide 5 –10mg PO/SC qid–q4h
- Haloperidol 1mg PO/SC bid–tid

- Advise not to drive
- Caution regarding falls

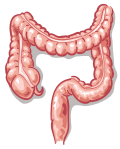


- Cautious dose escalation
- Consider neurological involvement due to cancer



- Dose reduction
- Switch opioids
- Hydration

- Dose reduction
- Oxygen support



- Take a detailed history of bowel habit
- Increase fluid intake
- Stool softeners, bowel stimulants, enemas, etc.

- Doxepin, naloxone, ondansetron, paroxetine

- Rule out urethral compression by fecal impaction
- Consider a urinary catheter

cancer patients may experience. Pain may not necessarily be the symptom that is having the greatest impact on a patient's quality of life at a given point in time. Furthermore, the experience of pain may affect the perception and expression of other symptoms, and vice versa. Moreover, the treatment of pain may lead directly to the worsening of other symptoms (e.g., opioid-related nausea and sedation). A tool that simultaneously measures the intensity of multiple symptoms, such as the Edmonton Symptom Assessment System (ESAS),[17] may facilitate recognition of the relationship between these symptoms.

Treatment

General Approach

The most common strategy for pain management is the use of analgesics. However, limited evidence exists for the outcome of pharmacological interventions for pain in older adults, since such patients have been systematically excluded from clinical trials. Older people appear to be more sensitive to the analgesic properties of drugs, especially those of opioids.[18,19] They also have a higher risk for adverse effects. Guidelines for age-adjusted dosing are not available for most analgesics due to the heterogeneity of the older adult population (e.g., chronological versus physiological age, comorbidities, pre-existing medications). As drug clearance is known to be reduced in older patients, a "start low and go slow" strategy is recommended.[20]

A suggested process for the treatment of cancer pain in older adults begins with an open discussion of the goals, expectations and trade-offs of possible therapies. A period of trial and error should be anticipated when new medications are initiated in order to achieve a balance between analgesic benefit and minimum adverse effects. The least invasive route of administration should be used. While the oral route is preferred, alternatives include subcutaneous, intravenous and rectal administration. The intramuscular route should be avoided because it is painful and inconvenient, and absorption is not reliable. Treatment should be started at the lowest possible dose and titrated slowly. Medications, doses and analgesic and adverse effects should be reviewed regularly, and seemingly ineffective drugs tapered and discontinued.

When adverse effects are seen, possible drug-drug interactions and physiological changes, such as dehydration, hypoalbuminemia, electrolyte imbalance, renal insufficiency and disease progression, need to be considered. Prolonged immobilization should be avoided whenever possible to prevent joint contracture, muscle atrophy, cardiovascular deconditioning and other unwanted outcomes. Psychosocial interventions should be introduced early in the course of the illness as part of a multimodal approach to pain management.

Pharmacological therapy is most effective when combined with non-pharmacological strategies to optimize pain management.[21] Typical non-pharmacological therapies in cancer pain management are listed in Table 1.

Non-opioid Analgesics

Mild cancer pain may respond to the non-opioid analgesics such as acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs should be used with caution in older adults, as the risk of gastrointestinal bleeding is significantly elevated in persons 60 years and older.[22] Moreover, older adults are susceptible to renal impairment and other drug-drug and drug-disease interactions associated with NSAIDs. Chronic opioid therapy, low-dose corticosteroid therapy or other non-opioid analgesic strategies may be associated with fewer life-threatening risks than long-term daily use of NSAIDs.

Opioids

Patients with moderate to severe cancer pain should receive regularly scheduled opioids, either as intermittent doses or by continuous infusion.[21,23] In addition, short-acting opioid should be administered as needed for breakthrough pain. Breakthrough analgesic doses are usually calculated as 5–10% of the total daily opioid dose,[10,24] but may be titrated according to effect. Opioid receptor ago-

Table 3: Adjuvant Analgesics in Management of Cancer Pain in Older Adults

Drug Class	Example with Starting Dose	Indications	Precautions and Suggestions
Corticosteroids	Dexamethasone 4mg PO daily to four times daily	Bone pain Visceral pain Neuropathic pain	Avoid high dose for long-term use if possible
Tricyclic antidepressants	Amitriptyline 10mg PO at bed time	Neuropathic pain	Frequent anticholinergic effects
Anticonvulsants	Gabapentin 100mg PO daily	Neuropathic pain	
Anti-arrythmic agents	Mexiletine 150mg PO daily	Neuropathic pain	Avoid in patients with heart disease Common side effects: tremor nausea, unsteadiness paresthesias
Bisphosphonates	Clodronate 1500mg IV/SC every 2 weeks Pamidronate 90mg IV every 4 weeks	Bone pain	Use cautiously in dehydration, renal insufficiency
Muscle relaxants	Baclofen 5mg PO daily	Muscle spasms	Monitor for weakness and urinary dysfunction
Psychostimulants	Methylphenidate 5mg PO in the morning	Opioid-induced sedation	Potential on-off syndrome

PO: orally; IV/SC: intravenously or subcutaneously

nists such as codeine, oxycodone, hydromorphone, morphine and fentanyl are effective analgesics (Table 2; page 27). Methadone may be particularly useful in situations of opioid tolerance and neuropathic pain, due to its ability to antagonize the N-methyl-D-aspartate receptor.[23] Other purported advantages of methadone include high oral bioavailability, lack of known toxic metabolites, minimal dependence on renal excretion and low cost. However, because of its long and unpredictable half-life and variable dose ratio relative to other opioids, methadone should only be initiated by clinicians experienced in its use.

Partial agonists and mixed agonists/antagonists such as buprenorphine, butorphanol or pentazocine are of limited value, as they may precipitate withdrawal when given to patients who have already been exposed to opioid agonists.[22,23,24] Meperidine is best avoided because of its short duration of action and association with neurotoxicity in patients with reduced renal function.[21,23,24] Propoxyphene is not recommended, as adverse effects may exceed analgesia due to its low potency.

Common adverse effects of opioids are shown in the accompanying Figure (pp. 28–29). Opioid-induced neurotoxicity is a more recently recognized syndrome, believed to be caused by accumulation of opioid metabolites.[24] One management option is to reduce the opioid dose. However, if the pain is not adequately controlled, other analgesic interventions must be applied. An alternative strategy is to switch or "rotate" the opioid.[25] The starting dose of the new opioid is calculated according to equivalency tables (Table 2), with a 20–30% reduction to account for incomplete cross-tolerance.

Adjuvant Analgesics

Most patients with cancer pain, including neuropathic pain, improve with opioid analgesics. Adjuvant analgesics may be added if dose-limiting adverse effects of opioids are reached.[24] Evidence for the effectiveness of adjuvant analgesics for neuropathic cancer pain is limited, as most studies have been conducted in non-cancer populations. Typical agents are listed in Table 3.

Conclusion

Cancer pain in older adults may be successfully controlled through disciplined multidimensional assessment, optimal use of pharmacological and non-pharmacological approaches, and consideration of the unique characteristics of this population. ◆

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