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Hospital Medicine: Current Concepts



Scott A. Flanders and Sanjay Saint • Series Editors

HOSPITAL-BASED PALLIATIVE MEDICINE

A PRACTICAL, EVIDENCE-BASED APPROACH

EDITED BY

**STEVEN PANTILAT • WENDY ANDERSON
MATTHEW GONZALES • ERIC WIDERA**

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Chapter 1

Hospital Care for Seriously Ill Patients and Their Families

Steven Z. Pantilat, Wendy G. Anderson, Matthew J. Gonzales,
and Eric W. Widera

Mrs Morton was an 82-year-old woman with ovarian cancer metastatic to the lung, liver, and peritoneum with massive ascites diagnosed 1 year ago. She had undergone many cycles of chemotherapy but stopped chemo several months ago due to progression of disease and increasing fatigue. Mrs Morton was living at home with her daughter, son-in-law, and three grandchildren. A few days earlier, she had stopped eating and drinking. She became sleepier and spent all of her time in bed. On the morning of admission, Mrs Morton's daughter awoke to find that her mother was not able to speak or even open her eyes and was moaning and breathing fast. Feeling panicked, her daughter called 911. The ambulance arrived within a few minutes. They found Mrs Morton hypotensive, tachypneic, tachycardic, hypoxic, and in respiratory distress. They asked about advance directives, but were told that Mrs Morton had not completed one. They started an IV, gave fluids, administered oxygen, and rushed Mrs Morton to the hospital.

On arrival in the emergency department, the emergency physician and nurse asked the family, "Would you like us to do everything possible?"

Her family responded, "Yes," as virtually anyone would to this question.

The emergency physician called the hospitalist on call STAT to the emergency department to admit Mrs Morton and notified the intensive care unit that she would soon be on her way up.

1.1 EPIDEMIOLOGY OF HOSPITAL CARE FOR THE SERIOUSLY ILL

For hospitalists, intensivists, emergency physicians, advance practice nurses, nurses, and all clinicians who practice in the hospital, the story of Mrs Morton is all too common. Overall, about one-third of Americans die in hospitals; many

more spend some time in a hospital in the last year of life [1]. Among Medicare beneficiaries, nearly 70% are hospitalized in the last 3 months of life, one-third receive ICU care in the last month of life, and over half die in a hospital or nursing home [2].

While it is arguable whether Mrs Morton needed hospital admission to receive quality care at the end of her life, as hospice or palliative care at home would likely have provided the care she needed, the reality is that for many people hospital care provides relief and recovery from exacerbations of chronic illness. People with acute shortness of breath from heart failure or chronic obstructive pulmonary disease (COPD), bowel obstruction from pancreatic cancer, altered mental status from liver failure, and pain from a pathologic fracture often experience rapid and dramatic improvement in symptoms and quality of life from hospital care. Even patients who prefer to avoid hospitalization may find that hospital care provides the quickest and best option for relief of symptoms. For example, Chapter 4 discusses options for treating patients with malignant bowel obstruction. In this clinical setting, hospitalization may offer the best option for relief of nausea, vomiting, and pain. At the same time, for a patient like Mrs Morton, there will likely come a time when hospitalization will not only fail to provide relief but may also impose additional burdens for her and her family. Although it can be difficult to predict which hospitalization will be the last one or whether hospitalization will provide more benefit than harm, each hospitalization for the seriously ill provides an opportunity to clarify goals of care to ensure that care is consistent with patient preferences, promotes benefit, and limits harm.

Studies of patients with serious illness have shown consistently what these patients need and want from the healthcare system: relief from pain and other symptoms; clear communication about their illness, prognosis, and treatment options; and psychosocial, spiritual, and practical support [3, 4]. Addressing these needs is critical for providing high-quality care to patients with serious illness, and as such provides the overarching organizational structure to this book. Further, it requires a team approach as no single clinician has expertise in all these domains. Hospitalists and other hospital-based physicians, nurses, social workers, and chaplains must collaborate to ensure that patient needs are attended to. Such collaboration can happen formally, as with a palliative care consultation team, or more informally through clinicians working together to share insights and develop and implement plans of care.

Increasingly, it is hospitalists and other hospital-based specialists who care for people with serious illness in the hospital like Mrs Morton [5]. Over time, hospitalists have come to care not only for people with classic medical conditions, such as pneumonia and COPD, but also for people with cancer and cardiac, neurologic, and surgical problems either as admitting physicians or through comanagement. The high frequency of hospitalization among the seriously ill and those approaching the end of life places the clinicians who work in these settings in an ideal position to promote optimal quality of life for these patients.

1.2 PALLIATIVE CARE

Palliative care is the field of medicine focused on providing the best possible quality of life to people with serious illness and those near the end of life. Palliative care is defined as follows:

...specialized medical care for people with serious illnesses. This type of care is focused on providing patients with relief from the symptoms, pain, and stress of a serious illness—whatever the diagnosis.

The goal is to improve quality of life for both the patient and the family. Palliative care is provided by a team of doctors, nurses, and other specialists who work with a patient's other doctors to provide an extra layer of support. Palliative care is appropriate at any age and at any stage in a serious illness, and can be provided together with curative treatment. [6]

There are several important parts of this definition that bear highlighting. First, palliative care is for people with *serious illnesses*. While palliative care is also about caring for people near and at the end of life such as Mrs Morton, fundamentally, palliative care is for people with serious illnesses such as heart disease, COPD, cirrhosis, cancer, and dementia and would have been appropriate for Mrs Morton from the time of diagnosis. The term *serious illness* is also helpful when talking with patients about the need for palliative care or the decision to involve palliative care specialists. Patients can easily relate to and understand that they have a serious illness and that additional care will be helpful to them. In the hospital, palliative care will also be appropriate for patients with fulminant acute illness such as massive intracranial hemorrhage and trauma. The important point for hospitalists to remember is that palliative care is not only for the terminally ill and also for those at the very end of life.

Palliative care is also *appropriate at any stage in a serious illness*, and patients can receive palliative care *while still pursuing curative intent treatment* such as chemotherapy, radiation therapy, percutaneous coronary interventions, surgery, and hemodialysis. Many patients and physicians harbor the misconception that receiving palliative care means that patients must forsake curative intent treatment. This misunderstanding is a common barrier that unnecessarily precludes patients from receiving palliative care. Patients admitted with exacerbations of heart failure or COPD, with complications of cancer or its treatment, and those with dementia all may benefit from symptom management, clarification of goals of care, and psychosocial support. One helpful question to ask for determining whether a patient would benefit from palliative care is, “Would I be surprised if this patient died in the next year?” This “surprise” question helps clinicians identify patients appropriate for palliative care [7]. If the question is difficult to apply to every patient, clinicians can also consider the types of patients who would be appropriate for palliative care (Table 1.1).

Consistent with what patients say they need from the healthcare system, palliative care seeks to *relieve the symptoms, pain, and stress of a serious illness*.

Table 1.1 Types of Patients Appropriate for Palliative Care

-
- Advanced heart failure, second readmission in a year
 - Breast cancer and malignant pleural effusion
 - Brain metastases
 - Dementia and aspiration pneumonia
 - New diagnosis of idiopathic pulmonary fibrosis
 - Cirrhosis, second admission for altered mental status
 - Awaiting solid organ transplant
 - “Would I be surprised if this patient died in the next year?”
 - If the answer is “No,” provide and/or refer for palliative care.
-

Relief of symptoms and pain is the first priority as patients can only focus on what is important to them and on having meaningful time when their symptoms are controlled. Control of symptoms allows patients to consider the issue that is at the heart and the ultimate goal of palliative care: *improving quality of life*. In fact, one helpful way to explain palliative care to patients and families is to state that the goal is to help patients “achieve the best possible quality of life for as long as possible.” This focus on promoting quality of life and understanding that it is defined uniquely by each patient is at the crux of what palliative care is about. It is also helpful to explain to patients that palliative care provides an *extra layer of support*. Few hospitalized patients would decline extra support, and the more seriously ill the patient, the more attractive and necessary the extra support becomes.

Hospitalized patients fall along a continuum of an illness trajectory, and palliative care plays a significant role in the care of patients throughout this continuum. The needs of these patients with serious illness will vary over the course of illness, and as shown in Figure 1.1, the relative focus on palliative care and curative intent treatment may change. Similarly, the depth and intensity of involvement with palliative care concerns will change over time, but from diagnosis to death, patients with serious illness will encounter situations where they will need and benefit from palliative care.

As will be highlighted throughout this book, there is considerable evidence for the efficacy and effectiveness of palliative care. A review of the evidence shows that palliative care relieves symptoms such as pain and depression, improves quality of life, increases satisfaction with care, and reduces resource utilization including ICU length of stay and costs of care [8–11]. Such an impact is easy to imagine when thinking about Mrs Morton. In addition, palliative care and conversations between patients and physicians about goals and preferences for care not only improve quality of care and life for patients but also improve outcomes for loved ones of patients who die [12, 13]. Those loved ones are less likely to experience complicated grief and depression 6 months after their loved one died.

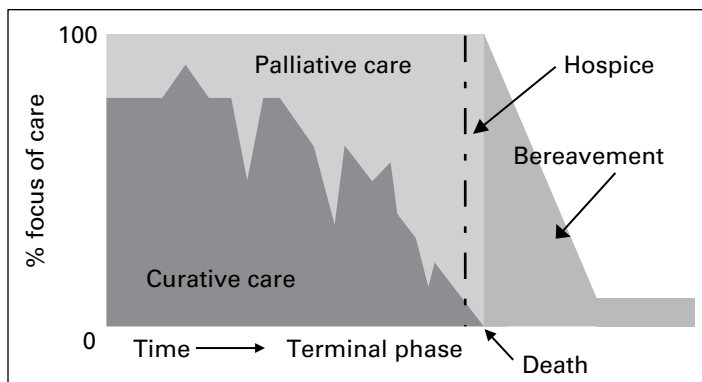


Figure 1.1 Concurrent model of palliative care. *Source:* © Steven Pantilat, MD and Regents of the University of California.

1.3 THE ROLE OF THE HOSPITAL-BASED CLINICIAN IN PALLIATIVE CARE

Hospitalists, intensivists, and other hospital-based clinicians frequently care for patients with serious illness and those approaching at the end of life like Mrs Morton. Hospitalists recognize the importance of palliative care to their practice and acknowledge a relative lack of education in pain management and palliative care during training [14]. Hospital-based clinicians can interact with palliative care in following four ways.

Refer to a Palliative Care Team: At a basic level, these clinicians need to identify patients who need palliative care and make appropriate referrals. Mrs Morton would be just such a patient. Many patients, like her, who need palliative care have complex symptom management and communication needs that require an interdisciplinary team of palliative care experts. In addition, when hospitalists are too busy with other patients to have extended goals of care conversations and family meetings, palliative care teams can assist to ensure that patient needs are met.

Work as a Member of a Palliative Care Team: Many hospitalists and other hospital-based clinicians will have extensive experience with palliative care and develop a strong interest in it. While currently the only path physicians in the US have to board certification in palliative medicine is through a 1-year clinical fellowship, many palliative care teams are challenged to find qualified physicians and advance practice nurses and would likely welcome experienced hospitalists dedicated to gaining continued education and experience in palliative care. Hospitalists, intensivists, and others can split their time between their primary specialty and working with a palliative care team, diversifying their professional responsibilities and income streams.

Become Board Certified in Palliative Care: Hospital-based clinicians who find palliative care compelling can pursue fellowship training in palliative care. The 1-year clinical fellowship is open to physicians from nearly all hospital-based disciplines. Understandably, taking a year away from practice to be a clinical fellow may be difficult financially. Some hospitals that have had difficulty hiring a board-certified palliative care physician have offered to supplement the salary of a hospital-based physician during fellowship in exchange for a guarantee of a certain number of years of work on the palliative care team. Given the shortage of palliative medicine-trained physicians, this arrangement can be a win–win for the hospital and the clinician and is often the fastest way of recruiting a board-certified palliative medicine physician. Nurses can also pursue board certification in palliative care. In addition, there are excellent educational courses for nurses in palliative care (End-of-Life Nursing Education Consortium (ELNEC) <http://www.aacn.nche.edu/elnec>), although there are few fellowships in palliative care for nurses.

Provide Primary Palliative Care: This option is the one that applies to all clinicians and could have the greatest impact on ensuring that all patients who need palliative care receive it [15]. For example, regardless of whether a hospital had a palliative care team, and many still do not [16], Mrs Morton needed to receive palliative care. All hospital-based clinicians should have a basic knowledge and facility with palliative care issues including pain and symptom management, discussing prognosis and goals of care, ensuring psychosocial and spiritual support to patients and families, and providing care that is culturally aware and sensitive. The tools, knowledge, and skills associated with palliative care—such as pain management and good communication—apply to the care of many, if not all, hospitalized patients. In addition to being able to address pain, hospital-based physicians should have facility with management of dyspnea, nausea, vomiting, bowel obstruction, depression, and anxiety. A thorough knowledge of good communication techniques including sharing bad news, running a family meeting, and discussing goals of care are critical activities for all hospital-based clinicians. Finally, addressing and attending to patients' psychological, social, emotional, and spiritual needs is important not only for patients nearing the end of life but also for many seriously and acutely ill patients. The fundamental goal of this book is to provide hospital-based clinicians with that knowledge base in an easy-to-use, evidence-based way with sufficient specificity and direction that will help guide care at the bedside.

Fortunately, there is large overlap in the knowledge, skills, and practice of hospital medicine, other hospital-based specialties, and palliative care. Clinical care in each realm includes interdisciplinary collaboration, seriously ill patients and those near the end of life, a wide range of clinical conditions, and a focus on improving quality of life and quality of care. This synergy across specialties can reinforce practice in each setting and help clinicians improve care overall.

1.4 THE STRUCTURE OF THIS BOOK

This book is divided into three parts that map the issues most important to seriously ill patients and their families and the major focus of palliative care: symptom management, clear communication, and psychosocial–spiritual support. The goal is to provide useful, practical, evidence-based information for busy hospital-based clinicians that forms the foundation of care for seriously ill patients and those near the end of life. This book also provides the science and the art of medicine and the science behind the art. In addition to evidence-based medicine, the authors share their clinical expertise and pearls of wisdom to put the evidence in context and offer guidance where evidence is lacking; akin to what they would impart in a consultation.

1.5 REWARDING PRACTICE

The care of seriously ill patients and those approaching the end of life can be challenging and richly rewarding [17]. Working with Mrs Morton and her family to help ease her respiratory distress; pausing the resuscitation long enough to understand her preferences for care; providing support, compassion, and empathy to her family; and implementing a plan consistent with her wishes allow the clinicians to use their heart as well as their head to provide the best possible care to patients and their families. In our technological age, it is easy to think that the only important aspects of medical care and the ones that patients value the most are the things we do to them. Such thinking grossly underestimates the importance that patients place in the human side of medicine and the caring that clinicians demonstrate by relieving symptoms and eliciting patient preferences carefully enough to really understand their goals and values and develop a plan to make those happen. In these cases, hospitalists and other hospital-based specialists can bring their humanism to bear on the care of the patient and can provide healing even, and especially, if cure is not possible.

1.6 CARING FOR MRS MORTON

A hospitalist or other hospital-based clinician well versed in palliative care can see the case of Mrs Morton as an opportunity to stop the onslaught of medical intervention for a patient who is dying and understand what her preferences would be to ensure she receives the care she and her family want. The hospitalist might start by asking, “How were you hoping we could help?” That question, much better in this situation than the one asked, could begin to elicit Mrs Morton’s preferences as expressed by her family [18]. The hospitalist could order opioids for the tachypnea and respiratory distress. If the family expresses understanding that Mrs Morton is dying and states that her wish in this setting is to have her care focused on comfort and dignity, the hospitalist might recommend admission or explore the possibility of Mrs Morton returning home with hospice services. The hospitalist might also ask about spiritual and religious issues to ensure that these are addressed in case

Mrs Morton dies soon. The hospitalist could provide a best estimate of prognosis and explain about the dying process. Finally, the hospitalist could provide guidance to the family about what they can say and do at the bedside to promote comfort, dignity, and healing. The skills and knowledge essential for providing this type of care are the essence of this book.

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Section 1

Symptom Management

Chapter 2

Pain Management: A Practical Approach for Hospital Clinicians

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2.1 ETIOLOGY AND TYPES OF PAIN

Pain is “localized physical suffering associated with a bodily disorder” or “acute mental or emotional distress or suffering” [1]. A comprehensive approach to diagnosing and understanding pain therefore requires evaluating not only the medical disorder causing the physical pain but also the psychosocial distress that contributes to the patient’s overall suffering. Since every patient has a psychosocial aspect and a spiritual/existential component to their pain, the question is not whether the patient has nonphysical pain but how much. For example, a postoperative patient’s pain may be 98% physical, 1.5% emotional, and 0.5% spiritual. A chronic cancer patient’s pain, however, may be 45% physical, 35% psychosocial, and 20% existential. In reality, the different pain domains interact (as in Fig. 2.1), and separating them is both impractical and often impossible.

However, understanding the different pain domains allows for a structured approach to address all of the patient’s sources of pain. Screening for depression and anxiety is important in all pain patients, but particularly in chronic pain patients. Generally when a patient rates their pain higher than a 10 out of a maximum 10 scale, they are saying they have more than just physical pain. The most important existential question to ask a pain patient is the meaning the patient gives to their pain. People are able to tolerate horrible pain, such as in childbirth, if they give the pain a positive meaning and see a purpose to their pain. However, if a patient gives a negative meaning to their pain, such as a cancer patient who interprets their pain as progression of their disease, then their ability to tolerate their pain worsens.

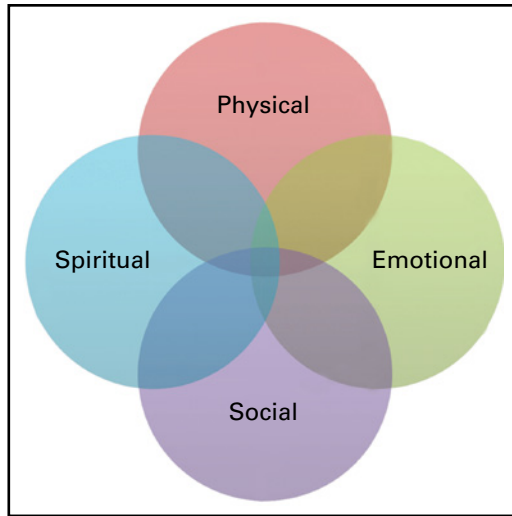


Figure 2.1 Biopsychosocial model of pain.

Even for physical pain, different categories have been suggested to divide the types of pain based upon etiologies and mechanisms. These categories include such terms as somatic, neuropathic, inflammatory, visceral, and nociceptive. However, the most useful or practical dichotomy of pain type is whether the pain is opioid responsive or opioid refractory. From a management standpoint, this distinction is the first point in the algorithm of treatment. If the patient's pain is opioid responsive, then the issue is finding the opioid dose needed to control the pain. If the patient's pain is opioid refractory, merely giving the patient more opioids gets the patient and the prescriber into more trouble, a phenomenon that occurs all too often.

The differential diagnosis for opioid refractory pain is relatively short. Neuropathic pain has an incomplete response to opioids, in that most patients with significant neuropathic pain say that opioids “take the edge” off the pain but do not relieve it [2]. The majority of patients with opioid refractory pain have some component of neuropathic pain. The second most common type of opioid refractory pain is inflammatory pain, such as metastatic bone pain, and the third is nonphysical pain. Less common but important causes of opioid refractory pain are complex regional pain syndrome (CRPS) and central pain syndrome. CRPS, previously called reflex sympathetic dystrophy, is an autonomic mediated pain from the sympathetic nervous system and thus presents with the classic triad of color and temperature changes, edema, and vague pain involving an entire limb. It occurs after trauma to a limb, particularly neurological or vascular trauma, regardless of severity. Central pain syndromes occur after damage to the central nervous system including spinal cord injury or strokes. Paradoxical pain occurs with opioids from accumulation of neurotoxic metabolites. This opioid-induced hyperalgesia typically occurs with chronic high-dose opioid use. Patients complain of escalating pain with increasing opioid doses.

Pain can also be divided by chronicity: acute, subacute, or chronic. Appreciating the chronicity of the pain allows for an appropriate response. In the hospital, clinicians often mistakenly respond to chronic pain with acute pain measures. Similarly, patients may have the erroneous expectation that their uncontrolled chronic pain will be controlled just because they are in the hospital. Overreacting to chronic pain with aggressive acute interventions can not only be nonbeneficial but also actually harmful to the patient and to the health system. On the other end of the spectrum, delays in diagnosing or treating a new or acute pain often occur, especially in patients who have chronic pain at baseline or those who are confused or nonverbal.

2.2 A PRACTICAL GENERAL APPROACH TO PAIN

Pain is the most common and important complaint for hospitalization and presentation to the emergency room. The consequences of pain include reduced quality of life, impaired physical function, extended recovery time, and high economic costs from hospital readmissions, longer lengths of stay, and repeated emergency room visits [3]. As patients' pain satisfaction scores become publicly reported, hospitals will be increasingly evaluated and ranked by their ability to manage pain. Improving pain management requires system changes in our hospitals. Fortunately acute care hospitals now have more resources to evaluate and address pain. Palliative care or pain consultations are increasingly available in hospitals for complex or refractory cases. Patients now have access to sophisticated pain therapies, such as ketamine or lidocaine infusions, epidural or intrathecal analgesia, and even surgical interventions for pain management.

The acute care setting poses challenges to good pain management. Acute illness not only increases the likelihood of pain but also increases the likelihood of complications from pain management. The ability of acutely ill patients to metabolize medications decreases when they develop acute kidney injury or acute hepatic failure. They are more sensitive to side effects of medications when they have exacerbations of their heart failure, COPD, or sleep apnea or when they have delirium or toxin-producing infectious colitis. Ironically when the patient most needs aggressive pain management, clinicians and hospital staff are the most fearful of giving them sufficient pain medications. The balance between the patient's comfort and an iatrogenic complication requires not only clinical skill but also an understanding of the patient's goals of care.

Management of acute pain requires a proactive, interdisciplinary approach. Frequent evaluation and adjustment of the treatment is more important than which initial therapy was started. The evaluation and treatment of pain in the hospital is everyone's responsibility, from the physician to nursing staff, case manager, pharmacist, social worker, occupational therapist, and physical therapist. Establishing expectations, an acceptable pain level, and functional goals for improvement are essential first steps for good pain management. While unidimensional pain scales, such as the visual analog or Wong–Baker FACES scale, are helpful in tracking the longitudinal severity of the patient's pain, multidimensional scales capture a fuller picture of the

patient's pain and should be administered at least once during the hospitalization, preferably on admission or on onset of the pain. Links to different pain assessment scales are shown in Table 2.1. Attention should be given to the patient's peak pain score of the day rather than the average pain severity, since studies show that the peak pain score correlate best with clinical outcomes, such as function and patient satisfaction.

Table 2.1 Web Resources

Opioid Conversion Calculator at <http://www.globalrph.com/opioidconverter2.htm>.

Opioid Conversion Tables

<http://www.globalrph.com/narcotic.htm>

<http://www.nhhpc.org/opioid.htm>

<http://champ.bsd.uchicago.edu/documents/Pallpaincard2009update.pdf>

Pain Guidelines

American Academy of Pain Medicine

http://www.painmed.org/Library/Clinical_Guidelines.aspx

WHO treatment guidelines on chronic nonmalignant pain in adults

http://www.who.int/medicines/areas/quality_safety/Scoping_WHOGuide_non-malignant_pain_adults.pdf

Management of persistent pain in older adults

http://americangeriatrics.org/health_care_professionals/clinical_practice/clinical_guidelines_recommendations/2009/

Palliative Care Fast Facts

<http://www.eperc.mcw.edu/EPERC/FastFactsandConcepts>

Free Mobile Applications

Pain Guide: Pain Management Quick

NPC Opioid Guidelines

PAIN Clinician

Pain Scales

Unidimensional

Wong–Baker FACES pain rating scale

<http://www.partnersagainstpain.com/printouts/A7012AS6.pdf>

Visual analog (0 to 10) scale

<http://ergonomics.about.com/od/ergonomicbasics/ss/painscale.htm>

Nonverbal or Observational

Pain Assessment in Advanced Dementia Scale (PAINAD)

<http://www.healthcare.uiowa.edu/igec/tools/pain/PAINAD.pdf>

Revised nonverbal pain scale

<http://ccn.aacnjournals.org/content/29/1/59/T4.large.jpg>

Multidimensional

McGill Pain Questionnaire

http://www.ama-cmeonline.com/pain_mgmt/pdf/mcgill.pdf

Brief Pain Inventory

<http://www.partnersagainstpain.com/printouts/A7012AS8.pdf>

Medication reconciliation is now required on admission to the hospital and is also part of good pain management. However, obtaining accurate medication reconciliation may be difficult in an acutely ill patient. Fortunately, most states now have electronic prescription drug monitoring programs (PDMP) that can help with the medication reconciliation process. These programs allow prescribers and pharmacists to look up an individual patient on the state's controlled substance database to see what pain medications they have received, when they received them, and from whom. Studies have shown that the use of PDMP actually increases (rather than inhibits) the prescribing of pain medications by reassuring the prescriber of the appropriate use of these medications [4]. PDMP can also help the care team identify patients who are at high risk for addiction or even pseudoaddiction (the appearance of drug-seeking behavior due to undertreatment of pain).

2.3 OPIOID ANALGESICS

2.3.1 Commonly Used Opioids (in the United States)

Table 2.2 summarizes the opioid medications that are commonly used in the United States. Morphine is the gold-standard opioid. It is available in short-acting and long-acting formulations. The benefits of morphine are that it is relatively inexpensive, is available in a liquid formulation, is ubiquitous, and is well known. Its familiarity translates to less medication errors in the hospital compared with other opioids. The liquid formulation is good for people who cannot swallow pills, have a tube feeding, or have poor bowel absorption (e.g., short bowel). Morphine is metabolized and glucuronidated in the liver to morphine-6-glucuronide and morphine-3-glucuronide. Both metabolites are renally excreted and are known neurotoxins. Accumulation of the metabolites leads to opioid-induced neurotoxicity which manifests as myoclonus, delirium, and then seizure. Morphine should be avoided in patients with moderate to severe renal impairment but can be used cautiously and for short term in patients with mild renal impairment.

Hydromorphone (Dilaudid) is more potent (mg to mg) than morphine but has no difference in efficacy. It is available in long-acting and short-acting formulations. However, the long-acting formulation is extremely expensive, not covered by insurance and cost prohibitive in most cases. Though not as neurotoxic as morphine, hydromorphone has toxic metabolites as well and is relatively contraindicated in patients with renal failure. The drawback of hydromorphone is its expense and the need to use a different opioid for long-acting pain relief.

Oxycodone is available in long-acting (OxyContin) and short-acting formulations. It is only available in oral formulations (pills and liquid) and not available in IV formulations. The disadvantage of long-acting oxycodone is its expense as it is not yet available in a generic formulation and therefore sometimes not covered by insurance. Additional drawbacks to long-acting oxycodone are its high potential for abuse and a high street value. Like hydromorphone, its metabolites are less neurotoxic than morphine's.

Table 2.2 Commonly Used Opioid Analgesics

Opioid	Dosage Form	Strength	Starting Doses of Short-Acting Opioids for Opioid-Naïve Patients
Morphine	Oral solution	2, 4, 20 mg/ml	5–10 mg PO q 60 min as needed
	Tablets ER (q 12 h)	15, 30, 60, 100, 200 mg	
	Tablets ER (q 24 h)	Kadian: 10, 20, 30, 50, 60, 80, 100, 150, 200 mg Avinza: 30, 45, 60, 75, 90, 120 mg	
	Tablets IR	10, 15, 30 mg	
	Injectable SC, IV, infusion	Check hospital-specific concentrations	2–3 mg IV q 30 min as needed
Methadone	Oral solution	1, 2, 10 mg/ml	NA
	Tablets	5, 10 (for pain); 40 mg (methadone maintenance clinics only)	
	Injectable IV, infusion	Check hospital-specific concentrations	
Fentanyl	Transmucosal (buccal)	Actiq: 200, 400, 600, 800, 1200, 1600 mg	
	Transdermal	Patches: 12 (delivers 12.5), 25, 50, 75, 100 mcg/hr	
	Injectable SC, IV, infusion	Check hospital-specific concentrations	25–50 IV mcg q 30 min as needed
Hydromorphone	Oral solution	1 mg/ml	2 mg PO q 60 min as needed
	Tablets ER (q 24 h)	8, 12, 12, 32 mg	
	Tablets IR	2, 4, 8 mg	
	Injectable SC, IV, infusion	Check hospital-specific concentrations	0.5 mg IV q 30 min as needed
Oxycodone	Oral solution	1, 20 mg/ml	5 mg PO q 60 min as needed
	Tablets ER (q 12 h)	10, 15, 20, 30, 40, 60, 80 mg	
	Tablets IR	5, 10, 15 mg	
Oxymorphone	Tablets ER (q 12 h)	7.5, 10, 15, 20, 30, 40 mg	5 mg PO q 60 min as needed
	Tablets IR	5, 10 mg	

The oral solutions of morphine, oxycodone, and hydromorphone are useful for enteral tube administration, and because they are short-acting, they are usually dosed every 4 h around the clock and/or as needed.

Methadone (in consultation with a palliative care specialist), because of its long duration of action, is an ideal “long-acting” opioid for enteral tube administration and is usually administered every 8 h.

Table 2.3 Advantages and Disadvantages of Transdermal Fentanyl Compared to Oral or IV/SC Opioids

Transdermal Fentanyl versus Oral Opioid	
Advantages of Transdermal Fentanyl	Disadvantages of Transdermal Fentanyl
Convenience	High cost
Continuous administration	Slower onset of action
Longer duration of action	More difficult to reverse side effects
Greater patient adherence	Slow titration
Avoids PO in patients with nausea/vomiting	Possible adhesive sensitivity
Transdermal Fentanyl versus Continuous IV/SC Opioid Infusion	
Advantages of Transdermal Fentanyl	Disadvantages of Transdermal Fentanyl
Less expensive	Slower onset of action
Easier for caregiver	More difficult to reverse side effects
Less invasive (no needles, no pumps)	Separate intermittent medication required for breakthrough pain

Fentanyl comes in many formulations including intravenous, transdermal (TD), intranasal, sublingual, and buccal. It is estimated to be 80 times more potent than morphine as an analgesic. Its lipid solubility, high potency, and low molecular weight make it ideal for administration systemically through a relatively small area of the skin or mucosa. One of the biggest advantages of fentanyl is that its metabolites appear to be inactive, conferring neither analgesia nor toxicity. Therefore, fentanyl does not have the neurotoxicity in the setting of renal impairment as seen in the other opioids listed earlier. Table 2.3 summarizes the advantages and disadvantages of TD fentanyl compared to orally and IV or SC administered opioids. A major disadvantage of fentanyl is its expense. Its absorption is unpredictable in cachectic patients and should not be used in this population. The Food and Drug Administration (FDA) black box warns that *the TD patch is not intended for opioid-naïve patients*. Absorption into serum begins approximately 4–8 h after application; however, therapeutic blood levels are not achieved for 12 to 16 h with mean time to maximum concentration between 29 and 36 h. At steady state TD fentanyl produces drug levels similar to those produced by intravenous or subcutaneous infusion with the same infusion rate. Levels vary between patients based on individual differences in skin absorption characteristics and fentanyl clearance rates. Patients with elevated body temperature (especially >102°F) must be carefully monitored and may need to be switched to an alternate oral or parenteral opioid. Fentanyl patches causing less constipation than other opioids is a myth. All opioids cause the same side effects.

2.3.2 Methadone Friend or Foe?

Methadone has several advantages but should be used in consultation with a palliative care or pain specialist. An important advantage is that it is very inexpensive, \$20–\$30

a month. Most patients can afford methadone even if it is not covered by their insurance. Methadone has no known active metabolites and only needs to be dose adjusted when renal function drops below 10%. It is the only long-acting opioid that comes in a liquid formulation and can therefore be given through feeding tubes or to patients with dysphagia who cannot swallow pills. In addition to its opioid activity, methadone also antagonizes the *N*-methyl-d-aspartate (NMDA) receptors, giving it a second analgesic effect. Because of its very low potential for abuse and hence, low street value, Methadone is the safest option in patients with a history of drug abuse or at risk for opioid diversion.

Methadone metabolism differs from other opioids in that it *does not* follow first order pharmacokinetics. Methadone has a biphasic pharmacokinetics: its opioid (first phase or plasma) effects peak in 2–3 h; its NMDA receptor antagonism (second phase or tissue) effect has an individually variable and long half-life and resultant peak. Therefore, methadone can be used both as a long-acting analgesic and a short-acting analgesic. Because methadone is long acting, it is usually prescribed every 8 h in younger patients and every 12 h in older patients, when used as a maintenance analgesic. As an as-needed, short-acting analgesic, it is used similar to other short-acting opioids. Although methadone quickly binds to the mu-opioid receptors, methadone takes 3–5 days to antagonize the NMDA receptors and become maximally effective. Because of this, methadone must be titrated slowly. *Increasing methadone doses more frequently than every 3–5 days is strongly discouraged given the possibility for overdose when the methadone reaches steady state.*

Opioid equivalency has only been established between oral morphine and methadone and uses a sliding scale that depends on the total amount of oral morphine equivalents required in 24 h (Table 2.4). This sliding scale is needed to account for its NMDA receptor blocking analgesic effect. As with all other opioids, there are variations of conversion tables in textbooks and online. The conversion ratio of oral to IV methadone is 2:1. Therefore, the IV methadone dose is half of the oral dose.

If overdosed, methadone requires a naloxone infusion to reverse. A negative side effect more common with methadone than other opioids is the risk for QTc prolongation.

Table 2.4 Morphine to Methadone Conversion

24 h Oral Morphine Dose	Oral Morphine–Oral Methadone
<100 mg	3:1
101–300 mg	5:1
301–600 mg	10:1
601–800 mg	12:1
801–1000 mg	15:1
>1001 mg	20:1

Please note that unlike the opioid equianalgesic equivalency chart above, given the variable metabolism of methadone, this chart can only be used left to right. Methadone should not be converted back to oral morphine equivalents using this chart. In the event the patient must stop methadone, retitration with an immediate-release opioid is recommended.