

Assessment and Management of Chemical Coping in Patients With Cancer

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ABSTRACT

Chemical coping is a working definition that describes patients' intake of opioids on a scale that spans the range between normal nonaddictive opioid use for pain all the way to opioid addiction. Most patients will fall somewhere between the two extremes in using opioid analgesics to cope with their psychological or spiritual distress. The degree to which patients use their medications in a maladaptive manner will determine their susceptibility to drug toxicity and harm. When there are no obvious cancer-related causes for increased pain intensity, chemical coping and other patient-related factors such as delirium, somatization, and depression should be considered. As part of the initial evaluation of patients with cancer-related pain, a brief screening tool such as the CAGE questionnaire should be used to identify patients who may be at risk for chemical coping. Identifying patients at risk will allow clinicians to avoid unnecessary opioid toxicity, control pain, and improve quality of life. A structured approach for managing opioid use should be adopted, including standardized documentation, opioid treatment agreements, urine drug screens, frequent visits, and restricted quantities of breakthrough opioids. All patients at risk should receive brief motivational interviewing with an objective, nonjudgmental, and empathic style that includes personalized feedback, particularly about markers of risk or harm. For chemical copers approaching the addiction end of the spectrum, with evidence of compulsive use and destructive behavior, referral should be made to substance abuse specialists.

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INTRODUCTION

Many patients treated for cancer have a high symptom burden, regardless of whether they are at the end of life or early in the cancer trajectory.¹ Moderate to severe levels of pain are reported in approximately 15% of ambulatory patients with cancer and in 70% of those referred to palliative care.² Patients presenting with these high-intensity pain levels require a longer duration of therapy and higher opioid doses to achieve pain control,³ and almost half may not respond at all.² Patients who report persistent, severe pain despite increasing doses of opioids are a challenge for the clinician, because cancer pain comprises physical, psychological, social, and spiritual dimensions. Determining the contribution of each dimension to the total pain experienced by the individual patient can be difficult. Cancer progression, new metastases, or complications such as pathologic fractures may account for increased pain in many patients who seem not to respond to analgesics. However, when there are no obvious cancer-related causes for the increased pain, clinicians should consider patient-related factors that may amplify pain expression, including delirium, somatization, depression, and chemical coping (Fig 1). Although a preliminary study showed that functional magnetic

resonance imaging⁴ can discriminate between acute cutaneous pain and a form of social pain, there is no objective measure for quantifying the chronic pain experienced by patients or determining the contribution of psychosocial factors that influence total pain. Unfortunately, some patients reporting severe pain may be requesting increasing doses of opioids to cope with their psychological, spiritual, or existential distress rather than their physical pain. These chemical copers are more likely to have a prior history of alcoholism or substance abuse,^{5,6} will typically receive a higher morphine equivalent daily dose (MEDD) for pain control, and are more likely to experience opioid adverse effects.⁷ Patients at risk for chemical coping should be screened and identified so that strategies can be implemented to improve patient care and aid health care providers facing the difficult dilemma of contributing to unnecessary opioid dose escalation and opioid adverse effects or perhaps undertreating a patient requiring high-dose opioids for pain control.

DEFINITION OF CHEMICAL COPING

Chemical coping is a working definition first used by Bruera et al⁸ that describes the intake by patients

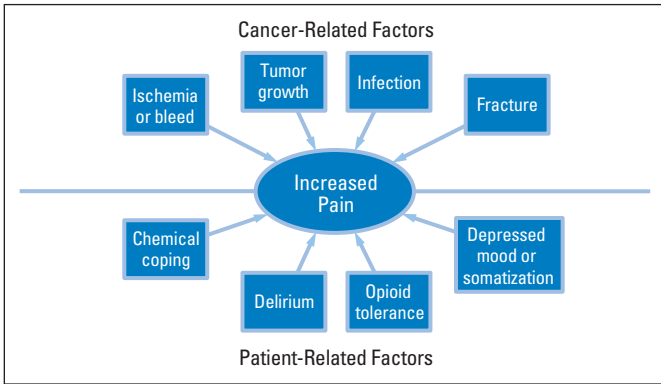


Fig 1. Cancer- and patient-related factors contributing to pain. Data adapted.⁴

with cancer of opioids on a scale spanning the range between normal nonaddictive opioid use for pain all the way to total addiction and its accompanying compulsive, destructive behavior. Most patients will fall somewhere between the two extremes, using their medications in nonprescribed ways to cope with their stress.⁹ The relationship between addiction and chemical coping is summarized by Kirsh et al⁹ as follows: “All addicts are chemical copers but not all chemical copers are addicts.”^{9(p221)} Mild chemical copers may not experience any major adverse effects, whereas those approaching the addiction end of the spectrum are at risk for increased morbidity and mortality. There is, therefore, a broad spectrum of chemical coping, and the degree to which patients use their medications in a maladaptive manner will determine their susceptibility to drug toxicity and harm. Chemical coping and addiction should be distinguished from physical tolerance and withdrawal syndrome when opioids are abruptly discontinued. Addiction is characterized by changes in brain structure and function that accompany chronic exposure to drugs of abuse.¹⁰

PREVALENCE

Opioid addiction was traditionally thought to be rare among patients treated for cancer.¹¹ However, some of the same risk factors for addiction found in patients without cancer might also be found in those with cancer, such as alcohol and tobacco abuse, depression, generalized anxiety disorder, post-traumatic stress disorder, psychological trauma, illicit drug use, psychotropic medication use, antisocial personality disorder, and childhood adversity.¹² This misconception about the low risk for opioid misuse, coupled with an ongoing legitimate worry about the inadequate treatment of cancer-related pain,¹³ has regrettably diminished clinicians’ concern about substance abuse and chemical coping in patients with cancer.

The prevalence of chemical coping among patients with cancer is uncertain; however, there is evidence that a history of alcoholism, one of the major risk factors for chemical coping, is common across the disease trajectory. The prevalence of alcoholism has long been underappreciated in general medical wards¹⁴ and among oncology patients. Between one third and 40% of male hospital patients are alcoholics¹⁵; however, a minority of these patients are identified, and an even smaller group is referred for treatment.¹⁶ Of 705 male patients with upper digestive tract tumors assessed preoperatively, 81% were alcohol misusers by Diagnostic and Statistical Manual of Mental Disorders

III criteria, although only 16% were detected by routine evaluation.¹⁷ Retrospective studies in patients with advanced cancer referred to palliative care have reported rates of alcoholism between 17%¹⁸ and 33%.⁸ Although few studies have been conducted in hospice patients, more than one third of hospices in Virginia report that abuse and diversion are problems in their hospices.¹⁹

COMPLICATIONS OF CHEMICAL COPING

Substance abuse can impede patients’ quality of life, increase the complexity of managing high physical and psychosocial needs, and lead to increased hospital admissions. As therapies for cancer treatment advance and patients survive for longer periods, the consequences of prolonged opioid use and high doses need to be considered.

Opioid-Induced Neurotoxicity

The risks to patients include opioid-induced neurotoxicity, such as excessive sedation, delirium,²⁰ myoclonus, and even seizures. These risks increase as a patient’s chemical coping becomes increasingly maladaptive and moves toward the addiction end of the spectrum. Higher doses of opioids are also associated with delirium in patients with cancer, and as a result, opioids may contribute to intractable delirium and a need for palliative sedation.²¹

Overdose

Although patients receiving chronic opioids are tolerant to the effects of respiratory depression, there is the potential for overdose. Prescription drugs, particularly opioids, are now the most common cause of overdose, outstripping illicit drugs such as heroin and cocaine combined.²² In a study evaluating the characteristics of deaths resulting from prescription drugs, a substance abuse indicator was present in 94.6% of decedents.²³ Although the rate of overdose is lower among patients with cancer compared with other patients, a study from the Veterans Administration showed an increased overdose risk among patients with cancer receiving opioid therapy, especially if patients were prescribed as-needed opioids alone compared with regularly scheduled opioids alone.²⁴

Combining Agents of Chemical Coping

Patients identified as positive after screening for alcohol misuse also have a higher frequency of nicotine use. Continued smoking despite a diagnosis of cancer should be considered maladaptive chemical coping, because continued smoking increases the risk for cancer recurrence, impairs treatment of the cancer, and impairs quality of life.²⁵ Patients who are coping chemically are also at increased risk for polysubstance abuse with illicit drugs such as cocaine and heroin and are more likely to use benzodiazepines,²⁶ increasing the possibility of excessive sedation or accidental opioid-related death.^{27,28}

SLIPPERY SLOPE: ANY BENEFIT OF CHEMICAL COPING?

Although we are concerned primarily with unnecessary dose escalation and the adverse effects of potentially addictive prescribed drugs, preliminary studies do suggest that pharmacologic agents for pain might decrease spiritual, psychological, or existential suffering. This by

no means condones the use of opioids for purposes other than pain relief, such as psychological distress. Clearly, the suffering of patients with cancer is compounded rather than diminished by substance abuse. There should be recognition, however, that some of these pain medications may ameliorate psychological and social components of total pain. Recent advances in neuroscience show that there is overlap in the neurobiologic foundations of physical and social pain²⁹ and that negative affect, pain, and cognitive control are anatomically and functionally integrated in the cingulate cortex.³⁰ Additional evidence of the mechanistic links between physical and social pain are provided by studies showing that opioids may decrease separation distress,³¹ and experimentally, acetaminophen has been shown to decrease distress in healthy people contemplating their own mortality.³²

MANAGEMENT OF CHEMICAL COPING

There may be health care providers who are skeptical about the value of identifying and managing patients with advanced cancer who are at risk for misuse of opioids. There may be an attitude that these patients have a limited life expectancy, and there is no additional harm from using excessive amounts of opioids.³³ However, if we are to manage symptoms optimally and allow patients to fulfill their maximal physical and psychosocial potential, we must avoid the adverse effects of high-dose opioids and their detrimental effects on patients' and families' quality of life.

A systematic review of chronic noncancer pain in patients who also have a substance use disorder concluded that little empiric data are available to guide clinicians in treating these patients.³⁴ There is even less information regarding patients with cancer, and much of the management is driven by the universal precautions approach^{35,36} to assessment and management advocated for noncancer patients with chronic pain.^{37,38} An adaptation of this universal management approach is summarized in Table 1. Patients identified as at risk should enter an opioid agreement that outlines expectations, including receiving prescriptions from a single provider. However, patients with advanced cancer and high symptom burden who break these agree-

ments present a difficult ethical challenge, because simply discharging them is not an option.

A multiagency federal effort to address prescription drug misuse was approved by the US Food and Drug Administration in 2012 and is also part of the national prescription drug abuse plan³⁹ announced by the Obama Administration in 2011 to combat prescription drug misuse and abuse. A risk evaluation and mitigation strategy will require opioid analgesic companies to make available education and training materials to health care professionals on proper prescribing practices and also distribute educational materials to patients on the safe use of pain medications. Patients who understand the risks of opioids are less likely to misuse their medications.

ASSESSMENT OF CHEMICAL COPING

As part of the initial evaluation of patients with cancer-related pain, a brief validated screening tool should be used to identify patients at risk for chemical coping. In the general population, there are strong associations between the early onset of alcohol use and family history of alcoholism with the development of prescription drug use disorders (sedatives, tranquilizers, opioids, stimulants).⁴⁰ Any patient with a history of coping chemically using alcohol or drugs is more likely to adopt a maladaptive coping strategy involving opioids when faced with the multiple psychosocial and physical burdens accompanying a diagnosis of cancer. Several brief screening tools for alcoholism or drug use are available⁴¹; however, there is no single instrument that can be recommended as the gold standard for assessment of substance misuse in patients with cancer.

CAGE Questionnaire

The CAGE questionnaire is a simple four-item validated screening tool.⁴² The screening need only take place at the initial assessment and does not distinguish between current versus past alcohol use. Without an assessment tool, alcoholism is undetected in more than 80% of patients referred to a supportive care clinic.¹⁸ Two positive answers (ie, CAGE positive) have sensitivity more than 90% and

Table 1. Approach to Managing Opioid Risk and Chemical Coping in Patients With Cancer Based on Universal Precautions

Step	Description
1	Differential diagnosis: identify tumor-related causes of pain and patient-related factors influencing pain perception and expression
2	History of risk factors for chemical coping: tobacco use, depression, history of substance abuse, personality disorder, somatization, sexual abuse
3	Screening instrument at first visit to identify those at high risk (eg, CAGE, SOAPP, ORT, STAR)
4	Informed consent including patient education about addiction, tolerance, and opioid adverse effects and treatment plan that de-emphasizes opioids as sole treatment for pain
5	Opioid agreement (written or verbal) that includes outline of patient obligations (eg, receive opioids prescriptions from single provider, no early refills, random UDS)
6	Pre- and postassessment of pain level and function; routine assessment of four As: analgesia, activities of daily living, adverse effects, and aberrant behavior ³⁸
7	Psychological support, motivational interviews, and increased vigilance and structure for those at high risk for opioid misuse (eg, pill counts, shorter intervals between visits); consider integrated comanaged model with interdisciplinary palliative care or chronic pain team
8	Periodically review differential diagnosis; contribution of tumor- and patient-related factors to pain may have changed (eg, patients with no evidence of disease should receive stable scheduled dose or tapered opioids, whereas patients with progressive advanced cancer will require additional breakthrough-dose opioids)
9	Documentation of all prescriptions, office visits, agreements, and instructions
10	Ethical concerns: discharging patient with advanced cancer and substance misuse; comanagement with substance abuse specialists should be initial step

NOTE. Data adapted.^{35,36,37}
Abbreviations: ORT, Opioid Risk Tool; SOAPP, Screener and Opioid Assessment for Patients With Pain; STAR, Screening Tool for Addiction Risk; UDS, urine drug screen.

specificity more than 95% to detect alcoholism.⁴³ Studies in patients with advanced cancer suggest that patients who cope chemically and are identified as CAGE positive tend to express a higher degree of symptoms, are referred earlier to palliative care, and are more likely to receive opioid therapy on referral.^{44,45} The CAGE-AID has been developed to include drugs in addition to alcohol on the four-item screening test.⁴⁶

Other Screening Tools

There are at least three screening instruments with only five items that take fewer than 5 minutes to administer. The Screener and Opioid Assessment for Patients With Pain (SOAPP) is a 14-item self-administered screening instrument originally used to assess risk for substance use disorders in patients with chronic noncancer pain.⁴⁷ An abbreviated five-item short form (SOAPP-SF) has been used in patients with cancer, and it was shown that those classified as high risk tended to have higher pain scores, MEDD, anxiety, and depression.⁴⁸ The Opioid Risk Tool (ORT) is a brief five-item yes-or-no self-report designed to predict aberrant behavior of patients receiving opioids for chronic pain⁴⁹; however, there are few studies in patients with cancer. The Screening Instrument for Substance Abuse Potential (SISAP) is a clinician-administered five-item instrument originally developed using data from the National Alcohol and Drug Survey (NADS; Canada) to identify patients with chronic noncancer pain at risk for opioid misuse.

Two slightly longer questionnaires have also been used to screen for risk. The Alcohol Use Disorders Identification Test (AUDIT) is a 10-item questionnaire requiring training for administration and was designed by the WHO to screen for hazardous or harmful alcohol intake in primary health care settings.⁵⁰ The Screening Tool for Addiction Risk (STAR) is a 14-item yes-or-no questionnaire that has the advantage of being self-reported.

Urine Drug Screening

Urine drug screening (UDS) is recommended for patients without cancer, but the extent to which this procedure should be implemented for patients with cancer-related pain is uncertain. Drug screens that show absence of an opioid should be concerning for noncompliance diversion and selling of prescription opioids. The presence of illicit drugs such as cocaine and heroin or nonprescribed sedating agents such as benzodiazepines is especially dangerous and would require referral to a substance abuse specialist for comanagement.⁵¹

TREATMENT

For many of the patients on the milder end of the spectrum, no specific intervention is needed, and as with all patients who initiate opioid therapy, they should be educated about potential opioid adverse effects. For patients who are farther on the spectrum, counseling and psychotherapy should be directed at managing comorbid conditions such as depression, demoralization, and existential distress that may be increasing suffering and opioid misuse. In addition, patients should

be given limited quantities of opioids, particularly breakthrough doses of immediate-release opioids. Survivors who have chronic stable pain should be treated with scheduled long-acting opioids, and immediate-release breakthrough opioids should be avoided.⁵² The use of opioids should be decentralized, emphasizing that opioids are not the sole focus of therapy but will be combined with other pharmacologic agents as well as nonpharmacologic modalities.⁵³ A structured approach by a nurse practitioner/clinical pharmacist-run clinic for managing opioids in patients with complex chronic noncancer pain successfully used standardized documentation, opioid treatment agreements, UDS, frequent visits, and patient education to support primary care providers and decrease pharmacy costs.⁵⁴ A similar, structured approach coupled with an individualized treatment strategy in patients with cancer should include an assessment of physical functioning and correlation with pain, feedback if patients are using unusually high doses of opioids, information about the risks of prolonged high-dose opioids, and advice regarding treatment options.

At follow-up visits, overuse must be identified and discussed in an open, honest manner. Providing personalized feedback, particularly about biologic markers of risk or harm, has been effective in patients with alcohol⁵⁵ or cocaine abuse.⁵⁶ This approach of brief motivational interviewing uses an objective, nonjudgmental, and empathic style and has been used successfully by a multidisciplinary inpatient palliative care service treating chemical copers with advanced cancer.⁸ In addition to discussion of the concepts of chemical coping and opioid misuse, positive reinforcement should be provided when a patient's function and socialization improve. For chemical copers approaching the addiction end of the spectrum, with evidence of compulsive use and destructive behavior, there should be referral to substance abuse specialists; however, this may be challenging if resources are limited. Nevertheless, poorly managed chronic pain and addiction overlap in that both lead to impaired function and quality of life, and it is necessary to treat both conditions simultaneously.⁵⁷

DISCUSSION

Pain expression is a patient-reported measure modulated by a patient's culture, personality, and cognitive ability. There are no objective measures for quantifying the pain experienced by an individual or the contribution by psychosocial factors. However, the mantra of "pain is what the patient says it is" should be abandoned in favor of a more complex model that acknowledges patient-related factors, including chemical coping, which may have a considerable influence on pain and its expression. This will allow us to avoid unnecessary opioid toxicity, control pain, improve quality of life, and simultaneously continue to provide the compassionate care that all our patients deserve.

AUTHOR'S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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