

Narrative Review

e Opioid Abuse in Cancer Pain: Report of Two Cases and Presentation of an Algorithm of Multidisciplinary Care

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Background: The growing awareness of opioid abuse and addiction in the chronic pain population, along with increasing cancer survivorship, has heightened our awareness of this potential problem in the cancer patient. An increasing number of patients who abuse opioids have been identified in our clinical setting.

Objective: We present an algorithm of multidisciplinary care for the treatment of cancer patients at risk for abusing opioids.

Setting: Two illustrative patient examples were identified recently from our clinic.

Results: These 2 patient examples demonstrate our multidisciplinary approach to treatment. A discussion of safe prescribing principles adapted from the literature is presented. Also, a brief point of added complexity is introduced; specifically, ethical considerations due to the unique nature of cancer pain.

Limitations: Although validation studies exist for the use of screening tools in patients with chronic noncancer pain, there have been no instrument validation studies on patients with cancer pain. The educational treatment model that we refer to regarding facilitating safe use of opioids also has not been studied on patients with cancer pain. Lastly, we express caution in generalizing our guidelines to patients with noncancer pain. Our patient population differs in the multiple co-existing stressors and symptom burden associated with cancer.

Conclusions: We have become increasingly aware of the problem of opioid abuse in the cancer pain population. With an approach to using safe prescribing principles adapted from chronic pain literature, and an ethically based multidisciplinary approach, clinicians can continue to treat pain successfully in the opioid-misusing cancer patient. We outline our approach in this article.

Key words: opioids, opioid abuse and addiction, substance abuse and addiction, multidisciplinary care

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Pain is a highly prevalent symptom and often a cause for severe distress in patients with cancer. A recent meta-analysis of the literature places the incidence of pain in those receiving active cancer treatment at 24-60%; 58-69% in patients with advanced cancer; and 33% in cancer survivors(1).

The basic approach to treat cancer pain was initially described as a 3-step analgesic ladder that was put forward by the World Health Organization in 1986. This 3-step analgesic treatment recommended prescribing according to need from non-opioids, to weak, and then strong opioids (2,3). Subsequent to

those recommendations, the Agency for Health Care Policy and Research (AHCPR) in 1994(4), the American Pain Society in 2005(5), and the National Comprehensive Cancer Network in 2000, updated in 2009(6,7), has put forth treatment guidelines to help with cancer pain management which include multidisciplinary and multimodal approaches, and pharmacological and non pharmacological methods.

In all recommended treatments there is acknowledgement that opioids are an important part of the armamentarium in the management of cancer pain. However, there has been a growing awareness of the abuse of prescription opioids. The risk of addiction to opioids remains a concern when initiating long-term opioid treatment (8). A literature review indicates that the prevalence of addiction to opioids varies from 0% up to 50% in chronic noncancer pain patients, and 0% to 7.7% in cancer patients, based upon the population studied and the criteria used (9,10). This may be an underestimation of the actual incidence of this clinical problem as awareness of opioid abuse, addiction and diversion increases in the chronic pain community and use of tools to identify misuse also increase (11). The abuse and addiction to prescription opioids presents an additional challenge in the management of these patients.

Risk stratification, even in cancer patients, may help to identify those at high risk for aberrant use of opioids. Being a "high risk" patient need not deter the physician from prescribing opioids, but should lead to increased vigilance and other strategies, including perhaps the use of a pain treatment agreement/informed consent form, frequent clinic visits, pill counts, and even urine toxicology screening using gas chromatography/mass spectroscopy. Patients with poor compliance to appropriate opioid use are more challenging to manage regardless of their cancer stage. These patients have a high incidence of co-morbid depression and anxiety. In advanced cancer, anxiety occurs in 13-79% and depression in 3-77% of patients (12-14). A multimodal treatment approach, including psychological care, is advocated to help the high risk patient. The consequences of patient noncompliance with following an opioid agreement differ according to disease status and across health care institutions. In the case of patients with pain from cancer, there is greater effort expended and leniency to help a patient become more compliant. Within our particular institution, there also is great importance on the pain physicians assisting the oncologists with their patients. Our view is that we are

all part of the patient's team.

Here we present 2 illustrative cases of patients with active cancer and substance misuse related issues from our clinic where we used multidisciplinary, multimodal treatment. Finally, we will present a discussion of our approach to the opioid-abusing cancer patient.

CASE 1

the patient is a 54-year-old male with a history of advanced metastatic lung cancer treated with chemotherapy and who recently has undergone palliative radiation. The patient continues to have chest pain for which he had been treated by the palliative care team for the past year. The palliative care team consulted our pain service for assistance in optimizing his pain control. He has a history of polysubstance abuse including alcohol, marijuana, heroin, cocaine, and tobacco abuse. He has a criminal record of driving under the influence of alcohol and for possession of cocaine and heroin. He has had numerous detoxification episodes, although he denies any illicit drug use for the past 3 years. His past medical history is significant for hypertension, cardiomyopathy, COPD, Hepatitis B and C, and bipolar mood disorder. His treatment course had been complicated by his ongoing misuse of medication and 2 emergency room visits for overdose of opioids and benzodiazepines. There had been several instances of early requests for refills due to inappropriate use and lost medications. He has demonstrated maladaptive "chemical coping" behaviors at several of the visits to previous physicians. For example, he takes opioids when stressed or when feeling despair. He also has a long history of chronic back pain for which he had been on multiple chronic opioids prior to his cancer diagnosis.

He presented to the pain center complaining of burning pain involving the left chest and dull ache in the left suprascapular region. There was a nociceptive and neuropathic component to his pain. His medications at the initial visit included oxycodone extended-release 80 mg 3 times a day, morphine immediate release 30 mg 4 times a day as needed for pain, venlafaxine, quetiapine, carvedilol, albuterol inhaler, and supplemental nasal oxygen. He reported an average pain score of 8/10 on a numerical rating scale (NRS) and felt that the morphine preparation provided more pain relief than the oxycodone. The patient also admitted to taking methadone that he had from previous prescriptions. He scored 4/4 on the CAGE for history of alcohol and substance abuse; and a 13/20 on the Screener and Opioid Assessment for Patients with Pain - Short Form

(SOAPP-SF). The name "CAGE" is an acronym formed by taking the first letter of key words from each of the following questions:

- Have you ever felt you should cut down on your drinking? YES/NO
- Have people annoyed you by criticizing your drinking? YES/NO
- Have you ever felt bad or guilty about your drinking? YES/NO
- Have you ever had a drink first thing in the morning (an eye opener) to steady your nerves or get rid of a hangover? YES/NO

He was under the care of a psychiatrist-addiction specialist to manage his depression, anxiety, insomnia, and opioid dependence and for supportive psychotherapy. The addiction specialist and psychologist both found him to have limited insight and judgment.

Upon coming to our pain center, a pain treatment agreement/ informed consent form was presented to the patient, reviewed, and signed. The patient and his wife agreed with the treatment plan that was discussed with them. A urine drug screen done at the initial visit was positive for morphine, methadone, and oxycodone, consistent with the patient's history. Since the morphine preparation was helping him, the oxycodone was discontinued and 400 mg of extended release morphine was initiated, with immediate release preparations for breakthrough pain and pregabalin for the neuropathic component. He was given a one week supply of medications and was scheduled to be seen at the pain clinic. Interventional therapy (blocks and intrathecal medications) were offered to optimize pain control, which the patient deferred. He was also to continue care with the psychiatrist and his medications for anxiety and depression.

In the following visit he had discontinued the pregabalin as it was causing him to have hallucinations. His pain was not adequately controlled with this regimen and the extended release morphine was increased to 600 mg/d over the next 6 weeks and hydromorphone initiated for breakthrough pain. At this point, a telephone call from another physician revealed that the patient was getting opioids prescribed by 3 other providers. He did confess to the psychiatrist that he was a "bad boy" and sought drugs from other sources as his current regimen was not adequately controlling his pain. His urine screen was positive for opioids and benzodiazepines consistent with history, and no illicit drugs detected. The pain agreement he had signed previously was reviewed and he was cautioned that noncompli-

ance on his part would necessitate us to discontinue opioids. Our team was designated as his sole provider (after discussions with his outside physicians) and his morphine dose was titrated up to 800 mg/d over the next 2 weeks. He was not satisfied with his pain control and an opioid rotation to methadone was done, starting at 60 mg/d with hydromorphone for breakthrough pain. Baseline ECG showed QTc to be within normal limits. The patient came back to the clinic in only 4 days as he had consumed his 2 week supply of methadone early.

This caused our team, including an addiction specialist and psychologist, to have an extensive discussion with the patient about our concerns of his misuse of pain medications and the importance of complying with his prescriptions. We had a lengthy discussion with the patient and wife to set firm limits, requiring him to have frequent visits (every week initially, transitioning as "earned" to monthly) to confirm proper use of his pain medications and optimize pain control. In spite of repeated warnings, the patient continued escalating opioids without our consent. His methadone dose had been slowly titrated up to 400 mg/d to satisfactory analgesia with breakthrough morphine. He did admit to the psychiatrist that the increased use of opioids was 50% pain-related and 50% was his "addiction." He was asked to maintain a pain diary documenting his level of pain, emotions, boredom, etc. and to identify patterns of opioid intake for "nonphysical pain." He was also encouraged by the psychiatrist to decrease his methadone dose by 10 mg/d per week which he has not been able to do. While on this stable regimen, he had one "panic attack" and was incarcerated overnight for possession of illicit drugs (which it appeared he did not ingest). His explanation for this was that the bottles of pain medications were with his wife and he was terrified of going into withdrawal if there was a delay in his next methadone dose and therefore sought alternative drugs. He was advised to attend Alcoholics Anonymous meetings to help prevent a relapse of illicit drug use, which he deferred.

With our help and "tough love" approach, he was able to realize that we would continue his treatment only if he was compliant. He worked hard to earn our trust and complied with his medical regimen and became stable. He was maintained on a 400mg/d dose of methadone and morphine for breakthrough pain for 6 months and continued with monthly follow-up visits. Repeat ECGs were done and showed QTc to be within normal limits. His pain was fairly well controlled and he

continued with his medications for anxiety and depression as well as monthly psychotherapy. He expressed regret over his behavior with medications in the past. He adopted a dog from the shelter and was able to walk the dog a few times daily. He has had repeat quantitative urine drug screens all revealing compliance with his opioid regimen.

He recently died of pneumonia but had a relatively stable clinical course with reasonable pain control for at least 6 months leading up to his death. His wife expressed gratitude for the compassionate care provided.

CASE 2

This patient is a 46-year-old African-American female with a history of HIV and hepatitis C seen at our institution for stage IIB squamous cell carcinoma of the cervix. Imaging of her abdomen and pelvis had demonstrated a right-sided hydronephrosis and a large necrotic cavitating mass in the cervix extending posteriorly into the uterosacral ligaments and the right piriformis muscle extending into the sciatic foramen. She was dispositioned to receive radiation without chemosensitization given her multiple co-morbidities. However, her radiation treatment was very protracted secondary to non-compliance with follow-up visits with her gynecologist.

The chronic pain service was consulted soon after she initiated oncologic treatment at our institution during a visit to the emergency department (ED) for intractable pelvic pain. At that time, she had already been started on a moderate dose regimen of extended release morphine 120 mg/d as well as hydrocodone and alprazolam for anxiety by her oncologist at the county hospital. She continued to use multiple illicit drugs, primarily crack cocaine and marijuana, and stated that she continued to use these drugs secondary to uncontrolled pain. We counseled her extensively regarding the inability to continue to provide opioid medications despite her active disease if she continued to use illicit drugs and was noncompliant with clinic policies outlined in the pain treatment agreement/informed consent. She agreed to the policies in the document and signed the pain clinic's agreement and consent form. She scored 14/20 on the SOAPP-SF screener.

Soon after this ED visit, she was admitted to the hospital for pelvic pain and was initiated on patient-controlled intravenous hydromorphone analgesia. She was discharged after having transitioned to oral morphine 180 mg/d and hydrocodone regimen and the addition of gabapentin. We planned to follow her up very closely at the clinic in one week and only provided

one week's worth of medication. At the clinic she denied any recent use of illicit drugs and appeared to be compliant with her pain medication regimen. She did still complain of suffering from increasing pelvic pain. Thus, her morphine regimen was rotated to methadone along with hydrocodone, and a week later she underwent a superior hypogastric plexus neurolysis which resulted in decreased pelvic pain intensity. Given her initial compliance, we decided to extend her next visit to 2 weeks and also have her see our pain psychologist for help with medication compliance and discontinuation of illicit substance use. Unfortunately, prior to this visit she presented to the ED, now with increasing left leg pain thought secondary to her sacral involvement of disease. Her medication regimen was then adjusted and she would be seen within the week at our pain clinic. During her follow-up visit, she was asked to provide a urine sample for toxicology, which she refused, leaving the clinic with a prescription for tramadol.

After this incident, she was lost to follow-up for more than a month when she was again seen in the ED, now with increasing pelvic pain exacerbated by a labial laceration. At this point, we again extensively counseled her on refraining from using illicit drugs due to our suspicions and gave her a week's worth of hydromorphone; she was allowed 4 tablets a day. She had progression of the disease and associated increased pain. So, in spite of her being noncompliant, we did give her a very limited supply of opioids. At her one week follow-up, the patient stated that her pain was better with her opioid regimen and appeared again compliant with her pain medications. Unfortunately, when asked to provide a urine sample she provided cold urine suggestive of tampering with the sample. She then admitted to continued use of crack cocaine and again was limited to treatment with tramadol. She did agree to drug detoxification/ rehabilitation, which are not available within our institute. With the help of our social worker, the patient was placed in contact with community drug rehabilitation programs. Unfortunately, secondary to ongoing cancer treatment, she did not qualify for any of the community programs.

Within the week, she was again seen at the ED for increasing pain at which point we decided to start her on a buprenorphine/naloxone sublingual preparation and local lidocaine gel, the latter to be applied over the genital area. She was seen in one week intervals and after a couple of visits and titration of buprenorphine/naloxone, she presented to the clinic with suicidal ideations, requiring immediate psychological consult. Our

psychologist deemed her appropriate for outpatient follow-up secondary to not being at acute risk for suicide. With the patient's permission, the psychologist did contact the patient's family and the family agreed to provide support and supervision of the patient. We scheduled the patient to be seen by a psychiatrist to assist with monitoring of chronic suicidal thoughts and medical management of depression. In an effort to improve pain control the patient was rotated again to a regimen of methadone 10 mg/d, with a restricted amount of hydromorphone for breakthrough pain and the addition of pregabalin. She would again be given a week's worth of medication and followed on a weekly basis. She seemed to be compliant with her medication regimen and follow-up at the pain clinic for several weeks. Unfortunately, she then presented to the ED with altered mental status and acute renal failure and required bilateral nephrostomy tube placement. During this admission, she again exhibited suicidal ideations and Psychiatry placed her on antipsychotic medications and again recommended adequate pain control. Her renal function improved and her neuroleptic medication adjusted accordingly and she was continued on her opioid regimen of methadone 20 mg/d and hydromorphone with good control days prior to discharge. After discussion with all members of the medical team and family, the patient opted for hospice care and followed with the hospice physician.

Discussion

As these 2 case presentations highlight, pain management in the setting of advanced cancer and a history of opioid and substance abuse can be challenging. Cancer pain is a biopsychosocial experience with significant contributions coming from sensory, emotional and cognitive components. There is the concern for inappropriate use of opioids for a patient's amplified "pain experience" due to suffering. In the case of patients with pain from cancer, there is greater effort expended and leniency to help a patient become more compliant to appropriate use of pain medications (15,16).

Pain treatment involves systematic attention to each of these components. This comprehensive approach to cancer pain management has been shown to decrease the dose of opioids required (17,18). Patients with a high level of anxiety tend to express higher levels of pain (12) and not addressing the anxiety may lead to inappropriate use of opioids. In patients with a history of opioid abuse and addiction, addressing their pain comprehensively with pharmacotherapy

and psychotherapy is of utmost importance to ensure appropriate use of opioids in context to treat the nociception, with the use of other modalities to treat the associated suffering.

Cancer pain management is complicated by multiple barriers, including systemic, professional, and patient related (4,18-21). Systemic barriers include the "drug war" waged against prescription opioid abuse and addiction, the cost and limited availability of opioids, and finally the lack of a multidisciplinary support system. Physician barriers include a lack of education and knowledge on assessment of pain and use of opioids and/or adjuvants, general medical "opiophobia," concern for regulatory scrutiny on the use of opioids and addiction, a "disease-based" rather than a "symptom-based" model of care, and finally the difficulty of compulsive follow-up care and meticulous appropriate documentation. Patient-related barriers include the reluctance to take medications as prescribed, confusion over the increased need of opioids for pain vs. craving for opioids, and concerns over addiction, dependence and being labeled a "drug seeker" (22,23). There is also the concern for some degree of "chemical coping" seen in these patients which will influence the expression of pain as well as management (17).

Adding another complexity is the significant ethical issue in the care of patients with cancer pain which is different than the chronic pain situation, particularly in the patient with active, progressive cancer. Whereas the noncompliant chronic pain patient can be determined not to be a candidate for chronic opioid therapy and discharged from the clinic, in the patient with active cancer and pain neither of these options are ethically satisfactory. In our case examples above, we monitored ongoing, unsanctioned opioid dose escalations through adequate assessment and multidisciplinary care of the patients throughout their evolving clinical cancer pain circumstances. It is also notable that we had to use a multidisciplinary approach in an attempt to optimize pain control and safely prescribe opioids for these high risk patients in an ongoing manner.

Pain physicians have adopted some structure in managing patients with noncancer pain and at high risk for abuse of opioids. Gourlay and Heit (24,25) have put forth "the ten principles of universal precautions" to manage chronic pain in patients with a history of addiction. These can be applied to the patient with cancer pain with some limitations. Kirsh and Passik (26) have outlined recommendations to help with pain management in the terminally ill with a history of substance

Table 1. Risk management strategies for treatment of cancer pain.

I.	Assessment and differential diagnosis
II.	Screening for substance abuse and opioid misuse risk factors
III.	Informed consent and treatment agreement
IV.	Opioid therapy and tolerance/addiction
V.	Adjuvant Pharmacotherapy and Interventional therapy
VI.	Ongoing Psychiatric, psychological and multidisciplinary support
VII.	Frequent outpatient visits and random screening for compliance with treatment
VIII.	Reassessment of pain and function; regularly re assess the "Four As" of pain medicine: Analgesia, Activity, Adverse Reactions, and Aberrant Behavior
IX.	Documentation
X.	Exit strategy and Ethical concerns

Adapted from Gourlay et al(24)

abuse. Adopting a tightened structure helps identify patients at risk for inappropriate opioid use and also reduces risk behaviors (27). There is scant literature on the management of pain in the cancer patient with substance/opioid abuse and/or addiction. We have adopted risk management strategies similar to the care of patients with noncancer pain, keeping in mind the complex nature and unique ethical considerations of cancer pain (Table 1). We are alert to the physiological, sensory, affective, cognitive, behavioral and sociocultural components to the experience of cancer pain (16). The pain physicians and psychologists at MD Anderson Cancer Center adopt a multidisciplinary approach to the care of these patients with use of multiple modalities at flexible times as indicated. We outline below some of the principles that guide us in optimizing care in this patient population.

I Assessment and differential diagnosis

The initial interview with the patient and their caregivers is crucial to establish a rapport as well as to begin to set limits. A thorough history and examination to identify the type of pain (i.e., nociceptive, neuropathic) and identification of comorbidities including anxiety and depression is key. The physiological aspect of pain is determined by a careful pain history and examination. In the cases discussed here, there is a component of nociceptive and neuropathic pain; pharmacotherapy is based accordingly. Both patients expressed high levels of anxiety associated with the progression

of disease and pain. They had some degree of ongoing depression. A psychosocial history will help guide the need for involvement of family members, social worker, physical therapist, psychologist and/or psychiatrist in the care of the patient. In our experience, most cancer patients will benefit from the involvement of these disciplines, at the very least family and psychological involvement.

II Screening for substance abuse and opioid misuse risk factors

Several screening tools such as Screener and Opioid and Assessment for Patients with Pain (SOAPP), SOAPP-SF (Fig. 1) and CAGE questionnaire can be used to identify patients at high risk in the noncancer population (28). There is evidence that a high score on SOAPP increases the likelihood of aberrant drug-related behavior in noncancer pain patients (29,30). We have been routinely using the SOAPP-SF for all new outpatient visits and other established patients at the discretion of the physician. This is a 5-item self report questionnaire that is used to help identify patients at high risk for opioid misuse and assess the need for more stringent monitoring. A score of ≥ 4 is considered high risk with 86% sensitivity and 67% specificity; whereas a score of < 4 is considered low risk. A high score has a 33% false positive rate which means it is less sensitive in identifying patients at low risk. Although less frequently than the SOAPP-SF, we also implement the CAGE when indicated. This measure is used frequently by our addic-

Screener and Opioid Assessment for Patients with Pain (SOAPP®) Version 1.0 - SF

Name: _____ Date: _____

The following are some questions given to all patients at the Pain Management Center who are on or being considered for opioids for their pain. Please answer each question as honestly as possible. This information is for our records and will remain confidential. Your answers alone will not determine your treatment. Thank you.

Please answer the questions below using the following scale:

0 = Never, 1 = Seldom, 2 = Sometimes, 3 = Often, 4 = Very Often

- | | |
|--|-----------|
| 1. How often do you have mood swings? | 0 1 2 3 4 |
| 2. How often do you smoke a cigarette within an hour after you wake up? | 0 1 2 3 4 |
| 3. How often have you taken medication other than the way that it was prescribed? | 0 1 2 3 4 |
| 4. How often have you used illegal drugs (for example, marijuana, cocaine, etc.) in the past five years? | 0 1 2 3 4 |
| 5. How often, in your lifetime, have you had legal problems or been arrested? | 0 1 2 3 4 |

Please include any additional information you wish about the above answers. Thank you.

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Figure 1. Sample of screener and Opioid and Assessment for Patients with Pain.

tion and palliative care specialists. The cases discussed above were considered high risk for opioid use based on history as well as their score on screening tools. Case 1 scored 4/4 on the CAGE and 13/20 on the SOAPP-SF; Case 2 scored a 14/20 on the SOAPP-SF; which put both these patients at high risk for opioid abuse and addiction. Validity of these tools in cancer patients is a topic of future research.

III Informed consent and treatment agreement

This is a crucial aspect of patient care for setting appropriate boundaries within the doctor-patient relationship. Our Informed Consent and Pain Treatment Agreement is a modified version of the Texas Pain Society treatment agreement with changes made to accommodate our cancer patient population. This document clarifies the risks associated with opioid use and concerns with continued substance abuse and/or opioid misuse is done at the first encounter and reiterated as indicated. This agreement provides a detailed explanation about the concerns with long-term use of opioids and harm to life with inappropriate use of opioids. Inclusive in this document is instruction on taking medications as prescribed and agreeing to not take any illegal or illicit drugs; not having early refills, and agreeing to random urine drug testing. Helping the patient understand the need for the appropriate use of opioids and adjuvants is an important therapeutic tool for optimizing pain control. There are times when we help patients understand that their goal for an excessive amount of opioids may not serve them well. Side effects associated with opioid use and abuse are discussed in detail with the patient and caregivers. This interchange also helps set realistic goals and limitations one faces at times with difficulty in managing intractable cancer pain. In these instances we help them shift their goals. Patient and family education plays a crucial role in the management of these patients with pain and substance abuse and addiction, and complex psychiatric co-morbidities. Ethical issues are raised by the introduction of a pain treatment agreement in the cancer pain setting. These are complex, and we have yet to abandon pain treatment in a patient with active cancer, yet we find the agreement a helpful "guidepost" when dealing with these difficult patients and issues.

IV Opioid therapy and addiction/tolerance

Pharmacological treatment with opioids and adjuvants are to be initiated as dictated by the type of pain.

Since both patient examples here have active cancer and are on chemotherapy, anti-inflammatory medications and acetaminophen are relatively contraindicated as they can mask fever. Opioids are usually the analgesic agents of choice, dosed according to patient requirement. Patients with a history of opioid abuse may have high opioid requirements due to tolerance. Our goal is to initiate at appropriate doses and titrate to optimal analgesic effect unless the patient has associated side effects. In the cases discussed above, our initial dose was high and had to be escalated rapidly. Opioid rotation remains an option when pain control is suboptimal on high dose opioids. Opioid tolerance complicates the treating physician's task when a patient suspected of abusing opioids complains of inadequate opioid doses. The physician's judgment is required to discern between tolerance and true increases in pain, or addictive-type behaviors. In patients with progressive cancer and an obvious source of nociception, we generally go with the patient's reported pain and titrate analgesics with a careful evaluation of their response. There are multiple patient and provider barriers that can complicate care in these cases (19-21,31). The patient may have concerns that include being labeled as a "drug abuser" which may compromise care. Patients also fear that inadequate analgesia and request for increased analgesic medications may be considered drug seeking behavior among the pain management staff. There is also patient concern about becoming addicted (or re-addicted) to the opioids (32). Health care providers fear legal/licensure ramifications as well as some unease about at-risk patients being on relatively high doses of opioids that may be required to obtain adequate analgesia. There may be a tendency to underdose the patient with a resulting poor outcome, and perhaps pseudo-addiction behavior.(33,34)

V Adjuvant pharmacotherapy and interventional therapy

Use of multiple adjuvants help to optimize analgesia and minimize side effects associated with opioids. There is some limitation as a majority of these patients are already on tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs) for depression or other medications for anxiety. Interventional treatments, such as neural blockade or implantable devices, can be added to the treatment algorithm to help optimize pain and may decrease the opioid requirement. The patient discussed in Case 1 did not consent to these modalities at least in part because of the fear that he may

lose or have to cut back on the use of opioids; whereas the second case did get some benefit from a block but had increased pain with disease progression. There is also some concern that patients who are “chemically coping” may perceive intrathecal medications as being helpful. Some patients with a history of opioid misuse and drug abuse have some element of chemical coping and may not do well if weaned off their medications. However, we believe in this analgesic approach within the context of the other principles presented here.

VI Ongoing psychiatric, psychological and multidisciplinary support

The cases described outline the different disciplines involved in the complex care of these patients. It is almost always necessary for the pain physician to work in coordination with a psychologist and/or psychiatrist. Following a careful psychosocial assessment, determination can be made on individually tailoring treatment to help patients. There is a growing body of evidence to support the use of multi-component psychological treatments (35). These could include cognitive behavioral therapy specifically focused on pain management. Other components of treatment might include aspects of positive psychology, meaning-finding therapy, dealing with end-of-life issues, interpersonal psychotherapy, and motivational interviewing. The challenge of addressing both the biomedical and psychosocial issues involved in pain is to develop rational and effective management strategies. Therapies directed primarily at psychosocial variables can also have a profound impact on nociception, and medical interventions directed at nociception can also have beneficial effects on the psychosocial aspects of pain. It is necessary to treat anxiety and depression with psychotropic medications and psychotherapy to avoid misuse of opioids for these symptoms. In the realm of psychotherapy, cognitive behavioral treatment could incorporate relaxation and meditation for anxiety and pain. Biofeedback could be useful to help with these symptoms; in our second patient it was difficult to incorporate these modalities early due to lack of compliance with appointments. The 2 patients presented here did receive pharmacotherapy and psychotherapy for their ongoing anxiety and depression along with parallel psychological interventions focused on cognitive behavioral strategies for improved coping and pain management. End-of-life issues were also dealt with and this proved to be very helpful. Family involvement was also utilized for assistance with medication-taking and also for support. Both our pa-

tients benefitted from family support at different time frames.

VII Frequent outpatient visits and random screening for compliance with treatment

Frequent outpatient visits are also useful to ensure compliance with medications and to establish adequate analgesia. This requires significant resource utilization and is oftentimes difficult, but may help to head off ED visits and after hours phone calls. These frequent visits also ensure ongoing education to the patient and family on appropriate use of medications. Pill counts and random urine drug screens may help recognize opioid and substance abuse and may deter the patient from noncompliance (36).

VIII Reassessment of pain and function

Regular clinic visits should be done, as is feasible within the context of declining physical health with documentation of response to care, as well as quantifying medication intake and overall symptoms, and compliance with treatment. Frequent visits may be necessary at the beginning to establish a regimen that will control the pain. In keeping with the tenets of good medical care, records should be kept outlining, at least, the 4 A's of Passik and Weinreb (37): Analgesia-response to analgesic therapy, Activity-functionality with better pain control, Adverse effects- opioid-related side effects, and Aberrant behaviors- such as medication overuse or misuse. In patients with high risk of poor compliance or worrisome behaviors, follow-up care needs to be diligent and frequent. We have found the aforementioned strategies very helpful in managing these difficult patients.

IX Documentation

This is a key component to keep track of events with patient care. A thorough documentation of the history, assessment and ongoing treatment plan will help guide all involved in the clinical care of these patients and also provide medicolegal protection. Keeping a record of clinical notes, prescriptions issued, drug screens and any identified “red flags” and aberrant behaviors are helpful in the care of this patient population. Both patients had multiple requests for early refills, noncompliance with recommended dosage of opioids, receiving prescriptions from multiple providers in Case 1, refusal to give a urine sample for screening

and frequent ED visits with Case 2. Documentation of these events guided us with safe care of these patients.

X Exit strategy and ethical concerns

“Discharging” a patient for noncompliance with pain treatment in the presence of active cancer may raise several ethical concerns and questions that must be addressed according to specific situations. From an ethics principles viewpoint, with focus upon beneficence and “does no harm” nonmaleficence, several questions arise. Physicians are obligated to “do no harm” to patients while providing some benefit to them. Treating pain is clearly a beneficent act concurrent with the nonmaleficence of avoiding the harm of continued suffering. However, in the setting of noncompliance, does the benefit of pain relief outweigh the potential harm of drug misuse? Is the prevention of misuse of opioid analgesics a higher priority than treating the pain? What are the physician’s ethical obligations to the patient? To the profession? To society? Is this a variation on the doctrine of double effect for opioids? From a consequences viewpoint, there are potential adverse impacts upon the patient, caregivers, and family, the prescriber, the health care system, and society as a whole. What is the relative hierarchy of importance of those consequences? Is it most important to relieve the individual’s pain? Or, is it equally necessary to protect caregivers and family, and society from the potential harms from misuse, abuse or diversion of opioids? What about the prescribing clinician’s professional obligations as part of a health care system? What roles and obligations does society play in this dilemma? What resources are available to the individual with concurrent cancer-related pain and drug misuse or abuse problems? Indeed, what comprises an ethical “exit strategy” in these situations

(if there is one)? These questions, and more, must be considered when working with these patients in these complex scenarios. There may be few clear answers, and a “best-fit” approach may be an acceptable option. Certainly our goal is to help these patients by managing their pain safely and satisfactorily. This requires skilled communication and interpersonal skills by a committed multidisciplinary pain team.

CONCLUSION

In conclusion, care of patients with active cancer and opioid misuse is challenging. Unlike patients with chronic pain, it is ethically difficult to discharge our patients with active cancer and pain in spite of noncompliance with opioids. In the case of patients with pain from cancer, there is greater effort expended and leniency to help a patient become more compliant. We have found it helpful to adopt and modify safe opioid prescribing guidelines used for the noncancer patient. Our specific strategies in brief include (Table 1): thorough assessment, informed consent/agreement; opioids and or adjuvants and interventional therapies as indicated; frequent outpatient visits, prescription writing/refills with small quantities, pill counts, referral to substance abuse programs, compliance counseling, and random or directed urine drug screens; and ongoing psychological/psychiatric treatment. If a full multidisciplinary team is not available to a community pain physician, appropriate consultations may be necessary when treating a high risk cancer pain patient. The clinician should be mindful of the different components of the experience of cancer-related pain and the importance of a multidisciplinary and multimodal approach as outlined in our monograph.

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