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Original Articles

Opioid Screening Practices in the Cancer Pain Patient

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Abstract

Background: Despite the growing use of opioids to treat cancer pain and the probability of opioid aberrancy in the cancer setting, clinical practice guidelines (CPGs) or recommendations for active screening and monitoring of opioid compliance are lacking.
Objectives: To evaluate the current practices and attitudes clinicians have toward monitoring and prescribing opioids in patients with cancer; to describe the current practice of screening and monitoring opioid compliance in the cancer setting; to provide insight into the role that CPGs may have in addressing opioid aberrancy in the oncologic population.
Hypothesis: Clinicians adopt diverse clinical practices and attitudes toward opioid screening and monitoring based on cancer status.
Design: A 24-question survey that evaluated the practices and attitudes that clinicians have when screening, monitoring, and prescribing opioids in patients with active cancer and history of cancer was completed by 105 pain management physicians. A comprehensive literature review was completed, evaluating the current state of available literature regarding opioid aberrancy and opioid risk in the cancer setting and CPGs for opioid monitor compliance in the cancer setting.
Setting: Multicenter, survey-based study to clinicians regarding pain management strategies in patients with active cancer, patients with a history of cancer, and patients with no history of cancer.
Results: Cancer status plays a role in the clinician's decision to screen and monitor opioid compliance in the oncologic population. For patients with active cancer, clinicians are more likely to prescribe opioids despite patient refusal for toxicology screen as well as history of substance abuse. For patients with no history of cancer, clinicians are more likely to refuse a prescription refill and eliminate opioids from treatment regimen.
Conclusions: Based upon the results of our study and evidence from current literature provided, the authors advocate for further investigation and development of CPGs to ensure the safe and prudent screening, monitoring, and prescribing of opioids in the oncologic population.

Keywords: cancer pain; clinical practice guidelines; compliance monitoring; opioid misuse, urine drug screening

Introduction

Pain is one of the most common symptoms reported in patients with cancer,[1] prevalent in ~50% of cancer patients undergoing chronic treatment and ~70% of cancer patients with advanced disease.[2] While cancer pain can vary significantly based on the primary site of the disease and the stage of disease,[2] most patients with cancer will require the use of opioids on a regular schedule to treat moderate and severe pain.[1,3,4] Debilitating treatment-related sequelae can necessitate the long-term use of opioid therapy for cancer survivors,[3] and even in cancer survivors who are 10 or more years past their cancer diagnosis, opioid prescribing is higher than in individuals with chronic, noncancer pain.[5] With the significant improvement in cancer remission rates during the past two decades,[6] the number of cancer survivors who are maintained on chronic opioid therapy has increased. Although many patients are initially managed by their primary care physician or oncologist, patients with more severe pain or those who require higher opioid doses are often referred to pain management specialists.[7]

Some cancer patients who report severe pain request increasing doses of opioids to cope with their psychological distress rather than their physical pain.[8] A recent review published by Carmichael et al. concluded that at least one in five patients with cancer may be at risk for an opioid-use

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disorder, and that the prevalence of opioid use-disorder risk is substantially higher among patients with cancer as compared with patients with no history of cancer.[9] Other studies have revealed that despite the use of screening tools to assess for risk of aberrant behavior before initiating opioids for treatment of cancer pain, opioid aberrancy still exists in the oncologic population.[10–15] A study published by Rauenzahn et al. reported that urine drug screening (UDS) aberrancies were common in ambulatory patients with cancer, and almost half of the patients tested were positive for nonprescribed opioids or potent illicit substances.[16]

The complexity of opioid use and misuse in the cancer setting is vast and encompasses medical, legal, psychological, financial, and ethical components. Clinicians have a dual obligation to ensure patients with cancer pain have access to opioid therapy and to guard from the public health risk that opioids can pose. Clinicians have been warned about the opioid epidemic, but at the same time, cancer pain remains undertreated in ~75% of patients with advanced cancer who experience moderate-to-severe pain.[17] This balance often requires a multidisciplinary approach consisting of primary care, oncologic, palliative, and pain management physicians who can ensure that the cancer-related pain is appropriately and adequately managed, while the risk of opioid misuse is judiciously and meticulously monitored and prevented.[3] This multidisciplinary approach is also effective in preventing burnout in individual clinicians who attempt to address the complexity of opioid management in the cancer setting alone.[3]

In recent years, international authorities, such as the National Institutes of Health (NIH), the National Cancer Institute (NCI), and the World Health Organization (WHO) have emphasized the importance of vigilant pain management strategies to ensure the proper use of opioids in patients with chronic pain,[18] but few guidelines and policies exist regarding the standardization of screening, monitoring, and prescribing opioids in the cancer setting. While the use of UDS as a diagnostic tool to guide pain management physicians' therapeutic decisions has been described in chronic noncancer pain, the use of UDS in patients with cancer pain has not been appropriately discussed. Similarly, while clinical practice guidelines (CPGs) exist on how to escalate opioid treatment in patients with cancer pain, these guidelines do not offer specific recommendations on how to actively screen and monitor opioid compliance for cancer patients and cancer survivors.

The authors hypothesize that clinicians adopt diverse clinical practices and attitudes toward opioid screening and monitoring based on cancer status due to the lack of CPGs that exist in the cancer setting. The aim of this study is to describe the current practice of screening and monitoring opioid compliance in the cancer setting, and to provide insight into the role that CPGs may have in addressing opioid aberrancy in the oncologic population.

Methods

This study was approved by the Memorial Sloan Kettering Cancer Center (MSKCC) Institutional Review Board and supported by MSKCC Support Grant (P30 Core Grant) as well as the Department of Anesthesiology & Critical Care.

A literature review was conducted using the Peer Review of Electronic Search Strategies (PRESS) 2015 guidelines to evaluate the current state of available literature regarding physicians' practices and attitudes in employing urine toxicology screens in patients with cancer and noncancer etiologies as well as opioid aberrancy and opioid risk in the cancer setting. Data were obtained from PubMed and EMBASE databases from inception to October 31, 2018 using MeSH terms: analgesics, opioid; cancer pain; substance abuse detection; practice guideline; and substance-related disorders. In addition, Google Scholar search engine was utilized to find gray literature. The quality of study, focusing on methodology and evidence, was evaluated by two reviewers using the GRADE system. Risk of bias, inconsistency, indirectness, imprecision, and publication bias were all used to guide reviewers. Any disagreements were resolved by consensus from a third independent reviewer.

A survey consisting of 24 questions was developed by investigators (see Supplementary Appendix A; Supplementary Data are available online at www.liebertpub.com/jpm) using a literature review and focus group to design the survey questions. The focus group was comprised of 12 pain management physicians who manage cancer pain. The clinicians were informed of the aims of the study and then divided into two groups and asked to review, modify, and/or challenge survey questions previously written by the authors. After a group discussion and consensus on survey questions, participants were also asked to form additional survey questions that they believed would help achieve the aims of the study.

All survey questions and answer choices were subsequently reviewed systematically by the authors so that the survey only included standard terms that are considered unambiguous to pain management physicians. Any term that may have been considered ambiguous was defined in the survey instrument. All survey questions were designed to collect data on three patient populations of interest: patients with active cancer, patients with a history of cancer, and patients with no history of cancer.

The survey included two sections; part one of the survey was created to better understand how pain management physicians employ urine toxicology screening in the three patient cohorts; part two of the survey was created to understand how pain management physicians prescribe opioids to the same three cohorts.

Numerical and/or ordinal scales were created with the goal of covering the full continuum of possible answer choices for each question. For questions in which more than one answer choice response was anticipated, respondents were given the option to include multiple answer choices. For questions in which alternative, nonlisted answers were anticipated, respondents were given the option to answer in a corresponding text box. A definition or reference frame was included in the question stem for all questions that required specific clarification.

The survey was delivered through electronic mail to 195 pain management physicians who were identified using a third-party service between July and August 2017. Physicians were identified through an electronic mailing list in which they self-identified as pain management specialists, and were invited to participate in the anonymous survey. Survey filters were used to further refine the study population so that only physicians who manage cancer pain were included. The inclusion criteria included physicians who currently specialize in pain management in the United States and actively manage

cancer-related pain. No limitations were placed on the length of time the physician has practiced cancer pain management or the type of training in pain management. An introduction and consent were included in the initial correspondence, which requested voluntary participation.

Statistics

Data were collected using online survey cloud-based software, and was analyzed by the investigators. Frequency distributions were calculated for all survey questions. For each question, chi-squared tests or Fisher's exact tests were used to test differences in rates of endorsement of answer choices regarding patients with active cancer, history of cancer, and no history of cancer. A p-value <0.05 was considered statistically significant. Analysis was performed in SAS version 9.4.

Results

Demographics

A total of 105 pain management physicians completed the survey (54.4% response rate). 72.1% of the responders were male, and 80.2% of responders noted formal training in cancer pain management. All 105 respondents had managed cancer pain as a part of their clinical practice, and a majority of responders were either <5 years or >20 years in practice. The average time to complete the survey was ~10 minutes (Table 1).

Screening practices

The clinicians who responded to the survey demonstrated variability in toxicology screening practices based on cancer status. Clinicians are three times less likely to require a toxicology screen for patients who have active cancer as compared with patients with a history of cancer and patients with no history of cancer (8.6% vs. 2.9% vs. 0%; p-value 0.004). All 105 physicians report using at least one type of toxicology screen for patient with no history of cancer; however, the same cannot be said for patients with active cancer and cancer survivors. Of the types of toxicology screens used, 93% of clinicians employ urine screens in their practice (vs. saliva or blood). For physicians who use more than one type of screen, cancer status does not play a role in their decision to use multiple types of screens.

Table 1. Physician Demographics (N=105)

Gender	
Male	72.1%
Female	27.9%
Years in pain management practice	
1–4 years	27.9%
5–9 years	18.6%
10–19 years:	20.9%
20+ years	32.6%
Have you had formal training in treating cancer pain?	
Yes	80.2%
No	19.8%
How frequently do you treat cancer pain?	
0% of patients	0%
Approximately 1–9% of patients	51.1%
Approximately 10–19% of patients	23.3%
Approximately 20–49% of patients	11.6%
50% or more of patients	14.0%

Before initiating opioid therapy, baseline toxicology screens are more often required in patients with no history of cancer and cancer survivors than in patients with active cancer (64.1% vs. 61.5% vs. 44.2%; p-value 0.043). Similarly, twice as many clinicians report ''never'' using a baseline screen in patients with active cancer as compared with patients with no history of cancer (9.6% vs. 4.9%; p-value 0.043).

For patients who refuse a toxicology screen, clinicians are almost twice more likely to refill a prescription without a completed screen for patients with active cancer than for cancer survivors or patients with no history of cancer (18.5% vs. 9.7% vs. 5.8%; p-value <0.0001). Similarly, while 92.2% of physicians endorsed that they would not refill an opioid prescription until the urine toxicology screen is completed for patients with no history of cancer, 68.0% of physicians noted that they would refill the prescription for patients with active cancer (p-value <0.001). Several clinicians noted (through free text boxes) that stage of cancer as well as the clinical scenario are also considered when deciding whether to refill the prescription.

Pain management physicians overall report feeling very comfortable managing pain caused by cancer and noncancer etiologies, although more clinicians report ''very comfortable'' if the patient's pain etiology is not due to cancer (85.9% vs. 79.8%; p-value <0.001). For patients with a history of substance abuse, clinicians are over four times more likely to report ''not comfortable'' in their treatment strategy if the pain is due to a noncancer etiology (21.5% vs. 5.3%; p-value <0.001). Of the physicians surveyed, more report ''doctor shopping'' on internet prescription monitoring programs in patients who have no history of cancer than in cancer survivors and patients with active cancer (65.7% vs. 38.1%; p-value 0.0003).

Prescribing practices

For patients who fail a toxicology screen, clinicians are twice more likely to prescribe a refill of opioid after a discussion about the importance of urine toxicology screen if the patient has active cancer as compared with if the patient has no history of cancer or is a cancer survivor (54.3% vs. 23.8% vs. 28.6%; p-value <0.0001). Similarly, physicians are nearly two times less likely to eliminate opioids from the treatment regimen if the patient has active cancer (26.7% vs. 48.6% vs. 50.5%; p-value 0.0005). One hundred percent of the physicians reported a reason to order a toxicology screen for patients with no history of cancer or patients who are cancer survivors, while the same cannot be said for clinicians caring for patients with active cancer.

While 83.9% of clinicians endorse that they would prescribe opioids to patients who have a history of substance abuse if they had active cancer, only 49.5% and 40.9% of clinicians endorses the same practice if the patient was a cancer survivor or had no history of cancer (p-value <0.0001). The same physicians surveyed are almost five times more likely to prescribe opioids to patients with active substance abuse if the patient has active cancer than if the patient is a cancer survivor or has no history of cancer (25.5% vs. 5.3% vs. 4.3%; p-value <0.0001).

Clinicians are more likely to prescribe sublingual tablets, sublingual spray, oral transmucosal lozenges, buccal tablets,

Table 2. Survey Questions with Significant Differences Regarding Patients with Active Cancer, History of Cancer, and No History of Cancer

Q2. Which toxicology screen do you use in your practice?
Urine; saliva; blood; more than 1
p-values >0.05
None
Active cancer: 9 (8.6%)
Cancer survivor: 3 (2.9%)
No history of cancer: 0 (0.0%)
p-value = 0.004

Q4. Do you require a baseline toxicology screen before initiating opioids?
Always
Active cancer: 46 (44.2%)
Cancer survivor: 64 (61.5%)
No history of cancer: 66 (64.1%)
Sometimes
Active cancer: 35 (33.7%)
Cancer survivor: 28 (26.9%)
No history of cancer: 28 (27.2%)
Rarely
Active cancer: 13 (12.5%)
Cancer survivor: 6 (5.8%)
No history of cancer: 4 (3.9%)
Never
Active cancer: 10 (9.6%)
Cancer survivor: 6 (5.8%)
No history of cancer: 5 (4.9%)
p-value = 0.043

Q11. For patients who refuse a toxicology screen, I:
Discuss the importance of a urine toxicology screen and prescribe refill without a completed screen
Active cancer: 19 (18.5%)
Cancer survivor: 10 (9.7%)
No history of cancer: 6 (5.8%)
Do not refill prescription until the urine toxicology screen is completed
Active cancer: 70 (68.0%)
Cancer survivor: 90 (87.4%)
No history of cancer: 95 (92.2%)
p-value <0.0001

Q12. For patients who fail a toxicology screen, I:*
Discuss importance of urine toxicology screen and prescribe refill
Active cancer: 57 (54.3%)
Cancer survivor: 30 (28.6%)
No history of cancer: 25 (23.8%)
p-value <0.0001
Eliminate opioids from treatment regimen
Active cancer: 28 (26.7%)
Cancer survivor: 53 (50.5%)
No history of cancer: 41 (48.6%)
p-value = 0.0005
Do not refill future prescriptions; Dismiss patient from practice; Refer patient to addiction medicine
p-values >0.05
**A toxicology screen is failed if the patient either (a) tested negative for the prescribed opioid, (b) tested positive for an opioid that was not prescribed, or (c) tested positive for other illicit substance(s)*

Q15. What is your reasoning for ordering toxicology screening?
It is a practice standard; Due to concerns about potential abuse; Due to concerns about potential diversion
p-values >0.05
Not sure
Active cancer: 5 (4.8%)
Cancer survivor: 0 (0.0%)
No history of cancer: 0 (0.0%)
p-value = 0.006

Q16. Do you prescribe opioids to patients who have a history of substance abuse?
Yes
Active cancer: 78 (83.9%)
Cancer survivor: 46 (49.5%)
No history of cancer: 38 (40.9%)
No
Active cancer: 15 (16.1%)
Cancer survivor: 47 (50.5%)
No history of cancer: 55 (59.1%)
p-value <0.0001

Q17. Do you prescribe opioids to patients who are active substance users?
Yes
Active cancer: 24 (25.5%)
Cancer survivor: 5 (5.3%)
No history of cancer: 4 (4.3%)
No
Active cancer: 70 (74.5%)
Cancer survivor: 89 (94.7%)
No history of cancer: 90 (95.7%)
p-value <0.0001

Q18. How would you describe your comfort level in treating pain caused by:
Cancer
Very comfortable: 75 (79.8%)
Somewhat comfortable: 17 (18.1%)
Not comfortable: 2 (2.1%)
Noncancer etiology
Very comfortable: 79 (85.9)
Not comfortable: 2 (2.2%)
Cancer in patient with history of substance abuse
Very comfortable: 44 (46.8%)
Somewhat comfortable: 45 (47.9%)
Not comfortable: 4 (5.3%)
Noncancer etiology in patient with history of substance abuse
Very comfortable: 45 (48.4%)
Somewhat comfortable: 28 (30.1%)
Not comfortable: 20 (21.5%)
p-value <0.0001

Q19. Do you prescribe Transmucosal Immediate-Release Fentanyl to your patients?
Sublingual tablet
Active cancer: 15 (14.3%)
Cancer survivor: 5 (4.8%)
No history of cancer: 3 (2.9%)
p-value = 0.003
Sublingual spray
Active cancer: 13 (12.4%)
Cancer survivor: 5 (4.8%)
No history of cancer: 2 (1.9%)
p-value = 0.006
Oral transmucosal lozenge
Active cancer: 23 (21.9%)
Cancer survivor: 6 (5.7%)

(*continued*)

TABLE 2. (CONTINUED)

No history of cancer: 4 (3.8%)
p-value <0.0001
Buccal tablet
Active cancer: 18 (17.1%)
Cancer survivor: 7 (6.7%)
No history of cancer: 3 (2.9%)
p-value = 0.0008
Buccal soluble film
Active cancer: 11 (10.5%)
Cancer survivor: 5 (4.8%)
No history of cancer: 2 (1.9%)
p-value = 0.024
Nasal spray
Active cancer: 11 (10.5%)
Cancer survivor: 4 (3.8%)
No history of cancer: 1 (1.0%)
p-value = 0.006
None
Active cancer: 62 (59.1%)
Cancer survivor: 83 (79.1%)
No history of cancer: 87 (82.9%)
p-value = 0.0001

Q20. Have you experienced any of the following situations of misconduct with your patients?
Abnormal toxicity screen
Active cancer: 71 (67.6%)
Cancer survivor: 77 (73.3%)
No history of cancer: 89 (84.8%)
p-value = 0.014
Doctor shopping on I-STOP
Active cancer: 40 (38.1%)
Cancer survivor: 58 (55.2%)
No history of cancer: 69 (65.7%)
p-value = 0.0003
Opioid hyperalgesia; difficulty weaning opioid once in cancer remission
p-value >0.05

Q22. Are the following treatments/therapies offered to treat pain?
Opioids
Active cancer: 92 (87.6%)
Cancer survivor: 83 (79.1%)
No history of cancer: 77 (73.3%)
p-value = 0.034
Implantable devices (i.e., spinal cord stimulator)
Active cancer: 66 (62.9%)
Cancer survivor: 82 (78.1%)
No history of cancer: 86 (81.9%)
p-value = 0.004
NSAIDs and/or acetaminophen; antiepileptics; antidepressants; intrathecal infusion therapy; alternative, nonpharmacologic therapies (i.e., acupuncture, physical therapy, massage therapy)
p-value >0.05

NSAID, nonsteroidal anti-inflammatory drug.

buccal soluble film, and nasal spray to patients with active cancer than to patients with a history of cancer or no history of cancer. In addition, clinicians are more likely to offer opioids in the treatment plan to patients with active cancer than to patients with a history of cancer or patients with no history of cancer (87.6% vs. 79.1% vs. 73.3%; *p*-value 0.034). Interestingly, physicians are more likely to offer implantable devices such as spinal cord stimulators to patients with no history of cancer than to patients with a history of cancer and patients with active cancer (81.9% vs. 78.1% vs. 62.9%; *p*-value 0.004) (Tables 2 and 3).

Discussion

The current study sought to build upon previous works that have investigated opioid aberrancy and opioid risk in the cancer setting, as well as CPGs for opioid monitoring compliance in the cancer setting. Data from this study provide evidence that there is variability among clinicians' clinical practice and attitudes toward opioid screening, monitoring, and prescribing based upon cancer status. Our results demonstrate that cancer survivors were managed differently than patients with active cancer; patients who are cured of cancer have different opioid monitoring, screening, and prescribing strategies than those patients who are currently living with incurable cancer or advanced cancer. While life expectancy was not examined as a possible factor in clinicians' decision making, this may also play a role in daily clinical practice.

The variability in clinical practice is likely a result of the lack of CPGs that exist when screening and monitoring opioids in the oncologic population.[16] Before establishing CPGs for the safe and prudent screening and monitoring of opioids in the cancer population, it is important to acknowledge previous key studies that have investigated opioid aberrancy and opioid risk in the cancer setting. By better understanding the risk factors for opioid aberrancy in the oncologic population, we can more effectively develop guidelines that can be used in clinical practice.

Opioid aberrancy and opioid risk in the cancer setting

In 2016, Carmichael et al. published a review that evaluated the current state of literature regarding opioid abuse and misuse in patients with cancer.[9] Thirty-four case studies, case series, retrospective observational studies, and narrative reviews were included in the review. The authors concluded that at least one in five patients with cancer may be at risk for an opioid-use disorder, and that the prevalence of opioid-use disorder risk is substantially higher among patients with cancer.[9] In addition, patients with specific cancer types that are related to tobacco and alcohol abuse, such as lung, esophageal, and head and neck cancers, are at even greater risk for opioid-use disorders.[19] While policies for screening patients for opioid misuse and abuse are routinely absent,[9] current evidence supports the need for assessing opioid risk in cancer patients. Of note, only 3 of the 34 clinical studies discussed the use of UDS in cancer patients.[11,20,21]

Three studies investigated the associated risk factors for opioid aberrancy in cancer patients. Kwon et al. completed a prospective, observational study to determine the risk predictors of opioid-related ''chemical coping'' among patients with advanced cancer.[10] The authors concluded that ~18% of the patients used opioids or other medications in a nonprescribed way to cope with various illness-related stresses. Interestingly, <25% of the patients found to be ''chemical coping'' had documentation of such aberrant behavior in their medical record. CAGE-positivity and younger age,

among other factors, were associated with a higher likelihood of chemical coping. Similarly, Arthur et al. completed a retrospective chart review to determine the factors associated with UDS test ordering in patients with cancer.[22] The authors observed that only 6% of patients underwent urine drug testing, and that younger age and CAGE positivity were considered significant predictors of urine drug testing ordering. A 2014 retrospective chart review by Barclay et al. examined the frequency in which risk factors for opioid aberrancy—such as substance abuse, diversion, and abnormal drug screens—exist in the cancer setting.[11] The authors noted that while opioids can be effective treatments for cancer-related pain, there is substantial risk for opioid abuse in the cancer population and, therefore, screening tools such as the Opioid Risk Tool (ORT) should be used to balance risk mitigation and treatment strategies.

Risk screening tools

The ORT and the Screener and Opioid Assessment for Patients (SOAP) tool are two self-reporting screening tools that can help clinicians assess for risk of aberrant behavior before initiating opioid therapy for cancer pain. Several studies exist that utilize these opioid risk screening tools to assess risk of opioid aberrancy in cancer patients. Koyyalagunta et al. utilized the SOAP tool to risk stratify opioid misuse among patients with cancer pain.[12] After reviewing over 500 patient charts, the authors concluded that patients classified as high risk by SOAP were generally younger, had comorbid depression and anxiety, and had higher morphine equivalent daily doses. Similarly, a retrospective analysis by Ma et al. made use of the ORT to risk stratify opioid misuse in cancer patients; the most common patient risk factors associated with opioid misuse were a history of depression and family history of alcohol abuse.[13]

Substance abuse and opioid risk

As seen in the studies by Koyyalagunta et al. and by Ma et al., comorbid psychiatric illness can play a significant role on the risk of opioid aberrancy in cancer patients. Comorbid substance abuse has also been studied as a risk factor for opioid misuse and abuse. Parsons et al. analyzed 665 patient charts to investigate the frequency of patients who screen positive for alcoholism in a palliative care outpatient clinic.[14] The authors concluded that patients who were CAGE positive were more likely to be on opioid therapy. Bruera et al. showed a similar finding in their retrospective study, noting that alcoholism is highly prevalent and underdiagnosed among terminally ill cancer patients.[15]

CPGs for opioid monitor compliance in the cancer setting

CPGs for the safe initiation and escalation of opioids in managing cancer pain have been published by various international societies and organizations. In 1986, the WHO created an analgesic ladder for cancer pain that provided clinicians with a step-wise approach to opioid prescribing, and in 1996 the WHO updated their prescribing guidelines.[23,24] Despite offering detailed recommendations regarding opioid prescribing practices, both the 1986 and 1996 guidelines drafted by the WHO lacked recommendation on opioid compliance monitoring.

Table 3. Survey Questions with No Significant Differences Regarding Patients with Active Cancer, History of Cancer, and No History of Cancer ($N = 106$)

Q1. Do you require a toxicology screen to monitor opioid compliance?
Q3. Does the toxicology screen you employ test only for the opioid you prescribe or does it also include other opioids and illicit drugs?
Q5. For a patient with NO history of substance or chronic opioid use, how frequently do you have the patient complete a toxicology screen to monitor compliance?
Q6. For a patient with a history of substance or chronic opioid use, how frequently do you have the patient complete a toxicology screen to monitor compliance?
Q7. When monitoring a patient's compliance with a toxicology screen, do you schedule it (patient is given advanced notice) or is it random (patient is not given advanced notice)?
Q8. What method do you use to decide when to screen your patient?
Q9. Are patients directly observed as they urinate for the urine toxicology screen?
Q10. Do you require a toxicology screen before every opioid refill?
Q13. For patients who fail a toxicology screen due to nonmedical cannabis use, I (do not refill future prescriptions; discuss importance of urine toxicology screen and prescribe opioid refill; dismiss patient from practice; eliminate opioids from treatment regimen; refer patient to addiction medicine)
Q14. Do you use a psychometric screening tool to risk stratify a patient's potential for opioid abuse?
Q21. Before prescribing opioids, are concerns about treatment side effects, dependence or tolerance discussed with your patients?

In 2012, guidelines introduced by the European Society for Medical Oncology (ESMO) outlined recommendations on cancer pain assessment, opioid escalation, and opioid side effect management.[25,26] This CPG, like earlier ones set forth by the WHO, did not define specific recommendation on opioid compliance monitoring in the cancer setting. In the same year, the European Association for Palliative Care (EAPC) updated their consensus guidelines regarding the use of opioids to treat cancer pain.[27] These guidelines, comprised of 16 evidence-based recommendations, provided guidance on initiating and titrating opioids for the treatment of cancer pain, but did not address the subject of opioid screening and monitoring.

In 2016, both the American Society of Clinical Oncology (ASCO) and the Centers of Disease Control (CDC) published CPGs regarding opioid treatment strategies. ASCO's guidelines centered on the use of opioids to manage chronic pain in adult cancer survivors.[28] This CPG noted that ''clinicians should incorporate a universal precautions approach to minimize abuse, addiction, and adverse consequences of opioid use'' and that tools such as urine drug testing are available and may mitigate risk. The CDC's ''Guideline for Prescribing Opioids for Chronic Pain'' also provided recommendations surrounding opioid prescribing practices for the treatment of chronic pain, but noted that their recommendations set forth

were not intended for patients who are in active cancer treatment, palliative care, or end-of-life care.[29] Both 2016 CPGs were not meant for patients with active cancer, and both omitted information regarding opioid compliance monitoring.

The National Comprehensive Cancer Network's 2017 ''Guidelines for Adult Cancer Pain'' advocated for the routine monitoring of abnormal patterns of opioid use that may suggest misuse or abuse.[30] While the NCCN guidelines recommend that prescribers make use of state prescription drug monitoring programs if available and consider the use of urine drug testing to document opioid adherence and screen for aberrant behavior, the guidelines lack specific instruction on exactly when and for which patients it would be appropriate to consider screening. The guidelines also note that prescribers should utilize risk factor screening tools, such as SOAP and ORT, and that the Food & Drug Administration is currently responding to the public health crisis of addiction, misuse, abuse, overdose, and death by establishing Risk Evaluation and Mitigation Strategy (REMS) programs for all patients receiving opioids analgesics.

To date, CPGs that identify specific recommendations for the active screening and monitoring of opioid compliance in the cancer setting do not exist.

Integral and interdependent strategies to mitigate opioid misuse in the cancer setting

UDS plays an integral role in monitoring for opioid aberrancy and is an important method to apply in clinical practice. If opioid misuse is diagnosed, clinicians can make informed decisions regarding possible alterations of pain management strategies and can enlist the guidance of an addiction specialist. However, drug screening is not the only solution to this complex problem and there are other interdependent strategies physicians can use to mitigate opioid misuse in the cancer setting. As in chronic, noncancer pain, universal screening through risk assessment tools and a thorough patient history that includes the use of a prescription-monitoring database is vital. Opioid management plans, opioid contracts, and comprehensive patient education on the risks and benefits of opioid use can also mitigate the risk opioid misuse. Close follow-up with continual vigilance and reassessment for aberrant behaviors is critical. If opioid aberrancy occurs, prompt referral to an addiction specialist is essential. A multidisciplinary approach consisting of primary care, palliative care, and psychiatric physicians can provide support to the patient and guide further management plans.

Limitations

A limitation in this study is the population of the survey that includes physicians who self-identify as pain management specialists but does not include other clinicians, such as primary care physicians, palliative care physicians, oncologists, and surgeons, who often initially manage cancer pain. Similarly, the type of formal training—whether fellowship-trained or otherwise—was not specified by the respondents. The aim of the study, to establish if there exists standard practice when screening and monitoring opioids in the cancer setting, did reach statistical significance even among pain management specialists trained in managing cancer pain. The authors believe that the results are generalizable and valuable to clinicians who do not have specialized training in pain management as the general principles of opioid screening are applicable to all physicians. In the future, the authors would like to extend the survey to primary care physicians, palliative care physicians, oncologists, and surgeons to investigate how these specialists screen and monitor opioid compliance in treating cancer pain.

Another study limitation is the 54.4% response rate, which may increase the likelihood of nonresponse bias, or error resulting from differences between those who respond to a survey and those who do not respond to a survey. However, this response rate is likely underestimated, as many physicians who received the survey do not manage cancer pain and did not complete the survey as they self-identified themselves as unsuitable candidates for the survey. In total, 105 of the 195 physicians completed the survey, allowing statistical significance to be assessed for all survey questions. Similarly, while the sample of 195 physicians is relatively small in comparison to the total number of pain physicians practicing in the United States, the sample size was large enough to detect statistically significant differences in responses regarding the three cohorts of patients.

Future directions

Based upon the results of our study as well as evidence from current literature, the authors advocate for the development of CPGs to help guide clinicians' therapeutic decisions when treating cancer pain. Certain populations, such as cancer patients with advanced disease and comorbid opioid use disorder, may require specific opioid monitoring guidelines. Investigation into the clinical practices and attitudes that primary care physicians and oncologists have when screening and monitoring opioids may provide further insight into the role that CPGs have in addressing opioid aberrancy in the oncologic population.

To better understand the complexity of opioid use and misuse in the cancer setting, further research into the potential barriers of implementing strategies to mitigate opioid misuse is needed. Considering that a multidisciplinary approach can be beneficial to both the patient and the clinician managing the cancer pain, further insight into the obstacles of instituting this multidisciplinary approach is warranted. In particular, research that can further elucidate specific practices clinicians can employ to confront opioid misuse can help clinicians cultivate and maintain safe opioid prescribing and monitoring techniques in clinical practice.

In the future, the authors would also like to investigate how clinicians employ urine drug testing when deescalating opioid therapy in cancer survivors. This information is critically needed, as remission rates continue to improve and increasingly more patients who once required opioids to control their pain are being titrated off chronic therapy. The authors are currently investigating international regional differences in opioid monitoring practices in the cancer setting to gain better insight into how regional and cultural differences may affect compliance monitoring. Future research into the cost effectiveness of different types of UDS may also help guide physicians on which screening tools to use in their practice.

Conclusion

For patients with active cancer, clinicians are more likely to prescribe opioids despite patient refusal for toxicology screen

and history of substance abuse. For patients with no history of cancer, clinicians are more likely to refuse a prescription refill and eliminate opioids from treatment regimen. The authors advocate for further investigation and development of CPGs to ensure the safe and prudent screening, monitoring, and prescribing of opioids in the oncologic population.

Author Disclosure Statement

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