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Navigating the Pain and Suicide Conundrum

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Abstract

Individuals that suffer from chronic pain typically experience a number of medical, social and psychiatric co-morbidities that greatly affect their quality of life. Patients with pain often experience depression, anxiety, and the prevalence of suicidal ideation and behavior is not inconsequential in this patient population. Suicide in patients with chronic pain has been a silent epidemic but there is an emerging literature in this area. This chapter will provide a review of the prevalence of suicide in both patients with pain and those with pain and substance use disorders, risk factors for suicide, possible mediators, assessment of risk for suicide, and risk mitigation and intervention strategies.

Introduction

There has been a great deal of scholarly activity devoted to the burgeoning rate of opioid misuse/abuse and opioid-related fatalities, particularly in the United States. However, this has overshadowed the silent epidemic of suicidal ideation (SI) and suicidal behavior (SB). Suicide has become a global problem. The World Health Organization published an executive summary, "Preventing Suicide, A Global Imperative".¹ In this summary, there were some alarming facts: every 40 seconds someone in the world dies of suicide; an estimated 804,000 suicide deaths occurred worldwide in 2012; the annual global suicide rate was 11.4/100,000 population (15.0 male and 8.0 female); and in the age group of 15-29 it is the second leading cause of death. Suicide constitutes 54% of the 1.5 million violent deaths per year globally. Over 75% of suicides occur in low and middle-income families, and all of these numbers continue to grow annually.

Pain and Suicide

A robust literature underscores that there is a high prevalence of SI and SB in patients with pain, ranging anywhere from 18%-50%.²⁻⁷ A systematic review by Tang and Crane⁵ revealed that the risk of successful suicide was doubled in patients with chronic pain as compared to non-pain controls. Ilgen et al² discovered in a large cohort from the United States Veterans Affairs' database (n=260,254) that veterans experiencing severe pain were more likely to end their life by suicide than veterans with no, mild, or moderate pain). Cheatle et al³ evaluated 466 patients with chronic nonmalignant pain treated in a behaviorally based pain program. Results revealed a high rate of SI (26%) and a logistic regression revealed that history of sexual abuse, family history of depression and being socially withdrawn were predictive of SI.

Suicidal Ideation and Behavior and Substance Use Disorder

Compared to the general population, individuals with an alcohol use disorder are almost 10 times more likely to die by suicide and those who inject drugs are approximately 14 times more likely to commit suicide.⁸ These individuals tend to have multiple risk factors for SB including having depressive symptoms and enduring a significant number of severe stressors such as loss of relationships, jobs, health and financial problems. Patients with co-occurring pain and substance use disorder (SUD) are particularly at high risk for attempting and ending their lives by suicide.

Pain and Suicidal Ideation and Behavior: Risk Factors

There are general, non-pain specific risk factors and pain-specific risk factors for suicidality. General, non-pain specific risk factors include gender (female); age (> 45 years old); having co-occurring mental disorders (especially depression and SUD); acute losses and stressors (relationships, job, finances); enduring chronic medical illnesses; experiencing conflict, disaster, discrimination; past psychiatric hospitalizations; frequency of SI; severity of psychiatric disorder; poor social support and the strongest predictor of suicide is a previous suicide attempt.^{1,9} While patients with pain commonly have a number of these risk factors,¹⁰ pain specific risk factors include pain duration, pain intensity, sleep disturbance, catastrophizing, mental defeat and opioid dosing. General and pain-specific risk factors for SI and SB are outlined in Table 1.

Pain Duration and Intensity

There is generally convincing evidence that pain intensity^{5,6} and pain duration⁵ are predictive of SI and SB. In a large cohort study, Ilgen et al⁶ analyzed data from the Veteran's Affairs' medical records database and the National Death Index (n=260,254)

evaluating the association between self-assessed pain severity and SB in veterans. They discovered after controlling for demographic and psychiatric factors that veterans with severe pain were more likely to die by suicide than ones with mild or moderate pain.

Sleep Disturbance

Sleep disturbance is very common in patients with chronic pain with the prevalence ranging from 50 to 80%^{11, 12,14} and has been postulated as a potential mediator of suicidal ideation in this patient population. Racine et al¹³ examined data of 88 patients with chronic pain who completed a number of self-administered questionnaires at intake to three pain clinics in Canada. They discovered that 24 % of these patients endorsed experiencing SI. Poor sleep quality was the only significant physical variable predictor of SI. There is also persuasive evidence that pain and sleep are bidirectional (pain leading to poorer sleep quality and sleep deprivation causing increased pain) which potentially could synergistically increase the risk of SI and SB. Although sleep disturbance is common in patients with pain it is often not evaluated or effectively treated.¹⁴

Opioid Dosing

Ilgen et al¹⁵ performed a retrospective data analysis on the risk of suicide by different opioid doses in Veterans with chronic nonmalignant pain. After controlling for demographic and other clinical features (depression, PTSD etc) results indicated that higher opioid doses were associated with increased risk of suicide mortality. These results suggest that when a patient is on higher doses of opioids clinicians should be more cognizant of an increased risk of SI and SB, especially if a patient has one or more of the known risk factors.

Pain and Suicidal Ideation and Behavior: Possible Mediators

There are a number of postulated mediators for suicide in patients with chronic pain. These include catastrophizing; burdensomeness/social isolation and mental defeat

Catastrophizing

Patients with chronic pain tend to engage pain-related catastrophizing which can be conceptualized as magnified, exaggerated negative focus on pain that can contribute to depression and disability and in turn exacerbate an individual's experience of pain and suffering.¹⁶ The association between SI and individual differences in the use of pain-related coping strategies and pain catastrophizing was assessed in a large cohort of 1,515 patients with chronic pain. In this sample, 32% reported recent SI. It was revealed that the extent of depression and pain catastrophizing best predicted the occurrence and the degree of SI.⁴

Burdensomeness and Social Isolation

A prevailing theory of SI and SB is based on the interpersonal theory of suicide by Joyner and colleagues.¹⁷ This theory proposes that thwarted belongingness (unfulfilled need for social interaction and connectedness), and perceived burdensomeness (perceiving oneself as a burden or a liability to others, particularly family members) are two primary factors that significantly contribute to the context that leads to SI and possible SB. These two factors are. In a study by Kranzler et al,¹⁸ 113 patients with chronic nonmalignant pain were evaluated and a logistic regression model revealed that one question measuring perceived burdensomeness was the only predictor of suicidal ideation. Cheatle et al³ also discovered that social withdrawal and isolation were predictive of SI in a cohort of 466 patients undergoing treatment at a pain center.

According to the interpersonal theory of suicide, the desire for suicide is caused by the confluence of thwarted belongingness and perceived burdensomeness and the capability for SB and attempts develop in response to repeated exposure to physically/emotionally painful and/or fear-inducing experiences. This is very pertinent to the patients with chronic pain, as two strong risk factors for suicide are pain duration and pain intensity.

Mental Defeat

A novel construct for increased risk of suicidal ideation in chronic pain is mental defeat, which has been defined as a state of mind marked by a loss of autonomy, agency and human integrity.¹⁹⁻²²

The link between mental defeat and suicide intent has been investigated in a recent study with 62 patients seeking specialist treatment from a hospital chronic pain self-management service.²³ Among these patients, 22.6% had a history of past suicide attempts, with 69% indicating that their wish to die during the last attempt being moderate to high. All participants completed a set of questionnaires assessing factors that have been linked to suicidality. Two hierarchical linear regression analyses were subsequently carried out to examine the effect of mental defeat – in competition with the remaining significant correlates of suicidality (pain intensity, anxiety, depression and pain catastrophizing) – on worst-ever suicide intent, as measured with the 21-item Beck Scale of Suicide Ideation.²⁴ Both regression models controlled for the effect of pain intensity (step 1), but in the first model mental defeat was entered to the equation first (step 2) before the three psychological predictors, namely anxiety, depression and pain catastrophizing (step 3), whereas in the second model, the entry order was reversed so

that mental defeat (step 3) was added to a full model of pain intensity (step 1), anxiety, depression, and pain catastrophizing (step 2) last. As expected, pain intensity alone was a significant predictor of predictor of worst-ever suicide intent in both models. When mental defeat was added to the model next, it improved the predictor by increasing the total amount of variance explained from 11% to 23%. In contrast, the combined power of anxiety, depression and pain catastrophizing was weaker and did not significantly improve the model's prediction of suicide intent. Also, none of the psychological predictors included in the model, except mental defeat, was found to be a significant predictor of suicide intent. These findings suggest that the effect of mental defeat on suicide intent is independent of pain intensity and that mental defeat may be a better predictor of suicide intent than anxiety, depression and pain catastrophizing, both as individual and as a combined set of predictors.

Screening for Risk of Suicide

Screening for risk of suicide in patients with chronic pain should include general mental health screening, SUD screening, assessing sleep disturbance and specific tools to assess SI and SB.

Mental Health Screening

There are a number of self-administered measures of depression for example the Beck Depression Inventory (BDI)²⁴, Profile of Mood States (POMS)²⁵, and Patient Health Questionnaire (PHQ-9).²⁶ Two measures of anxiety that are highly valid and reliable are the Beck Anxiety Inventory (BAI)²⁷ and the State-Trait Anxiety Inventory.²⁸ There are also tools that assess both depression and anxiety such as the Hospital Anxiety and Depression Scale.²⁹

Substance Use Disorder Assessment

While patients with pain have an elevated risk for SI, those patients with both pain and SUD are particularly vulnerable to the risk of SI and SB. Assessing the presence of a SUD, therefore, is critical in this patient population.

Examples of assessment tools for SUDs include the CAGE-AID (Cut down, Annoyed, Guilty, Eye-opener Tool)³⁰ which assesses for both alcohol and drug abuse,; and the DAST (Drug Abuse Screening Test).³¹

Risk assessment tools for potential prescription opioid misuse and abuse include the Opioid Risk Tool (ORT)³² and the Screener and Opioids Assessment for Patients with Pain (SOAPP).³³ These two instruments are examples of assessing risk for potential aberrant drug-related behavior (ADRB) prior to the initiation of long-term opioid therapy. Examples of assessment tools to monitor misuse once opioid treatment has been initiated include the Current Opioid Misuse Measure (COMM)³⁴ and the Prescription Drug Use Questionnaire(PDUQ).³⁵ A recently developed tool, the ORT-OUD, has been demonstrated to predict the risk of developing an opioid use disorder with good specificity and sensitivity.³⁶

Screening Tools for Sleep Disturbance

Measures for insomnia predominantly include patient self-report in questionnaire and daily sleep diary to capture the subjective experience of sleep disturbance, but may also include objective measures such as actigraphy and polysomnography to provide objective estimates of sleep patterns and for the assessment of possible concomitant sleep disorders (e.g., sleep apnea, restless leg syndrome/period limb movement disorder,

narcolepsy etc.). Self-report measures assess different aspects of sleep disturbance. Moul et al provide a review of the various sleep assessment scales.³⁷

Screening Tools for Mental Defeat

The Pain Self Perception Scale (PSPS) has been developed to assess the sense of mental defeat in relation to pain experiences.¹⁹ The PSPS contains 24 items that describe negative thoughts and feelings people may have about themselves due to a specified recent episode of intense pain. All items begin with the referent “Because of the pain...”, followed by statements such as “...I felt defeated by life”, “...I felt destroyed as a person.” Respondents rate the extent to which each item applied to their specified recent episode of pain on a 5-point scale (0-4), where 0 is anchored with “not at all/never” and 4 “very strongly”. Scores of each item are then summed to give a total score that ranges from 0-96, with higher scores indicating higher levels of mental defeat in relation to pain.

Screening Tools for Suicide

The Columbia Suicide Severity Rating Scale (C-SSRS) has been frequently used for clinical trials on new medications and in clinical practice. The C-SSRS assesses a number of domains including ideation, intensity, behaviors, severity of self-injury and potential lethality of suicide attempts.³⁸ The C-SSRS provides greater precision in the assessment of SB and SI but due to its length can be cumbersome with regards to clinical practice.

Another example of a commonly used assessment for risk of suicide is the Suicide Assessment Five-Step Evaluation and Triage (SAFE-T) assessment tool that was

developed in collaboration with Substance Abuse and Mental Health Services Administration (SAMHSA).³⁹ The SAFE-T includes assessment of risk factors such as suicidal behavior, current and past psychiatric disorders, family history, change in treatment and access to fire arms; protective factors, both internal, such as the ability to cope with stress, spiritual or religious beliefs and frustration tolerance, and external, such as responsibility to children or others and having a positive therapeutic relationship and good social supports; suicidal inquiry which asks specific questions about thoughts, plans, behaviors, intents, risk level and intervention; assesses the risk level based on the clinical judgment after completing the first three steps. Patients are stratified into low, moderate and high risk, with specific interventions indicated for each risk level.

Prevention and Treatment Strategies

Preventative Measures

Patients who present with moderate to severe depression with or without endorsing SI or plans should be co-managed with a behavioral health specialist. Patients who acknowledge active SI may require inpatient treatment depending on certain factors such as: depression and SI severity; if they have vague or specific plans for completing suicide including having access to means (potentially lethal medications or own a gun); history of past SB or impulsivity. During an acute phase the patient will require meaningful treatment both consisting of pharmacotherapy and intensive psychotherapy. The pharmacotherapy strategy should include managing depressive symptomatology, sleep disturbance, and pain. If opioid or benzodiazepine use is necessary, these medications should be prescribed cautiously, in small amounts and held and administered by a family member.¹⁰

Interventions/Treatment

There are a number of pharmacologic and nonpharmacologic interventions to mitigate the risk of SI/SB.

Pharmacologic Treatment to Manage SI/SB in Patients with Pain

For suicidal patients with or without pain, the general pharmacological strategy is to treat comorbid illness that leads to increased suicide risk, including depression, anxiety, sleep disorder, psychosis, and uncontrolled pain.

- Medications that show benefit for reducing suicidality

Four medications have been shown to decrease risk of suicide: lithium, clozapine, and ketamine and buprenorphine. Lithium is a first line treatment for bipolar depression and also may be used to augment antidepressants in treatment resistant depression. It has been shown to decrease suicidality in patients with mood disorders.⁴⁰ Clozapine is an atypical antipsychotic frequently used for treatment resistant schizophrenia and schizoaffective disorders, and has also been shown to decrease suicides in these populations.⁴¹ Ketamine is a NMDA receptor antagonist that has recently been shown to have potent and rapid antidepressant and pain relieving effect. In several small studies ketamine has shown promise in rapidly reducing SI.⁴² Most recently buprenorphine has shown promise in abating even acute SI.⁴³

- Medications that treat comorbid risk factors for suicidality: Depression, Sleep, and Anxiety

Patients with pain often have comorbid anxiety, sleep and mood disturbance, which can increase risk of SI/SB. Many of these comorbidities may be treated with

antidepressants. Augmenting strategies including anxiolytics, sleep aids, and antiepileptics, may also be employed.

a) Antidepressants

For suicidal patients with comorbid depression, anxiety and pain, treating with an antidepressant should be considered. There is no clear data showing that any single antidepressant works better than another, so the choice of antidepressant depends on the patient's comorbidities, the side effect profile, and whether the goal is to add additional pain control. Selective serotonin reuptake inhibitors (SSRIs) and serotonin/norepinephrine reuptake inhibitors (SNRIs) are first line agents for treating depression and anxiety disorders. SSRIs may be better tolerated, while SNRIs also treat pain. For SNRIs and SSRIs, it is often good to start at a low dose, even half of the typical recommended starting dose, because initial side effects can include elevated anxiety, prompting anxious patients to discontinue the drug before it has a chance to take effect. Other side effects can include sexual dysfunction, nausea and diarrhea, insomnia and weight gain. Of note, SSRIs and SNRIs, while effective for depression, anxiety and pain, have been shown to disrupt and fragment sleep.⁴⁴

Tricyclic antidepressants (TCAs) such as amitriptyline and doxepin are a good choice for patients with depression, anxiety, and sleep disorder, and also have benefit for pain.¹⁴ However, this benefit must be carefully weighed by their risk in suicidal patients, as they are extremely lethal in overdose.⁴⁵ Other significant side effects include anti-cholinergic and adrenergic effects and cardiac conduction delay.

b) Anxiolytics

Although many clinicians avoid benzodiazepines, a long acting benzodiazepine such as clonazepam can be useful in the short term to reduce anxious agitation in a suicidal patient, since such agitation potentially contributes to completed suicide.⁴⁶ They ought not to be combined with opioids, and as with TCAs given in small or observed doses. Other medications potentially useful for anxiety include buspirone, hydroxyzine, and antiepileptic drugs.

c) Anticonvulsants

Like antidepressants, antiepileptics may be used to treat not just pain, but also anxiety and sleep disturbance. Gabapentin and pregabalin both have some benefit for both sleep and anxiety.⁴⁷

d) Sleep aids

As mentioned above, the tricyclic antidepressants can be effective for treating sleep. Many patients may need additional assistance to fall asleep and stay asleep, so adding a dedicated sleep aid is an option. Eszopiclone not only treats sleep but also anxiety. Trazodone is an antidepressant that at low doses is indicated for sleep. Mirtazepine similarly is an antidepressant that improves sleep.¹⁴

- Special consideration: Risk of Suicidality with Antidepressants and Anticonvulsants

Antidepressants (of all classes) and antiepileptic drugs have the additional complication of possibly leading to SI/SB in some patients. In 2004 the FDA issued a black box warning, regarding an increased risk of SI/SB in children and adolescents, which was extended to young adults (age 18-25) in 2006.⁴⁸ This warning was based on a meta-analysis showing approximately 2-fold increase in risk of SI/SB in these

populations. Of note, there were no completed suicides and no distinctions among class of antidepressant. Antidepressants in older patients (age 65 and older) are actually protective against SI/SB. A similar analysis of antiepileptic drugs showed an increased risk of SI/SB in patients with various disorders taking any antiepileptic drug, again showing approximately 2-fold increased risk in those taking anticonvulsants over placebo, with no distinction among age.⁴⁹

On balance, the risk of untreated depression on suicide in a general population outweighs the risk of treating with an antidepressant.⁴⁸

Behavioral Interventions

- Cognitive Behavioral Therapy

CBT has been highly efficacious in treating mood and anxiety disorders and the basic principles of CBT have been applied to other conditions including pain, sleep and substance use disorders (SUD).

a) CBT-Pain

CBT can include various techniques to assist and support the patient in identifying maladaptive behaviors and/or dysfunctional thought patterns that may diminish the patient's ability to adjust to and cope with their chronic pain thus contributing to their related depression and anxiety.

The process of CBT typically involves the patient acquiring specific skills which can include mindfulness-based stress reduction, progressive muscle relaxation training, pacing, effective communication, cognitive restructuring, which is followed by skill consolidation, rehearsal and relapse training.⁵⁰

There is a robust literature supporting the clinical efficacy and cost-effectiveness of CBT in improving mood, anxiety and functionality in a number of chronic pain disorders.

CBT-Insomnia

CBT tailored to insomnia has also been effective in improving sleep disturbance. As noted above, sleep disturbance is highly prevalent in patients with chronic pain, pain and sleep are bidirectional and sleep disturbance is a known risk factor for SI/SB in patients with chronic nonmalignant pain.

There is evidence that CBT-Insomnia (CBT-I) in patients with chronic primary insomnia, is equally effective or even superior to pharmacotherapy in multiple outcomes.⁵¹

A course of CBT-I typically includes: psychoeducation about sleep and insomnia; stimulus control; sleep restriction; sleep hygiene; relaxation training; and cognitive restructuring.

CBT, Pain and SUD

There is emerging evidence that CBT can reduce the risk of prescription opioid misuse and abuse in high-risk patients indirectly by improving mood, anxiety, sleep and pain coping skills and also in improving outcomes in patients with pain who have a history of a SUD. In a recently published pilot study,⁵² patients with Hepatitis C who also experienced chronic pain and had a history of SUD were enrolled in an 8-session integrated group CBT program for chronic pain and SUD. Results revealed improvement in key outcomes including pain-related interference, reduction in cravings for alcohol and other substances, and a decrease in past-month alcohol and substance use.

Conclusions

Patients suffering from persistent pain often present with complicating medical and psychiatric comorbidities including mood and anxiety disorders and a substantial subgroup of this patient population experience SI and engage in SB. A number of risk factors for SI/SB have been identified in the general population including gender, age, social isolation, past history of suicide attempts and several more specific to the pain population such as sleep disturbance, pain intensity and duration, and opioid dosing as well as potential mediators of pain and SI/SB such as burdensomeness, sleep disturbance and mental defeat. Many of these risk factors and mediators are modifiable thus reducing the potential of SI and SB in this vulnerable patient population. Clinicians need to be cognizant of the potential of SI/SB when managing patients with chronic nonmalignant pain, routinely screen for and treat or refer for treatment of concomitant mood, anxiety, sleep and substance use disorders and develop a plan of action if patients endorse active SI/SB.

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Table 1. Risk Factors for Suicide

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| <ul style="list-style-type: none">➤ Gender (female)➤ Age (> 45 years old)➤ Acute losses and stressors➤ Chronic medical illnesses➤ Previous suicide attempts➤ Concomitant mental health history (especially depression and SUD)➤ Social isolation/poor social support➤ Experiences conflict, discrimination | <ul style="list-style-type: none">➤ Frequency of Suicidal Ideation➤ Severity of psychiatric disease➤ Past psychiatric hospitalizations➤ Past suicide attempt➤ Pain Type *➤ Pain Intensity *➤ Pain Duration *➤ Sleep disturbance *➤ Opioid dosing * |
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* pain specific risk factors