

*Invited Review***Chronic Pain and Opioid Use in Older People With HIV****Vasudev C. Mandyam, MD; R. Douglas Bruce, MD, MA, MS**

*Chronic pain is common among older people with HIV. Etiologies of chronic pain are multifactorial in this population. A careful and thorough initial assessment of pain is important. Associated conditions that can contribute to pain should be explored and managed as indicated. Special consideration is warranted for some of the unique aspects of pain in people with HIV. Chronic pain management is multimodal; a variety of pharmacologic and nonpharmacologic strategies are effective. Among medications, opioids can be used but carry a risk of significant harms. The use and monitoring of opioids is discussed here, and recommendations are made for the safe prescribing of opioids for chronic pain.*

**Keywords:** HIV, chronic pain, opioids, older adults, aging

**Introduction**

Although chronic pain is prevalent among the general population, it is more common among people with HIV, especially among older people with HIV.<sup>1-3</sup>

Pain is a subjective experience. Although some organic processes generate pain, pain can be caused by a wide variety of pathologies and experiences, which complicates its evaluation and treatment. The underlying mechanisms of pain in people with HIV are multifactorial. Evaluating a person with HIV who has chronic pain requires a careful and thorough assessment. In this article, we have detailed approaches to treatment that begin with the assessment and evaluation of pain, management strategies in people with HIV, and the use and risks of opioids in this population.

**Assessing and Evaluating Chronic Pain**

People who present with a complaint of pain may often feel judged. Patients may fear that they will be seen as weak or unable to cope with the pain. They may also fear that the health care practitioner will assume that they are faking pain in search of medications.

As a result, it is important to begin by validating the patient's complaint of pain: "I am so sorry to hear that you are experiencing this pain." Although acute pain may present, for example, with a swollen, erythematous joint, chronic pain does not necessarily present with objective evidence of pain. Patients with "silent" chronic pain can feel dismissed by others; providing validation can lead to improvement in attitudes and approaches to their symptoms.<sup>4</sup>

Pain influences and is influenced by a variety of individual factors. These can include depression, post-traumatic stress, substance use disorders, sleep disturbance, reduced antiretroviral adherence, missed HIV clinic visits, and unemployment.<sup>5</sup>

Taking a detailed history and conducting a proper physical examination are crucial to the accurate assessment of pain.<sup>6</sup> Medical and psychiatric evaluation can provide evidence of comorbidities, which can contribute to the perception and severity of pain, as described previously. Quality of life assessment is important, as is screening for substance use disorders.

Formulating a diagnosis is an important next step. This can be difficult in the setting of the multifactorial

nature of pain. Pain sources include neuropathic, musculoskeletal, inflammatory, and visceral processes. The use of opioids for pain management can itself lead to pain, caused in part by the adaptation of opioid receptors over time. These and other factors should be considered when formulating a diagnosis.

Frequent reevaluation over time provides information about the progression of pain, response to treatment, and clues for alternate or new interim diagnoses. The Pain, Enjoyment, General Activity (PEG) scale is an easy-to-use 3-item scale that monitors pain severity and impact longitudinally. It is brief enough for practical use in clinical settings. By tracking the patient's PEG score, the practitioner can monitor and assess the response to treatments over time (Figure).<sup>7</sup> Furthermore, re-evaluations are too often simply an endorsement of the current treatment plan, and this approach can miss opportunities to confirm or modify a diagnosis as new data are available. Repeating examinations can bring to light changes that warrant further investigation. For example, a patient may have worsening lower back pain that is being treated as a flare of a musculoskeletal problem, but reexamination may reveal it is actually rheumatologic in nature.

HIV has unique pathophysiologic mechanisms that cause chronic pain; therefore, the evaluation of pain in people with HIV warrants added considerations.<sup>8</sup> The HIV-1 virus itself has neurotoxic effects. Proteins expressed by the person with HIV can lead to an increase in inflammatory cytokines; activation of the immune system stimulates nociceptors. Medications that treat HIV also can have neuropathic

**1. What number best describes your pain on average in the past week?**

0 1 2 3 4 5 6 7 8 9 10  
 No pain Pain as bad as you can imagine

**2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?**

0 1 2 3 4 5 6 7 8 9 10  
 Does not interfere Completely interferes

**3. What number best describes how, during the past week, pain has interfered with your general activity?**

0 1 2 3 4 5 6 7 8 9 10  
 Does not interfere Completely interferes

**Figure.** Pain, Enjoyment, General Activity (PEG) scale. Medical practitioners can use this scale to evaluate the severity of a patient's pain over time and adjust treatment accordingly. Adapted from Krebs et al.<sup>7</sup>

adverse effects. As a result, chronic pain remains a significant problem in people with HIV and is associated with functional impairments and reduced quality of life.

### Management of Chronic Pain in Older People With HIV

Treatment for pain is multidisciplinary and multimodal. The Infectious Diseases Society of America (IDSA) has published clinical practice guidelines on the management of chronic pain in people with HIV, including older people.<sup>9</sup> This and other guidelines emphasize a multidisciplinary approach. In addition to the patient's primary prescriber, the treatment team can include a mental health clinician, case manager, pain specialist, physical therapist, acupuncturist, peer support, and others.

A variety of nonpharmacologic treatments have also been studied and are recommended. Cognitive behavioral therapy is one treatment modality that has been shown to improve adaptive behaviors to pain and subsequent outcomes. Interventions such as yoga, physical therapy, and acupuncture may also provide benefit.

Because HIV itself can injure nerves and create pain, the use of antiretroviral therapy may treat and prevent HIV-

associated neuropathy. Gabapentin is an anticonvulsant medication used in a variety of applications, including a wide range of chronic pain conditions. Efficacy is questionable for many of the conditions in which gabapentin has been commonly used, but it is recommended for treatment of HIV-associated neuropathic pain. Gabapentin can cause sedation, which can be beneficial for people with insomnia, but it can also increase the risk of adverse events. Neuropathic medications such as tricyclic antidepressants, serotonin norepinephrine reuptake inhibitors, and pregabalin may also be used. Other beneficial agents include topical capsaicin, alpha-lipoic acid, and medical cannabis. Non-neuropathic pain can be managed with acetaminophen and non-steroidal anti-inflammatory drugs.

### Opioids in Chronic Pain Management

Though they carry serious risks, opioids do play a role in the management of

chronic pain in people with HIV. Opioids require close monitoring given the risk of developing opioid use disorder, and this monitoring is an important part of ongoing chronic pain management.

Given the risk of addiction, an opioid agonist should not typically be used as a first-line agent. The multimodal approach described in the prior sections is important for initial management and, if opioids are added, as an ongoing foundation in conjunction with the opioid therapy. Before the patient starts opioids, it is valuable to estimate the patient's baseline risk of developing harms or opioid use disorder. A variety of tools and calculators have been created to assist with this, including the Screener and Opioid Assessment for Patients with Pain (SOAPP), the revised SOAPP (SOAPP-R),<sup>10</sup> and the Opioid Risk Tool (ORT) (Table).<sup>11</sup>

The Centers for Disease Control and Prevention (CDC) has published a guideline for prescribing opioids for chronic pain.<sup>12</sup> This guideline provides several helpful strategies on how to safely select a patient who may benefit from opioids, start that patient on opioids, and monitor the patient for

**Table.** Opioid Risk Tool (ORT). A person's total score on an ORT assessment helps calculate their baseline risk of developing harms or an opioid use disorder ( $\leq 3$  = low risk; 4–7 = moderate risk;  $\geq 8$  = high risk). Adapted from Webster et al.<sup>11</sup>

Mark each box that applies	Female	Male
Family history of substance abuse		
Alcohol	1	3
Illegal drugs	2	3
Prescription drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Prescription drugs	5	5
Age between 16-45 years	1	1
History of preadolescent sexual abuse	3	0
Psychologic disease		
Attention deficit disorder, obsessive-compulsive disorder, bipolar disorder, schizophrenia	2	2
Depression	1	1
Scoring totals		

harms. When patients have moderate-to-severe pain that has not responded to first-line and second-line therapies, opioids can be started as a time-limited trial. Practitioners should start with the lowest effective dose and exercise caution when increasing the dose. The use of morphine milligram equivalents (MME) is a common measure of the overall daily strength of a patient's opioid regimen. The measure is calculated by summing up the total dose of all opioids prescribed in a 24-hour period and converting this total to the equivalent amount of oral morphine. The CDC has resources to help with this calculation.<sup>13</sup> A dose higher than 50 MME/day can increase the risk of overdose and warrants close attention. Immediate-release, rather than extended-release, preparations may provide faster relief and can be titrated with a lower risk of overdose than longer acting medications. An important caution is that fast-acting opioids with short half-lives may carry an increased risk of abuse. Extended-release opioids should only be considered for patients who have severe continuous pain and who have been stabilized on an immediate-release medication first. Close interval follow-up should be arranged to evaluate the response to therapy and any adverse effects.

The pharmacodynamic effects of some medications change as people age. Many of the psychotropic effects are augmented in older adults. Older patients are also at increased risk of medication-induced confusion and delirium. In particular, opioids may carry an increased risk of medication-related adverse effects in older people. As an example, tramadol, a weak opioid with inhibitory activity on serotonin and norepinephrine reuptake, has been reported to cause severe hyponatremia, mostly in women above the age of 65 years in the initial week of therapy.<sup>14</sup> In addition to the pharmacodynamic effects, older adults with HIV are often on multiple medications. This polypharmacy, plus age-related changes in metabolism,<sup>15</sup> can result in unpredictable pharmacokinetic interactions, which may increase the risk of respiratory depression or other adverse

events (eg, QT corrected for heart rate prolongation). Therefore, it is prudent when starting an older patient on an opioid to begin at the lowest dose and the longest intervals for dosing. Titration of the medication should account for the medication's half-life and the time to reach steady state, with repeated monitoring of the patient to avoid an adverse outcome. If practitioners are unclear on the timing of dosing or the rate of titration, they should consider speaking with pharmacy staff or reaching out to pain management specialists.

The use of patient-practitioner agreements, also known as controlled substance agreements or "pain contracts," is common for people on long-term opioid therapy. These are used for shared decision making and informed consent. Patients should be explicitly counseled on the risks and harms of opioids, including overdose and addiction. Assigning responsibility to the patient to self-monitor for the development of harms can be empowering to the patient, and it can help to focus on patient safety and risk-benefit analysis rather than on assigning blame. The practitioner, however, should keep in mind that HIV can be a proxy for risk-taking behavior. A person started on opioids should always be monitored for safety, and someone with a history of risk-taking behavior may be particularly vulnerable to taking risks with opioids as well.

Consideration should be given to prescribing intranasal naloxone as a rescue medication in case of overdose. Risk factors for overdose include a higher total opioid dose, concurrent use of other sedating medications such as benzodiazepines, history of substance use disorder, and comorbid medical conditions that can decrease clearance of medications (eg, liver and kidney disease) or increase risk of respiratory depression (eg, obstructive lung disease).

Urine toxicology is a widely used tool in monitoring for harms from opioids. The goal of urine drug testing (UDT) is to detect the presence of prescribed substances and to screen for the presence of nonprescribed substances.

UDT should be performed with open communication about the intent, namely as a monitoring tool for a potentially harmful treatment, rather than as an attempt to catch bad behaviors. There are limited data regarding the efficacy and optimal frequency of UDT in detecting concerns for the patient's treatment. Interpretation of UDT can be complicated and requires knowledge of drug metabolites, assay interference, and false positives and negatives. For example, the ingestion of poppy seeds has the potential to cause low levels of morphine in the urine, which prompted most immunoassays to move from 100 ng/mL to 300 ng/mL for thresholds for a positive opiate urine test. Another example in some laboratories is the use of trazodone, which can cause a false positive amphetamine assay. When a false positive result is suspected, immunoassay tests can be sent for confirmation testing with gas chromatography and mass spectroscopy. Major management changes should not be made based solely on initial UDT results without further investigation.

There are other tools used for monitoring the safety of opioids. Prescription drug monitoring program (PDMP) data at the state level help look for inconsistencies in prescription-filling patterns. Pill counts can detect an escalation in a patient's dosage beyond prescribed limits, or they can detect a diversion of their medication.

Aberrant behaviors can be challenging to address. They may arise from an unrecognized substance use disorder, but they may also be due to inadequately managed pain and poor coping skills. The response to aberrant behaviors should be individualized and should take into account patient-specific factors and the overall safety profile of opioid treatment. It is very important that hospital and clinic staff feel safe and protected; in rare cases, a patient may be discharged from a clinic due to their behavior, but all efforts should be taken to address the situation first.

If routine close monitoring reveals concerns for an opioid use disorder, a thoughtful, patient-centered approach

is recommended. This includes consultation with practitioners who have expertise in the management of substance use disorder. Practitioners should continue to treat chronic pain and support the patient, even when discontinuing the opioid is the safest choice. In most cases, an opioid taper should not be initiated abruptly or unilaterally by the prescriber; a taper plan should instead be formulated with the patient's input and, depending on the situation, may require a slow, prolonged taper. There are exceptions where a rapid taper may be appropriate, such as the safety of a patient at acute risk of overdose. If the taper plan is not successful, consultation with or referral to a pain or addiction specialist is appropriate.

## Conclusion

Older people with HIV have a high burden of chronic pain due to a variety of factors. It is important to inquire about chronic pain as it can impact health outcomes. Management of chronic pain requires a multimodal approach including both pharmacologic and non-pharmacologic interventions. Opioids can play a role among medications that manage chronic pain, and given their potential for significant harms, practitioners should be familiar with their use and understand how to monitor them.



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