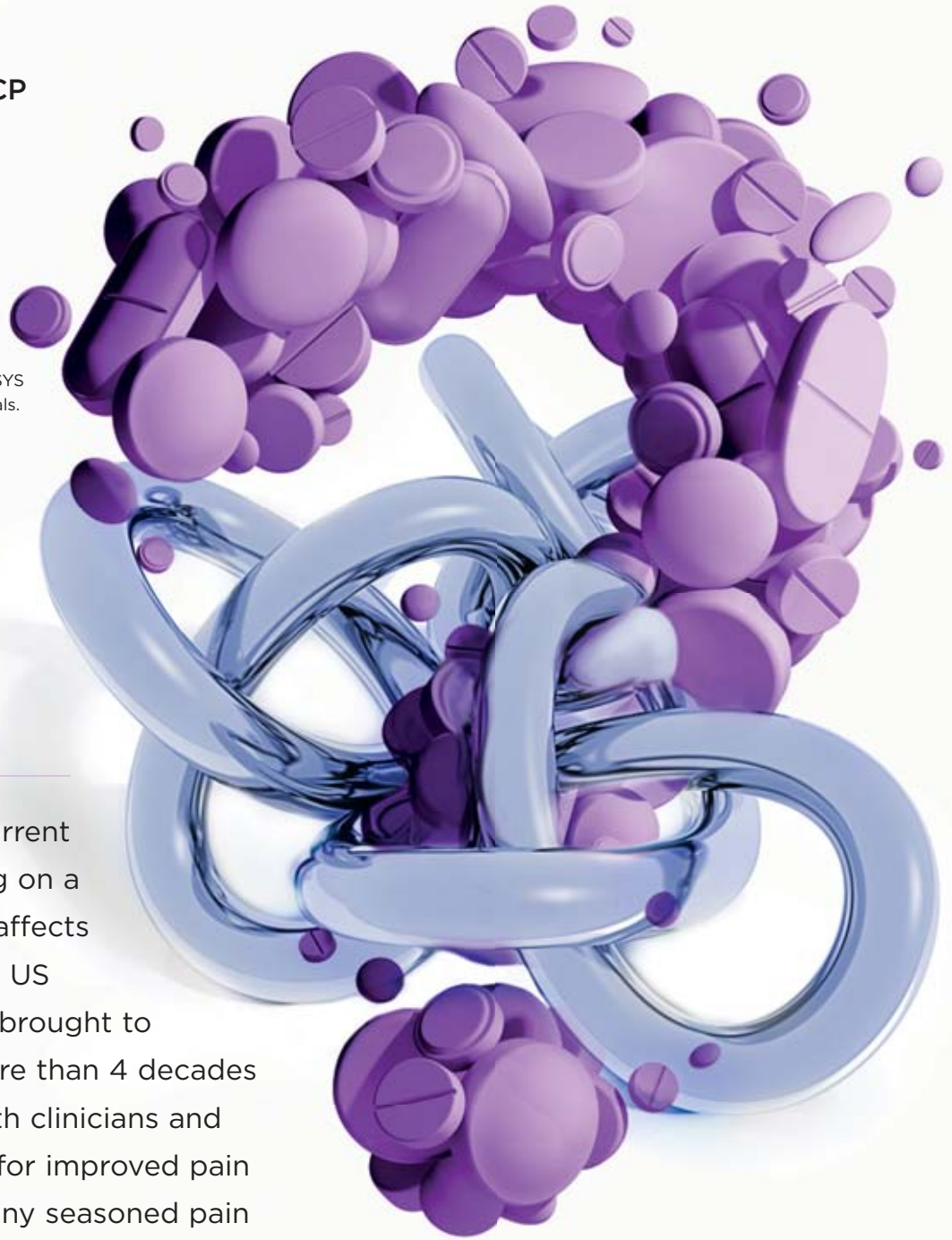


The Use of Opioids in Chronic Pain: Complexity and Practice

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Chronic or recurrent pain occurring on a regular basis affects more than 25% of the US population.¹ This was brought to national attention more than 4 decades ago to encourage both clinicians and patients to advocate for improved pain care. At that time, many seasoned pain physicians considered opioid therapy as not only safe, but also as a mainstay of chronic pain treatment.

However, those same physicians have grown sanguine about the use of opioids, as the downside of the class has become more apparent. There has been a lack of progress in the treatment of chronic pain and a paucity of physicians who specialize in the field of pain medicine.² Furthermore, the environment for the treatment of pain has become inimical and antagonistic, as state and federal agencies, committees, legislators, and regulators focus on physician prescribing of scheduled medications in an apparent effort to reduce abuse, misuse, addiction, and overdose deaths. This myopic approach, brought on by an election year and the need for re-election funds and media attention, has had unfortunate and significant negative consequences.³ There is no one answer to the problem of scheduled medication or illicit drug abuse, misuse, addiction, or overdose deaths, just like there is

no one answer to the treatment of chronic pain. Opioids have a role in the treatment of chronic pain, as part of a multidisciplinary multimodal program, and can be effective in the appropriately selected patient, but they are not a panacea. Although the treatment of these patients is fraught with complexity, it is how that selection should occur that this review attempts to elucidate.

When approaching a chronic pain patient it is critical to keep in mind that the effective evaluation, diagnosis, and treatment are complex and require a multimodal and open philosophy. This multimodal approach is supported by research that demonstrates the lack of efficacy of many of the unimodal interventions, both pharmacologic and nonpharmacologic.⁴ Weisman's warning about minimizing the complexities of the treatment of chronic pain came a decade ago; unfortunately, his caution has not been heeded.⁵

From the perspective of the busy clinician, the treatment of chronic pain can be viewed as overwhelming. Furthermore, given the scarcity of trained pain practitioners and the burgeoning number of patients with chronic pain, a new approach is needed that values the complex nature of chronic pain. There is no simple treatment approach to these patients; the complex nature of chronic pain takes time and effort.

Opioids can be a potent tool in the treatment of chronic pain but should never be the default standard. Some patients respond well to opioid therapy, others do not, and for some the risk outweighs any potential benefit. A comprehensive evaluation can aid in determining the most appropriate therapeutic approach for an individual patient. Although a focused approach to evaluation and treatment selection might be useful for certain diseases, in chronic pain only a comprehensive and full evaluation that also assesses potentially confounding factors is the appropriate course. Comorbidities and confounders will hinder success with any treatment approach. The categories listed in Table 1 may affect chronic pain and should be assessed with any evaluation of a patient with chronic pain.^{6-21,24} These criteria are not listed in order of importance because each of these domains is important and needs to be evaluated for each individual chronic pain patient. The only exception is pain intensity, which is purposefully listed at the end in this list because a parochial focus on a number is not the appropriate approach to these patients.

Evaluation

All patients entering a chronic pain treatment program should be given and sign a pain management agreement (it is best to describe and label these as "agreements" rather than the legally loaded term *contract*).^{22,23} The pain management agreement is an essential part of the initial evaluation and can be administered by office staff, but should always be discussed, in detail, directly with the patient by the practitioner. This agreement can specify what the clinic and physician will do

Table 1. Domains That Affect Chronic Pain Treatment

Medical comorbidities ^{6-21,24}
Other concomitant symptoms (symptom clusters)
Psychiatric and psychological comorbidities
Scheduled medication diversion and abuse risk
Number of chronic pain problems
Number of past surgeries
Tobacco usage
Head trauma history
Body mass index
Goal setting
Sleep disorders
Educational level and employment status
Current pharmacotherapy regimen
Level of social support
Physical conditioning
Current pain intensity

for the patient and what is required of the patient in return. The pain management agreement should never be a list of “thou shalt not’s,” but rather a template for how treatment will proceed and what is required from both the patient and physician. The agreement should never be used as punishment, or as a tool to discharge patients. As with urine drug monitoring (UDM), the agreement can be used as an opportunity for discussion with the patient concerning violations, issues with office staff, and the patient’s progress. Furthermore, the agreement should be given to all patients, regardless of the specific treatment regimen.

The evaluation of a patient with chronic pain starts with a full and complete history and physical examination (Table 2). A “focused examination” should never be the approach in the treatment of these patients.²⁴ For example, on average a chronic pain patient has 3.2 pain problems when he or she presents for the major pain complaint. Interestingly, data shows that low back pain will reduce pain thresholds in other areas of the body.¹⁰ If a focused evaluation is conducted, these pain generators and other issues will be missed, and treatment will more likely be unsuccessful.

This evaluation should set the stage for everything that follows. The history should establish the most consistent diagnoses and the physical examination helps to support those diagnoses. The initial evaluation will help define clear goals that can be set by patient and physician. Furthermore, it may find evidence of overt and concealed comorbidities that need to be addressed. Although this first evaluation is time-intensive, the time spent may well be more than made up for in future visits by a thorough knowledge of the patient’s pain problems and medical condition. Again, management of chronic pain is a complex medical paradigm. Although it should be obvious, full and complete documentation is a critical part of every patient visit. Documentation is one of the major weaknesses of prescribers who have problems with regulatory boards or federal agencies.²⁵ As part of the initial evaluation, obtaining a record of previous treatments and treating physicians also is critical. These records can establish patterns of concern and suggest treatments that have been successful or those that should be avoided. Additionally, they may suggest potential problems in a given patient’s care, such as a high risk for abuse of scheduled medications or addiction.

As with any medical intervention, informed consent is the foundation by which we engage in any treatment.^{23,24} Patients need to be apprised of the potential risks and benefits of any treatment and this is no less true with scheduled and controlled medications. The potential for side effects (eg, constipation or nausea, the potential risk for addiction, potential drug interactions, endocrinopathies, and sleep apnea), should be clarified for the patient. Appropriate documentation of this process should be present in the record and chart as well.

Patients with chronic pain frequently have multiple

Table 2. Overview of the Approach to the Chronic Pain Patient

Complete evaluation, history, and physical
Psychiatric evaluation and screening (eg, Beck, Zung, etc)
Risk evaluation for opioids (eg, ORT or SOAPP)
Pain agreements
Prescription monitoring programs
Understand federal and state laws and regulations pertaining to pain clinics and use of opioids
If opioids are used, no weekend or after-hours prescriptions or call-ins
Use of methadone: Make sure you understand its complexities
Review of the complexity domains (Table 1)

ORT, Opioid Risk Tool; **SOAPP**, Screener and Opioid Assessment for Patients with Pain

comorbidities.^{23,24} For example, sleep apnea (central or obstructive), frequently under diagnosed, may be more common, especially in patients on chronic opioid therapy.²⁶ The pain patient being treated with opioids who also has sleep apnea may be at risk for death.¹⁶ Additionally, insomnia and sleep disturbance, and endocrinopathies, are common in chronic pain.²⁷ Frequently, these patients have underlying psychiatric comorbidities (eg, anxiety and depression) that often go untreated.^{22,23,28} Numerous screening tools to evaluate for underlying psychiatric problems are available and should be used. The Zung Self Rating Depression and Anxiety scales and the Beck Depression Inventory are such screening tools.²⁹⁻³¹ These tools can be given simply and easily to patients by office staff and can identify those in need of treatment or those in need of a more thorough psychological evaluation. Furthermore, a number of screening tools have appeared in the literature within the past few years to aid in risk stratification for potential opioid abuse.^{22,23} Passik and his colleagues have conducted a thorough comparison of available tools and recommend the Opioid Risk Tool, when brevity is needed, and the Screener and Opioid Assessment for Patients with Pain, a good choice among the longer measures.³² It should be noted that these screening tools are not substitutes

Table 3. Staying Out of Trouble

Follow the complete evaluation of a chronic pain patient (Table 2).

Discontinue treatment that fails.

Document well and document everything.

Reassess, reassess, reassess.

Know your limitations.

Refer for addiction counseling, do not continue opioid treatment in active addicts.

Refer to pain specialist when needed.

for a psychological assessment by a trained pain psychologist. Regardless of what treatment a chronic pain patient is given, it is important to screen for and treat the disease of addiction.

Knowing which patient to start on opioids is not a simple question; neither does the answer to this question lend itself to protocols or a “set of rules.” It depends on a gestalt based on previous treatments, patient risk, psychological profile, and other factors. Once the gestalt identifies a patient who might benefit from opioids, treatment can be started. However, there should always be an exit strategy, which should be discussed with the patient up front.²² Additionally, if your evaluation and diagnoses suggest that opioids might be one aspect of a patient’s treatment plan, long-acting rather than short-acting opioids should be considered.³³ Furthermore, the lowest dose that provides the best pain relief, improved function, and quality of life should be used. In addition, the patient should be required to use only one pharmacy for all scheduled medications.³⁴

Most patients in this population may benefit from adjuvant medications, such as antiepileptics, tricyclic antidepressants, serotonin norepinephrine reuptake inhibitors, α -agonists, and others.^{22,23} As mentioned previously, old medical records can help with this data collection. They also can elucidate if the patient was on a therapeutic dose of a previously tried medication, which might suggest a retrial with titration to higher and more effective doses (eg, venlafaxine [Effexor, Pfizer] at 75 mg per day). The addition of adjuvants can provide a synergistic benefit. One pilot study found the use of an adjuvant (gabapentin) with morphine created a synergistic effect, reducing the dose of both agents.³³ Furthermore, a recent Cochrane collaboration review has shown that combination therapy has “superior efficacy” compared with single-drug therapy.³⁵ Additionally, pain psychology and behavioral therapy, physical therapy, manipulative therapies, and interventional pain

medicine all should be considered and applied when appropriate. Again, this is part of a multidisciplinary, multimodal approach to the treatment of chronic pain.

Patient and physician goals for any treatment are critical and these should be established in documentation from the initial evaluation. What does the patient want to achieve? All patients with chronic pain want “less pain”; however, improved function and quality of life must be discussed and included when setting goals. Each goal should be listed in the original evaluation and readdressed as the treatment regimen is instituted and the patient is followed. Unrealistic expectations may cause treatment failure and must be addressed. Furthermore, a rigorous adherence to reduction in pain numbers should be avoided. Function and quality of life are much more important goals and markers of success than a single pain number, again reflecting the complexity of this chronic syndrome. One possible, and easy, measurement of patient function is the 6-Minute Walk.³⁶ Office staff can administer this easily.

Setting clear rules and expectations at the initial visit can be done both verbally as well as in the pain agreement. It is critical that we keep boundaries and clear consequences should those boundaries be crossed and violated. However, boundaries should be occasions for discussion with the patient, and not a tool to discharge or punish them. A practitioner may refuse to prescribe scheduled medications to a patient who has violated boundaries, but instead may offer addiction treatment, treatment of potential withdrawals, antidepressants, adjuvants, and so on.

UDM should be a consistent part of any chronic pain program in which chronic opioid therapy is being considered. Although UDM can be a very useful test to help identify abuse, misuse, or addiction, its use both by pain specialists and primary care physicians is surprisingly low (8%-30%).^{37,38} There is a risk for misinterpreting UDM results and potentially harming a patient. This is one reason why practitioners should have a good understanding of the UDM report and a good relationship with whatever laboratory is being used. The UDM should never be used to penalize a patient, but rather to open up dialogue. A UDM that is positive for cocaine is a potential opening to discuss the patient’s need for treatment. Although clear research data on UDM efficacy in reducing “abuse, misuse, addiction, and overdose deaths”^a does not exist, many professional organizations, regulatory agencies, and others recommend the use of UDM.²³ Have a clear plan on how to deal with inconsistent UDM results, results that you don’t understand, and how to generally incorporate UDM into your practice. For more information, see Peppin et al.³⁹

Reassessment

Although a full and thorough history and physical are critical to the initial evaluation of the patient with chronic pain, continued treatment requires constant reassessment (Table 3). Patients are not static in time,

they are fluid and things can change quickly. New pain states, the discovery of abuse or addiction not found on the initial evaluation, and new comorbidities all can affect the success of treatment. The 4 A's can help formalize this reassessment when it comes to opioids.⁴⁰

The 4 A's are:

- Analgesia (pain relief)
- Activities of daily living (ADLs; functional outcomes)
- Adverse effects (side effects)
- Aberrant drug-related behaviors (appropriate use and adherence vs misuse or addiction-related outcomes).

However, the assessment for potentially developing complications of therapy, sleep issues, psychiatric issues, and so on, also should occur. This cannot be emphasized enough and is a critical, often overlooked, piece in the appropriate treatment of chronic pain patients on chronic opioid therapy. Patients should be seen more frequently when medications are changed or increased, but once a patient is stable, the time between visits can be longer. Most regulatory boards state that physicians and providers who are prescribing scheduled medications must see their patients "regularly," although rarely is this defined.⁴¹ The Drug Enforcement Administration (DEA) allows physicians to write class II prescriptions with a "do not dispense" label, which specifies when prescriptions can be filled. This allows physicians to write multiple prescriptions at once but prevents early filling before the dates specified on the prescription. Physicians must fully understand federal and regulatory laws and guidelines before writing a prescription for any scheduled medication.⁴²

Patients with exacerbations of chronic pain should not go to the emergency department (ED). The pain agreement should specify that the patient will be seen in the clinic as soon as possible to treat his or her exacerbation; however, the ED is "off limits" for chronic pain. Clearly explain to patients that any other issue (ie, shortness of breath, chest pain, etc) still indicates they should indeed go to the ED. The 4 A's should be assessed at every visit, especially in patients on opioids.^{22,40}

Pill counts are another way to check on patient compliance with scheduled medications. It should always be done in front of the patient with a witness present. The pills should be counted twice and the patient, physician, or nurse, and the witness should sign a form indicating how many pills were present. This documentation should be in the patient's permanent record. A DEA registrant cannot take possession of any patient's scheduled medications; this is a federal felony.⁴³ However, if a medication trial has failed and there are leftover medications, having the patient dispose of them appropriately in the office is acceptable.

It is still not clear if prescription monitoring programs (PMPs) have a significant effect on diversion, but they do represent a standard of care in states where they exist and should be used. An example of PMP is KASPAR (Kentucky All Schedule Prescription Electronic

Reporting).⁴⁴ How often to order a PMP report on a given patient is not clear. Again, it is critical for physicians to know their state's regulations and laws. Recent legislation in Kentucky requires that PMP reports be obtained on all patients on opioid therapy.⁴⁵

When treating a number of chronic pain patients with opioids, physicians must get to know local law enforcement and work with them. Although the current regulatory and legislative environment is antagonistic to good pain care, there are members of law enforcement who understand the importance of treating chronic pain. Too often, physician offices have a lack of prescription pad security.⁴⁶ Physicians should consider having prescriptions that are "uncopyable" and sequentially numbered. For each prescription, the individual script number, patient name, and date should be documented. All prescription pads should be signed for and locked up. Blank prescriptions should be treated as money, and should be protected from theft or misuse. Each scheduled prescription should include the generic name of medication, doses in both alpha and numeric form, the strength, and the patient's address.⁴⁷ Anyone who comes to the office to pick up a prescription, especially for scheduled medications, should be required to show a photo identification. This should be spelled out in the pain agreement. Office personnel should document the person picking up the prescription, and photocopy the identification. Additionally, the pain agreement should clearly state that no prescriptions will be provided after hours, on weekends, or vacations. Patients should be responsible with their medications, and waiting until 5 PM on a Friday to request a refill is not responsible.

When treatment fails, it should be discontinued; although obvious, physicians frequently get themselves into legal and regulatory trouble for this very reason.⁴⁸ If a patient is placed on a scheduled medication and there is no improvement in his or her pain levels, quality of life, or function, the treatment should be modified or changed. For primary care physicians who wish to treat chronic pain patients, getting a second opinion from a pain specialist can be very helpful. Their consultation helps document the treatment regimen and goals of therapy.

The use of methadone for chronic pain should be approached very cautiously. This medication carries with it great complexity and uncertainty. It requires experience and understanding of its pharmacology and potential drug-drug interactions. Comorbidities such as sleep apnea or congenital prolonged QT interval syndrome must be identified. Furthermore, the as-needed use of methadone must be strictly avoided.⁴⁹ Patients should be counseled in detail about this medication. They should call the prescribing physician before starting any new medications, or the consulting physician should call the prescribing physician to discuss the potential for interactions. Prescribers who do not feel comfortable with this medication should get training, or leave it for an experienced expert.

Conclusion

The treatment of chronic pain is complex and there is no simple or easy approach to treat these patients. The use of opioids in the treatment of chronic pain is complicated; there is no easy approach to their use. Furthermore, they are not a panacea or magic answer to patients' pain. The use of opioids requires knowledge of pharmacology, comorbidities, medication side effects, appropriate outcomes, addiction, and abuse, as well as psychiatric disorders. All chronic pain patients should receive a full and thorough initial history and physical examination, without which treatment of these patients may well fail. Additionally, these patients should be reassessed with every visit. Although complicated, treating these patients can become part of a non-pain specialist practice, which can provide much needed care to this patient population. Office staff can administer some of the assessments and reassessments. Furthermore, computers allow screening tests

to be administered by the patient him or herself, and so on. Those practitioners who are interested easily can obtain further training and even board certification through professional organizations and CME programs. Subscribing to a pain journal and reading current literature also can be of help. However, the complexities of chronic pain cannot be minimized, and treating these patients must take these complexities into account.

^a The terms *abuse*, *misuse*, *addiction*, and *overdose deaths*, have been goal terms in FDA discussion (although they are poorly defined). (Rappaport BA. Food and Drug Administration Elements of the proposed REMS for long-acting and extended-release opioid drug products. Slide presentation, June 22, 2010, Joint meeting of the Anesthetic and Life Support Drugs and Drug Safety and Risk Management Advisory Committees).

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