Managing Side Effects and Complications of Opioid Therapy for Chronic Pain

This fact sheet accompanies the 2017 VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain and was created to aid with treatment of adult populations. Department of Veterans Affairs (VA) and Department of Defense (DoD) employees who use this information are responsible for considering all applicable regulations and policies throughout the course of care and patient education. The goal of this factsheet is to explain how to properly manage side effects of opioid therapy (OT) in DoD and VA primary care settings. Co-occurring conditions and side effects are common consequences of OT, and may occur during both short-term and long-term opioid therapy (LOT).

Risk Mitigation

The greatest risk factors for the development of opioid-related adverse events are the duration and dose of opioid analgesic use.[1] Many other factors also increase the risk of adverse outcomes and must be considered when prescribing opioid medications (see Significant risk factors).

Providers should consider and implement risk mitigation strategies before prescribing opioid medications. The provider should discuss the potential risks and benefits as well as alternative therapies with the patient and if possible, obtain the patient's informed consent regarding the patient care plan, including risk mitigation strategies. Risk mitigation strategies may include:

- Ongoing random urine drug testing and appropriate confirmatory testing
- Frequent face-to-face follow-up appointments to assess for co-occurring conditions and side effects
- Monitoring for overdose potential and suicidality
- Providing overdose education, including prescribing of naloxone rescue
- Checking state prescription drug monitoring programs

Evaluation of the benefits of continued opioid therapy and risk for opioid-related adverse events every three months (at a minimum) is recommended.

Significant risk factors

- Duration and dose of OT
- Severe respiratory instability
- Sleep disordered breathing (e.g., sleep apnea)
- Acute psychiatric instability or intermediate to high acute suicide risk (suicidality)
- Traumatic brain injury
- Mental disorders
  - Current or history of substance use disorder (SUD) (untreated SUD confers additional risk)
  - Depression or history of depression[2]
  - Generalized anxiety disorder
  - Borderline personality disorder
  - Antisocial personality disorder
  - Posttraumatic stress disorder (PTSD)
- History of drug overdose
- Under 30 years of age
- Evidence for or history of diversion of controlled substances
- Intolerance, serious adverse effects, or a history of inadequate beneficial response to opioids
- Impaired bowel motility unresponsive to therapy
- Pain conditions worsened by opioids (e.g., fibromyalgia, headache)
- True allergy to opioid agents (that cannot be resolved by switching agents)
- Co-administration of a drug capable of inducing fatal drug-drug interactions

Clinical reminders:

- Evaluate risk factors for opioid-related harms
- Conduct a suicide risk assessment and intervene when necessary
- Check the Prescription Drug Monitoring Program (PDMP) for high dosages and prescriptions from other providers
- Use urine drug testing to identify prescribed substances and undisclosed use
- Refer for opioid use disorder treatment if indicated

STOP Avoid prescribing concurrent benzodiazepines and opioids

Spectrum of Side Effects

Carefully consider side effects (e.g., depression, weight gain, headaches, nightmares, problems with intimacy, paresthesias) during monitoring and adjust treatment in order to minimize the side effects pursuant to individual patient preferences. Slower initiation and titration improves tolerability.

Managing Adverse Effects

It is imperative that providers discuss possible adverse effects of OT with patients and family members. If adverse effects are unmanageable and therapy is a greater detriment than benefit as determined by discussion with the patient and family, OT should be discontinued. See the chart below for more information on some of the potential adverse effects.

Adverse Effects	Symptoms	Protocol for Management
Respiratory depression	▪ Drowsiness ▪ Slow or shallow breathing ▪ Difficulty staying awake ▪ Difficulty awakening ▪ Loud or unusual snoring	▪ Administer the lowest effective opioid dose necessary to achieve satisfactory pain control – start low and go slow STOP Avoid other central nervous system (CNS) depressants, especially benzodiazepines because this combination has been identified in opioid-related deaths ▪ Alert family members or caretakers of the important warning signs to watch for that may indicate that the opioid should be decreased or stopped: — Difficult or slow breathing — Difficulty staying awake — Loud or unusual snoring — Difficulty being awakened
Mental status changes	▪ Confusion ▪ Bad dreams ▪ Hallucinations ▪ Restlessness ▪ Agitation ▪ Dysphoria ▪ Significantly depressed level of consciousness ▪ Seizures	▪ Evaluate underlying cause; consider role of primary therapy – hallucinations can be due to a variety of causes, including change in surroundings and sleep deprivation ▪ Evaluation of hallucinations is often performed by "trial and error" techniques – eliminate nonessential CNS-acting medications (e.g., steroids) ▪ Re-evaluate and treat underlying process if appropriate ▪ Dysphoria is more common with mixed opioid agonists/antagonists and antidopaminergic medications ▪ If hallucinations persist: — Consider a trial of an antipsychotic in consultation with behavioral health specialty, or — Switch to another opioid
Opioid induced endocrinopathy	▪ Loss of libido ▪ Impotence ▪ Fatigue ▪ Mood alterations ▪ Loss of muscle mass and strength ▪ Abnormal menses ▪ Infertility	▪ Ask all patients on opioids about symptoms of opioid-induced endocrinopathy (e.g., hypogonadism) ▪ Determine cause of symptoms through lab work and/or consultation with an endocrinologist ▪ For males, consider testosterone patch therapy, as research indicates it may improve androgen deficiency symptoms, sexual function, mood, depression and hematocrit levels ▪ NOTE: There is insufficient data to recommend routine laboratory screening for endocrinopathy in asymptomatic patients on OT
Severe respiratory instability or sleep disordered breathing (sleep apnea or COPD)	▪ Loud snoring ▪ Excessive daytime sleepiness ▪ Fatigue ▪ Morning headaches (cerebral vasodilation) ▪ Depression and/or emotional instability ▪ Short-term memory loss ▪ Impaired concentration ▪ Irregular pauses in breathing	▪ Strongly consider discontinuing OT and obtain sleep studies ▪ The type of sleep apnea should be evaluated to determine if it is obstructive or central ▪ Central sleep apnea is a relative contraindication to OT, and discontinuation of OT should be considered if sleep apnea is severe or life-threatening ▪ Instruct patients to avoid alcohol and medications that cause drowsiness

References

1 Opioid Therapy for Chronic Pain Working Group, Department of Veterans Affairs & Department of Defense. (2017). VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain. Version 3.0. Retrieved from https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPG022717.pdf

2 Management of Major Depressive Disorder Working Group, Department of Veterans Affairs & Department of Defense. (2016). VA/DoD Clinical Practice Guideline for the Management of Depressive Disorder. Version 3.0. Retrieved from http://www.healthquality.va.gov/guidelines/MH/mdd/VADoDMDDCPGFINAL1.pdf

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