Background: Opioid withdrawal can occur in anyone with physical dependence on opioids who stops opioid use suddenly, has a rapid reduction in opioid dose, or receives an opioid antagonist such as naloxone or high dose of a partial agonist like buprenorphine. Physical dependence on opioids is a normal and predictable neurophysiological response to regular treatment with opioids for more than 1-2 weeks. Continuous or near continuous opioid blood levels are required for physical dependence (one oxycodone-acetaminophen tablet per day will is not sufficient). Physical dependence is not the same as addiction or opioid use disorder, although nearly all patients with OUD will also have physical dependence. While OUD has a neurobiological basis, fundamentally it is defined behaviorally, and is characterized by impaired control over opioid use, use of opioids despite harm (physical/medical, social/interpersonal, vocational, legal), and craving.

Signs and symptoms: Signs and symptoms of the opioid withdrawal syndrome include yawning, sweating, lacrimation, rhinorrhea, anxiety, restlessness, insomnia, dilated pupils, piloerection, chills, tachycardia, hypertension, nausea/vomiting, cramping abdominal pains, diarrhea, and muscle aches and pains. Unlike withdrawal from alcohol or benzodiazepines, opioid withdrawal is not life threatening. Emergence of withdrawal symptoms varies with half-life of the particular opioid: often within 6-12 hours after the last dose of a short-acting drug or 72-96 hours following methadone (see Fast Facts #75, 86). Duration and intensity of withdrawal are related to clearance of the drug such that withdrawal is shorter (5-10 days) and more intense for opioids like morphine and less severe and more protracted with methadone and buprenorphine. A validated tool to assess severity of withdrawal symptoms as well as aid in appropriate medication management is the Clinical Opioid Withdrawal Scale (COWS).

Prevention: Opioid withdrawal syndrome should be prevented as much as possible. Patients treated with opioids for more than one to two weeks should be instructed to gradually reduce the opioid before discontinuing use and given basic education about withdrawal symptoms. Clinics should establish reliable systems to refill opioid prescriptions on-time so patients do not inadvertently run out. Near the end-of-life, patients with physical opioid dependence need to have careful dose and route adjustments to ensure they receive adequate opioid dosing even as they lose the ability to swallow. When done intentionally, opioid tapering should be done slowly to prevent withdrawal, and the rate of tapering should be adjusted as needed to minimize withdrawal symptoms. The current CDC recommendations are to decrease the dose by 10% per month for patients on opioids greater than one year and a decrease of 10% per week for patients with weeks to months on opioid medications. See Fast Fact #413 for more about opioid tapering.

Symptomatic treatment: Sometimes withdrawal symptoms are unavoidable (e.g. the patient or clinician’s preference is to rapidly taper and is willing to accept some withdrawal symptoms). There are many medications useful in the symptomatic treatment of opioid withdrawal. Standard medications include alpha-2-adrenergic agonists such as clonidine and lofexidine, which can be used to treat autonomic hyperactivity symptoms. The major drawback of clonidine therapy is the tendency to cause hypotension. Skeletal muscle relaxants such as tizanidine or cyclobenzaprine help with both myalgias and sympathetic symptoms without causing hypotension. Other agents used for palliating withdrawal symptoms include: NSAIDS and acetaminophen (for muscle aches), diphenoxylate/atropine (Lomotil) (for diarrhea), bismuth and ondansetron (for nausea and GI distress), gabapentin (1600 mg/day may reduce subjective coldness, diarrhea, muscle tension and yawning), hydroxyzine (for pruritus, anxiety, and musculoskeletal pain), trazadone (for insomnia), cyclobenzaprine and dicyclomine hydrochloride for abdominal cramping. All these agents can be discontinued after approximately a week.

Reinstating opioids for patients experiencing withdrawal: For patients experiencing withdrawal due to an unintended stopping of opioid therapy (e.g., patient ran out of opioid medications despite intentions to continue opioid therapy) reinstituting opioid therapy is appropriate and will typically rapidly resolve the withdrawal. Depending on how long a patient has been without opioids it may not be safe to reinstate the full opioid dose immediately (especially for long-acting opioids). In this case patients should go through a dose-titration phase with short-acting opioids to safely achieve analgesia. Importantly, intentionally
stopping opioids and initiating withdrawal, with a plan to mitigate the withdrawal primarily through starting buprenorphine-based opioid therapy, is a common strategy to transition a patient onto buprenorphine for OUD and/or chronic pain. Symptomatic treatment of withdrawal with the above medications is still important for these patients and the above medications can be used. See Fast Fact ###.

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References:


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