Unintentional overdose in a patient on high dose opioids
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Story from the frontline

A woman in her 50s with chronic pain and anxiety established care at a new clinic. At that time, she was on morphine ER 60mg tid, oxycodone 30mg q6h prn, diazepam 10mg bid prn, and temazepam 30mg qhs. Her pain was from osteoarthritis of the knees and hips. During that initial visit, the patient was resistant to trying other therapies for control of her anxiety and was insistent on maintaining her prior opioid regimen. Her oxycodone was decreased from 30mg to 15mg q6h prn given the provider's discomfort with her total daily morphine equivalent dose and the high short acting opioid dose, otherwise her regimen was maintained without change. Her new physician agreed to three months of benzodiazepine refills to allow the patient time to establish care with a mental health provider prior to planning a rapid taper of these medications.

Over the next 5 months, the patient twice was found to have obtained opioid and sedative medications from another clinician, in violation of her pain contract. She was advised that one more violation would result in an immediate cessation in opioid medications prescribed by the office. She agreed to this, and set up an appointment with mental health. Unfortunately, before the appointment with the mental health provider, the patient forgot if she had taken her medications, and took a double dose of morphine ER and oxycodone, and also consumed both wine and marijuana. She was admitted to the medical ICU after being found down at home. She was fortunately only hospitalized for 36 hours. On discharge, her doses of both opioid and benzodiazepines were continued by the discharging physician.

Teachable moment

Since 1999, prescriptions of opioid pain medications have quadrupled[1]. Deaths from opioid overdose have tripled since 2000, and deaths from drug overdose now exceed those from motor vehicle accidents[2]. The concern about the risks of opioid overuse has led to the US Surgeon General sending a letter to all physicians, urging them to "turn the tide" on the opioid epidemic[3], and the CDC released guidelines for chronic opioid prescribing[4]. Because of the rapid development of this opioid epidemic, patients and clinicians may struggle with the decision to taper opioid medications, and in this particular case a patient suffered overdose and an ICU stay because of her medications.

Evidence of the risk of opioid overdose at a dose higher than 100 morphine equivalent dose (MED) is robust, and is reflected in the CDC recommendation to carefully evaluate and clearly justify any decision to prescribe any patient more than 100 MED per day. Even with

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[1] Paulozzi LJ, Jones C, Mack K, Rudd R. Vital signs: overdoses of prescription opioid pain relievers—United States, 1999–2008. MMWR Morb Mortal Wkly Rep 2011;60:1487–92.
[2] CDC. Wide-ranging online data for epidemiologic research (WONDER). Atlanta, GA: CDC, National Center for Health Statistics; 2015. Available at http://wonder.cdc.gov
[3] Murthy, Vivek (2016, August 25). Letter from the Surgeon General. *Turn the Tide.* Retrieved from: http://turnthetiderx.org/
[4] Dowell, Deborah, Tamara M. Haegerich, and Roger Chou. "CDC guideline for prescribing opioids for chronic pain—United States, 2016." JAMA 315.15 (2016): 1624-1645.

doses as low as 50-100 MED, the risk of serious opioid overdose is 2.2 times higher than at lower doses[5]. At doses above 100 MED, relative risk of overdose is 4-8 times higher, for an absolute risk of overdose of about 1.8% per year[6]. This patient was taking 270 MED, and was therefore at high risk for opioid overdose even without considering her co-occurring benzodiazepine use. She also had other risk factors for opioid misuse and potential overdose, including receiving prescriptions from more than one provider, and using other substances (alcohol and marijuana). Although patients may be very reluctant to taper their chronic opioid medications, there is strong evidence that the risks of chronic opioid doses of more than 100 MED has a high risk of harm, and there is no evidence of long-term benefit (longer than one year) in terms of pain control.

As recommended by the CDC, and as this patient's case demonstrates, patients who are taking more than 100 morphine equivalents per day for chronic pain should be tapered to a dose below this range to reduce risk of opioid overdose. Also, while not the focus of this article, it should be noted that the risk of a repeat overdose is related to the dose of opioids prescribed after an overdose. Research would indicate that this individual has a 17% chance of repeat overdose in the next two years if her opioid dose is not decreased[7].

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[5] Zedler, Barbara, et al. "Risk factors for serious prescription opioid-related toxicity or overdose among Veterans Health Administration patients." Pain Medicine 15.11 (2014): 1911-1929.
[6] Dunn, Kate M., et al. "Opioid prescriptions for chronic pain and overdose: a cohort study." Annals of internal medicine 152.2 (2010): 85-92.
[7] Larochelle, Marc R., et al. "Opioid prescribing after nonfatal overdose and association with repeated overdose: a cohort study." Annals of internal medicine 164.1 (2016): 1-9.