

A practical guide to tapering opioids

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Abstract

Tapering opioids is one of the most daunting dilemmas in clinical practice today. The decision to taper opioids is based on many factors, including a lack of efficacy, unacceptable risk, perioperative management, noncompliance, or patient preference. Tapering in the perioperative setting is quite common, though more complex in patients previously taking chronic opioid therapy. Outside of a medical emergency, opioid tapers are best managed in an outpatient setting, allowing for adjustments and more long-term nonopioid pain management, if necessary. No single strategy can be applied to all patients, and very few published guidelines are available for reference. Dose reductions and schedules are highly variable across available guidelines and literature. Dose reductions range from 10% to 50%, with a frequency ranging from daily reductions to every 2 weeks. Most guidelines address the concern of preventing physical withdrawal symptoms; however, few address the psychological ramifications of tapering. Individualized regimens and a willingness to adjust schedules and doses allows for improved patient comfort. The goal is to complete tapering without any symptoms of withdrawal; however, this is not always possible. Several available agents may help ameliorate these symptoms, including antihypertensives, antihistamines, antiemetics, antidepressants, anticonvulsants, and antipsychotics. Opioid tapering is rarely easy but should be a manageable process.

Keywords: Opioid tapering, opioid withdrawal, pain management

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Introduction

Recent statistics indicate that health care providers wrote 259 million prescriptions for opioids in 2012, enough for every American adult to have received at least one prescription in that year.¹ This reflects an upward trend over the past 15 years. Providers in a variety of settings now routinely see patients who are taking large doses of

opioid (eg, more than 100 mg of morphine equivalents), either as new referrals or as the result of a long-term dose escalation. Providers are faced with an ethical and clinical dilemma of how to manage this analgesic therapy, how long to continue it, and how to stop it if necessary. Concerns about opioid management are seen across health care settings, ranging from short-term opioid exposure in an acute pain setting to patients with long-standing opioid use. Surgeons need to plan opioid tapers after surgery, as acute postoperative pain is expected to improve. Oncologists may need to initiate and manage opioid tapers for patients in cancer remission who may no longer need or benefit from this type of therapy. This review will focus on tapering approaches in patients who have been taking consistent opioid therapy (at least 60 mg morphine equivalent per day for at least 7 consecutive days) in a nonaddiction setting. The tapering methods and



maintenance therapies used in the setting of addiction are outside the scope of this review.

Reasons to Consider a Taper

From the health care provider and the patient perspectives, an opioid taper should be considered for many reasons. Generally, tapers should be completed when there is no perceived benefit derived from the therapy. Lack of efficacy can be measured in many ways but is usually considered if there is no improvement in function, inadequate analgesia, or failure to reach established treatment goals. Some types of pain do not generally respond well to opioid therapy (eg, fibromyalgia, myofascial pain syndrome) and individual patient response (eg, pharmacogenetic variability) is also a factor. Analgesic therapy is expected to improve patient function and quality of life. If this is not achieved, despite regular dose increases and/or opioid rotation, tapering or switching to nonopioid therapy is indicated.

Unacceptable risk, from the patient's or the provider's perspective, is another reason to taper. The innumerable opioid-related adverse effects may lead patients and providers to question the risks versus benefits of opioid therapy. These effects include cognitive compromise or sedation, refractory constipation, concerns about respiratory depression, hypogonadism, and osteoporosis. Another consideration is the phenomenon of opioid-induced hyperalgesia, one of the controversies in chronic opioid management, which suggests that in certain patients, chronic exposure to opioids results in an increased sensitivity to pain.²⁻⁴ Although not necessarily a health risk, some patients may think the stigma of opioid use is too great or that the risk to their home and life are too great. Some employers prohibit opioid therapy in the workplace and may perform urine toxicology screens routinely.

Researchers have established that patients taking chronic opioid therapy before surgery require up to 3 times more opioid after surgery than opioid naive patients.⁵⁻⁷ The definition for chronic opioid therapy is variable and tends to be defined on a practitioner-specific or institution-specific basis. For example, an institution may consider chronic opioid therapy to be a regimen of at least 60 mg of morphine equivalent daily for at least a month. Though there are no published data to support it, surgeons may request that patients stop opioid therapy before surgery to improve mu receptor sensitivity and avoid greater postoperative opioid requirements. The period of abstinence before mu receptor resensitization occurs is not known in humans but is roughly 3 weeks in an animal model.⁸ Just as they might taper before surgery, surgeons also need to consider a plan to taper opioids after surgery, as acute postoperative pain is expected to improve.

TABLE 1: Definition of opioid tolerance^{9,a}

Patients considered opioid tolerant are those receiving any of the following for 1 week or longer:

- At least 60 mg oral morphine/day
- 25 µg transdermal fentanyl/hour
- 30 mg oral oxycodone/day
- 8 mg oral hydromorphone/day
- 25 mg oral oxymorphone/day

^aDoses used in this table are considered to be approximately equianalgesic

Providers may think there is a need to taper opioids in a patient who is noncompliant or is misusing or abusing the medication. Patients may request an increase in dose without indication of worsening conditions or presence of a new condition. Other issues include compulsive use, overuse, abnormal urine drug screening results, and use for reasons other than pain (eg, a nonmedical use or a medical use for a non-pain-related condition, such as anxiety). These situations may call for referral to a mental health or chemical dependency specialist.

Patient Populations

Acute Care Setting

Opioid use is often considered a primary modality in the treatment of acute pain in many settings, including post-surgical somatic pain, as mentioned previously. Acute injury or surgical pain usually peaks within a couple days and then improves as the underlying pathophysiology resolves. Patients without previous chronic opioid therapy usually receive short-acting products, and most patients' opioid requirements steadily decrease as their pain improves. Complex tapering regimens and psychological support are not as critical in this population. However, for patients who have undergone extensive surgeries or those who were taking chronic opioid therapy before surgery, providing a structured taper is usually appropriate. If a patient becomes opioid tolerant (eg, requires a dose of at least 60 mg of oral morphine equivalents per day for a week or more after surgery), he or she will likely need a tapering regimen to prevent opioid withdrawal. See Table 1 for more information about the definition of opioid tolerance.

Patients with chronic pain who present with an acute illness or injury (or surgery) also require ongoing pain management, and this may require continuing or increasing opioids. Some providers will consider tapering opioids for a chronic condition that is not related to the acute presenting illness.(eg, a patient with chronic low back pain who is admitted with acute abdominal pain). In some situations the philosophy is "as long as the patient is here

we might as well get rid of these opioids.” Despite the desire to address several concerns during an acute care admission, however, this setting is not the optimal time to taper chronic opioid therapy, as it may cloud the treatment of the presenting complaint (causing tachycardia, complaints of pain, anxiety, poor sleep, and so on). If medical reasons dictate that a taper must be initiated for safety reasons, providers may choose a tapering regimen that is quicker, as more intensive monitoring is available in the inpatient setting. The emergency department is also not an appropriate place to initiate a taper, unless medical safety requires it. These patients may be referred to their primary care providers for management or referred to a specialist to initiate and complete an opioid taper.

Outpatient Setting

Chronic opioid therapy users in the outpatient setting can be divided into 2 groups. The first group includes patients who take low-dose short-acting opioids on a long-term basis but have intermittent or sporadic use (generally fewer than 8 tablets/day) on an as-needed basis. The second group includes patients who use long-acting agents and/or short-acting agents as a regular daily regimen. The former group is not likely to need a formal tapering regimen, as the patients are not considered opioid tolerant. Although there is no official definition for opioid tolerant, the FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics considers this to be the equivalent of 60 mg morphine daily for 7 consecutive days (see Table 1).^{9,10} The former group is not as likely to have withdrawal symptoms and not as likely to have psychological dependence on the opioid as they are not taking a large enough dose of the opioid on a consistent basis. The latter group will need a more structured tapering regimen to avoid withdrawal. This regimen may need to be spread out over several weeks to months. The latter group will also need psychosocial support, particularly if the patient has been taking opioids for years. Patients may feel dysphoric and “not normal” when they taper off opioids.

Approaches to Tapering

Many practitioners, particularly specialists, tend to have their own formulas for managing opioid tapers. However, there is no single strategy that can be applied to all patients, and each situation must be handled on an individual basis.

The literature is not clear with respect to the dose intensity and schedule for opioid tapers. As can be seen in Table 2, dose reductions and schedules are highly variable across a variety of published clinical guidelines.¹¹⁻¹⁵ These dose reductions range from 10% to 50%, with frequency

of dose reduction suggested from daily to every 2 weeks. These guidelines also offer differing opinions with respect to the actual opioid being used and dosing parameters. In one of the seminal pain management textbooks, suggests that a simple 10% to 20% daily reduction in opioid dose is well tolerated by most people.¹⁶ This same textbook asserts that withdrawal can be avoided when a dose reduction is 25% or less than the previous usual daily dose. This variability, even within the same reference, leads to uncertainty when establishing a tapering regimen.

It is useful to remember that there are multiple factors to consider with respect to determining the rate of an opioid taper. The data discussed in the previous paragraph primarily focus on avoidance of a withdrawal reaction secondary to physical dependence. As such, avoidance of the physical sequelae with an opioid taper would appear to be accomplished in most patients in very short order (eg, 1 or 2 weeks). At the same time, many of these patients may require a more individualized approach because of various physical and psychological comorbidities. Examples where a slower, individualized approach will likely be necessary include patients with comorbid cardiorespiratory disease, anxiety, or psychological dependence on opioids or patients who request a slow taper.^{11,14}

Once a decision to taper is made, use of long-acting agents (eg, controlled-release hydrocodone, morphine, oxycodone, oxymorphone, and methadone), given on a consistent schedule every 8 to 12 hours is preferable. Use of short-acting agents (eg, hydrocodone or oxycodone combination products or immediate-release morphine, oxycodone, oxymorphone, hydromorphone), especially on an as-needed schedule, is not recommended. One guideline suggests switching patients to morphine, especially if they are experiencing addiction with oxycodone or hydrocodone.¹⁴ In doing so, the guideline recommends starting the taper at 50% of the calculated equianalgesic dose conversion due to incomplete cross-tolerance. In a similar fashion, two guidelines describe converting transdermal fentanyl to an oral long-acting opioid to facilitate the tapering process.^{13,14}

Additional considerations include frequency of assessment and access to medication. Frequent monitoring visits are likely necessary for many patients and should be scheduled in a manner that facilitates assessment of the patient’s pain status and function and occurrence of any withdrawal symptoms. The frequency at which medication is prescribed and dispensed should match a patient’s ability to appropriately control and manage his or her opioid use. This may dictate that some patients will require smaller quantities provided at short intervals, possibly as often as daily. Holding or discontinuing a taper may become necessary for a specific patient. Events such

TABLE 2: Opioid tapering guidelines

American Pain Society/ American Academy of Pain Medicine (2009) ¹¹	Veterans Affairs/Department of Defense (2010) ¹³	Canadian National Opioid Use Guideline Group (2010) ¹⁴	ASIPP (2012) ¹² Agency Medical Directors Group (2010) ¹⁵
<p>Slow</p> <ul style="list-style-type: none"> • 10% reduction weekly 	<p>Variable</p> <ul style="list-style-type: none"> • Taper by 20% to 50% weekly 	<p>Slow</p> <ul style="list-style-type: none"> • Taper by 10% of the total daily dose every 1 to 2 weeks 	<p>Decrease by 10% of the original dose per week</p> <p>Some patients may be weaned more rapidly over 6 to 8 weeks</p>
<p>Rapid</p> <ul style="list-style-type: none"> • Rapid 25% to 50% reduction every few days • Anecdotal evidence of rapid tapering at oral morphine doses > 200 mg daily • Slow taper of oral morphine equivalent doses of 60 to 80 mg daily 	<p>Slower tapering may be warranted</p> <p>Rapid Tapers</p> <p>Decrease by 20% to 50% daily until 30 mg daily</p> <p>Methadone:</p> <ul style="list-style-type: none"> • Decrease to 30 mg daily • Then reduce by 5 mg daily every 3 to 5 days until 10 mg daily • Then reduce by 2.5 mg daily every 3 to 5 days until discontinued <p>Morphine:</p> <ul style="list-style-type: none"> • Decrease to 45 mg daily • Then decrease by 15 mg daily every 2 to 5 days until discontinued <p>Oxycodone:</p> <ul style="list-style-type: none"> • Decrease to 30 mg daily • Then reduce by 10 mg daily every 2 to 5 days until discontinued 	<p>Rapid</p> <ul style="list-style-type: none"> • Taper by 10% of the total daily dose every day <p>Once one-third of original dose is reached reduced rate of taper by at least 50%.</p> <p>Consider switching patient to morphine if previously experiencing addiction with hydromorphone or oxycodone. Use 50% of the calculated equianalgesic dose to begin the tapering process.</p>	

as withdrawal, pain crisis, worsening of mood, or impairment of physical function may be predictors for slowing or stopping the tapering process.¹⁴

Adjusting Taper Regimens

Individual patients may have differing responses to the tapering regimen chosen. Patients who have been on long-term opioid therapy may have fear and anxiety about reducing and/or eliminating their opioid(s). Patients may be concerned about the recurrence or worsening of pain. These patients may also be concerned about developing withdrawal symptoms. Typically, the last stage of tapering is the most difficult. The body adapts fairly well to the proportional dosage reduction to a point. As illustrated in some publications, the rate of taper may need to be slowed upon reaching approximately 30 to 45 mg of oral opioid/day.²³ This is the point when tapers usually need to be slowed to about 50% of the dose reduction to avoid withdrawal. For example, if a taper has

been decreasing at a rate of 10 mg per week, consider decreasing at 5 mg per week to prevent withdrawal. This threshold phenomenon seems to be the case across opioids. See Boxes 1 and 2 for further examples. Furthermore, patients may not be emotionally ready for the next stage of dose reduction. If the patient has been making a reasonable effort and has followed through with the tapering plan, slowing the taper may be the most reasonable adjustment. Refer to Boxes 1 through 4 for examples of several tapering schedules.

Adjunctive Therapy

Patients should always be made aware of the signs and symptoms of opioid withdrawal so that they may contact the provider to adjust the taper or provide appropriate supportive therapy. Opioid withdrawal is typically not dangerous, but it may cause considerable discomfort. Patients with significant cardiac or psychiatric comorbidities should be monitored closely to avoid a hypertensive

BOX 1: Methadone tapering regimen

A patient who has been taking methadone for back pain has required escalating doses during the past 3 months without any noted pain relief. Because her pain is not opioid-responsive, you would like to taper her off methadone and try another approach. She is currently taking 40 mg methadone three times a day; there is no acute need to taper her rapidly, so a slow taper is reasonable.

Proposed regimen starting with 10 mg methadone tablets:

Week 1: 30 mg three times a day

Week 2: 20 mg three times a day

Week 3: 15 mg three times a day

Week 4: 10 mg three times a day

Week 5: 10 mg every day before noon, 5 mg every day at noon, 10 mg every day after noon or in the evening

Week 6: 5 mg every day before noon, 5 mg every day at noon, 10 mg every day after noon or in the evening

Week 7: 5 mg every day before noon, 5 mg every day at noon, 5 mg every day after noon or in the evening

Switch to 5 mg methadone tablets:

Week 8: 5 mg every day before noon, 2.5 mg every day at noon, 5 mg every day after noon or in the evening

Week 9: 2.5 mg every day before noon, 2.5 mg every day at noon, 5 mg every day after noon or in the evening

Week 10: 2.5 mg three times a day

Week 11: 2.5 mg twice a day

Week 12: 2.5 mg daily

Then discontinue

or psychiatric crisis upon withdrawal. Other medications, such as antihypertensives, may need to be adjusted to cover for this potential consequence. With a gradual taper, there is less likelihood of the occurrence of withdrawal symptoms.¹⁷

BOX 2: Tapering with the same opioid

A patient is having intolerable constipation with controlled release morphine, and you have tried every option for a bowel regimen without success. The patient has had to go to the emergency department for bowel evacuation twice. You believe an opioid rotation and/or taper off of the morphine is the most reasonable option. The patient is currently taking 120 mg morphine twice a day (total 240 mg daily).

Proposed regimen starting with 30 mg morphine extended-release tablets:

Week 1: 90 mg twice a day

Week 2: 60 mg twice a day

Week 3: 30 mg twice a day

Switch to 15 mg tablets:

Week 4: 15 mg every day before noon, 30 mg every day after noon or in the evening

Week 5: 15 mg twice a day

Week 6: 15 mg daily

Then discontinue

BOX 3: Tapering after surgery

About 8 weeks after orthopedic surgery, a patient is ready to taper off her regular schedule of hydrocodone/acetaminophen. She is currently taking 2 tablets every 6 hours (8 tablets per day).

Option A: Rapid taper (duration 10 days)

1 tablet every 6 hours \times 1 day (4/day), then

1 tablet every 8 hours \times 3 days (3/day), then

1 tablet every 12 hours \times 3 days (2/day), then

1 tablet every daily \times 3 days (1/day), then

Discontinue

Option B: Slow taper (duration 3 weeks)

Reduce by 1 tablet/day every 3 days until off

If withdrawal symptoms do occur, pharmacologic adjunctive agents can decrease the severity of the symptoms (see Table 3).¹⁸ Some providers will add clonidine to attenuate autonomic symptoms such as hypertension, nausea, cramps, diaphoresis, and/or tachycardia. The use of clonidine may be limited by hypotension or bradycardia, making it difficult to use in an outpatient setting.¹⁷

Some data support the use of anticonvulsants and antidepressants as adjuncts for opioid withdrawal symptoms. Gabapentin, at doses up to 1600 mg per day over 3 weeks was found to reduce symptoms of coldness, dysphoria, diarrhea, yawning, and muscle tension. This appeared to be dose related.¹⁹ Topiramate has also been reported to alleviate opioid withdrawal effects in 3 patients.²⁰ Small studies support the use of venlafaxine or buspirone in managing withdrawal symptoms.^{17,21} Quetiapine, at a dose of up to 600 mg/day, has been reported to reduce cravings and anxiety during opioid

BOX 4: Fentanyl patch taper

A patient has been using 100 μ g/hour fentanyl patches, changed every 72 hours. He is not certain this has been helping his pain very much, and it is quite expensive. He would like to taper off this regimen.

Option A: Reduce by 50% every 6 days:

50 μ g/hour \times 6 days (new patch on third day)

25 μ g/hour \times 6 days (new patch on third day)

12 μ g/hour \times 6 days (new patch on third day)^a

Discontinue

Option B: Reduce by 25 μ g/hour (25%) every 15 days

75 μ g/hour every 3 days \times 15 days (1 box of 5 patches)

50 μ g/hour every 3 days \times 15 days (1 box of 5 patches)

25 μ g/hour every 3 days \times 15 days (1 box of 5 patches)

12 μ g/hour every 3 days \times 15 days (1 box of 5 patches)^a

^aConsider providing an immediate-release opioid such as morphine sulfate 15 mg every 6 hours as needed for about a week to manage withdrawal symptoms.

TABLE 3: Pharmacologic management of opioid withdrawal symptoms^{18,22}

Symptom	Possible Treatment
Aches/pains/myalgias	Nonsteroidal anti-inflammatory drugs: Ibuprofen 400 to 600 mg orally 4 times daily or Acetaminophen 650 to 1000 mg orally every 6 hours as needed
Diarrhea	Loperamide 2 to 4 mg orally as needed (up to 16 mg/day)
Constipation	Laxative; will need to reduce and eventually stop over time
Nausea/vomiting	Prochlorperazine 5 to 10 mg orally every 6 hours as needed or Haloperidol 0.5 to 1 mg orally every 8 to 12 hours as needed or Ondansetron 4 to 8 mg orally every 6 hours as needed
Anxiety, irritability, lacrimation, cramps, rhinorrhea, diaphoresis, insomnia	Hydroxyzine 25 to 50 mg orally 3 times daily as needed or Quetiapine up to 300 mg daily
Insomnia	Trazodone 25 to 100 mg orally at bedtime
Autonomic symptoms (hypertension, nausea, cramps, diaphoresis, tachycardia)	Clonidine 0.1 mg twice a day up to 4 times daily Reassess in 3 to 7 days. Taper upon symptom resolution

tapering.²² Benzodiazepines, however, are not recommended.

The selection of adjunctive agents should be carefully considered, as drug-drug interactions can affect opioid metabolism, particularly when tapering methadone. Pharmacokinetic interactions must be accounted for, which can inhibit (eg, fluoxetine) or induce (eg, phenobarbital) drug metabolism. Also, the lowest effective doses should be used for adjunct treatments, keeping in mind the potential for pharmacodynamic interactions such as increased sedation or QTc interval prolongation (eg, quetiapine, haloperidol).

Advising Patients on Emergency Tapering²³

If patients are unable to refill or obtain opioid medications because of bad weather or other circumstances, they should be counseled on what to expect if opioid withdrawal occurs. The symptoms of withdrawal will vary depending on the particular medication and how long the patient was taking the opioid. Patients taking immediate-release products like morphine, hydromorphone, or oxycodone may experience withdrawal symptoms within 6 to 12 hours of the last dose. Those taking methadone or controlled-release opioids will experience symptoms 1 to 4 days after the last dose. Typically, withdrawal from morphine continues for 5 to 10 days, while withdrawal from methadone or other long-acting opioids take longer. The best way to avoid serious withdrawal symptoms is to reduce the dose by 25% per day, or by 25% every other day. This may result in some withdrawal symptoms, but it is better than abruptly stopping it. Encourage patients not to tamper with long-acting agents in any way. Breaking or opening these

capsules or cutting patches can release the entire dose at once, causing overdose and possible death. Encourage patients to stay hydrated and calm, and reassure the patient that the symptoms will pass.

Summary

Prolonged exposure to opioid analgesics can lead to physical dependence in essentially any patient. This can occur within a week of consistent dosing of opioids. An appropriate management plan for opioid analgesics should include consideration of how best to discontinue these agents. Discontinuation may be considered for numerous reasons, including noncompliance, aberrant behavior, and lack of analgesic efficacy. In the event discontinuation becomes necessary, an approach that limits patients' negative experiences is paramount.

From a pharmacologic standpoint, a variety of approaches are available to reduce or taper opioid doses. In general terms, the process includes reducing the total daily opioid dose at specific time intervals. Consideration should be given to the length of time a patient has been exposed to opioids as well as the type and dose of opioid the patient is using. In the event that a patient experiences worsening of pain or withdrawal phenomena, the tapering schedule can be modified or appropriate adjunctive therapy offered.

Preparing patients for an opioid taper is vitally important, especially if they are psychologically dependent on opioids or have a comorbid psychiatric condition. In these settings, a tapering schedule that includes psychological monitoring and support should be considered. The goal is to ensure that patients successfully reduce or discontinue opioids in a manner that does not lead to other, protracted adverse sequelae.

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