

Frequently Asked Questions on Breakthrough Pain



Responded to by
Michael J. Brennan, MD
The Pain Center of Fairfield
Fairfield, Connecticut
Senior Attending Physician
Department of Medicine
Bridgeport Hospital
Bridgeport, Connecticut

1. *What is breakthrough pain?*

Breakthrough pain has a specific accepted definition by the FDA. It is kind of a funny thing that we have to use the FDA to allow us to define a condition, but because that is how all the current drug indications are based, it is probably a reasonable stance. So the FDA's current working definition for breakthrough pain is that it needs to occur in cancer patients and individuals who have moderate-to-severe around-the-clock pain that is well controlled over a 24-hour period continuously with an opioid analgesic on board, and the pain occurs in that context. So, someone who takes a medication episodically cannot have breakthrough pain. Someone who has pain that comes once in a blue moon outside the context of continuous pain cannot have breakthrough pain. It does not mean they do not have a severe episodic recurrent acute pain problem, but breakthrough pain has this very specific categorical kind of definition that needs to be understood. There are three subtypes of breakthrough pain.

2. *How do we address the types of breakthrough pain?*

I mentioned that of the three subtypes of breakthrough pain – end-of-dose failure, incident pain, and idiopathic pain – end-of-dose failure is generally the easiest to address, but we need to take a good and thorough history about the effects of an analgesic to make sure that we know whether we should increase the frequency of dosing or the strength of the analgesic that is being prescribed. Very often by asking the patients when their analgesic effect kicks in, how long it lasts for, and if it is associated with any side effects, we can determine whether or not we should be increasing dose in frequency or increasing dose in strength. With idiopathic breakthrough pain, we often have to use drugs that affect the nervous system such as antiepileptics or antidepressants because in that context,

idiopathic, pain more often than, is not neuropathic in nature. So by adding drugs that might actively block pain signals such as anti-seizure drugs, or improve innate analgesic pathways such as antidepressants, we can sometime enhance the analgesic role of the opiate. But it is very important for us to make sure that with an idiopathic pain presentation, that if their pain is rapid in onset and if it is relatively short in duration, we try and match the most effective analgesic to it, particularly if it is associated with a quality of life or functional compromise.

Where we often have the most difficulty structuring an effective regimen is in the incident-related breakthrough pain. For instance, when bed mobility or ambulation aggravates bone pain, trying to make sure our patients understand that an ounce of prevention is worth a pound of opioids, sorry about the bad pun, but if we can make sure they understand to think through their activities before embarking upon them, we can very often reduce the need for analgesics of any type by using readily available nonopioid, nonpharmacologic mechanisms to help reduce pain, whether it is bracing, using ambulatory devices, or other therapy such as ice or wrapping an impaired limb.

3. How do you differentiate true breakthrough pain for adequate pain control and addiction when the patient is asking for more medication or claiming they take more medication than prescribed?

I think that if you talk to those of us who treat a lot of patients with breakthrough pain, I think every time we are facing patients in the clinic who complain of breakthrough pain, this question comes up. So I think you have to back to your basics and view breakthrough pain in the whole greater construct that the patients themselves is suffering with pain. So for instance, the individual who has been managing their pain along with your therapies, they have been integrating other interventions, not just focusing on pharmacologic therapy, but have incorporated rehabilitation, interventions, meditation, the whole panoply of things that we can offer patients. And when those patients respond in a way that is overtly positive to you and to the people who are caring for that patient, that is kind of one of my main focal point to determine if somebody is taking medicine as prescribed or if they are losing control of drugs. Howard Heit likes to talk that addiction is a complete loss of control, so patients who are addicted to their medicines will be out of control not just with their around-the-clock medicine but with their breakthrough medicine as well. So I think you cannot make the diagnosis of breakthrough pain absence in assessment and management of the

long-acting pain or around-the-clock pain, you need to make the assessment in the whole context of how the patient is responding to therapy. And so you assess, you intervene, you evaluate your assessment and your treatment, then you reassess, monitor your intervention, assess the outcome, and that continuous loop of assess, intervene, evaluate your intervention, that will help protect you and protect your patient, but it is a very good question and I think we wrestle with it every day, especially when some of our patients come in and they may not be following all of our requests and orders, but they are doing it mostly. Another way that I think you can help differentiate is, and I like to use this explanation with family members of the patients, if a medication or routine is demonstrably improving somebody's function, odds are they are not addicted to a drug. Conversely, if the drug is interfering with functionality, however you want to define that, there may be a condition of addiction or misuse that is present.

4. What type of medication is used for breakthrough pain that is not a part of the opioid family?

Really all drugs from the analgesic and coanalgesic or adjuvant analgesic family might benefit. So for instance, steroids are very frequently used in patients with metastatic disease, particularly disease to the spine, and they can have a very beneficial analgesic effect. Similarly, nonsteroidals, particularly for bone pain, can be quite effective as a breakthrough pain medicine. Now you might not think of them as a breakthrough pain medicine, but for instance, in a rehabilitation unit or a palliative care unit where we know an individual is going to need to transfer at a specific time to either use the restroom, go to gym, or some other therapy, we will pre-medicate those patients an hour beforehand with an immediate-release or a regular-acting NSAID, assuming the patient can tolerate it and there is no other contraindications. It may be an adequate analgesic and it might make the other opioid that we may have to use more effective thru a synergistic mechanism. Other drugs other than NSAIDs, steroids and acetaminophen include some of the antidepressant therapies and anti-seizure drugs for those patients who have idiopathic breakthrough pain. Pathophysiologic and nosologic presentation of patients with idiopathic breakthrough pain is generally neuropathic in etiology. Therefore, we want to use drugs to treat the source of the breakthrough pain, meaning dysfunctional nervous system in the patients suffering with pain, by trying to reduce the episodes of breakthrough pain. So that is kind of a cheap answer I just gave because we are really not treating the incidents per se, we are trying to prevent the incident. So this is not just about opioid therapy when we

talk about treating breakthrough pain and it is not just about medical therapy. We can use rehabilitation interventions, anesthetic interventions, physical therapy interventions all to try and help mitigate the frequency, severity, and impact that breakthrough pain episodes might have.

How can opioid abuse be diagnosed in patients who come to our pharmacy? That is for part 1 and part 2. Can tramadol be used in patients who are opioid resistant? And that is from D. Colston. So how can opioid abuse be diagnosed in patients who come to your pharmacy? Boy, that is a good question. So I am going to assume you are a pharmacist. You know, it is interesting and this is more to the physicians who are listening. Our community pharmacists really are front guards to patients who get in trouble with us. I never hang up on a pharmacist and I never ever try to be rude to a pharmacist. When pharmacists call, I take it very seriously because they see patients in an entirely different light than I see patients. Now it is a two-way street, we like to exchange information about patients within privacy restrictions, but I would like to hear how a patient is presenting themselves outside of the very strict confines of my office. So how can you tell somebody is abusing? Well there is a classic sign or suggestive signs of early refills, lost prescriptions, and multiple providers. Those are probably key. The second next sensitive would be individuals who come in saying that only one drug type works versus another, those who are brusque, rude, or in a hurry within the pharmacy might be another sign. What I would urge the pharmacists and physicians to do is to collaborate in your communities and lend each other an attentive ear so that you can be clear on what each person is thinking so as to have the best outcomes for the patient as well as for yourself.

Now what about using tramadol? So tramadol is an odd analgesic. I am sure everybody listening is familiar. It is an opioid-like drug that also has adrenergic and serotonergic effects that relieve pain, also much of its analgesic basis is dependent on its primary metabolite M1. Now tramadol is a tricky drug. There is boxed warnings that suggests that it cannot be administered with opioids nor can it be administered with antidepressants of any kind. For that reason, I typically will not use it in patients with breakthrough pain since they are already on an opioid by definition, but in individuals who do not tolerate opioids, it is a reasonable drug to try. I think another drug, tapentadol, might be a better option as it is more potent, cleaner, and does not have the boxed warnings that tramadol has.



Responded to by
Lynn R. Webster, MD, FACPM, FASAM
Medical Director
CRILifetree
Co-Founder, LifeSource
Salt Lake City, Utah

5. *What do you do if you think there is abuse?*

Well, I guess it depends upon who you are, I mean if you are a physician or a prescriber, somebody who is writing the scripts, I think that you need to confirm that it is abuse. You need to assess why there is an abuse problem. Most often in people who have chronic pain, the single greatest reason why they overuse medicine, if that is how you are going to define abuse, is that their pain is not well controlled. They do not have good coping skills, and they are using the medication to try to manage that pain. Now if the individual has pain but they are abusing medication because of a mental disorder or they just find it is a useful way to escape, then I think that there should be a lot of counseling. Sometimes, you have to take them off of the medicines, sometimes they cannot control the use of the medication, and it is too dangerous for them to be on it, so you have to assess what is the risk of them continuing on this medicine, assuming that they have pain. So, if you have somebody who has a significant pain problem but is also abusing, this is a real challenge, and you need to do several things. One is, that you have to thoroughly document that there is a reason to continue the medication. Two, I think if you are not a psychiatrist, you need to send the patient to a psychiatrist or a psychologist to get some help in evaluating and managing the mental health problem for which the drug is being misused. Three, try to look for an alternative treatment; it could even be an interventional treatment, an injection of some type, or a different approach to treating the pain than the use of pharmacotherapy. So the bottom line is, if you think somebody is abusing, you need to assess it, you need to document it, you need to refer when needed, you need to consider looking for alternative treatments, and you have to demonstrate in your notes what the risk and benefit would be if you were to continue to provide them medications.

6. *What is the most ideal analgesic for treating breakthrough pain?*

Well again, it depends. There is no one opioid that works better than another opioid for everybody. I mean it all depends upon the type of pain, the intensity of the pain, and the speed of onset. Remember, breakthrough pain usually occurs very quickly, so the onset of action of the medications listed here are all immediate-release opioids, not rapid onset. So if you've got somebody who has a rapid-onset pain, somebody who has a sudden lancinating pain, and they are otherwise safe for rapid onset medication and they are opioid tolerant because they are on an extended-release opioid, then a rapid onset would probably be better. I do not believe methadone should be used for breakthrough pain. If you read any of what I have written, I think that is a dangerous drug to be used as PRN or for breakthrough pain and should never be used for that purpose. It has to be scheduled. It has to very, very cautiously used. I think it is an excellent analgesic, but you really need to know how to use it, and it should not be used PRN or for breakthrough pain.



Responded to by
Jeffrey A. Gudin, MD
Director
Pain Management Center
Englewood Hospital and Medical Center
Englewood, New Jersey

7. What is the TIRF REMS program?

TIRF stands for transmucosal immediate-release fentanyl REMS. At the website TIRFREMSaccess.com, you can read about all of the requirements for the TIRF REMS program. Remember this is new to all of us. In pain management, we have not been involved with a class of medications before where the pharmacy has to enroll in the educational program, the clinicians have to enroll in the educational program, and the patients have to sign a patient-prescriber agreement, which ensures that they have been given all of the pros and cons, as well as the safety and benefit features of these medications. This closes the loop so that everybody is involved with education, from clinician to pharmacist to the patient. That is the essence of the TIRF REMS program.

8. Would NSAIDs be a good choice for patients with breakthrough pain, and if so, do you have any recommendations?

Basically most NSAIDs work through a similar mechanism of action. Some, as you know, are more selective for cyclooxygenase-1 enzyme blockade, some are more selective for COX-2. The only agent that we have left in this country from a COX-2 blocking standpoint is celecoxib or Celebrex. So if I have any patients that I am concerned about platelet dysfunction, bleeding issues, I tend to favor Celebrex, remembering there are some contraindications or warnings for Celebrex. All of the NSAIDs have some warning about GI, renal, and cardiovascular dysfunction, but it turns out that for some types of pain, let's say like inflammatory pain or bone pain, NSAIDs are a good choice. Recently a new form of diclofenac in a liquid filled capsule has been marketed and appears to work well for acute pain. Remember, although we use NSAIDs commonly, when patients have truly severe levels of pain, we tend to favor the rapid-onset opioid preparations.

9. Can you address the importance of keeping an open relationship with your local pharmacist or at the local pharmacy where the patients get their controlled medications filled?

Now, that is certainly critical. I recommend welcoming pharmacists into your practice; I have them see patients with me, and get an idea of how we prescribe. It becomes a learning experience for all of us because we learn a little bit about what they do every day, and they learn a little bit about what we do. Almost every pharmacist that has rotated through my practice has been amazed when they hear the patients' stories, hear about the illness/trauma, and they realize just how much pain their patients have, and gain insight in to their underlying disease. They get a better understanding of their disease state and the affects of pain on their function. They look at the patient once a month when they come to the pharmacy, and they may not look like they are in pain, but this patient has had his kidney taken out, or this guy had this nerve injured somehow. I think it really broadens the relationship with the pharmacists. It also helps that pharmacists are great advocates for us when they see patients who come in intoxicated or doctor-shopping and filling prescriptions from multiple physicians. They are also on the lookout for potential for drug-drug interactions. The pharmacist is critical for playing a role in screening pain patients. So I have always been a big advocate for getting to know your local pharmacists, inviting them into my practice, and supporting local educational initiatives. Some communities have set up town hall meetings and invite the pharmacists to discuss complex chronic and breakthrough pain patients. Remember, when it comes to breakthrough pain, that it is a separate component of the patient's overall pain. You have to ask your patients to tell you about their around-the-clock pain, you have to say, "Tell me about your breakthrough pain," and we treat those differently. For the patients who have a majority of around-the-clock pain, they get an around-the-clock or an all-day-long analgesic. For the patients who have breakthrough pain, they are going to need something that usually works quick because when their pain strikes, it comes on quick and may not last that long; usually they require a rapid-onset/short-acting analgesic.