New Effective Treatment for Opioid-Induced Constipation

It’s not a glamorous topic, but severe constipation due to opioid (narcotic) medications is a major issue in managing pain from cancer. Opioid medications like morphine, oxycodone, dilaudid, and fentanyl are often needed to manage cancer-related pain effectively, but they come with some baggage. Although I strongly encourage my patients who need narcotics to not worry about becoming addicted (you can become dependent, which may be unavoidable with appropriate use but is a physiologic effect, not a desire or need to abuse these agents), but opioid-induced constipation is the most common and challenging side effect we encounter as the downside of achieving good pain control that many cancer patients need. In fact, there’s an old quote in medicine, “The hand that writes the narcotic prescription is the hand that writes the laxative prescription.” Not exactly poetry, but I think of it every time I write a prescription for a needed narcotic, and I also write for one or more bowel medications to counter-balance the constipating effects of narcotics. Otherwise, you’re pretty much asking for trouble.

Even with many of the agents available, from stool softeners to laxatives to suppositories and enemas and more, some patients who need significant amounts of narcotics can get pretty miserable from constipation, and we find ourselves sometimes wondering how to balance the competing problems of pain and severe constipation. So when a new and effective treatment for opioid-induced constipation is tested and becomes commercially available, it can represent a major benefit for the people who need it.

That new agent is called relistor, or methynaltrexone, and unfortunately it is only able to be administered as an injection under the skin, like insulin, but it was the subject of a recent randomized study published in the New England Journal of Medicine that showed the benefit it can offer (abstract here). This drug blocks a subset of the opioid receptors, called mu receptors, that are along the gut and cause constipation when turned on by opioids, but this drug also can’t get through the blood brain barrier to reverse the pain control effects of opioids.

This trial enrolled 133 patients who had been on narcotics for at least two weeks and who were experiencing problematic constipation despite taking all of the usual medications. They were then randomized to receive subcutaneous (SC, = under the skin) injections of either the active drug every two days for up to two weeks. The main target of the study was to assess the proportion of patients who had a bowel movement (termed, “laxation”, a new fancy term for bowel movement, in their paper) within four hours of the first injection of the active drug, and also who moved their bowels within four hours for at least two of the first four treatments.

It worked. Of the patients who received relistor, 48% had a BM within 4 hours after the first dose, vs. just 15% in the control group who received placebo. And 52% of those receiving active drug moved their bowels promptly after at least two of the first four treatments, vs. only 8% of the placebo recipients (both results highly statistically significant). Moreover, as a bonus, about half of the time, patients achieved relief of their constipation within 30 minutes after the injection. This must have been an odd study to run, with investigators probably standing over
patients with a stopwatch after the injection, then all eyes on the patient until they excused themselves to go to the bathroom. I don’t know if they rang a bell or something from the bathroom to note the time of their success, or maybe yelled, “woohoo” to stop the clock.

I actually haven’t had occasion to prescribe this medication, which is meant for patients to self-administer, but it seems as if this could really be a meaningful new treatment for a truly significant problem. While it does require an injection, if patients can achieve good pain control and avoid the most common and sometimes severe side effect of narcotics, it’s likely to be a welcome option.