INSTITUTE TO ENHANCE PALLIATIVE CARE

PALLIATIVE CARE CASE OF THE MONTH

Treatment of acute pain in a patient taking buprenorphine for addiction

Julie Childers, MD

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Case: Ms. O is a 44-year-old woman with Stage III B cervical cancer; on a recent gynecological exam, there was noted to be a cavitating lesion in her cervix, and involvement of her pelvic sidewalls. She also has a long history of heroin addiction but has been clean for three years, ever since she found a physician to prescribe buprenorphine. Buprenorphine is a newer opioid agonist/antagonist used primarily for addiction treatment in the United States. Ms. O has made several attempts on her own to taper herself off the buprenorphine, but has had withdrawal symptoms and restarted the medication. She presents now for local radiation treatment to the cervix, and she is in excruciating pain from having the radiation device implanted. She is on a hydromorphone PCA and using 0.2 mg every 10 minutes, as well as a continuous rate of 1.0 mg, with little effect. How should her pain be treated?

Discussion: Buprenorphine is a mixed opioid agonist/antagonist. There are several receptors at which opioids act, including mu (μ), kappa (κ) and delta (Δ). The μ receptor is responsible for most of the analgesic effects of opioids. Buprenorphine binds tightly to μ receptors but only partially activates them, leading to pain relief up to a certain level. It also blocks the κ receptors (without exerting an effect). Kappa opioid receptors are responsible for some analgesia, as well as respiratory depression and dysphoria. Some studies have found that a "ceiling effect" exists for analgesia with buprenorphine. The agonist (analgesic) effects of buprenorphine may increase linearly with increasing doses of the drug until, at moderate doses, they reach a plateau and no longer continue to increase with further increases in dose. Buprenorphine's analgesic effects only last for 6 to 12 hours, but at high doses it occupies the μ receptor for 24 to 60 hours, preventing other opioids from binding. This blocking of other opioids is key to its use in opioid addiction treatment.

Buprenorphine has been available in the United States in the sublingual form as Subutex, and also mixed with naloxone as Suboxone. The addition of naloxone is intended to avoid IV buprenorphine abuse: if the sublingual Suboxone tablet is dissolved and injected, it cannot produce a high because of the presence of naloxone. Several other forms of buprenorphine are marketed for pain. A parenteral analgesic form of buprenorphine, Buprenex, is available in the U.S., and a transdermal form of buprenorphine is used widely in Europe for pain but is not yet available in the U.S. The typical daily buprenorphine dose for opioid addiction ranges from 4 to 32 milligrams taken once daily. The half life of buprenorphine in the sublingual form is from 24 to 60 hours. In the United States, the use of buprenorphine for the treatment of opioid addiction is restricted to qualified physicians who have received training and received a waiver to practice medication-assisted opioid addiction therapy.

When patients on buprenorphine therapy are in acute pain, the antagonist activity of buprenorphine on opioids receptors limits the effectiveness of opioids used in the usual doses for pain. There have been no clinical trials testing how best to treat acute pain in patients taking buprenorphine for addiction therapy but federal guidelines and experts have suggested several strategies:

1. If acute pain, such as for an elective surgical procedure, is anticipated, clinicians should arrange for adjuvant analgesics and interventional procedures such as nerve blocks in advance if available.
2. For patients who require opioid therapy for the short term, federal guidelines recommend holding the buprenorphine and rotating to short-acting opioid agonists. Buprenorphine should be discontinued 2-3 days in advance if the pain is anticipated as part of an elective procedure. With unanticipated pain, buprenorphine should be stopped immediately. While the buprenorphine wears off (20 to 60 hours), the patient may require higher opioid doses to compete with the presence of buprenorphine on μ receptors. The patient should be monitored carefully in the initial period to titrate the opioid agonist dose downward as its effect becomes greater. Before restarting buprenorphine, the patient should be opioid-free for 12 to 24 hours to avoid precipitating withdrawal; this process should be overseen by an approved buprenorphine provider.
3. For patients with mild to moderate acute pain who are able to take medication by mouth, consider treating the pain with buprenorphine alone. The total daily dose of buprenorphine may be increased (to a maximum of 32 mg sublingual/day) and should be given in divided doses sublingually every 6 to 8 hours.

4. Another option is to continue buprenorphine (perhaps increasing the dose) and use short-acting opioid agonists at high enough doses to overcome buprenorphine antagonism. Opioids which have a strong affinity for the μ receptor, including morphine, fentanyl, or hydromorphone, are all options, while weaker opioids such as hydrocodone or codeine should be avoided.
5. Consideration could also be given to replacing buprenorphine with methadone at 30 to 40 mg/day to prevent withdrawal and allowing additional opioids to meet the short-term analgesic needs.

A patient such as Ms.O, who has a life-limiting illness which is expected to cause significant pain, may not be a good candidate for continuation of buprenorphine maintenance.

References:

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3. Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction at http://buprenorphine.samhsa.gov/Bup_Guidelines.pdf