INSTITUTE TO ENHANCE PALLIATIVE CARE

PALLIATIVE CARE CASE OF THE MONTH

Methylnaltrexone for Opioid Induced Constipation

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Case: CH is a 56-year-old woman with metastatic breast cancer to bone, liver and brain. She is admitted to the hospital with increasing lethargy and a marked decrease in her oral intake. She has also not had a bowel movement for 10 days. Further interview reveals that she has been on a fentanyl patch 75 mcg for months, senna and colace, and hydrochlorothiazide. Her diuretic is stopped and she is placed on intravenous fluids. Except for dehydration, a metabolic work up is unremarkable. Her exam reveals hypoactive bowel sounds, a scaphoid abdomen with palpable mobile masses, and soft stool in the rectal vault. She is disimpacted. No active bm follows despite suppositories. She is also not able to retain enemas. She has increasing nausea and anorexia. Given her inadequate response to a bowel regimen from below and inability to tolerate an oral regimen, she is dosed with methylnaltrexone subcutaneously x1. She has a large formed bm 2 hours later.

Discussion: Constipation is a well recognized side effect from opioids. Tolerance does not occur. In fact, the dose that can cause constipation is ¼ of an analgesic dose. Opioids exert their constipating effects by decreasing GI motility, gastric emptying, increasing ileocecal valve tone, increasing fluid resorbtion, and decreasing the reflex to defecate.

Methylnaltrexone (MNTX) is a mu receptor antagonist that unlike naloxone does not cross the blood brain barrier as it is a quaternary amine. Naloxone has been used in the past for opioid induced constipation. However, this use has also been associated with opioid withdrawal and decreased pain relief. MNTX was approved for the treatment of opioid induced constipation by the FDA last year. Given its expense, many institutions have tried to limit its use. Our institution has made a Palliative Care consult one of three consultation services that can approve dosing.

The phase three clinical trials that led to approval of MNTX involved patients either enrolled in hospice or as part of a palliative care program, and opioids were thought to be the primary cause of the constipation. They must have been receiving opioids for two weeks and on a stable opioid and laxative regimen for three days. Enrolled patients had had no bowel movement in greater than 48 hours or had had less than 3 bowel movements the week prior. Bowel obstruction, fecal impaction or other acute abdominal processes were ruled out. In addition, patients with peritoneal dialysis catheters and fecal ostomy bags were excluded. While 80 percent of the patient population had cancer, patients with cardiovascular disease, AIDS, dementia, and COPD were also included. MNTX is administered subcutaneously based on the patient's weight. After administration of MNTX, greater than or equal to 50% of the study group had a bowel movement within 4 hours. Most patients had a bowel movement within 30-70 minutes. As compared to placebo, the most frequent side effects were abdominal cramping, nausea, dizziness, increased body temperature and flatulence. However, the number of patients who discontinued therapy secondary to side effects was similar to that in the placebo group. No decrease in pain control or signs of opioid withdrawal were noted as compared to the placebo group.

There are many medications and dosage forms that are available for opioid induced constipation. Previously, routes of administration have been oral and rectal. Dysphagia, nausea or decreased mental status can greatly hinder an adequate regimen by mouth. Rectal routes of suppositories and enemas can also be tried. Inability of the patient to participate can limit effectiveness of enemas. In properly selected patients, MNTX may be able to aid in relief of opioid constipation without adversely affecting pain control

References:

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