PALLIATIVE PEARLS
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Hiccup Management
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Patient Case

VL is a 69-year-old woman admitted to hospice recently with a terminal diagnosis of gastrointestinal stromal tumor with metastases to the liver and pancreas. She has no comorbidities and current medications are listed below.
Over the past few days, VL has experienced nausea, retching, abdominal cramping, bloating and worsening gastric reflux. A trial of simethicone and ondansetron, left over from her moderately emetogenic chemotherapy, has provided minimal relief. Two days ago, bouts of hiccups began, interfering with her sleep and quality of life.

VL is able to perform some activities of daily living and has a Karnofsky performance score of 60. Her primary goals include maintaining control over her daily activities and minimizing symptoms. Her appetite is diminished despite changing her diet to small frequent meals and reduced intake of spicy foods and drinks. She has also tried non-pharmacological remedies such as drinking lemon juice without response.

VL's physician ordered chlorpromazine 25mg po every 8 hours as needed for hiccups, hoping it would also relieve some nausea as well. VL's nurse has concerns related to the high price of this medication and needs an alternative recommendation. Her other medications include:

- Morphine extended-release 60mg every 8 hours for pain
- Ondansetron 8mg every 8 hours for nausea
- Dexamethasone 2mg every morning for pain
- Diphenhydramine 25mg capsule every 6 hours as needed for itching
- Omeprazole 20mg capsule every morning for esophagitis
- Docusate calcium 240mg twice daily for opioid-induced constipation
- Oxycodone IR 10mg every 4 hours as needed for pain
- Simethicone 125mg four times daily as needed for gas and bloating
- Sulfamethoxazole-trimethoprim DS one tablet twice daily for 10 days for skin infection
- Diazepam 10mg twice daily for anxiety

Why do hiccups occur?

Patients may develop hiccups for a myriad of reasons. Hiccups are involuntary, intermittent, spasmodic contractions of the diaphragm and intercostal muscles. Most patients experience spontaneous resolution within 48 hours of onset. Hiccups persisting for greater than 48 hours may warrant treatment.

What conditions are associated with increased prevalence of hiccups?

- Gastrointestinal disorders
- CNS disorders
- Infectious disease
- Metabolic changes and toxins
- Psychogenic causes

What medications may precipitate hiccups?

- Chemotherapy
- Sulfonamides and other antibiotics
- Barbiturates (phenobarbital)
- Benzodiazepines (diazepam, midazolam)
- Corticosteroids (dexamethasone, methylprednisolone)

How are hiccups managed pharmacologically?

- Hiccups related to reflux, dyspepsia or stomach distension
    - Antacids (Mylanta®, Tums®)
    - Anti-flatulent therapy (simethicone)
    - Prokinetic agent (metoclopramide)
- Hiccups NOT related to reflux, dyspepsia or stomach distension
    - Anticonvulsants (carbamazepine, gabapentin, valproic acid)
    - Antipsychotics (haloperidol, chlorpromazine)
    - Muscle relaxers (baclofen)

Pharmacist Assessment

In patients with abdominal malignancies, especially those with other accompanying epigastric symptoms such as bloating, belching, nausea, reflux, hiccups are typically a direct result of significant gastric distension. For this reason, the antipsychotic therapy consisting of chlorpromazine that the doctor recommended may not be effective. VL's opioid-induced constipation is poorly managed and is contributing to gastric distension. In addition, VL takes dexamethasone and a sulfonamide antibiotic that may precipitate hiccups. Targeting her abdominal distension may prove to be key in relieving not only hiccups, but other symptoms as well.

Recommendations to reduce gastric distension and resulting hiccups

- Initiate metoclopramide 5mg three times daily for hiccups. Monitor and assess response.
- Increase omeprazole to 20mg twice daily for reflux symptoms that could contribute to gastric distension
- Evaluate if dexamethasone is needed and consider discontinuing via taper if no longer indicated.
- Initiate Senna-S 1 tablet twice daily for opioid-induced constipation. A stool softener alone is ineffective; recommend discontinuing docusate calcium.

For additional information on this topic, please review these references:

- Enclara Pharmacia's On Demand Educational Webinar, "Management of Less Common but Troubling Symptoms in Hospice: Pruritus, Hiccups, Cough, Muscle & Bladder Spasm". Click here to log in.
- Farmer, C. Center to Advance Palliative Care Fast Fact #81: Management of Hiccups. [cited 2015 Dec 17].Available at: https://drive.google.com/file/d/0BylFEWCSwGsUajZ3c1Bxby1jX3M/view?pref=2&pli=1
- Friedman NL. Hiccups: A treatment review. *Pharmacother. 1996;16(6):986-995.*
- Guelaud C, Similowski T, Bizec JL, Cabane J, Whitelaw WA, Derenne J-P. Baclofen therapy for chronic hiccups. *Eur Respir J. 1995;8(2):235-237.*

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- Rousseau P. Hiccups. *South Med J. 1995;88(2):175-181.*
- Rousseau, P: Hiccups in terminal illness. *Am J Hosp Palliat Care 1994; 11:7-10.*
- Smith HS, Busracamwongs A. Management of hiccups in the palliative care population. *Am J Hosp Palliat Care. 2003;20(2):149-154.*