PALLIATIVE CARE CASE OF THE MONTH

"Management of Hiccups"

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Case: Ms. K is a 54-year-old woman with a remote history of opioid use disorder and a current history of alcohol use disorder and Hepatitis C/alcoholic cirrhosis (MELD 15, Child B-9) complicated by ascites requiring large volume paracentesis. She was admitted with recurrent hematemesis, hematochezia, and anorexia. EGD showed duodenal ulcers. The critical care team admitted the patient and managed her bleeding, hypovolemic shock, and acute kidney injury. After she stabilized, palliative care saw her for goals of care and symptom management. On symptom assessment, the patient reported having had bothersome hiccups intermittently for the last several months.

What is the physiology of hiccups?
Hiccups are involuntary, intermittent contractions of the diaphragm and intercostal muscles accompanied by sudden inspiration that ends with closure of the glottis. This reflex consists of an afferent limb, including the vagus nerve, phrenic nerve, and sympathetic chain; a central hiccup center, which is thought to be located in hypothalamus; and an efferent limb, extending through the phrenic nerve to the diaphragm. Hiccups can be persistent, lasting more than 48 hours but less than one month, or intractable, which is defined as lasting more than one month.[1]

What causes hiccups?
There are many etiologies of hiccups, as any irritation along the reflex arc can trigger this phenomenon. Causes of transient hiccups include gastric distension, such as from overeating; carbonation; or alcohol ingestion. Common causes of persistent hiccups derive from pathology along the gastrointestinal tract, thoracic viscera, or central nervous system.

Common causes of persistent hiccups are:

- Vagus or phrenic nerve irritation (pharyngitis, goiter)
- Gastrointestinal disorders (gastroesophageal reflux disorder, peptic ulcer disease, pancreatitis, tumor)
- Medications (steroids, benzodiazepines)
- Central nervous system disorders (head trauma, encephalitis, stroke)
- Toxic-metabolic disorders (hyponatremia, hypocalcemia, uremia)
- Psychogenic factors (stress)
- Post-operative (anesthesia, intubation)

What are treatment options for hiccups?
If possible, treat the underlying cause and stop causative medications. Evidence supporting specific pharmacologic interventions are limited to case reports and one double-blind, randomized controlled trial of baclofen studied in four men with idiopathic hiccups.

This study was a placebo-controlled, crossover design that showed an improvement in hiccup severity but not frequency in the setting of idiopathic hiccups. The low sample size of four participants makes this study difficult to interpret.[2] Other pharmacologic treatment options evaluated in case series or case reports include: dopamine antagonists (chlorpromazine, haloperidol, metoclopramide), baclofen, gabapentin, phenytoin, valproic acid, and carbamazepine.

Non-pharmacologic treatment options include acupuncture, breath holding, performing Valsalva maneuver, swallowing sugar, sipping cold water, breathing into a paper bag, sudden fright, and digital rectal massage. Acupuncture is the only non-pharmacologic treatment evaluated in the literature. The studies evaluating acupuncture all included a high risk of bias and did not include placebo arms. Thus, systematic review was impossible, and making inferences regarding clinical implications is difficult.

There are no randomized-control trials that compare the effectiveness of non-pharmacologic and pharmacologic treatment. To date, there is insufficient evidence to support treatment recommendations for either non-pharmacologic or pharmacologic management of hiccups.[3]

Resolution of the case:
Given the patient had experienced hepatic encephalopathy in the past, the palliative care team worried that treating her hiccups with a pharmacologic agent would trigger delirium. Instead, we focused on treating the underlying causes of her hiccups. Ms. K started on twice daily proton pump inhibitor therapy and underwent paracentesis which alleviated her hiccups. The gastroenterology team planned for transjugular intrahepatic portosystemic shunt (TIPS) procedure as an outpatient to mitigate her ascites, while appreciating the risk of potentially worsening hepatic encephalopathy.

References:
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2. Ramirez FC, Graham DY. Treatment of intractable hiccup with baclofen: Results of a double-blind randomized, controlled, cross-over study. Am J Gastroenterol.1992; 87:1789–1791.
3. Moretto EN et cal. Interventions for treating persistent and intractable hiccups in adults. Cochrane Database of Systematic Reviews, 2013. https://doi.org/10.1002/14651858.CD008768.pub2