

Hiccups in palliative patients: a mini review

Introduction

Hiccups can be defined as involuntary, intermittent, spasmodic contractions of the diaphragm and intercostal muscles, which result in sudden inspirations and end with abrupt closures of the glottis. Hiccups often occur with a frequency of 4 to 60 per minute.¹ Hiccups are considered persistent when last for more than 48 hours, and intractable when last for more than a month.² Intractable hiccups can occur in 3.9 to 4.5% of advanced cancer patients in palliative care.³ If not properly managed, hiccups can result in exhaustion, fatigue, malnutrition, weight loss and even death.⁴

Etiology

Hiccups can result from injuries compromising phrenic and vagus nerves, sympathetic chain and efferent neural connections to the glottis and intercostal muscles.^{5,6} Main causes in palliative care are cerebrovascular accidents, mechanical injuries of central nervous system (tumours, inflammation or traumatism), vagus and phrenic nerve irritation (mediastinal or esophageal masses, pharyngitis, laryngitis), gastric distension or gastroparesis, chemotherapy (especially cisplatin, carboplatin or etoposide), drugs (dopamine agonists, aripiprazole, benzodiazepines, dexamethasone), invasive procedures (pacemakers, central venous catheters), metabolic disorders (hyponatremia, hypocalcaemia, hypokalemia), cardiopathies and psychological causes.^{7,8}

Clinical evaluation

Persistent and intractable hiccups should be carefully evaluated through clinical history, including duration, relationship with meals, gastric symptoms, associated diseases, previous abdominal surgeries, abdominal pain, intestinal constipation, medications (including chemotherapy), abdominal masses or signs of central nervous injuries. Laboratory tests can be useful, as well as computed tomography (thorax, abdomen or brain). Upper endoscopy can help in patients with gastroesophageal symptoms. It is important to emphasize that every exam request should be preceded by individual risks and benefits. During end-of-life stage, tests can be dropped.

Treatment

If there is a treatable etiology for hiccups, it should be primarily addressed. Surgery or radiotherapy can be performed to manage mediastinal, esophageal or brain masses. Treatment of gastroesophageal reflux or *H. pylori* infection can also provide relief. Medications apparently involved with hiccups should be discontinued wherever possible. In cancer patients in use of dexamethasone, an exchange of the drug for another corticosteroid (methylprednisolone, for example) can help.⁹⁻¹¹

Non-pharmacological approaches

Some popular procedures can help in hiccups relief, which include breath holding for a couple of seconds, breath inside a bag, hyperventilation, swallow bread or crushed ice, drink from the far side of a glass, gently rub the eyes, digital ocular globe pressure, belching, stimulation of vagus nerve (pulling knees to chest, for example), fractionated diet, stimulate the uvula with a gauze, or swallow a

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tablespoon with xylocaine gel plus sugar and lemon juice.^{3,12-18} A recent systematic review about the use of acupuncture for persistent hiccups concluded that there are not high quality studies to support its indication, but available results are encouraging.¹⁹⁻²³ A small study demonstrated efficacy of vinegar nasal instillation in advanced cancer patients with persistent hiccups.²⁴ Descriptions of behavioral conditioning, hypnosis and even prayer can also be found, but there is no strong evidence for support their indication.

Pharmacological approaches

Lack of consistent data about pharmacological therapy enhances its use only when etiology is not manageable and non-pharmacological procedures failed. Chlorpromazine is the most popular drug, although there are just a few studies available. Recommended dose of chlorpromazine is 25-50 mg orally every 6-8 hours for 3 to 7 days. Parenteral use of chlorpromazine (25-50 mg intravenously or intramuscularly) can be more effective than oral administration, but hypotension is a major problem in this approach, which should be minimized through preloading the patient with 500-1000 ml of intravenous fluid. In any case, chlorpromazine is often associated to drowsiness, hypotension and dizziness, even when given orally, and should be avoided in elderly.^{25,26} If chlorpromazine failed, gabapentin can be considered (recommended dose 300-1200 mg orally/24 hours), with hiccups relief reported in 66.7-88.4% of patients.^{3,16,18,27} If there is associated gastric distension, metoclopramide can be useful (10-40 mg orally every 8 hours for 7 to 10 days), alone or in combination with proton-pump inhibitors.²⁸⁻³¹

Baclofen was evaluated in small studies involving patients with previous use of chlorpromazine, metoclopramide and/or diazepam. A significant improvement in hiccups frequency and intensity was observed, but drowsiness and dizziness were reported. Association of baclofen and olanzapine was also described, with promising results.^{17,32-35}

Invasive procedures

Surgical phrenic nerve ablation has been advocated for intractable cases that are unresponsive to other treatment, as well as phrenic blocked with local anesthetic. This drastic approach may be associated

with considerable morbidity and is not universally successful. So, temporary blockade as upfront strategy is advisable. Electrical stimulation of phrenic nerve (with a respiratory pacemaker) had also been described as effective.^{7,36–39}

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Conflict of interest

None.

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