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Assessing the Current Evidence on Singultus (Hiccups): Epidemiology, Pathophysiology, Differential Diagnosis, and Management

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ABSTRACT

Hiccups are sudden involuntary contractions of the diaphragm that A variety of causes, such as factors like eating too quickly or too much, and drinking carbonated beverages can make someone hiccup. Stress is another known trigger, and there are certain medical conditions that can also lead to frequent hiccups. Symptoms of hiccups include repeated, sudden closure of the glottis, producing a characteristic sound. Most people don't realize that a hiccup is really a spasm of the entire diaphragm (not just one half as in normal breathing), accompanied by one half of the brain working differently from the other. The record for the longest bout of hiccups is held by a man who hit up for 68 days back in 1970. Although hiccups are usually self-limiting and harmless, persistent or severe cases can disturb and disrupt daily life. Treatment options for hiccups range from simple home remedies, such as holding one's breath or drinking water, to pharmacological interventions, including antacids and anxiolytic medications. In some cases, underlying medical conditions may need to be addressed to alleviate hiccup symptoms. This review aimed to provide an overview of the causes, symptoms, and treatment options for hiccups, highlighting the importance of proper diagnosis and management.

INTRODUCTION

Involuntary sounds produced by diaphragmatic spasms are known as hiccups. The medical term for hiccups is "*singultus*," which comes from the Latin word "*singult*," which means to catch one's breath while sobbing. Abrupt, involuntary contractions of the diaphragm and intercostal muscles cause hiccups. The contraction that results in the distinctive 'hic' sound is followed by the abrupt closing of the glottis. It can occur in adults, children, babies, and unborn children. Hiccups have a physiological purpose in the fetus: to condition the respiratory muscles for breathing and to act as a response to stop the aspiration of amniotic fluid. Although hiccups usually go away on their own within a few minutes, persistent hiccups that last for days or weeks could indicate an underlying medical condition. It is typically a self-limiting illness, which means that many episodes would end on their own without any obvious clinical

consequences. Overeating, eating too quickly, consuming hot food, drinking carbonated drinks, using alcohol, smoking excessively, and other behaviors are thought to cause self-limiting hiccups. People who take certain medications, such as those used for epilepsy, may become more prone to hiccups. A single hiccup episode may last for a few seconds to several days.

EPIDEMIOLOGY:

Hiccups can occur from infancy to old age. Hiccups are more prevalent in conditions that affect the central nervous system or the gastrointestinal tract. Hiccups were categorized according to their duration. Acute hiccups occur less often than 48 hours apart, persistent hiccups remain for more than two days, and intractable hiccups linger for more than a month. There are various causes of hiccups, including idiopathic, organic, psychogenic, and drug-induced ones. Unquestionably, frequent hiccups may be a sign of more significant underlying issues.

- **Acute hiccups**: The duration of an acute hiccup attack is less than 48 h. Acute hiccups are a well-known occurrence that both adults and children encounter frequently. Acute hiccups are most commonly associated with digestive processes, including gastroesophageal reflux disease (GERD) and related hiatal hernias; it has been reported that up to 10% of GERD patients experience hiccups. Common correlations include stomach distension caused by heavy metals, fizzy drinks, spicy foods, and alcohol. Most research has focused on chronic and intractable hiccups because acute hiccups are self-limited and usually undetectable. Acute hiccups can be stopped by a variety of physical maneuvers, such as holding, or breathing into a paper bag when discomfort occurs.
- **Persistent hiccups**: More than two days pass between persistent hiccups. The most likely explanation for chronic hiccups is an underlying clinical, anatomical, or biological illness condition. More than a month of persistent hiccups is typically a sign of a major biological disruption. Constant hiccups make it difficult for the patient to eat if they can't be stopped. socially and sleep-wise, resulting in a marked decline in life quality. Patients with specific conditions, such as Parkinson's disease, advanced cancer, and gastroesophageal reflex disease (GERD), are more likely to experience persistent hiccups.
- **Intractable hiccups:** If the attack continues for a month, uncontrollable hiccups will occur. Intractable hiccups can result in extreme discomfort, sadness, and even death if treatment is not received. An unusual ratio of 2:4 indicates that older males and those with higher height and weight are more likely to experience intractable hiccups

A thorough examination of the patient's medical history is necessary when evaluating someone who experiences hiccups. Ask about any trigger events, such exposure to heavy metals, excitement, or strain in the mind. Ask about any associated symptoms, such as stomach pain, indigestion, coughing, or weight loss. Ask about any neurological symptoms that would indicate a medullary stroke, multiple sclerosis, or Parkinson's disease. Although they are uncommon, pulmonary, neurological, or esophageal issues can elicit tic tacs during sleep, ruling out a psychogenic explanation. Ask about known cancer, recent surgery, and chemotherapy. A comprehensive evaluation of all prescribed medications may identify a likely cause; causality is established if quitting the problematic medication produces a noticeable improvement. Investigating organic causes is the best course of action when hiccups are severe and persistent. Goiters, tonsillitis, pharyngitis, lumps, hair, or a foreign body pressing against the tympanic membrane are among the diseases that may be discovered during a thorough exam by HEENT specialists. Listen to the lung sounds to rule out thoracic causes such as empyema or pneumonia.

PATHOPHYSIOLOGY:

The diaphragm an, intercostal muscles contract myoclonically and spontaneously during hiccups. The idea that a "reflex arc" comprising afferent, central, and efferent components causes hiccups was initially put forth by Bailey in 1943 and is now generally acknowledged. From the phrenic, vagus, and sympathetic nerves (T6–T12) to the central processing area in the midbrain, which includes the periaqueductal gray and subthalamic nuclei, the reflex arc contains afferents. The motor fibers of the phrenic nerve lead to the diaphragm, while the accessory nerve leads to the intercostal musculature.

- The afferent limb sends somatic and visceral sensory impulses, including those of sympathetic, vagus, and phrenic nerves [thoracic outflow].
- The reticular formation, brainstem in the medulla oblongata, close to the respiratory center, upper spinal cord, and hypothalamus appear to be parts of the central nervous system that are engaged in the hiccup response.
- The accessory nerves supplying the intercostal muscles and the phrenic nerve supplying the diaphragm constitute the efferent portion of the reflex.

Depending on the person, hiccups often occur in cycles of 4-60 per minute. The left hemidiaphragm is more frequently affected than the right hemidiaphragm, and diaphragmatic spasms are frequently unilateral. Following diaphragmatic spasm, the recurrent laryngeal nerve is activated, closing the glottis and completing the reflex. Hyperventilation occurs if the glottis is not closed. Because the medulla's single nucleus is overactive, hiccups persist as diaphragmatic myoclonus.GABA-ergic medications (such as baclofen and gabapentin), vagal movements, dopamine agonists (such as amantadine) or antagonists (such as chlorpromazine, haloperidol, and metoclopramide), and increases in partial pressure of carbon dioxide (PCO2) can all help avoid tic episodes.

ETIOLOGY:

The etiology of hiccups involves many different factors that can irritate the nerves controlling breathing. When these factors nerve provoke the wrong response from the diaphragm, it leads to the sudden, involuntary contraction of this muscle. The etiology of hiccups is multifactorial and encompasses a wide range of physiological and pathological triggers. Common benign causes include gastric distension due to overeating or consumption of carbonated beverages, sudden temperature changes, emotional stress, and excitement. Chronic hiccups may be present in as many as one in four patients with esophageal tumors. Similarly, extreme excitement or anxiety can trigger the hiccup response, especially if it is accompanied by air swallowing or hyperventilation. Alcohol consumption in particular is associated with hiccups when taking a lot of medications. Irritation of the phrenic or vagus nerves due to conditions such as gastroesophageal reflux disease (GERD), laryngitis, or thoracic tumors can also provoke hiccups. Central nervous system disorders including stroke, traumatic brain injury, encephalitis, and multiple sclerosis may disrupt the hiccup reflex arc. Metabolic and toxic causes such as uremia, diabetes mellitus, electrolyte imbalances (particularly hyponatremia or hypocalcemia), and adverse drug reactions (e.g., corticosteroids, benzodiazepines, or chemotherapy agents) have also been implicated. In rare cases, persistent or intractable hiccups may be idiopathic and require thorough diagnostic evaluation to exclude underlying serious diseases. The respiratory causes include pneumonia, asthma, and pleuritis. Certain drugs can induce hiccups via CNS or GI stimulation, such as corticosteroids, benzodiazepines, chemotherapeutic agents such as cisplatin, dopamine agonists, and barbiturates. Psychogenic causes are more common in persistent hiccups without organic pathologies such as anxiety, stress, hysteria and somatization disorders. Infectious diseases include neurosyphilis, tuberculosis, influenza, herpes simplex, herpes zoster, asthma, bronchitis, diaphragmatic tumor, or hernia, empyema, lymphadenopathy, mediastinitis, neoplasms, pleuritis, pneumonia, and pulmonary embolus. Intra-thoracic illnesses include: surgery: tracheostomy, post-operative bronchoscopy, stomach insufflation during endoscopy, anesthetic medications (barbiturates, bupivacaine epidural, isoflurane, methohexital, Propofol), and sedation during endoscopy (20%).

SYMPTOMS:

- Primary symptoms: Involuntary, repetitive contractions of the diaphragm followed by a sudden closure of the vocal cords, producing the characteristic “hic” sound.
- Associated or Secondary symptoms: Mild chest or throat discomfort due to repeated contractions. Sensation of tightening of the chest, abdomen, or throat. Interruption in speech or eating caused by spasms. Fatigue or sleep disturbance, especially in patients with prolonged hiccups. Social embarrassment or anxiety, particularly in persistent cases.
- Prolonged or Persistent hiccups (lasting >48 hours) may include weight loss due to disrupted eating. Dehydration, insomnia, depression or irritability and aspiration risk, especially in patients with neurological or swallowing disorders.

DIAGNOSIS:

The best factors for guiding further imaging or therapy include the duration of hiccups, history, and physical exam findings. For persistent or uncontrollable hiccups associated with neurologic symptoms or signs, brain imaging using computerized tomography (CT) or magnetic resonance imaging (MRI) may reveal causes such as stroke, multiple sclerosis, tumor, syringomyelia, neuromyelitis optica, aneurysm, or vascular malformation. Chronic and intractable hiccups are typically benign and do not require a workup, thus a thorough evaluation is necessary to identify a therapeutic reason. To assess electrolyte imbalances or rule out infectious or malignant processes that were missed during the physical examination and history, laboratory work makes sense. Laboratory tests for blood urea nitrogen (BUN), lipase, creatinine, electrolytes, calcium, and liver function can be beneficial. A chest radiograph can help identify the underlying cause of hiccups, such as pneumonia, empyema, diaphragmatic hernia, adenopathy, or aortic disease. It is very important to review the blood gases of any ventilated patient who is having hiccups. Serious hemodynamic or respiratory events can arise from hiccups in a patient receiving ventilation, including severe respiratory disruptions, large hemodynamic swings, and ventilator desynchronization.

TREATMENT:

In general, transient hiccups are self-limited, and unless they return, they do not require etiological assessment or prompt treatment. Clear-cut standards are sparse and the therapeutic approach for recurrent hiccups is primarily based on observational studies and case series. Once ailment-causing hiccups have been discovered, the primary goal of treatment is to address the underlying cause. Anecdotal data suggests that a few simple physical measures help prevent hiccups during their acute phase. The majority of approaches focus on a portion of the hiccup reflex arc. Hiccup frequency lowers with increasing PCO_2, therefore holding your breath, blowing into a paper bag, and doing Valsalva techniques could be beneficial. When using the supra-supramaximal inspiration technique, the patient takes a deep breath, holds it for ten seconds, and then exhales fully. The participant next takes two more breaths without exhaling, holding them for five seconds each time. The Valsalva maneuver, pulling on the tongue, sipping vinegar, swallowing sugar, stimulating the uvula or posterior nasopharynx (with smelling salts or nasal vinegar), applying pressure to the carotid artery, the eyeballs, or both external auditory canals, gargling, gagging, or even self-induced vomiting are other techniques. Other odd techniques, like digital rectal massage and sexual stimulation, have also been reported. There have been reports of suboccipital release and osteopathic/chiropractic manipulation techniques. All of these techniques appear to perform noticeably better during the acute phase.

Non - pharmacological treatment: First-line treatments for hiccups include physical techniques like stopping regular breathing (e.g., breath holding, Valsalva maneuver), stimulation the nasopharynx or uvula (e.g., drinking cold water, gargling with water, or swallowing a teaspoon of dry sugar), increasing vagal stimulation (e.g., pressing on the eyeballs), and countering diaphragm irritation (e.g., pulling knees to chest, leaning forward to compress the chest). The fundamental idea behind several physical techniques is to suppress or stop a reaction arc. When physical measures have not been successful in treating hiccups, medication should be administered.

Interventional treatment: Approaches based on local intervention inside the hiccup reflex arc at the central or peripheral level should be considered, in addition to attempting to address hiccupping methodically. Surgical resection can provide relief if the tumor affects the nerve structures that cause hiccups. Hiccups were successfully treated with blocking by injecting local anesthetics into the cervical epidural space or near the phrenic nerve. Transesophageal diaphragmatic pacing and radiofrequency ablation of the phrenic nerve have also been reported to be successful. Accurate application of the injectate or electrodes near the phrenic nerve is made possible by ultrasonography.

Pharmacological treatment: The pharmacological treatment of hiccups is considered when hiccups are persistent (lasting more than 48 hours) or intractable (lasting more than a month), and non-pharmacological methods fail. The most commonly used medications include chlorpromazine, which is FDA-approved for hiccups and acts as a dopamine antagonistic; metoclopramide, a prokinetic agent with dopamine antagonist effects; and baclofen, a GABA-B receptor agonist that can reduce diaphragmatic excitability. Other agents, such as gabapentin, haloperidol, and nifedipine, have also been shown to be effective in some cases. The choice of drug depends on the patient's overall health, underlying cause of hiccups, and potential side effects. Treatment should be tailored to individual responses and tolerated side effect profiles.

CONCLUSION

In conclusion, hiccups are a complicated condition that involves abrupt, uncontrollable contractions of the intercostal and diaphragm muscles. Hiccups are generally innocuous and self-limiting, yet they negatively affect quality of life and may indicate serious medical problems. Management requires knowing the causes and the symptoms, as well as the basic treatments that exist. Understanding what you're dealing with is vital to effective management. Hiccups are generally harmless, but they can cause you to lose your train of thought or even your temper. The pathophysiology of hiccups isn't well understood, and neither is why some people get them regularly or for extended periods.. Healthcare providers can provide comprehensive care and enhance patient outcomes by recognizing the complex nature of hiccups.

Declarations

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- Kugalur Ganesan Parthiban — Supervision; Methodology; Critical review; Validation.
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Competing Interests

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