ANNALS OF MEDICINE
2025, VOL. 57, NO. 1, 2474173
https://doi.org/10.1080/07853890.2025.2474173

REVIEW ARTICLE

OPEN ACCESS | Check for updates

Pathogenesis and treatment of perioperative hiccups: a narrative review

Jiahui He[a*], Ao Guan[b*], Tingting Yang[a], Lijuan Fu[c], Yourui Wang[d], Shaoshuang Wang[a], Haomin Ren[a], Ling Chen[e], Yaomin Zhu[a] and Bin Deng[a]

[a]Department of Anesthesiology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China; [b]School of Medicine, Xiamen University, Xiamen, China; [c]Department of Infectious and Liver Disease, Xiang'an Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China; [d]Key Laboratory of Resource Biology and Modern Biotechnology in Western China, Ministry of Education, Northwest University, Xi'an, China; [e]Department of Philosophy, Xiamen University, Xiamen, China

ABSTRACT

Introduction: Hiccups affect 0.05% of general in-patients and up to 10% of patients with gastroesophageal reflux disease. Hiccups are typically self-limited. In certain cases, they can become persistent and intractable, suggesting a potentially more serious underlying pathological condition. Treatment of hiccups in the perioperative period is challenging as it is difficult to identify their causes, and the existing literature is mainly based on case studies. This review aims to comprehensively explore the aetiology, mechanisms and treatment of perioperative hiccups to provide new insights.

Methods: A systematic search was conducted in multiple databases such as PubMed, Embase, and Web of Science, for literature published within the past three decades. Search terms included 'Hiccups, Perioperative, Pathogenesis, Treatment, Lidocaine', etc. Inclusion criteria included original research articles, review papers and case reports that provided relevant information on the topic. Exclusion criteria were non-relevant studies, duplicates and articles with insufficient data.

Results: Surgical, anaesthesia- and patient-related aetiological factors and mechanisms of perioperative hiccups were systematically analysed. Management strategies across different perioperative phases were summarized, highlighting the emerging evidence of lidocaine's therapeutic efficacy. Current understanding of perioperative hiccups is limited as it mainly depends on case reports and observational studies, lacking strong evidence from controlled clinical trials. Preoperative risk stratification, intraoperative dynamic assessment, and postoperative multimodal safety protocols are clinically essential.

Conclusion: Research on the pathogenesis and treatment of perioperative hiccups requires further enhancement. Large-scale prospective studies are needed to validate the proposed management strategies and treatment recommendations, which will be beneficial for improving the clinical management of this condition.

KEY MESSAGES

- A comprehensive review of the causes and mechanisms of hiccups, with a specific focus on hiccups in the perioperative period.
- Presenting clinical evidence supporting the prevention or prompt and safe management of hiccups in the perioperative period.
- Offering corroborating evidence for the use of lidocaine as a viable treatment option for hiccups in the perioperative period.

ARTICLE HISTORY
Received 23 April 2024
Revised 18 February 2025
Accepted 20 February 2025

KEYWORDS
Hiccups; perioperative; pathogenesis; treatment; lidocaine

Introduction

Hiccups, characterized by involuntary contractions of the diaphragm and sudden closure of the glottis, are a common yet often overlooked issue, especially in the perioperative period. Although hiccups might appear to be of minor consequence in daily life, their occurrence during the perioperative period can exert a substantial influence on both the surgical procedure itself and the subsequent recovery of patients. This process is accomplished by a reflex arc composed of structures such as the phrenic, vagal and sympathetic pathways, as well as the central processing units of the brainstem [1], which involves an imbalance in the

CONTACT Bin Deng xajxdb@126.com Department of Anesthesiology and Center for Brain Science, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China; Yaomin Zhu yaomin_zhu@126.com Department of Anesthesiology & Center for Brain Science, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China
*These authors contributed equally to this work.

levels of various neurotransmitters in the peripheral and/or central nervous system [2].

The incidence and prevalence of hiccups are difficult to determine because it is not usually a major phenomenon in various systemic diseases. For general inpatients, the probability of hiccups is approximately 0.054% [3]. This probability is even higher among patients with digestive system diseases, nervous system disorders, abnormal mental states or those taking specific medications [4]. Gastroesophageal reflux disease (GERD) and related hiatal hernias in patients are common causes of acute hiccups, with the incidence reaching 10% [5]. Among patients with oesophageal tumours, about 27% experience hiccups for more than 48 h [6]. In stroke patients, due to cerebrovascular lesions that disrupt the hiccup neural pathway, approximately 0.3% of patients experience hiccups [7]. In addition, approximately 3.9%–4.5% of cancer patients taking chemotherapy drugs also experience hiccups [8]. Notably, the occurrence of hiccups appears to be specific to gender. A community hospital conducted a retrospective analysis of all patients over a five-year period and found that out of the 54 hiccups patients, 91% were male, who were typically over the age of 50 and often had comorbidities, while 9% were female [3]. Major comorbidities seem to include central nervous disorders or gastrointestinal cancer. Of 71 patients with hiccups of Central Nervous System (CNS) origin (0.5% of all patients), 59(83%) were men, with a mean age of 50 [9]. Among the 160 cancer patients receiving chemotherapy, hiccups occurred in 24(65%) male patients and 13(35%) female patients [10]. Some studies present conflicting conclusions regarding the prominence of gender differences in hiccups. They suggest that male gender is more significantly associated with hiccup of non-CNS origin (peripheral or drug-related causes) (OR 11.72, $p < 0.001$), but not hiccup of CNS origin (OR 1.74, $p = 0.072$). This difference may be attributed to variations in patient population, aetiology, study design and sample size [11]. Mechanistically, male susceptibility to hiccups may be attributed to lower synaptic thresholds in the hiccup reflex arc, making it easier to excite afferent or efferent nerves [12]. In addition to gender differences, taller height seems to be an independent risk factor for hiccups, but the exact mechanism is unclear [13].

The severity of hiccups usually depends on their duration, and most hiccups are acute and self-limiting (lasting less than 48 h), which is common in healthy individuals. This type of hiccups tends to subside on their own and rarely require medication [6,14]. However, in exceptional cases, hiccups may also be chronic and persistent, which often indicates the presence of a serious underlying pathological process. Hiccups require medical intervention when they last more than 24 h or interfere with eating, breathing, or sleeping [15,16]. The causes of these hiccups are often complex and diverse, including infections, trauma, tumours, as well as gastrointestinal, metabolic, and psychological diseases, which may ultimately lead to fatigue, loss of appetite, weight loss, dehydration and even death [17]. Mechanistically, any factors that can affect the structure or function of the reflex arc of the hiccups process can trigger hiccups. Hiccups in the perioperative period, typically arising as a reflex response to an acute cause, present a complex issue that warrants further investigation. In contrast to hiccups during the non-operative period, which are mainly induced by factors like diet, gastrointestinal diseases and mental factors, hiccups during the perioperative period result from complex elements such as surgical manipulation, anaesthesia and patients' underlying diseases. Preoperative hiccups can postpone surgeries by increasing patient anxiety, raising aspiration risk and hindering doctors' preoperative assessment. During surgery, hiccups disrupt surgical operations and anaesthesia management, prolonging the operation time and increasing complication risks. Post-operative hiccups impede wound healing, trigger respiratory issues, delay gastrointestinal function recovery and reduce patient comfort. Due to the multiple pathophysiological processes in disease development and hiccups being a possible concurrent symptom, it's arduous to determine the cause and targeted treatment, with most interventions only validated by case reports.

This narrative review aims to bridge the knowledge gap by comprehensively exploring the aetiology, pathogenesis and management strategies of perioperative hiccups, with no contain quantitative data. By analysing surgical, anaesthesia and patient-related factors in detail, we hope to provide a more in-depth understanding of this underrecognized complication. Special attention will be given to the emerging evidence regarding the therapeutic efficacy of lidocaine, which has shown promise in recent years. The ultimate goal is to enhance clinical awareness, stimulate further research, and establish more effective management guidelines to optimize patient outcomes during the perioperative period.

1. Aetiology and classification of hiccups

Transient hiccups, which are caused by irritation of the gastrointestinal or respiratory tract from alcohol, smoking, carbonated beverages, and other substances, are common in healthy individuals and usually resolve on their own. Persistent and intractable hiccups often signal the presence of an underlying pathology [3,18], especially common in gastrointestinal diseases (62.5%) and central nervous system diseases (33.3%). The causes of hiccups are often categorized as idiopathic, organic (central and peripheral), psychiatric, and others. Table 1 summarizes the reported aetiology of this condition, including non-perioperative hiccups. In addition, many drugs also cause hiccups, but the precise mechanism is rarely reported [13,19–21]. However, it is often challenging for many patients to pinpoint the cause of hiccups due to the unclear direct link between individual pathophysiologic processes and hiccups.

2. Pathophysiologic mechanisms of hiccups

For the origin of hiccups, Straus et al. first posited that hiccups could be a recurrence of archaic motor patterns because the hiccup-associated ventilatory motor patterns in mammals bear resemblance to those in lower vertebrates. The neural circuit for hiccups may have persisted in mammals, facilitating the development of pattern generators for functions such as suckling or normal breathing [22]. Karabacak and Danner expanded mechanisms of hiccups from a phylogenetic exploration to a focus on central respiratory regulation, highlighting the role of the central nervous system in the generation of hiccups [23]. The mechanism of hiccups involves a complex reflex arc, which includes the balance of various neurotransmitters in both the central and peripheral nervous systems. The hiccup reflex arc involves a complex neural network of multiple anatomical structures, relying on the 'hiccup center' to coordinate and connect multiple afferent and efferent pathways (Figure 1). Most studies generally agree that the reflex arc of the hiccup is as follows: the afferent pathway of hiccups includes the sensory fibres of the vagal nerve, glossopharyngeal nerve, the phrenic nerve and sympathetic nerves from Th6 to Th12 [24,25]. The centres structures related to hiccups mainly include the nuclei related to the medulla such as the ventrolateral medulla of the brainstem and the reticular formation, the phrenic nerve nucleus, spinal cord segments such as C3–C5 in the cervical region and their associated nerves, as well as the higher-order centres of the cerebrum [26,27]. The efferent pathway of hiccups involves the phrenic nerves to the diaphragm, accessory nerves to the intercostal muscles, the cervical spinal nerves to the anterior scalene muscles, and the recurrent laryngeal portion of the vagal nerve to the glottis, resulting in glottal closure. Other studies explain the mechanism of hiccups as a neurogenic dysfunction affecting the 'valve function' between the inspiratory complex and the glottis closure complex [28]. In addition, the hiccups reflex arc function is mediated by various central neurotransmitters (dopamine (DA), serotonin, opioid, glycine, and gamma-amino butyric acid (GABA), peripheral neurotransmitters

Table 1. Aetiology of persistent and intractable hiccups.

Type	Disease/Disorder	Reference
Central nervous system		
Vascular	Ischaemic/haemorrhagic cerebrovascular insult, cavernoma, systemic lupus erythematosus related vascular disorders and aneurysms (posterior inferior cerebellar artery)	[7,100–103]
Tumor	Astrocytoma, carvenoma and brain stem tumors	[48,104]
Structural	Brain injury	[47]
Inflammation	Demyelinating disorders (neuromyelitis optica and multiple sclerosis)	[105,106]
Miscellaneous	Seizure, cranial nervous herpes infection, lateral medullary syndrome and parkinsonism	[41,107,108]
Peripheral pathway		
Gastrointestinal tract	Gastro-oesophageal reflux disease, oesophageal tumours, hiatus hernia, stomach volvulus, stomach distension, *H. pylori* infection, gallbladder disease, peptic ulceration, pancreatitis, hepatitis, abdominal abscess, abdominal tumours, bowel obstruction	[109–115]
Cardiovascular	Atrial pacing, myocardial ischemia, pericarditis, aortic aneurysm and post-myocardial myocardial infarction	[116–118]
Pulmonary	Bronchitis, pneumonia, asthma, bronchial carcinoma, tuberculosis, pulmonary emboli	[119–121]
Otolaryngologic	Goiter, neck cyst, herpes zoster, rhinitis, otitis, pharyngitis, endotracheal intubation and foreign body in nose or ear	[122–125]
Chest cavity	Bronchitis, mediastinal diseases, lymphadenopathy, pleural effusion, chest wall herpes, empyema and diaphragmatic tumours	[125–128]
Other causes		
Surgery	Anaesthetic agents, pharyngeal intubation, thoracic and upper abdominal surgical, gastric insufflation and sedation during endoscopy, bronchoscopy and central venous catheterization	[64,125,129–132]
Drugs	Ethanol, steroids, dopamine agonists, platinum-based agents, benzodiazepines, opioids, barbiturate, sulphonamides, dexamethasone and azithromycin	[21,41,131,133–137]
Psychogenic disorders	Anxiety, excitement, stress, sleep deprivation and fear	[27,138]
Infectious Disorders	Helicobacter pylori, herpes simplex virus, herpes zoster virus, influenza, malaria, neurosyphilis, tuberculosis, meningitis, encephalitis	[112,117,123,139–141]
Metabolic disorders	Electrolyte imbalance (hyponatremia, hypokalaemia, hypocalcaemia, hypocapnia), uraemia, diabetes mellitus	[142–144]

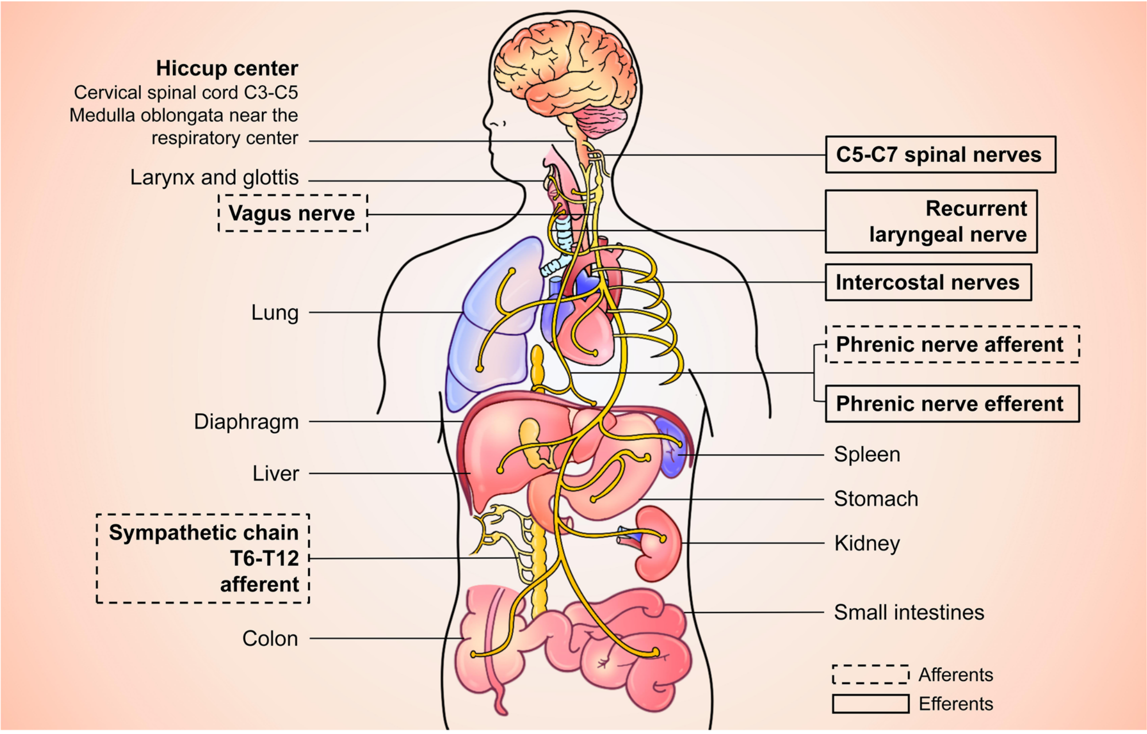

Figure 1. The reflex arc of hiccup. The dotted line box represents the afferent nerve pathway of hiccups, while the solid line box represents the efferent nerve pathway. The afferent pathway includes the sensory fibres of the vagal nerve, glossopharyngeal nerve the phrenic nerve, and sympathetic nerves from Th6 to Th12. The hiccup centers mainly include the medulla oblongata, the periaqueductal grey, sub-thalamic nuclei, phrenic nerve nuclei, reticular formation, and C3 to 5 cervical cord. The efferent pathway includes the phrenic nerves to the diaphragm, accessory nerves to the intercostal muscles, the cervical spinal nerves to the anterior scalene muscles, and the recurrent laryngeal portion of the vagal nerve to the glottis, which causes glottal closure. Figure 1 was developed by the authors.

(epinephrine, norepinephrine and histamine) [29] (Table 2). Hiccups may be triggered by various factors that stimulate the structure and function of the flex arc, including tumours, inflammation, systemic lesions and drugs. These factors can disrupt the normal balance of the hiccups reflex arc's function. The specific mechanisms and the cross-action of certain drugs in regulating hiccups are illustrated in Figure 2. The development of a disease typically involves multiple pathophysiological processes, and hiccups may simply be a concurrent symptom of the disease, making it more challenging to determine the cause and target treatment for hiccups.

2.1. Central neurotransmitter

2.1.1. Gamma-amino butyric acid (GABA)

GABA is an important central nervous system inhibitory neurotransmitter, formed by the decarboxylation of precursor glutamate through glutamate decarboxylases (GADs), and most synaptic sites in the brain and spinal cord use it as a transmitter and regulate body functions. The allosteric sites of its three receptors ($GABA_A$, $GABA_B$ and $GABA_C$) can precisely regulate the inhibitory level of neurons in brain-related regions [30]. The GABA pathway is also the site of action of many neuroactive drugs such as benzodiazepines, barbiturates and volatile anaesthetics. Research has proven that low levels of GABA are linked to mood, sleep hypo-function and other advanced brain functions [31]. In addition, GABA seems to be involved in hiccups reflex. Oshima T et al. confirm that the nucleus raphe magnus (the lower brainstem), which contains GABA cells, is the most important region likely to inhibit inputs from the ergoreflex arc [32]. A number of drugs seem to exert a therapeutic effect on hiccups by modulating the GABA pathway. Gabapentin, a GABA-like molecule, may act as a partial agonist at the glycine modulatory site of the NMDA receptor, and increase endogenous GABA production and release. At the same time, gabapentin may block the inward flow of calcium at neuronal voltage-gated calcium channels, increase GABA release and lead to excitatory inhibition of the diaphragm [8]. Valproic acid also plays a role in the treatment of hiccups by enhancing GABA [33]. Pregabalin, a relatively new GABA analogue, has a role in the treatment of intractable hiccups through inhibiting voltage operated calcium channels to reduce

Table 2. Drugs involved in neurotransmitter pathways to treat hiccups.

Drugs associated with central neurotransmitters	Possible Mechanisms	Reference
GABA		
Gabapentin	As a partial agonist at the NMDA receptor and block the inward flow of calcium at neuronal voltage-gated calcium channels to increase endogenous GABA production and release, leading to excitatory inhibition of the diaphragm	[145]
Valproic acid	By enhancing GABA	[33]
Pregabalin	By inhibiting voltage operated calcium channels to reduce calcium influx and increasing serotonin levels to affect the presynaptic terminals of respiratory muscles	[34]
Baclofen	By reducing the release of dopamine in the central nervous system, or acting as a GABA type B receptor agonist mediating an inhibitory effect on presynaptic hyperpolarization in the spinal hiccup reflex arc	[36]
Midazolam and morphine	By acting on benzodiazepine receptors, forming the benzodiazepine-GABA receptor-chloride ionophore complex to open the chloride channels, hyperpolarize neurons, and to reduce their excitability	[37]
Dopamine		
Rotigotine and pramipexole	As dopamine agonists, may be related to the high affinity of dopamine agonists to D_3 receptors to involve in the regulation of hiccup reflex arc	[146]
5-HT		
Tandospirone	As a major metabolite of tandospirone, 1-PP is a centrally acting α_2-adrenergic antagonist, which increases 5-HT release and availability	[49]
Olanzapine	Antagonizes the postsynaptic serotonergic receptors to reduce the phrenic motor neuron activity	[47]
Sertraline	Selectively reuptakes inhibition of 5-HT	[48]
Risperidone	High $D_{2/5}$-HT_{2A} affinity	[45]
aripiprazole	By activation of 5-HT_{1A} receptor and antagonism of 5-HT_{2A} receptor	[54]
Drugs associated with peripheral neurotransmitters		
Norepinephrine and epinephrine		
Methylphenidate	A receptor modulator of norepinephrine	[56]
Carvedilol, amitriptyline and sertraline	As α_1/β-receptor antagonist	[147]
Chlorpromazine	By blocking α adrenergic receptors of the ascending activating system of the reticular structure	[60]
Histamine		
Omeprazole	Inhibits H_2 receptors and proton pumps to reduce neural input from the gastrointestinal tract to the hiccup centre	[62]

GABA: gamma-amino butyric acid; NMDA: N-methyl-D-aspartic acid; D_3: dopamine receptor; 5-HT: 5-Hydroxyl tryptamine; 1-PP: 1-(2-pyrimidinyl)-piperazine; 5-HT_{1A}, 5-HT_{2A}: receptor types of 5-hydroxytryptamine; D_2: dopamine receptor; H_2 receptor: histamine receptor.

calcium influx and increasing serotonin levels to affect the presynaptic terminals of respiratory muscles [34]. The mechanisms of baclofen inhibiting hiccups may reduce the release of dopamine in the central nervous system, or by acting as a GABA type B receptor agonist mediating an inhibitory effect on presynaptic hyperpolarization in the spinal hiccup reflex arc [35,36]. Midazolam acts on benzodiazepine receptors, forming the benzodiazepine-GABA receptor-chloride ionophore complex to open the chloride channels, hyperpolarize neurons, and to reduce their excitability. When used in combination with morphine, midazolam does control intractable hiccups in cancer patients [37]. Interestingly, at low doses, benzodiazepines are associated with the development of hiccups, while at high doses they may be useful in the treatment of hiccups.

2.1.2. Dopamine

In the central nervous system, dopamine, as an important catecholamine neurotransmitter of the nervous system, is involved in cognitive, emotional and neuroendocrine regulation and presents as a local paracrine substance in the peripheral nervous system, mainly affecting sodium homeostasis, vascular tone and hormone secretion [38]. Based on biochemical and pharmacological properties, dopamine receptors can be classified into two major groups containing D1-like receptors (D1 and D5 receptors) and D2-like receptors (D2, D3 and D4 receptors). D1-like receptors, D2-like receptors are coupled to stimulatory and inhibitory G-protein-coupled receptors, respectively, which either elevate or reduce adenylyl cyclase activity [39]. Evidence that dopamine agonists induce hiccups and anti-dopaminergic drugs successfully treat hiccups has been reported, which supports the role of dopamine as a central neurotransmitter in the pathogenesis of hiccups [40,41]. Rotigotine and pramipexole (dopamine agonists) have a higher chance of inducing hiccups in male PD patients [42]. The mechanism may be related to the high affinity of dopamine agonists to D3 receptors to involve in the regulation of hiccup reflex arc [43]. Paradoxically, some anti-dopaminergic drugs also seem to cause hiccups [40]. This suggests that both high and low levels of dopamine are linked to hiccups, possibly because of the unclear understanding of the specific receptors targeted by dopamine agonists or drugs. In conclusion, while the role of dopamine as a central neurotransmitter in the development of hiccups is established, it remains unclear

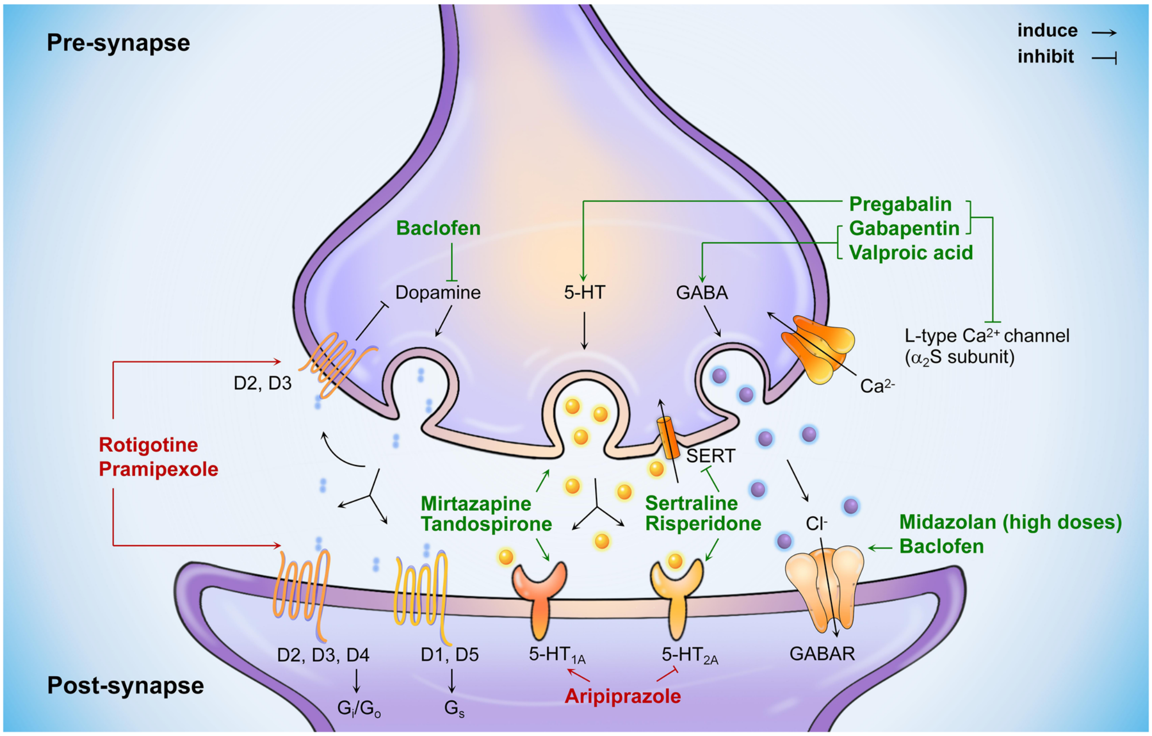

Figure 2. The cross-action mechanism of multiple drugs that can regulate hiccups. Red represents the drug that induces hiccups, while green represents the drug that inhibits hiccups. D1, D2, D3, D4, D5: five types of dopamine receptors; G_i/g_o, G_s: G protein-coupled receptors; 5-HT, 5-Hydroxytryptamine; 5-HT_{1A}, 5-HT_{2A}: receptor types of 5-hydroxytryptamine. GABA: Gama-amino butyric acid; GABAR: Gama-amino butyric acid receptor; SERT: serotonin transporter. Figure 2 was developed by the authors.

whether hiccups are mediated by dopaminergic activation or inhibition. Therefore, blindly blocking dopaminergic receptors alone may not cure hiccups.

2.1.3 5-Hydroxyl tryptamine (5-HT; serotonin)

5-HT is an important neurotransmitter that regulates neural activity in the brain and can strongly constrict blood vessels in peripheral tissues. The classification of 5-HT receptors is complex, which can be divided into seven families (5-HT_1-5-HT_7), a total of 14 subtypes. Except for 5-HT_3 receptor, which is a ligand-gated ion channel, the rest belong to G protein-coupled receptors [44]. In addition to the dopaminergic system, the serotonin system may also be involved in some pathophysiology of hiccups [45]. Animal studies have shown that 5-HT can promote phrenic nerve activity at the level of spinal cord, involved in the excitation of diaphragm in hiccups [46]. Hiccups during cisplatin and dexamethasone combination chemotherapy may be caused by the release of serotonin from intestinal pigment cells and vagal afferents induced by cisplatin [21]. In addition to the above evidence that the 5-HT system mediates hiccups, a number of case studies have reported successful treatment of hiccups, and the mechanisms also seem to be inseparable from the serotonergic system. Olanzapine antagonizes the postsynaptic serotonergic receptors to reduce the phrenic motor neuron activity to treat hiccups of brain injury cases [47]. Sertraline was shown to selectively reuptake inhibition of 5-HT to treat hiccups [48]. Tandospirone, an anxiolytic and 5-HT_{1A} receptor agonist, is effective in intractable hiccups [49]. Some drugs that target the dopaminergic system may instead initiate or treat hiccups primarily through the serotonergic system. One case report shows that a patient with intractable hiccups completely eliminated hiccups 6 h after risperidone administration but did not respond to haloperidol, despite both being potent inhibitors of dopamine D_2 receptors. This may be due to the many times higher D_2/5-HT_{2A} affinity of risperidone than haloperidol [50]. Moreover, aripiprazole shows the strongest association with hiccups induction among antipsychotics, and tandospirone has similar efficacy [51–53]. Aripiprazole is an antipsychotic that acts as a functional antagonist in the mesolimbic dopamine pathway and reduces the extent of dopaminergic pathway activity. Studies have shown the occurrence of persistent hiccups with low doses of aripiprazole, especially when anti-dopaminergic activity has not yet begun. This may be triggered by activation of 5-HT_{1A} receptor and antagonism of 5-HT_{2A} receptor. The complete disappearance of hiccups after a small dose of gabapentin and immediate discontinuation of aripiprazole suggests that gabapentin is an ideal drug for the acute treatment of hiccups caused by aripiprazole [54]. Centrally acting α_2-adrenergic antagonists such as tandospirone and mirtazapine may be thought to inhibit hiccups by increasing the release and availability of serotonin or by primarily activating 5-HT1A receptors to indirectly activate the serotonergic system [49]. This seems to contradict previous mechanisms, probably because drugs have multiple effects on the 5-HT system and are difficult to fully characterize with one mechanism.

2.2. Peripheral neurotransmitters

2.2.1. Norepinephrine and epinephrine

Norepinephrine and epinephrine are catecholamine transmitters with central and peripheral nervous system centres of action, respectively. Norepinephrine has a potent but nonselective effect on α receptors, a very weak agonist effect on β1 receptors, and almost no effect on β2 receptors. Epinephrine pairs primarily activate α and β receptors [55]. Studies have shown that methylphenidate, a receptor modulator of norepinephrine, is effective in treating hiccups [56]. Carvedilol, amitriptyline and sertraline, α_1/β-receptor antagonist, are effective in cases of intractable hiccups [57–59]. Chlorpromazine has long been considered a successful treatment for persistent and intractable hiccups by blocking α adrenergic receptors of the ascending activating system of the reticular structure [60]. However, due to its adverse effects, such as hypotension, urinary retention and glaucoma, it is often used in combination with other drugs. Anisodamine (M-receptor blocker) can improve microcirculation, relieve smooth muscle spasticity, and help overcome the side effects of chlorpromazine. It has been proved that acupoint injection of chlorpromazine combined with anisodamine is better than chlorpromazine alone in the treatment of intractable hiccups after stroke [60].

2.2.2. Histamine

Histamine is one of the main mediators involved in immune response and inflammation and binds to specific subtypes of receptors as a mediator or neurotransmitter, including four subtypes H1, H2, H3 and H4. H2 receptors are mainly distributed in gastric parietal cells and vascular smooth muscle cells, which can promote gastric acid secretion and telangiectasia [61]. Omeprazole inhibits H2 receptors and proton pumps to reduce neural input from the gastrointestinal tract to the hiccup centre to treat hiccups [62].

3. Hiccups in the perioperative period

3.1. Causes and mechanisms of hiccups in the perioperative period

Hiccups in the perioperative period are typically reflexes caused by acute factors and present a challenging problem that deserves further investigation. During a surgical procedure, the occurrence of hiccups in patients who are not intubated can lead to potential complications such as airway obstruction, a reduction in minute volume and respiratory rate, and in severe cases, even apnoea. Following a hiccup attack in intubated patients, potential manifestations may include hyperventilation, respiratory alkalosis and ECG artifacts [63]. Therefore, it is particularly important to fully identify the aetiology and potential mechanisms of perioperative hiccups. The factors of hiccups are primarily examined from three perspectives: surgical factors, anaesthetic factors and the patients factors.

Surgical factors frequently trigger hiccups as a result of intraoperative stimulation of various organs, including the diaphragm and stomach. For instance, during gastroscopy, the sudden distension of oesophagus and stomach cavity can stimulate the gastric vagus nerve, thereby exciting the afferent nerve of the hiccup reflex arc and leading to the occurrence of hiccups [64]. During laparoscopic surgery, the stimulation of the diaphragm by the CO_2 pneumoperitoneum can also increase the risk of hiccups [65]. The risk of hiccups may also be increased by the pressure difference caused by temporary or continuous relaxation of the lower oesophageal sphincter (LES) in patients with gastroesophageal reflux disease [12]. When hiccups manifest, a pressure gradient is observed in the LES, potentially leading to the regurgitation of gastric contents into the oesophagus, particularly in severe cases. This phenomenon can result in reflux and aspiration, posing significant risks for patients undergoing anaesthesia during surgical procedures [65]. In addition, for some special requirements of general anaesthesia surgery (such as the prohibition of muscle relaxants when nerve monitoring is required), the management of hiccups is more troublesome [66]. Therefore, surgeons should take care to prevent hiccups when conducting abdominal manoeuvres and patient positioning.

For the patient factors, individuals who have experienced chronic and uncontrollable hiccups in the past, especially those with underlying central nervous system or gastrointestinal issues, may still be at risk of hiccups, even if they exhibit no symptoms at the time of their visit. Patient's preoperative fasting duration is less than 6 h, undigested food in the stomach may reflux and stimulate the vagus nerve, causing diaphragmatic spasm and thus leading to hiccups [67]. These greatly increase the perioperative challenge. In addition, hiccups may also occur in patients with renal impairment, particularly in those with uraemia who have electrolyte imbalances [68]. Patients with a history of digestive, nervous, respiratory system-related diseases or with perioperative electrolyte disorders may have an increased risk of hiccups during surgery.

The effect of anaesthetics and anaesthesia techniques on inducing hiccups in the perioperative period is noteworthy. For patients with general risk non-cardiothoracic surgeries, depending on factors such as the type and duration of the surgery, approximately 60%-80% of patients require mechanical ventilation [69]. It has been observed that positive pressure ventilation can trigger hiccups, which cease as airway pressure decreases [70]. The laryngeal mask airway (LMA) has become a common auxiliary means for airway management during the perioperative period, thanks to its advantages of simple operation and reduced throat pain. Meanwhile, the impact of a laryngeal mask on intraoperative hiccups cannot be underestimated, with an incidence from 1% to 5% [71]. Studies have shown that this incidence is largely related to anaesthesia techniques and varies with the type and dosage of anaesthetic-inducing drugs [72]. Specifically, hiccups may be triggered by the insertion and positioning of the laryngeal mask airway or by inflating the LMA cuff [71]. This could be due to placing the distal end of the laryngeal mask airway near the proximal end of the oesophagus, which stimulates local mechanoreceptors and triggers excitation of the vagal nerve [73]. In addition to the airway management, different anaesthesia methods also have an impact on hiccups. A case of obstetric analgesia and anaesthesia *via* epidural injection of levobupivacaine revealed that the parturient experienced hiccups lasting 1–2 h both during the initial administration of levobupivacaine and upon additional dosing. This may be related to the changes in cerebrospinal fluid pressure caused by the epidural injection [74]. Drug-induced hiccups are a relatively infrequent occurrence, however, the administration of perioperative anaesthetics and sedatives, including benzodiazepines, opioids, are believed to be potential triggers for hiccups in the perioperative period. Sedatives, such as midazolam, have been found to induce hiccups in a dose-dependent manner among patients undergoing endoscopic gastrointestinal surgery. Furthermore, it has been observed that men are more susceptible to experiencing this side effect, which may be attributed to differences in physiological characteristics, drug metabolism, and hormone levels [12]. Interestingly, it has been observed that opioids, including fentanyl, may induce hiccups. However, in Ardhanari' s case report, it was demonstrated that a low dose of 30 mcg of intravenous fentanyl effectively ceased the occurrence of hiccups [75]. Anaesthetic-related causes of hiccups include the type of anaesthesia, airway management and the use of specific anaesthetic drugs.

3.2. Treatment of hiccups in the perioperative period

3.2.1. Preoperative period

During the preoperative period of the perioperative period, it is of great importance to comprehensively understand the past medical history that may trigger hiccups in advance, pay attention to the emotional state, reasonably arrange the diet and fasting time and prevent hiccups in a timely manner. This is because if hiccups occur during the intraoperative period, more serious consequences may be triggered. For most patients with a relatively good physical condition and without serious underlying diseases, non-pharmacological methods such as psychological intervention [76], dietary management [64] and respiratory training [4] can be the first choice. For patients with high-risk factors for hiccups, such as a history of hiccups, severe gastrointestinal dysfunction, mental illness, etc., non-pharmacological methods alone are not sufficient for effective prevention. It is necessary to use pro-kinetic agents [77], anticholinergic drugs [78], etc. in advance to enhance the preventive effect. If trying multiple methods fails, it has been documented that patients have effectively alleviated hiccups through the implementation of a technique known as sub-occipital release. This procedure entails the application of gentle traction and pressure to the posterior region of the neck, as well as the stretching of the suboccipital muscles and fascia. The proposed mechanism involves the manual decompression of the vagus nerve, and potentially the phrenic nerve, in order to disrupt the hiccup reflex and restore normal autonomic function [79].

3.2.2. Intraoperative period

When hiccups occur during the intraoperative period of the perioperative period, the selection of treatment methods needs to be considered comprehensively based on multiple factors. First and foremost, it is necessary to assess the severity of the condition. If the patient's hiccup symptoms are mild and have little impact on the surgical operation and vital signs, non-drug methods can be tried first. For example, adjusting the patient's position, modifying the ventilation parameters of the ventilator, pausing the surgical operation briefly to observe whether the hiccups can be alleviated. In addition, there are also successful cases of some other slightly more complex non-drug methods, such as increasing the pressure of carbon dioxide in the alveoli [80], lung inflation [81] and acupuncture [82]. An efficacious approach for managing intraoperative hiccups has been previously documented in the literature, involving the stimulation of the pharynx at the C2 and C3 vertebrae through the insertion of a catheter or the application of local anaesthesia-lubricated airway [83]. Nasopharyngeal stimulation appears to be the optimal approach for mitigating the adverse effects of multi-drug therapy and preventing the occurrence of acute hiccups during surgical procedures [84]. In the context of persistent hiccups in the perioperative period, the utilization of ultrasound-guided phrenic nerve block may serve as a viable therapeutic approach in cases where conventional physical and medical interventions prove ineffective [85].

However, if the hiccups are severe or occur during a complex and critical surgical stage, making the surgical operation difficult to carry out or causing significant fluctuations in vital signs, drug treatment should be immediately prioritized (Table 2). Initially, it is common to attempt to inhibit the hiccup reflex by appropriately deepening anaesthesia using general anaesthetics like propofol. Intravenous chlorpromazine (total 5 mg) may be a suitable treatment option for relieving hiccups in patients who cannot be treated with muscle relaxants under general anaesthesia [66]. If the hiccups are suspected to be related to abnormal gastrointestinal peristalsis and changes in gastric pressure, metoclopramide can be selected to relieve smooth muscle spasms [86]. Anticholinergics and muscle relaxants may also be used [67].

It is noteworthy that in cases of hiccups in the perioperative period, when conventional medications such as intravenous anaesthetics, central anti-emetics, muscle relaxants, hormones, etc. prove to be ineffective or result in adverse effects, some other medications can also effectively manage hiccups. Ephedrine appears to be a viable and uncomplicated method for managing refractory hiccups during the perioperative period, but it is linked to cardiovascular adverse effects, including tachycardia and hypertension [87]. The suppression of hiccups in the perioperative period through the use of dexmedetomidine, a selective alpha-2 adrenergic receptor agonist, is anticipated to serve as an alternative to ephedrine, thereby mitigating the associated side effects such as elevated blood pressure [88].

The use of intravenous subanaesthetic doses of lidocaine is a viable alternative treatment option. The potential impact of lidocaine on hiccups is frequently disregarded due to its routine administration prior to propofol to alleviate pain during injection. Propofol itself is known to be associated with hiccups, thus hiccups are preemptively treated under uncertain circumstances, despite the fact that the dosage administered is considerably lower than that used for hiccup treatment [89]. The supporting effect of lidocaine pretreatment on hiccups in the perioperative period is that it can prevent hiccups caused by methohexitol sedation [90]. Cohen reported that lidocaine was administered as a treatment for a patient experiencing intractable hiccups following an exploratory laparotomy. After the failure of various conventional drugs such as phenothiazine and butanophenone for treating hiccup, the administration of two intravenous injections of lidocaine proved to be effective in inhibiting hiccup without any recurrence. The first injection consisted of 1.5 mg/kg of lidocaine on the first day, followed by a second injection of 0.75 mg/kg on the subsequent day [91]. In addition, several case studies have supported the role of lidocaine, especially when administered intravenously within 24 h for anaesthesia-induced hiccups [92,93]. In addition to intravenous administration, alternative methods such as oral 2% lidocaine gel [94], continuous subcutaneous infusion of lidocaine (480 mg(24 ml)/day) [95], and intradermal injection of lidocaine around the sternocleidomastoid muscle to stimulate the vagus nerve [96] have proven to be effective in managing intractable hiccups. This approach may provide valuable guidance for patients who are unable to receive intravenous lidocaine due to either relative or absolute contraindications, and who experience hiccups outside of surgical procedures. Furthermore, a comparative study investigating the efficacy of lidocaine and ephedrine in the management of hiccups determined that the ephedrine group (96%) exhibited a higher success rate in controlling hiccups compared to the lidocaine group (56%). Additionally, the ephedrine group was able to suppress hiccups in a greater proportion of patients within a shorter duration of time. This phenomenon could potentially be associated with the use of ephedrine as a bronchodilator and nocturnal decongestant, or its function as a central stimulant [97]. The precise mechanism through which lidocaine inhibits hiccups remains unclear. Some scholars posit that the intravenous administration of lidocaine has the potential to inhibit calcium channels, stabilize membrane potential, and block sodium channels in sensory neurons. This mechanism of action is believed to reduce neuronal excitability and ectopic discharge, ultimately increasing the nerve excitation threshold at each stage of the hiccup reflex arc. The intended outcome is to prevent the occurrence of hiccups [95,98]. For instance, Weksler confirmed that the administration of lidocaine can effectively prevent methohexitone-induced hiccups during elective dilatation and curettage procedures for uterus evacuation. This finding is attributed to the membrane stability properties exhibited by lidocaine. Lidocaine has the ability to decrease the excitability of all neural structures that are implicated in this reflex [92]. When conventional medications are ineffective or cause adverse reactions in the treatment of perioperative hiccups, intravenous sub-anaesthetic doses of lidocaine can be an alternative. However, it is necessary to strictly adhere to the indications and contraindications of lidocaine. The dosage should be precisely adjusted according to the patient's condition, and adverse reactions should be closely monitored. Attention should also be paid to the interactions between drugs.

3.2.3. Postoperative period

The management of hiccups during the postoperative period of the perioperative period requires an analysis of the underlying causes and consideration of the severity and duration of the hiccups, as well as the overall condition of the patient. Often, a combination of pharmacological and non-pharmacological approaches is used. Depending on the specific circumstances, the selection of the two methods may also have different emphases. If hiccups are caused by factors such as insufficient gastrointestinal motility, dyspepsia, or gastrointestinal flatulence, gastrointestinal prokinetic drugs such as metoclopramide can be tried first. Meanwhile, non-pharmacological methods such as abdominal massage, hot compress, and position adjustment should be combined. For hiccups caused by nerve - related factors such as nerve stimulation during surgery and mental stress, non - pharmacological methods like distraction and acupoint massage can be initially adopted to regulate nerve function. If these methods are ineffective, drugs with central regulatory effects such as chlorpromazine and diazepam can be used. In addition, Lee AR reported three cases of using stellate ganglion block (SGB) to treat persistent postoperative hiccups, including reducing the frequency and intensity of hiccups, and eventually stopping the hiccups completely [99].

4. Conclusions and prospect

This study comprehensively reviews the aetiology and pathogenesis of hiccups. With a focused exploration of perioperative hiccups, we systematically analysed surgical-, anaesthesia- and patient-related etiological factors and mechanisms. We summarized management strategies across preoperative, intraoperative, and postoperative phases, with particular emphasis on emerging evidence supporting lidocaine's therapeutic efficacy in recent years. This review aims to enhance clinical awareness and stimulate scholarly interest in managing this underrecognized perioperative complication.

However, the current understanding remains constrained by predominant reliance on case reports and observational studies, with a critical paucity of robust evidence from controlled clinical trials. Given the unique challenges of perioperative settings, we emphasize the clinical imperative for preoperative risk stratification based on comorbidities and symptomatic evaluation, intraoperative dynamic assessment of hiccup severity with tailored interventions, and postoperative multimodal therapeutic safety protocols. In the future, it is necessary to conduct large-scale prospective studies with standardized diagnostic criteria and quantitative outcome measures. Such investigations are crucial to establish evidence-based management algorithms and optimize clinical outcomes for perioperative hiccup management.

Authors' contributions

Bin Deng and Yaomin Zhu: Conceptualization, Methodology, Funding acquisition. **Jiahui He:** Writing-Original draft preparation and Reviewing. **Ao Guan and Yourui Wang:** Visualization and Investigation. **Tingting Yang and Ling Chen:** Software and Supervision. **Lijuan Fu, Shaoshuang Wang and Haomin Ren:** Validation and Editing.

All authors have read and approved the final work.

Author contributions

CRediT: **Jiahui He**: Methodology, Project administration, Writing – original draft; **Ao Guan**: Resources, Supervision; **Tingting Yang**: Supervision, Validation; **Lijuan Fu**: Formal analysis, Visualization; **Yourui Wang**: Validation, Visualization; **Shaoshuang Wang**: Conceptualization; **Haomin Ren**: Visualization; **Ling Chen**: Conceptualization, Investigation; **Yaomin Zhu**: Validation, Writing – review & editing; **Bin Deng**: Validation, Visualization, Writing – review & editing.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was supported by the General Project of Natural Science Basic Research Program of Shaanxi Province (Program

No. 2023-JC-YB-654), the General Program of China Postdoctoral Science Foundation(Program No. 2023M744105), the Fujian Health Science and Technology program (Program No. 2021GGB038), the Medical 'Basic-Clinical' Integration Innovation Project of Xi'an Jiaotong University (Program No. YXJLRH2022030), the fund of the First Affiliated Hospital of Xi'an Jiaotong University (Program No. 2022MS-26).

Data availability statement

Data sharing not applicable – no new data generated.

References

[1] Chang FY, Lu CL. Hiccup: mystery, nature and treatment. J Neurogastroenterol Motil. 2012;18(2):123–130. doi: 10.5056/jnm.2012.18.2.123.

[2] Gilson I, Busalacchi M. Marijuana for intractable hiccups. Lancet. 1998;351(9098):267. doi: 10.1016/S0140-6736(05)78270-2.

[3] Cymet TC. Retrospective analysis of hiccups in patients at a community hospital from 1995-2000. J Natl Med Assoc. 2002;94(6):480–483.

[4] Steger M, Schneemann M, Fox M. Systemic review: the pathogenesis and pharmacological treatment of hiccups. Aliment Pharmacol Ther. 2015;42(9):1037–1050. doi: 10.1111/apt.13374.

[5] Rey E, Elola-Olaso CM, Rodríguez-Artalejo F, et al. Prevalence of atypical symptoms and their association with typical symptoms of gastroesophageal reflux in Spain. Eur J Gastroenterol Hepatol. 2006;18(9):969–975. doi: 10.1097/01.meg.0000230081.53298.03.

[6] Khorakiwala T, Arain R, Mulsow J, et al. Hiccups: an unrecognized symptom of esophageal cancer? Am J Gastroenterol. 2008;103(3):801. doi: 10.1111/j.1572-0241.2007.01612_4.x.

[7] Itabashi R, Endo K, Saito T, et al. Supratentorial infarcts accompanying hiccup. Brain Behav. 2019;9(11):e01439. doi: 10.1002/brb3.1439.

[8] Porzio G, Aielli F, Verna L, et al. Gabapentin in the treatment of hiccups in patients with advanced cancer: a 5-year experience. Clin Neuropharmacol. 2010;33(4):179–180. doi: 10.1097/WNF.0b013e3181de8943.

[9] Keane JR. Hiccups due to central nervous system disease: analysis of 71 inpatients. Can J Neurol Sci. 2010;37(6):870–872. doi: 10.1017/s0317167100051611.

[10] Ergen M, Arikan F, Fırat Çetin R. Hiccups in cancer patients receiving chemotherapy: a cross-sectional study. J Pain Symptom Manage. 2021;62(3):e85–e90. doi: 10.1016/j.jpainsymman.2021.02.012.

[11] Lee G-W, Kim RB, Go SI, et al. Gender differences in hiccup patients: analysis of published case reports and case-control studies. J Pain Symptom Manage. 2016;51(2):278–283. doi: 10.1016/j.jpainsymman.2015.09.013.

[12] Liu CC, Lu CY, Changchien CF, et al. Sedation-associated hiccups in adults undergoing gastrointestinal endoscopy and colonoscopy. World J Gastroenterol. 2012;18(27):3595–3601. doi: 10.3748/wjg.v18.i27.3595.

[13] Hosoya R, Uesawa Y, Ishii-Nozawa R, et al. Analysis of factors associated with hiccups based on the Japanese Adverse Drug Event Report database. PLoS One. 2017;12(2):e0172057. doi: 10.1371/journal.pone.0172057.

[14] Kolodzik PW, Eilers MA. Hiccups (singultus): review and approach to management. Ann Emerg Med. 1991;20(5):565–573. doi: 10.1016/s0196-0644(05)81620-8.

[15] Howard RS. Persistent hiccups. BMJ. 1992;305(6864):1237–1238. doi: 10.1136/bmj.305.6864.1237.

[16] Rouse S, Wodziak M. Intractable hiccups. Curr Neurol Neurosci Rep. 2018;18(8):51. doi: 10.1007/s11910-018-0856-0.

[17] Wilcox SK, Garry A, Johnson MJ. Novel use of amantadine: to treat hiccups. J Pain Symptom Manage. 2009;38(3):460–465. doi: 10.1016/j.jpainsymman.2008.10.008.

[18] Park MH, Kim BJ, Koh SB, et al. Lesional location of lateral medullary infarction presenting hiccups (singultus). J Neurol Neurosurg Psychiatry. 2005;76(1):95–98. doi: 10.1136/jnnp.2004.039362.

[19] Lee G-W, Oh SY, Kang MH, et al. Treatment of dexamethasone-induced hiccup in chemotherapy patients by methylprednisolone rotation. Oncologist. 2013;18(11):1229–1234. doi: 10.1634/theoncologist.2013-0224.

[20] Gilbar P, McPherson I. Severe hiccups during chemotherapy: corticosteroids the likely culprit. J Oncol Pharm Pract. 2009;15(4):233–236. doi: 10.1177/1078155209102336.

[21] Liaw C-C, Wang C-H, Chang H-K, et al. Cisplatin-related hiccups: male predominance, induction by dexamethasone, and protection against nausea and vomiting. J Pain Symptom Manage. 2005;30(4):359–366. doi: 10.1016/j.jpainsymman.2005.08.008.

[22] Straus C, Vasilakos K, Wilson RJA, et al. A phylogenetic hypothesis for the origin of hiccough. Bioessays. 2003;25(2):182–188. doi: 10.1002/bies.10224.

[23] Bacak BJ, Danner SM. Hiccups are a manifestation of central respiratory arrhythmias. Med Hypotheses. 2023;179:111165. doi: 10.1016/j.mehy.2023.111165.

[24] De Vloo P, Dallapiazza RF, Lee DJ, et al. Long-term relief of intractable hiccups with vagal nerve stimulation. Brain Stimul. 2018;11(6):1385–1387. doi: 10.1016/j.brs.2018.08.002.

[25] Kondo T, Toyooka H, Arita H. Hiccup reflex is mediated by pharyngeal branch of glossopharyngeal nerve in cats. Neurosci Res. 2003;47(3):317–321. doi: 10.1016/s0168-0102(03)00225-6.

[26] Arita H, Oshima T, Kita I, et al. Generation of hiccup by electrical stimulation in medulla of cats. Neurosci Lett. 1994;175(1-2):67–70. doi: 10.1016/0304-3940(94)91079-0.

[27] Kohse EK, Hollmann MW, Bardenheuer HJ, et al. Chronic hiccups: an underestimated problem. Anesth Analg. 2017;125(4):1169–1183. doi: 10.1213/ANE.0000000000002289.

[28] Askenasy JJ. About the mechanism of hiccup. Eur Neurol. 1992;32(3):159–163. doi: 10.1159/000116815.

[29] Nausheen F, Mohsin H, Lakhan SE. Neurotransmitters in hiccups. Springerplus. 2016;5(1):1357. doi: 10.1186/s40064-016-3034-3.

[30] Tovar-Gudiño E, Guevara-Salazar JA, Bahena-Herrera JR, et al. Novel-substituted heterocyclic GABA analogues. enzymatic activity against the GABA-AT enzyme from pseudomonas fluorescens and in silico molecular modeling. Molecules. 2018;23(5):1128. doi: 10.3390/molecules23051128.

[31] Akyuz E, Polat AK, Eroglu E, et al. Revisiting the role of neurotransmitters in epilepsy: an updated review. Life Sci. 2021;265:118826. doi: 10.1016/j.lfs.2020.118826.
[32] Oshima T, Sakamoto M, Tatsuta H, et al. GABAergic inhibition of hiccup-like reflex induced by electrical stimulation in medulla of cats. Neurosci Res. 1998;30(4):287–293. doi: 10.1016/s0168-0102(98)00011-x.
[33] Jacobson PL, Messenheimer JA, Farmer TW. Treatment of intractable hiccups with valproic acid. Neurology. 1981;31(11):1458–1460. doi: 10.1212/wnl.31.11.1458.
[34] Matsuki Y, Mizogami M, Shigemi K. A case of intractable hiccups successfully treated with pregabalin. Pain Phys. 2014;2;17(2;3):E241–E242. doi: 10.36076/ppj.2014/17/E241.
[35] Baumann A, Weicker T, Alb I, et al. Baclofen for the treatment of hiccup related to brainstem compression. Ann Fr Anesth Reanim. 2014;33(1):e27-8–e28. doi: 10.1016/j.annfar.2013.10.023.
[36] Turkyilmaz A, Eroglu A. Use of baclofen in the treatment of esophageal stent-related hiccups. Ann Thorac Surg. 2008;85(1):328–330. doi: 10.1016/j.athoracsur.2007.07.059.
[37] Wilcock A, Twycross R. Midazolam for intractable hiccup. J Pain Symptom Manage. 1996;12(1):59–61. doi: 10.1016/0885-3924(96)00051-6.
[38] Tintner R, Jankovic J. Dopamine agonists in Parkinson's disease. Expert Opin Investig Drugs. 2003;12(11):1803–1820. doi: 10.1517/eoid.12.11.1803.21881.
[39] Grace AA. Dysregulation of the dopamine system in the pathophysiology of schizophrenia and depression. Nat Rev Neurosci. 2016;17(8):524–532. doi: 10.1038/nrn.2016.57.
[40] Bagheri H, Cismondo S, Montastruc JL. Drug-induced hiccup: a review of the France pharmacologic vigilance database Therapie. 1999;54(1):35–39.
[41] Coletti Moja M. Hiccups associated with non-ergoline dopamine agonists in Parkinson's disease. Mov Disord. 2010;25(9):1292–1292. doi: 10.1002/mds.23056.
[42] Lertxundi U, Marquínez AC, Domingo-Echaburu S, et al. Hiccups in Parkinson's disease: an analysis of cases reported in the European pharmacovigilance database and a review of the literature. Eur J Clin Pharmacol. 2017;73(9):1159–1164. doi: 10.1007/s00228-017-2275-6.
[43] Lester J, Raina GB, Uribe-Roca C, et al. Hiccup secondary to dopamine agonists in Parkinson's disease. Mov Disord. 2007;22(11):1667–1668. doi: 10.1002/mds.21583.
[44] Artigas F. Serotonin receptors involved in antidepressant effects. Pharmacol Ther. 2013;137(1):119–131. doi: 10.1016/j.pharmthera.2012.09.006.
[45] Nishikawa T, Araki Y, Hayashi T. Intractable hiccups (singultus) abolished by risperidone, but not by haloperidol. Ann Gen Psychiatry. 2015;14(1):13. doi: 10.1186/s12991-015-0051-5.
[46] Schmid K, Böhmer G, Merkelbach S. Serotonergic control of phrenic motoneuronal activity at the level of the spinal cord of the rabbit. Neurosci Lett. 1990;116(1-2):204–209. doi: 10.1016/0304-3940(90)90411-2.
[47] Alderfer BS, Arciniegas DB. Treatment of intractable hiccups with olanzapine following recent severe traumatic brain injury. J Neuropsychiatry Clin Neurosci. 2006;18(4):551–552. doi: 10.1176/appi.neuropsych.18.4.551.
[48] Musumeci A, Cristofori L, Bricolo A. Persistent hiccup as presenting symptom in medulla oblongata cavernoma: a case report and review of the literature. Clin Neurol Neurosurg. 2000;102(1):13–17. doi: 10.1016/s0303-8467(99)00058-x.
[49] Takahashi T, Murata T, Omori M, et al. Successful treatment of intractable hiccups with serotonin (5-HT)1A receptor agonist. J Neurol. 2004;251(4):486–487. doi: 10.1007/s00415-004-0377-4.
[50] Reimold M, Solbach C, Noda S, et al. Occupancy of dopamine D(1), D (2) and serotonin (2A) receptors in schizophrenic patients treated with flupentixol in comparison with risperidone and haloperidol. Psychopharmacology (Berl). 2007;190(2):241–249. doi: 10.1007/s00213-006-0611-0.
[51] Davies MA, Sheffler DJ, Roth BL. Aripiprazole: a novel atypical antipsychotic drug with a uniquely robust pharmacology. CNS Drug Rev. 2004;10(4):317–336. doi: 10.1111/j.1527-3458.2004.tb00030.x.
[52] Caloro M, Pucci D, Calabrò G, et al. Development of hiccup in male patients hospitalized in a psychiatric ward: is it specifically related to the aripiprazole-benzodiazepine combination? Clin Neuropharmacol. 2016;39(2):67–72. doi: 10.1097/WNF.0000000000000129.
[53] Silverman MA, Leung JG, Schak KM. Reply to: comment on: aripiprazole-associated hiccups: a case and closer look at the association between hiccups and antipsychotics. J Pharm Pract. 2015;28(2):134–134. doi: 10.1177/0897190014568680.
[54] Carbone MG, Tagliarini C, Della Rocca F, et al. Protracted hiccups induced by aripiprazole and regressed after administration of gabapentin. Case Rep Psychiatry. 2021;2021:5567152. doi: 10.1155/2021/5567152.
[55] Jovanovic P, Wang Y, Vit J-P, et al. Sustained chemogenetic activation of locus coeruleus norepinephrine neurons promotes dopaminergic neuron survival in synucleinopathy. PLoS One. 2022;17(3):e0263074. doi: 10.1371/journal.pone.0263074.
[56] Maréchal R, Berghmans T, Sculier P. Successful treatment of intractable hiccup with methylphenidate in a lung cancer patient. Support Care Cancer. 2003;11(2):126–128. doi: 10.1007/s00520-002-0411-y.
[57] Stueber D, Swartz CM. Carvedilol suppresses intractable hiccups. J Am Board Fam Med. 2006;19(4):418–421. doi: 10.3122/jabfm.19.4.418.
[58] Parvin R, Milo R, Klein C, et al. Amitriptyline for intractable hiccup. Am J Gastroenterol. 1988;83(9):1007–1008.
[59] Vaidya V. Sertraline in the treatment of hiccups. Psychosomatics. 2000;41(4):353–355. doi: 10.1176/appi.psy.41.4.353.
[60] Wang J, Zhu Q, Zhang S, et al. Observation of clinical efficacy of anisodamine and chlorpromazine in the treatment of intractable hiccup after stroke. Biomed Res Int. 2022;2022:6563193. doi: 10.1155/2022/6563193.
[61] Branco ACCC, Yoshikawa FSY, Pietrobon AJ, et al. Role of histamine in modulating the immune response and inflammation. Mediators Inflamm. 2018;2018:9524075–9524010. doi: 10.1155/2018/9524075.
[62] Petroianu G, Hein G, Petroianu A, et al. Idiopathic chronic hiccup: combination therapy with cisapride,

omeprazole, and baclofen. Clin Ther. 1997;19(5):1031–1038. doi: 10.1016/s0149-2918(97)80055-0.

[63] Brouillette RT, Thach BT, Abu-Osba YK, et al. Hiccups in infants: characteristics and effects on ventilation. J Pediatr. 1980;96(2):219–225. doi: 10.1016/s0022-3476(80)80806-7.

[64] Tey HK, Talley NJ. Use of cricoid pressure to facilitate gastric insufflation and stop hiccoughs during gastroscopy. Gastrointest Endosc. 1996;44(6):760–761. doi: 10.1016/s0016-5107(96)70076-7.

[65] McVey FK, Goodman NW. Gastro-oesophageal reflux and hiccough on induction of anaesthesia. Anaesthesia. 1992;47(8):712–712. doi: 10.1111/j.1365-2044.1992.tb02400.x.

[66] Shimada K, Inokuchi R, Tominaga K, et al. Effective treatment of intraoperative hiccups with chlorpromazine under general anesthesia without muscle relaxants: a case report. A A Pract. 2022;16(6):e01597. doi: 10.1213/XAA.0000000000001597.

[67] Canonica S, Eze R, Carlen F, et al. Chronic hiccups: diagnosis and treatment. Rev Med Suisse. 2024;20(874):991–995. doi: 10.53738/REVMED.2024.20.874.991.

[68] Krahn A, Penner SB. Use of baclofen for intractable hiccups in uremia. Am J Med. 1994;96(4):391. doi: 10.1016/0002-9343(94)90074-4.

[69] Boyer T, Sigaut S, Puybasset L, et al. From preoperative evaluation to stroke center: management of postoperative acute ischemic stroke. Anaesth Crit Care Pain Med. 2016;35(4):299–305. doi: 10.1016/j.accpm.2015.11.007.

[70] Kyogoku M, Inata Y, Takeuchi M. Ventilator-induced hiccups. J Pediatr. 2017;189:238. doi: 10.1016/j.jpeds.2017.06.065.

[71] Kanaya N, Nakayama M, Kanaya J, et al. Atropine for the treatment of hiccup after laryngeal mask insertion. Anesth Analg. 2001;93(3):791–792. doi: 10.1097/00000539-200109000-00047.

[72] Bapat P, Joshi RN, Young E, et al. Comparison of propofol versus thiopentone with midazolam or lidocaine to facilitate laryngeal mask insertion. Can J Anaesth. 1996;43(6):564–568. doi: 10.1007/BF03011767.

[73] Fass R, Higa L, Kodner A, et al. Stimulus and site specific induction of hiccups in the oesophagus of normal subjects. Gut. 1997;41(5):590–593. doi: 10.1136/gut.41.5.590.

[74] Kanniah SK. Acute transient hiccups after epidural injection of levobupivacaine. Int J Obstet Anesth. 2009;18(2):193–194. doi: 10.1016/j.ijoa.2008.12.004.

[75] Ardhanari A. Intravenous fentanyl as the treatment for intraoperative hiccups: a case report. Agri. 2018;30(1):38. doi: 10.5505/agri.2017.33603.

[76] Al-Mahrouqi T, Al-Sabahi F, Al-Harrasi A, et al. Psychogenic hiccups in an older adult: a case report and literature review. J Taibah Univ Med Sci. 2023;18(3):560–565. doi: 10.1016/j.jtumed.2022.10.017.

[77] Hiyama T, Yoshihara M, Tanaka S, et al. Effectiveness of prokinetic agents against diseases external to the gastrointestinal tract. J Gastroenterol Hepatol. 2009;24(4):537–546. doi: 10.1111/j.1440-1746.2009.05780.x.

[78] García Callejo FJ, Redondo Martínez J, Pérez Carbonell T, et al. Hiccups. attitude in otorhinolaryngology towards consulting patients. A diagnostic and therapeutic approach. Acta Otorrinolaringol Esp. 2017;68(2):98–105. doi: 10.1016/j.otoeng.2017.02.005.

[79] Kwan CS, Worrilow CC, Kovelman I, et al. Using suboccipital release to control singultus: a unique, safe, and effective treatment. Am J Emerg Med. 2012;30(3):514.e5-7–514.e7. doi: 10.1016/j.ajem.2011.01.012.

[80] Lavernhe, Bisquerra. Carbon dioxide; medication of hiccups during anesthesia. Afr Fr Chir. 1948;4(7-8): 163.

[81] Baraka A. Inhibition of hiccup by pulmonary inflation. Anesthesiology. 1970;32(3):271–273. doi: 10.1097/00000542-197003000-00020.

[82] Wang B. Eighty cases of intractable hiccup treated by acupuncture. Zhongguo Zhen Jiu. 2011;31(2):181–182.

[83] Salem MR. An effective method for the treatment of hiccups during anesthesia. Anesthesiology. 1967;28(2):463–464. doi: 10.1097/00000542-196703000-00036.

[84] Orlovich DS, Brodsky JB, Brock-Utne JG. Nonpharmacologic management of acute singultus (Hiccups). Anesth Analg. 2018;126(3):1091–1091. doi: 10.1213/ANE.0000000000002789.

[85] Renes SH, van Geffen GJ, Rettig HC, et al. Ultrasound-guided continuous phrenic nerve block for persistent hiccups. Reg Anesth Pain Med. 2010;35(5):455–457. doi: 10.1097/aap.0b013e3181e8536f.

[86] Madanagopolan N. Metoclopramide in hiccup. Curr Med Res Opin. 1975;3(6):371–374. doi: 10.1185/03007997509114789.

[87] Sohn YZ, Conrad LJ, Katz RL. Hiccup and ephedrine. Can Anaesth Soc J. 1978;25(5):431–432. doi: 10.1007/BF03006576.

[88] Koteswara CM, Dubey JK. Management of laryngeal mask airway induced hiccups using dexmedetomedine. Indian J Anaesth. 2013;57(1):85. doi: 10.4103/0019-5049.108583.

[89] Krishnakumar M, Srinivasaiah B, Naik SS, et al. Propofol-induced hiccups in MRI suite treated with dexmedetomidine. Saudi J Anaesth. 2023;17(3):450–451. doi: 10.4103/sja.sja_816_22.

[90] Landers C, Turner D, Makin C, et al. Propofol associated hiccups and treatment with lidocaine. Anesth Analg. 2008;107(5):1757–1758. doi: 10.1213/ane.0b013e3181853605.

[91] Cohen SP, Lubin E, Stojanovic M. Intravenous lidocaine in the treatment of hiccup. South Med J. 2001;94(11):1124–1125. doi: 10.1097/00007611-200111000-00018.

[92] Weksler N, Stav A, Ovadia L, et al. Lidocaine pretreatment effectively decreases the incidence of hiccups during methohexitone administration for dilatation and curettage. Acta Anaesthesiol Scand. 1992;36(8):772–774. doi: 10.1111/j.1399-6576.1992.tb03562.x.

[93] Dunst MN, Margolin K, Horak D. Lidocaine for severe hiccups. N Engl J Med. 1993;329(12):890–891. doi: 10.1056/NEJM199309163291222.

[94] Neuhaus T, Ko YD, Stier S. Successful treatment of intractable hiccups by oral application of lidocaine. Support Care Cancer. 2012;20(11):3009–3011. doi: 10.1007/s00520-012-1533-5.

[95] Kaneishi K, Kawabata M. Continuous subcutaneous infusion of lidocaine for persistent hiccup in advanced cancer. Palliat Med. 2013;27(3):284–285. doi: 10.1177/0269216312448508.

[96] Kocak AO, Akbas I, Betos Kocak M, et al. Intradermal injection for hiccup therapy in the Emergency Department. Am J Emerg Med. 2020;38(9):1935–1937. doi: 10.1016/j.ajem.2020.03.044.
[97] Bahadoori A, Shafa A, Ayoub T. Comparison the effects of ephedrine and lidocaine in treatment of intraoperative hiccups in gynecologic surgery under sedation. Adv Biomed Res. 2018;7:146. doi: 10.4103/abr.abr_82_18.
[98] Boulouffe C, Vanpee D. Severe hiccups and intravenous lidocaine. Acta Clin Belg. 2007;62(2):123–125. doi: 10.1179/acb.2007.021.
[99] Lee AR, Cho YW, Lee JM, et al. Treatment of persistent postoperative hiccups with stellate ganglion block: three case reports. Medicine (Baltimore). 2018;97(48):e13370.), doi: 10.1097/MD.0000000000013370.
[100] Zingale A, et al. Distal posterior inferior cerebellar artery saccular and giant aneurysms: report of two new cases and a comprehensive review of the surgically-treated cases. J Neurosurg Sci. 1994;38(2):93–104.
[101] Inami K, Tsutsumi S, Asagiri H, et al. Recurrent hiccups associated with ipsilateral intracerebral hemorrhage and chronic subdural hematoma with immediate resolutions after evacuations. Radiol Case Rep. 2024;19(10):4610–4613. doi: 10.1016/j.radcr.2024.07.081.
[102] Puppala S, et al. Dorsal medullary cavernous hemangioma presenting as obstinate hiccups and its surgical treatment: illustrative case. J Neurosurg Case Lessons. 2023;5(10):83–88.
[103] Muñoz-Zúñiga JR, Tamayo-Delgado ADM, Shinchi-Tanaka AM, et al. Postrema area syndrome in the context of systemic lupus erythematosus: case report. Heliyon. 2025;11(1):e40614. doi: 10.1016/j.heliyon.2024.e40614.
[104] Tay SS, Yadav RR. Novel use of baclofen in cancer patients for the treatment of hiccups. Ann Acad Med Singap. 2010;39(2):154–154. doi: 10.47102/annals-acadmedsg.V39N2p154.
[105] Shibahara T, Yamanaka K, Matsuoka M, et al. A case of neuromyelitis optica spectrum disorder complicated with aquaporin-4-antibody-associated organizing pneumonia. Mult Scler. 2025;24(7):112–156. doi: 10.1177/13524585241310397.
[106] Misu T, Fujihara K, Nakashima I, et al. Intractable hiccup and nausea with periaqueductal lesions in neuromyelitis optica. Neurology. 2005;65(9):1479–1482. doi: 10.1212/01.wnl.0000183151.19351.82.
[107] Sampath V, Gowda MR, Vinay HR, et al. Persistent hiccups (singultus) as the presenting symptom of lateral medullary syndrome. Indian J Psychol Med. 2014;36(3):341–343. doi: 10.4103/0253-7176.135397.
[108] Alan S, Vural SN, Aliefendioglu D, et al. A case of early infantile epileptic encephalopathy due to KCNQ2 gene mutation presenting with episodes of hiccups. Cureus. 2022;14(12):e33164. doi: 10.7759/cureus.33164.
[109] Redondo-Cerezo E, Viñuelas-Chicano M, Pérez-Vigara G, et al. A patient with persistent hiccups and gastro-oesophageal reflux disease. Gut. 2008;57(6):763, 771–763. doi: 10.1136/gut.2007.119347.
[110] Félix-Téllez FA, Jiménez-Castillo RA, Remes-Troche JM. Identifying the hiccup-induced esophagogastric waveform: a case series report using high-resolution manometry. ACG Case Rep J. 2024;11(10):e01541. doi: 10.14309/crj.0000000000001541.
[111] Senior A, Hari C. A rare case of acute on chronic gastric volvulus with Borchardt's triad. J Surg Case Rep. 2014;2014(11):1–3.
[112] Yang Q, Shang Q, Wei GQ, et al. Jinghuaweikang capsules combined with Quadruple therapy in the treatment of Helicobacter pylori infection: a multicenter, randomized, controlled, clinical study. Zhonghua Yi Xue Za Zhi. 2019;99(4):295–300. doi: 10.3760/cma.j.issn.0376-2491.2019.04.012.
[113] Kumar S, Sharma P, Muthu R, et al. Management of empyema of gallbladder with percutaneous cholecysto-duodenal stenting in a case of hilar cholangiocarcinoma treated with common bile duct metallic stenting. Indian J Radiol Imaging. 2011;21(4):298–300. doi: 10.4103/0971-3026.90695.
[114] Hopkins C, Bansari A, Ladna M, et al. Prolonged intractable hiccups associated with HSV (I&II) esophagitis and H. pylori gastritis. Case Rep Infect Dis. 2023. 2023;2023:3561895.
[115] Muraki N, Asahina K, Hori K, et al. Intra-abdominal abscess caused by mycobacteroides abscessus in a peritoneal dialysis patient: a case report. Intern Med. 2024;10(8):232–236. doi: 10.2169/internalmedicine.4048-24.
[116] Cotoi S, Moldovan D, Georgescu C. Diaphragmatic action potentials recorded on standard electrocardiogram. A clinical and experimental study. Med Interne. 1982;20(4):267–269.
[117] Ramrattan A, Aguilar C. Hiccups: an atypical manifestation of miliary tuberculosis and myocardial ischemia. Cureus. 2024;16(2): p:e53595. doi: 10.7759/cureus.53595.
[118] Jolobe OMP. Liver abscess with hiccups and the potential association with pericarditis and colorectal cancer. QJM. 2021;114(6):431–432. doi: 10.1093/qjmed/hcaa006.
[119] Karakonstantis S, Pitsigavdaki S, Korela D, et al. Lower lobe pneumonia presenting as singultus (hiccups). Caspian J Intern Med. 2018;9(4):403–405. doi: 10.22088/cjim.9.4.403.
[120] Patiño-Galeana JL, Reveles-García MP, Niño-Rodríguez CM, et al. Spontaneous pneumomediastinum associated with severe and persistent episode of hiccups. Bol Med Hosp Infant Mex. 2021;78(5):485–488. doi: 10.24875/BMHIM.20000332.
[121] Perry S, Stevenson J. An unusual cause of hiccups. J Accid Emerg Med. 1996;13(5):361–362. doi: 10.1136/emj.13.5.361.
[122] Teles LMF, Neto ID, Macedo BLF, et al. Intractable hiccups as the presenting symptom of toxic nodular goiter. Porto Biomed J. 2018;3(3):e19. doi: 10.1016/j.pbj.0000000000000019.
[123] Hayashi Y, Ueda N, Shibata H, et al. Clinical characteristics of intractable or persistent hiccups and nausea associated with herpes zoster. Clin Neurol Neurosurg. 2021;207:106751. doi: 10.1016/j.clineuro.2021.106751.
[124] Sueyoshi S, Shin B, Nakashima T. [Repeated syncope episodes caused by intractable hiccups; a case report]. Nihon Jibiinkoka Gakkai Kaiho. 2013;116(10):1120–1125. doi: 10.3950/jibiinkoka.116.1120.

[125] Khatri S, Hannurkar P. Understanding and treating laryngeal mask airway-induced intraoperative hiccups. Cureus. 2024;16(9):e69782. doi: 10.7759/cureus.69782.
[126] Sadiq AM, Raza FM, Abdulrahimu YR, et al. Idiopathic fibrosing mediastinitis with esophageal varices: a case report. Heliyon. 2023;9(5):e15780. doi: 10.1016/j.heliyon.2023.e15780.
[127] Lee AF, Lee HW, Yen ZS. Persistent hiccups as a rare presenting symptom of empyema: a case report. Int J Emerg Med. 2024;17(1):29. doi: 10.1186/s12245-024-00603-7.
[128] Hong MK, Han AY, Long JL. Intractable hiccups caused by diaphragmatic eventration. Cureus. 2022;14(4):e24430. doi: 10.7759/cureus.24430.
[129] Neumann M, Lazo KG, Stover D. Sarcoidosis presenting as hiccups. Respirol Case Rep. 2020;8(6):e00605. doi: 10.1002/rcr2.605.
[130] Yoshida Y, Nakajima Y, Tokuda K, et al. Recurrent hiccups caused by malposition of the peritoneal catheter of a lumboperitoneal shunt: a case report. No Shinkei Geka. 2016;44(2):129–133. doi: 10.11477/mf.1436203243.
[131] Arroyo-Cózar M, Grau Delgado J, Gabaldón Conejos T. Hiccups induced by midazolam during sedation in flexible bronchoscopy. Arch Bronconeumol. 2012;48(3):103. doi: 10.1016/j.arbr.2011.11.007.
[132] Parlak M, Sancak T, Arat M, et al. Tunneled catheters placed in bone marrow transplant patients: radiological and clinical follow-up results. Diagn Interv Radiol. 2006;12(4):190–194.
[133] Tammineedi SN, Singla R, Cornejo Leon M, et al. Unforeseen effects: hiccups unveiled by high-dose steroids in demyelination. eNeurologicalSci. 2024;35:100509. doi: 10.1016/j.ensci.2024.100509.
[134] Xausa G, Escher M, Singovski S, et al. Recurrent persistent hiccups on opioid treatment: a case report and literature review. J Pain Palliat Care Pharmacother. 2023;37(1):82–90. doi: 10.1080/15360288.2022.2157070.
[135] Garcia Ramos J, Cobian Solorio A. On the glottal activity of experimental hiccup. Arch Med Res. 1995;26(2):155–161.
[136] Ehret CJ, Le-Rademacher JG, Martin N, et al. Dexamethasone and hiccups: a 2000-patient, telephone-based study. BMJ Support Palliat Care. 2024;13(e3):e790–e793. doi: 10.1136/bmjspcare-2021-003474.
[137] Surendiran A, Krishna Kumar D, Adithan C. Azithromycin-induced hiccups. J Postgrad Med. 2008;54(4):330–331. doi: 10.4103/0022-3859.43521.
[138] Wu B, Ling Y, Zhang C, et al. Risk factors for hiccups after deep brain stimulation of subthalamic nucleus for Parkinson's disease. Brain Sci. 2022;12(11):1447. doi: 10.3390/brainsci12111447.
[139] Harris J, Smith T, Preis J. Intractable hiccups due to herpetic esophagitis in an immunocompromised patient. IDCases. 2016;4:34–37. doi: 10.1016/j.idcr.2016.01.001.
[140] Barry M, Traoré FA, Sako FB, et al. Ebola outbreak in Conakry, Guinea: epidemiological, clinical, and outcome features. Med Mal Infect. 2014;44(11-12):491–494. doi: 10.1016/j.medmal.2014.09.009.
[141] Hasebe M, et al. Asymptomatic meningitis diagnosed by positron emission tomography in a patient with syndrome of inappropriate antidiuretic hormone secretion: a case report. J Med Case Rep. 2021;15(1):390.
[142] Pandey PK, Pandey D, Andrews R. Hiccups and acute symptomatic hyponatremia: a rare manifestation of COVID-19. Cureus. 2022;14(4):e24090. doi: 10.7759/cureus.24090.
[143] Nguyen V, Deeb K, Rathakrishnan R. Hiccups: you got to be kidney me!. SAGE Open Med Case Rep. 2020;8:2050313x20962641. doi: 10.1177/2050313X20962641.
[144] Yuvaraj A, Abraham G, Kurien A, et al. A maintenance hemodialysis diabetic patient with unexplained pulmonary and gastrointestinal involvement. Hemodial Int. 2016;20(1):E12–5. doi: 10.1111/hdi.12337.
[145] Got T, Vivas L, Fan C, et al. Treatment of hiccups in stroke rehabilitation with gabapentin: A case series and focused clinical review. Topics in Stroke Rehabilitation. 2021;28(6):475–480. doi: 10.1080/10749357.2020.1834274
[146] Emekli AS, Hanagasi HA. Dopamine Agonist-Associated Hiccup in Parkinson's Disease: A Case Report. Noro Psikiyatr Ars. 2021;58(3):253–254. doi: 10.29399/npa.23625
[147] Bilgiç A. Possible Sertraline-Induced Hiccups in a Boy With Obsessive-Compulsive Disorder and Attention-Deficit/Hyperactivity Disorder. Clin Neuropharmacol. 2019;42(1):17–18. doi: 10.1097/WNF.0000000000000311