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Ketamine for Intractable Singultus: A Case Report

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Introduction: Singultus, or hiccups, are typically self-limited but may become persistent or intractable (lasting over 48 hours), leading to significant distress that may result in a visit to the emergency department (ED). When traditional treatments fail, management becomes exceptionally challenging. This case report presents a novel therapeutic option using low-dose ketamine for intractable singultus.

Case Report: A 39-year-old man presented to the ED with five days of persistent singultus secondary to lower-lobe pneumonia. The patient failed an extensive course of conventional pharmacologic therapies, including chlorpromazine, antihistamines, benzodiazepines, and antiemetics. Ultimately, a low-dose intravenous injection of ketamine was administered over two minutes, which achieved immediate and complete cessation of the symptoms.

Conclusion: Managing intractable singultus in the ED remains a challenge, with limited and inconsistently effective therapeutic options. This case demonstrates that low-dose ketamine may serve as a rapid, practical, and effective rescue therapy. Further research is warranted to define indications for use, determine efficacy and safety, and delineate an optimal dosing strategy. [Clin Pract Cases Emerg Med. 2026;X(X):XXX–XXX.]

Keywords: *singultus; hiccups; ketamine; emergency medicine; case report.*

INTRODUCTION

Singultus - defined as sudden, involuntary contractions of the diaphragm and intercostal muscles immediately followed by abrupt glottic closure - produces the characteristic "hic" sound as air rushes into the lungs.[1-2] Singultus is classified by duration: self-limited episodes resolve spontaneously; persistent hiccups last more than 48 hours; and intractable hiccups may persist beyond one to two months.[1,3]

The pathophysiology of singultus involves a reflex arc with both peripheral and central components.[1,4] The peripheral limb includes the phrenic nerve which innervates the diaphragm, vagus nerve, and sympathetic chain from the sixth to twelfth thoracic level.[1,4] The central component involves modulation in the brainstem, particularly the medulla, with additional input from the hypothalamus and temporal lobe.[1,5] Any irritation along this pathway, whether mechanical, chemical, inflammatory, or neoplastic, can induce singultus.[1]

Persistent singultus can represent a significant deterioration in quality of life, and various etiologies may affect multiple organ systems, some with serious underlying pathology. Central causes include cerebral ischemia (particularly medullary or pontine lesions), space-occupying lesions, and trauma.[5-6] In rare cases, singultus may be the initial presentation of underlying neurological pathology, including lesions of the medulla oblongata.[7] Peripheral causes most commonly include gastric distention and gastroesophageal reflux disease and less commonly myocardial ischemia, tumors compressing the phrenic or vagus nerves, and diaphragmatic irritation.[8] Metabolic disturbances, medications (including anti-parkinsonian drugs,

anesthetics, steroids, and chemotherapy), and infections can also precipitate singultus.[4]

CASE REPORT

A 39-year old man without any significant past medical history presented to the emergency department (ED) complaining of 5 days of persistent singultus associated with cough, body aches, and subjective fever. Chest radiography was notable for a left lower-lobe consolidation, and he was diagnosed with community acquired pneumonia. The singultus was initially treated with chlorpromazine 25 mg intramusclar (IM) which resulted in the complete resolution of his symptoms. The patient was discharged with a prescription for antibiotics, however, he returned to the ED several hours later due to recurrent singultus.

During the second encounter, the patient was noted to have persistent singultus with episodes occuring every few seconds. The patient reported the episodes were causing significant emotional distress. Diagnostic testing which included a complete blood count, comprehensive metabolic panel, serum lactic acid, troponin, and electrocardiogram were remarkable only for a mild leukocytosis, 13.9 x 10^3/uL [4.0-11.0 x 10^3/uL]. Despite receiving additional doses of chorpromazine 50 mg IM, famotidine 40 mg per os (PO), aluminum hydroxide-magnesium hydroxide-simethicone 30 mL PO, diphenhydramine 25 mg intravenous (IV), midazolam 2 mg IV, 1 L normal saline IV, ceftriaxone 1 g IV, azithromycin 500 mg IV, and prochlorperazine edisylate 10 mg IV, the singultus persisted. Eventually, an injection of ketamine (0.25 mg/kg) over 2 minutes was administered which resulted in the immediate cessation of the singultus.

The patient was subsequently discharged with a referral to a primary care physician. A review of the electronic health record showed no return visits for recurrent singultus to the primary health system within 72 hours of ketamine administration; however, this does not exclude a return visit to an outside facility, and longer-term outcome data were not available.

CPC-EM Capsule

What do we already know about this clinical entity?
Intractable hiccups often resist chlorpromazine, the only Food and Drug Administration-approved agent, and other therapies with inconsistent success.

What makes this presentation of disease reportable?
Ketamine resolved refractory post-pneumonia hiccups after chlorpromazine, antihistamines, benzodiazepines, and antiemetics all failed.

What is the major learning point?
Low-dose intravenous ketamine may rapidly and completely terminate refractory singultus when standard first-line agents have failed.

How might this improve emergency medicine practice?
Ketamine offers physicians a practical rescue option for refractory hiccups beyond current standard therapy.

DISCUSSION

Persistent or intractable singultus may prompt ED evaluation given its impact on sleep, emotional well-being, and quality of life.[1,3] Most episodes resolve spontaneously and rarely require medical attention. However, singultus lasting more than 48 hours are more likely to be associated with underlying pathology. Intractable singultus may persist for weeks to months and are often refractory to standard therapies.[3]

Peripheral causes are more common and encompass a broad range of thoracic and abdominal processes. Pulmonary pathology, particularly lower-lobe pneumonia as was likely the causative etiology in our patient, may provoke singultus through inflammation of the diaphragmatic pleura or irritation of the phrenic nerve, thereby activating the afferent limb of the reflex arc.[7-8] Other factors such as persistent coughing and mechanical diaphragmatic irritation may further contribute to afferent limb activation. Prior literature has noted that singultus may occasionally serve as an initial symptom of underlying thoracic disease, highlighting the importance of identifying and treating the underlying cause rather than focusing solely on symptom management.[9]

The treatment of intractable singultus remains challenging due to limited evidence guiding therapeutic management. Dopamine antagonists such as chlorpromazine, metoclopramide, and haloperidol are commonly used. However, chlorpromazine is the only medication approved by the Food and Drug Administration for hiccups.[9] Other agents, such as baclofen and gabapentin, target the gamma-aminobutyric acid (GABA) pathway and have been used in refractory cases.[10] Despite these options, treatment response remains inconsistent, and no single agent has demonstrated consistent efficacy across patient populations.[10]

Although ketamine has been infrequently used as a treatment for refractory singultus, it offers a potential therapeutic option in refractory cases. Prior studies have reported the use of ketamine in the postoperative period when traditional treatments were ineffective, although this has not been described or expanded upon in nearly 50 years.[11-12] One proposed mechanism is ketamine's noncompetitive N-methyl-D-aspartic acid receptor antagonism and its modulation of

neurotransmitters involved in reflex regulation, including glutamate, dopamine, and GABA.[13-14] Through its effects on central neurotransmitter networks, ketamine may act on central pathways involved in the singultus reflex, leading to symptom resolution.[14]

In this case, a low dose of ketamine resulted in immediate resolution of intractable singultus after failure of multiple pharmacologic agents, including chlorpromazine, famotidine, antacids, diphenhydramine, midazolam, and prochlorperazine. The decision to trial ketamine was guided by extrapolation from its established use in analgesia and procedural sedation, along with the treating team's familiarity with prior literature describing ketamine for refractory singultus. The rapid response following the administration of ketamine suggests a therapeutic effect rather than spontaneous resolution, however, the effects of medications given prior to the injection of ketamine are unknown. Given ketamine's widespread availability and familiarity among emergency physicians, it may offer a practical rescue therapy for refractory singultus in the ED setting, although more research is warranted to determine efficacy.

CONCLUSION

Persistent or intractable singultus can cause significant emotional distress and frequently results in an ED visit. Singultus may arise from a broad range of etiologies, including central nervous system, cardiothoracic, infectious, metabolic, and inflammatory conditions. In this case it is likely the patient's singultus arose secondary to diaphragmatic irritation from a left lower lobe pneumonia. Therapeutic options for refractory cases remain limited and are inconsistently effective. This case demonstrates that low-dose ketamine may provide rapid and effective symptom resolution after failure of conventional therapies and offers an additional rescue therapy for refractory singultus. Further research aimed at expanding ketamine's clinical indications to include refractory singultus as well as safety and efficacy, optimal dosing strategies, and treatment failure rates is warranted.

Patient consent has been obtained and filed for the publication of this case report.

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