

Case Report

40-year-old male presents to the emergency department complaining of hiccups for the past year. Patient states the hiccups used to occur intermittently a couple times a week but over the past several weeks have become constant. The patient denies any pain but says the hiccups are very bothersome and make it difficult for the patient to eat and sleep. He recently discovered that self-induced vomiting will make the hiccups subside for several hours and hence the patient has been self-inducing vomiting multiple times a day for the past several days. The patient has a past medical history of HIV and is on HAART therapy. On exam the patient's vitals are within normal limits, he is well-appearing, and only notable for constant hiccups throughout the interview and exam. The patient was given one dose of **chlorpromazine 25 mg orally** with cessation of his hiccups in the emergency department and discharged home with follow-up.

Clinical Question

What is the current evidence behind the treatment of intractable hiccups in adults?

Background

Hiccups, or singultus, is an uncommon presenting complaint to the emergency department. The name comes from the unique sound made from a sudden, involuntary, spastic contraction of the diaphragm and inspiratory respiratory muscles as well as sudden closure of the glottis. Generally, **hiccups will resolve on their own, but if they last longer than 48 hours are considered persistent and if greater than one month are considered intractable.** Each individual generally has a constant rate of hiccups anywhere from four to 60 a minute. Although not life-threatening, hiccups can be a significant factor in quality of life and ability to eat, drink, and sleep. Many different causes for hiccups have been identified including **gastric distention, alcohol consumption, carbonated beverages, very hot or very cold drinks, stress, anxiety, advanced cancers, lesions of the central nervous system, drug-induced especially benzodiazepines and corticosteroids, infectious, and idiopathic.** Several different treatments for hiccups have been suggested including medications such as **chlorpromazine, metoclopramide, and baclofen, as well as pharyngeal stimulation, ocular pressure, and acupuncture** [1].

Evidence:

- **Most of the current evidence is based on single patient case reports or small observational studies that do not compare treatment to placebo.**
- A Cochrane review published in 2013 aimed to look at the evidence behind the different treatment modalities. Unfortunately, only 4 studies with a total of 305 patients met their inclusion criteria and they were not able to perform a meta-analysis given the different research methods. The 4 studies all evaluated acupuncture for the treatment of hiccups. However, the studies were weak with high degree of bias. The randomization was poorly performed, the groups were not well matched, the intervention was not compared to placebo, and the acupuncture was varied from patient to patient with no one protocol. Therefore, no real conclusions can be drawn from these studies. [1]
- A case series from 1955 looked at **chlorpromazine** for the treatment of intractable hiccups. 50 patients were given intravenous chlorpromazine 25-50 mg and a second dose

in 2-4 hours. 81% had cessation of hiccups after the treatment, but **long-term efficacy was not measured**. Only mild side effects were reported. However, multiple case reports have also been reported over the years that showed **no change** in hiccups with chlorpromazine treatment. [2]

- A randomized controlled cross-over study from 1992 looked at treating intractable hiccups with **baclofen**. Four male patients with hiccups longer than 6 months unresponsive to previous medical therapy were treated with increasing doses of baclofen. When treated with baclofen versus placebo the nurses noticed increased hiccup-free periods and the patients reported decreased hiccup severity; however, there was no change in frequency of hiccups. [1]
- A recent study published this year looked at treating intractable hiccups with **metoclopramide** versus placebo for 15 days. 34 patients were included and the patient's treated with metoclopramide had statistically significant cessation of hiccups versus placebo with a relative risk of 2.75 for cessation. However, the metoclopramide arm also had increased side effects of fatigue, upset mood, and dizziness. Therefore, further larger studies would need to be performed to validate these results and assure no adverse side effects. [3]

Conclusion

Currently, **very little quality research exists on the treatment of intractable hiccups**. Also, due to the rarity of the symptom, a large scale clinical trial would be difficult to perform. Therefore, clinicians most currently go with the suggested treatments based on case reports until further research is performed. The **only FDA approved medication for hiccups is chlorpromazine but may not work for all patients and other adjunct therapies should be considered**. Determining and treating the underlying cause of the hiccups should also be attempted and patients referred for follow-up as clinically indicated.

References:

1. Moretto EN, Wee B, Wiffen PJ, Murchison AG. Interventions for treating persistent and Intractable hiccups in adults. Cochrane Database Syst Rev 2013; Jan 31.
2. Friedman NL. Hiccups: a treatment review. Pharmacotherapy 1996; 16 (6): 986-995.
3. Wang T, Wang D. Metoclopramide for patients with intractable hiccups: A multi-center, randomized controlled pilot study. Intern Med J 2014; Jul 29.