

CASE STUDY

Hiccup No More: The Emerging Role of Baclofen in Recurrent Hiccups- A case series on the management of hiccups with Baclofen

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Received: 22 May 2023

Accepted: 25 June, 2023

ABSTRACT:

Background

Recurrent hiccups are a challenging condition with limited effective treatment options. Baclofen, a GABA agonist used for spasticity, has been studied as a potential treatment for recurrent hiccups. This review evaluates current evidence for the use of baclofen in the treatment of recurrent hiccups.

Methods

We present a case series of 5 patients along with a literature review affected by recurrent and chronic hiccups which was successfully treated with baclofen.

Results

Hiccups stopped in all patients after the administration of a short course of baclofen. While the optimal dosage is not well established, starting doses of 5 to 10 mg three times a day with gradual titration to a maximum of 30 to 40 mg per day were found to be effective.

Conclusions

Despite numerous available options, recurrent hiccups remain an enigma in terms of response to treatment. We observed a fast and adequate response on baclofen where other modalities failed or were ineffective. Baclofen may be a valuable addition to the treatments for recurrent hiccups, but further research is needed to determine the optimal dosage, duration, and safety of baclofen for the treatment of hiccups.

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Introduction:

Hiccups, also known as singultus, are involuntary contractions of the diaphragm and intercostal muscles followed by the sudden closure of the glottis, which generally resolves themselves without complications. [1,2] While hiccups are generally benign and self-limiting, recurrent hiccups can be debilitating and interfere with daily activities. Hiccups are usually a self-limited disorder; "transient" hiccups last less than 48 hours, while "persistent" or "chronic" hiccups last 48 hours or more, or they occur with recurrent attacks. Hiccups lasting longer than 2 months are termed "intractable hiccups." [2,3]

There are various pharmacological and non-pharmacological treatments available for hiccups, but the efficacy of these treatments is often limited.

In recent years, baclofen has emerged as a potential treatment for recurrent hiccups. Baclofen is a gamma-aminobutyric acid (GABA) receptor agonist that is commonly used in the treatment of spasticity. Its mechanism of action is thought to involve the inhibition of neurotransmitter release, resulting in decreased muscle tone. The drug is believed to exert its antispasmodic effects by increasing the threshold for excitation (cell hyperpolarization), reducing excitability, resulting in depression of synaptic transmission in the spinal cord, and thus depressing reflex hiccup activity. [4] Baclofen has also been shown to have an effect on the central nervous system, leading to sedation and analgesia.

Case Reports:

CASE 1 A 30-year-old female diagnosed with schizophrenia and stable on 2 mg of risperidone for 3 years presented to the outpatient department with a complaint of intractable hiccups for 6 months. The frequency of hiccups was around 10–12 times per minute and continued throughout the day, leading to significant socio-occupational distress. The patient had been receiving medical treatment for the last 4 months for the same, including metoclopramide and chlorpromazine, along with trying breath-holding, breathing in a bag, relaxation exercises, and drinking cold water, but symptoms persisted. Her ECG, chest X-ray, complete blood counts, and other blood investigations, including the blood urea level, were unremarkable. A CT scan of the brain was normal. The patient was given baclofen 10 mg three times per day. Within one week, the patient had a dramatic response, and complete remission was achieved in two weeks. Treatment was also well tolerated. Slowly, the drug is tapered over 3 weeks, and the patient didn't report any recurrence of symptoms during further follow-ups for his psychiatric illness.

Case 2: A 26-year-old female presented with a hiccup for 5 consecutive days. The frequency of hiccups was initially 5–6 times per minute, then increased to 10–15 times per minute and continued throughout the day, causing significant socio-occupational distress and even causing eating and drinking problems. After the first two days, the patient went to the physician, where chlorpromazine, pantoprazole, and domperidone were prescribed, but the hiccup persisted, even during sleep hours. After 3 days, the patient visited our internal medicine OPD. The physical exam and medical history were negative. Routine blood tests, electrocardiography (ECG), and chest X-ray were normal. Metoclopramide and pantoprazole were discontinued, and baclofen 10 mg twice daily was prescribed, but no significant improvement was seen. Therefore, the dose of baclofen was increased to 10 mg TDS, after which the patient reported significant improvement in 4–5 days, resulting in the remission of the hiccup without recrudescence within 8–10 days. Further administrations were not needed.

Case 3 A 41-year-old male is present in the OPD with a 2-year history of hiccups. At the time the patient visited our hospital, he had been receiving medical treatment for GERD-like symptoms that had started developing since the intractable hiccup began. All routine investigations, including blood urea nitrogen levels, were normal. The chest x-ray and ECG were normal. An endoscopy was performed by a gastroenterologist, but no significant findings were present. EEG and brain magnetic resonance imaging (MRI), also performed, showed normal findings. Before the visit, he had been treated by multiple

specialists but did not report any significant improvement. The patient had no significant prior medical history, and no abnormal findings were present. About four months before the visit to our OPD, his hiccups had worsened, and on a visit, he hiccupped approximately 20–25 times per minute. He was a salesman and complained of severe discomfort and embarrassment caused by hiccups during his work. The hiccup also disturbed his sleep. He visited our department, and 10 mg of baclofen was administered three times daily. On a visit after 3 days, the patient reported that the bout of hiccups had decreased significantly after taking the medication. After three days, the hiccup frequency is 4–5 per minute. In addition, the GERD-like symptoms had also disappeared. His hiccups had decreased by the next follow-up, which was one week later, and he had hiccups 4–5 times throughout the day. His hiccups completely disappeared after 20 days on the same dose. The quantity of the dose was reduced over the next week and then stopped within 15 days. At a follow-up performed 1 month after stopping his medication, the hiccups had not recurred, and the patient is currently free from hiccups and gastrointestinal symptoms.

Case 4 A 28-year-old male presented with hiccups for 2 years. The frequency of hiccups is 6–7 times per minute. When he tries to stop them, his anxiety level increases. He was diagnosed with dissociative and conversion disorders. Due to this problem of hiccups, the patient went to the physician and was given metoclopramide and pantoprazole. The patient took it for 10 days but didn't get better. His routine blood investigations, ECG, and chest x-ray are also normal. Then the patient came to the psychiatry OPD in our hospital, where he was started on baclofen 10 mg BD. The patient initially reported improvement, but within 3–4 days of starting medication, the frequency of hiccups again increased. We further hiked the dose up to 20 mg BD. Of course, his hiccups disappeared after 30 days.

Case 5: A 28-year-old female with obsessive-compulsive disorder who had been in remission on treatment (fluoxetine 40 mg) for 5 years presented with hiccups for the past 12 years. Though most of the time her hiccups were low in frequency and not much trouble, they got worse even with mild stress and anxiety and became intractable. She has visited multiple physicians and gastroenterologists and gone through multiple investigations, including endoscopy, barium meal radiography, a CT abdomen, tests for autoimmune disorders, etc., and numerous treatment regimens, but didn't see any improvement. Later, the patient was initiated on 10 mg baclofen BD doses, and she reported improvement on a single dose. After 10 days, her hiccups almost disappeared.

DISCUSSION

In the above case series, we discussed the use of baclofen in the treatment of both transient and persistent hiccups. All of our cases showed significant improvement on baclofen acutely within a week and complete remission in around 2–3 weeks. Many options are available for the treatment of intractable hiccups, like chlorpromazine, haloperidol, gabapentin, metoclopramide, carbamazepine, and benzodiazepines.^[5,6] Antipsychotics like olanzapine and quetiapine, haloperidol, as well as antidepressants like amitriptyline and dothiepin, were also used anecdotally by a few physicians, but the majority of them did not show much efficacy or reliability in the treatment of the same.^[7,8,9,10] Since baclofen is a GABA_B receptor agonist that reduces synaptic transmission at the spinal cord, it produces an anti-spastic effect and is able to interrupt the hiccup's reflex arc.^[11]

Our observation of five patients on the administration of baclofen starting at 5 mg and ranging up to 40 mg, all of whom showed significant improvement in 2–3 days and had complete recovery in an average of 15 days. Baclofen administration can be beneficial because determining the cause of hiccups and conducting specific investigations from the vast armamentarium can take a long time and cause significant distress to the patient. The use of baclofen has the advantage of being faster, relatively safer, and more tolerable.^[5,6,12] Only mild sedation and dizziness were reported as early side effects, which subsided shortly in the above cases. It is also easily available and especially useful in the context of disorders with spastic components and comorbid alcohol dependence. Despite its therapeutic advantage, the case series has certain limitations, like low sample size, a lack of longitudinal follow-up, and a patient's subjective bias.

In conclusion, the available evidence suggests that baclofen is an effective treatment for recurrent hiccups. Multiple studies and our observations have demonstrated a reduction in the frequency and duration of hiccups with the use of baclofen. While the optimal dosage of baclofen for the treatment of hiccups is not well established, starting doses of 5 to 10 mg three times a day with gradual titration to a maximum of 30 to 40 mg per day are commonly used. Side effects are generally mild and include sedation, dizziness, and muscle weakness. Further research is needed to determine the optimal dosage, duration, and safety of baclofen for the treatment of hiccups. Nonetheless, given the lack of effective treatment options for recurrent hiccups, baclofen may be a valuable addition to the armamentarium of treatments for this condition. Thus, Baclofen can be an agent that may provide us with a therapeutic advantage alone or in combination with other psychotropics.

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