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Successful treatment of persistent idiopathic hiccup with ondansetron

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Abstract
We report a case of idiopathic persistent hiccup rebellious to many medication and that has been resolved after ondansetron administration. This case report is the occasion to discuss different etiologies of persistent and intractable hiccups and to review different medication proposed to such annoying symptom.

Keywords: idiopathic hiccup, ondansetron

Introduction
Hiccup is a spasmodic involuntary contraction of the diaphragm which triggers a sudden inspiration and an abrupt closure of the glottis with a characteristic sound. Regarding its duration, it is classified as hiccup attack, persistent hiccup or rebellious or intractable hiccup.

Case report
A 41-year-old patient, healthy without medical problems, was admitted at the emergency department for acute intractable hiccups for 10 days. His history revealed that the patient had repetitive hiccups lasting for a whole day that was worse while speaking, could hardly be controlled for 1–2 minutes and was still present at night perturbing his sleep. There was no associated pain abdomen, retrosternal burning, digestive hemorrhage, difficulty in breathing, coughing, or swallowing of food. Hiccups caused marked distress and professional difficulty. No neurological deficit on clinical examination was reported.
Before admission he sought medical consultation and all investigations such as ECG, chest X-ray, upper gastrointestinal endoscopy, ultrasonography of abdomen, cerebral scan, fasting blood sugar, hemogram, liver and kidney function tests were within the normal limits.
He has received various oral medication: omeprazole (40 mg, twice daily), metoclopramide (10 mg, 3 times daily) then domperidone (10 mg 3 times daily), chlorpromazine (25mg, 4 times daily) and haloperidol (2 mg, 3 times daily) without any relief.
His hemodynamic and respiratory values were normal, routine blood tests were still normal and He obtained partial improvement for 1 hour from intravenous ranitidine and metoclopramide and hiccups returned as intense as at the admission. Then Ondansetron 8 mg was the injected intravenously, 5 minutes later which the hiccups stopped (figure 1). The patient was relieved and discharged from the hospital the next day. Two months later, the patient has retrieved his normal activity and reported no relapse in his symptoms.

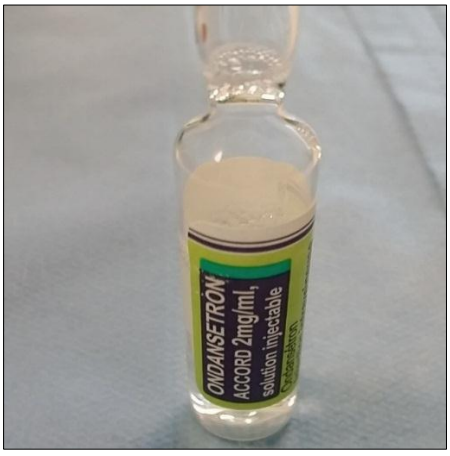

Fig 1: ondansetron 8 mg.

Discussion
A hiccup is a reflex arch that consists of a sudden contraction of the diaphragm and intercostal muscles followed immediately by laryngeal closure. Hiccups are fairly common and are usually transient and self-limited but may become protracted. When hiccups last for more than 48 hours, they are defined as persistent; hiccups lasting longer than 2 months are labeled as intractable [1].

Protracted hiccups are responsible for approximately 4000 hospitalizations in the United States [2]. However, the exact incidence of persistent and intractable hiccups in the cancer population is unclear. Hiccups that are persistent or intractable can result in significant morbidity and substantial symptom burden for patients. Common symptoms associated with intractable hiccups include vomiting, poor caloric intake, dehydration, fatigue, disrupted sleep, depressive symptoms, and anxiety [3].

The etiology of intractable hiccups may include structural or functional disturbances of the medulla, afferent or efferent nerves to the respiratory muscles, metabolic and endocrine disorders, drugs, general anesthesia, and psychological problems [2]. in our case, no neurologic deficit was noted and all investigations were negative.

Non pharmacological treatment methods such as breath holding, drinking cold water, and inserting a nasogastric tube are found ineffective in cases of persistent hiccups. However, several pharmacological agents have been proposed for the management of persistent or intractable hiccups. There is a paucity of data over which agent may be superior to another.

Chlorpromazine is the only Food and Drug Administration–approved medication for hiccups; but its use can be limited by untoward side effects such as sedation, confusion, hypotension, urinary retention, and extrapyramidal symptoms [4]. Other frequently utilized medications include metoclopramide, haloperidol, and baclofen [5, 6, 7]. Baclofen showed significant reduction in hiccup severity and in several cases has been shown to successfully treat persistent and intractable hiccups [8, 9]. Anticonvulsants including phenytoin, valproic acid, and carbamazepine have been used for severe hiccups [3]. More recently, gabapentin has been shown to reduce or eliminate persistent and intractable hiccups including in those with cancer [6, 10]. Individual case reports of the use of sertraline, nifedipine, nimodipine, carvedilol, amantadine, and methylphenidate have also shown promise [11, 12]. In addition, intravenous lidocaine, nebulized lidocaine midazolam, and nefopam have also been successfully utilized to manage severe hiccups [13, 14, 15].

Ondansetron is a potent, highly selective, competitive antagonist at 5-HT3 receptors and acts on the Central nervous system as well as on the peripheral nervous system [16]. While all mechanisms of ondansetron's effects are not fully understood, it clearly lacks dopamine receptor antagonist property [17]. Ondansetron reduce visceral sensitivity and have inhibitory effects on motor activity in the distal intestine. Early clinical studies suggest that these agents may have a role in painful, diarrhea-predominant Irritable bowel syndrome (IBS), patients with IBS experienced significantly fewer daily episodes of pain while on ondansetron [18]. Ondansetron may be ineffective in the treatment of intractable hiccups, in our patient, it was immediately efficient while all other medication failed to relieve the persistent hiccup.

In addition to pharmacological therapy, interventional methods such as ultrasound-guided phrenic nerve block have also been advocated for the treatment of intractable hiccups and offers a plausible treatment modality for symptomatic long-term relief [19, 20]. It is necessary to block the both phrenic nerves with a security interval. In case of fail of the phrenic nerve bloc, US guided radiofrequency lesioning can be proposed to stop the hiccup.

Conclusion

Persistent and intractable hiccups is an annoying situation perturbing the patient life and have various etiology. Ondansetron have his place with the several medications in the treatment of intractable hiccups. In case of fail of medications guided US phrenic nerve block may save the situation.

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