

Amantadine for the intractable hiccup when weaning a patient with a brainstem lesion-a case study

Dear Editor,

The occurrence of hiccups in a critically ill patient is a common encounter in an intensivist's practice.

Though hiccup bouts are usually benign and transient, persistent singultus can last for more than 48 hours, adding to a patient's discomfort and thereby impeding synchronised mechanical ventilation and appropriate patient care. The diaphragm, phrenic nerve, vagus nerve, brainstem, hypothalamus, and their inter-neuronal connections comprise the hiccup reflex arc, the disruption or stimulation of which can trigger hiccups.^[1] Intractable hiccups has been reported as the presenting symptom of underlying central nervous system (CNS) lesions,

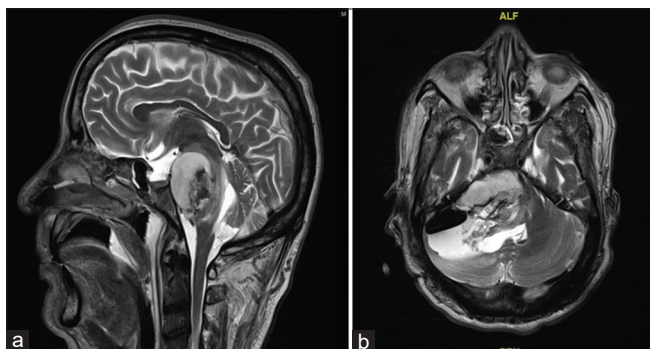


Figure 1: T2-weighted magnetic resonance imaging scans of the brain in the sagittal (a) and the axial (b) showing partially excised right cerebellopontine angle (CPA) tumour with right retromastoid suboccipital craniotomy defect with haemorrhagic residue and oedema in the right cerebellar hemisphere, right middle cerebellar peduncle, and the right hemipons, with additional haemorrhage and loculated blood mixed cerebrospinal fluid in the right CPA cistern

namely, brainstem tumour, vascular malformations, demyelinating disease, and posterior circulation cerebrovascular syndromes^[2] secondary to associated medullary compression or distortion. Non-response to induction of emesis, hyperventilation, and the Valsalva manoeuvre demands the need for pharmacotherapy with peroral (PO) or intravenous (IV) agents. Baclofen, metoclopramide, gabapentin, chlorpromazine, carbamazepine, haloperidol, amitriptyline, lidocaine, nimodipine, and valproate have been the initial choices of pharmacotherapy.^[1] Hypnosis, acupuncture, vagus and phrenic nerve blockade or pacing are reserved for medically refractory hiccups. Surgical extirpation of a brainstem tumour has been reported to resolve hiccups in a patient with medullary tumour.^[3]

We report the management course of a patient with a partially excised unilateral cerebellopontine angle meningioma with infiltration into the brain stem [Figure 1]. The postoperative course in the neurocritical care unit was complicated by intractable hiccups beginning from the 7th postoperative day and lasting till the 30th postoperative day. He had no associated comorbid illness, gastroesophageal reflux disease, gastric distension, cardiac illness, or ear, nose, and throat problems. The correctable causes, namely, dyselectrolytemia, uraemia, hyperglycaemia, and pharmacotherapy-induced hiccups due to macrolides, benzodiazepines, steroids, and opioids were ruled out. Initial pharmacotherapy IV pantoprazole, IV metoclopramide 20 mg, twice a day PO doses of chlorpromazine 50 mg, and gabapentin 75 mg was unsuccessful. Ventilator asynchrony hindered optimal mechanical ventilation and subsequent readiness to

successful weaning from the ventilator.^[4] A purely neurological cause in the form of a tumour residue abutting the medullary centre for maintaining a hiccup reflex arc explained the persistence of hiccups and prompted us to attempt escalation of pharmacotherapy using the dopamine agonist amantadine. Combination of chlorpromazine, gabapentin, and amantadine at a dose of 100 mg once a day for five days progressively reduce the frequency of episodes, leading to the hiccups' complete disappearance by the end of the prescription. Treatment was de-escalated with progressive discontinuation of chlorpromazine, gabapentin, and amantadine at 24-hour intervals between each. The patient could be subsequently weaned from the ventilator. Discontinuation of the drug did not cause recurrence of hiccups. The patient was followed up for a year later and had no recurrence of persistent hiccups.

The neurocognition promoting property of amantadine dictates its significance in neurointensive care practice. Two recent case reports in literature introduced its utility in the amelioration of hiccups in a survivor of pancreatic cancer with associated Parkinson's disease^[5] and in another patient with terminal stage of vascular dementia who had a 4-year history of intractable hiccups, both before treatment with amantadine.^[6] This report reiterates the wider therapeutic applicability of amantadine to benefit patients with intractable hiccups, despite the presence of an organic CNS cause. However, its mechanism of action in this context remains to be elucidated.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient consented to his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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REFERENCES

1. Steger M, Schneemann M, Fox M. Systemic review: The pathogenesis and pharmacological treatment of hiccups. *Aliment Pharmacol Ther* 2015;42:1037-50.
2. Lee KH, Moon KS, Jung MY, Jung S. Intractable hiccup as the presenting symptom of cavernous hemangioma in the medulla oblongata: A case report and literature review. *J Korean Neurosurg Soc* 2014;55:379-82.
3. Eisenächer A, Spiske J. Persistent hiccups (singultus) as the presenting symptom of medullary cavernoma. *Dtsch Arztebl Int* 2011;108:822-6.
4. Saravanan R, Nivedita K, Karthik K, Venkatraman R. Role of diaphragm ultrasound in weaning mechanically ventilated patients: A prospective observational study. *Indian J Anaesth* 2022;66:591-8.

5. Wilcox SK, Garry A, Johnson MJ. Novel use of amantadine: To treat hiccups. *J Pain Symptom Manage* 2009;38:460-5.
6. Hernandez SL, Fasnacht KS, Sheyner I, King JM, Stewart JT. Treatment of refractory hiccups with amantadine. *J Pain Palliat Care Pharmacother* 2015;29:374-7.

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