



## **Hiccup in patients with advanced cancer successfully treated with gabapentin: report of three cases**

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Chronic hiccup is an infrequent but distressing symptom in patients with advanced cancer. A series of drugs (chlorpromazine, haloperidol, nifedipine, metoclopramide, baclofen) have been proposed to treat hiccup without definitive results. Some authors have suggested a possible role of gabapentin in the treatment of idiopathic chronic hiccup in patients not affected by neoplasms.<sup>1,2</sup> We report three cases of hiccup in patients with advanced cancer successfully treated with gabapentin observed at the Supportive Care and Rehabilitation Unit of the Medical Oncology Department, University of L'Aquila, Italy.

### **Case 1**

A 62-year-old man with a history of colon cancer metastasised to the liver was admitted for chronic hiccup, nausea and fatigue. He was previously treated by his family physician with metoclopramide and dexamethasone without effect. At admission the patient was suffering and distressed due to continuous hiccup and sleep deprivation. Chlorpromazine (25 mg iv bid) was started with relief of hiccup but with postural hypotension and severe drowsiness. After two days hiccup recurred; chlorpromazine was stopped and gabapentin (300 mg tid) was introduced. We registered a prompt relief of hiccup with only sporadic episodes successfully treated with empiric methods. Sleep was restored. No side effects related to gabapentin were noted. After six days the patient developed jaundice and died by progression of disease. No recurrence of hiccup was observed.

### **Case 2**

A 43-year-old man affected by pancreatic cancer was referred for pain, nausea and chronic hiccup.

Hiccup and nausea were treated with metoclopramide (1 mg/kg) and haloperidol (5 mg sc continuous infusion) with good results. After one week hiccup recurred accompanied by anxiety, nervousness and sleep deprivation.

Gabapentin (300 mg tid) was added to the treatment with a prompt resolution of the symptom. Hiccup recurred after ten days with lower intensity; gabapentin was increased to 400 mg tid with remission of the symptom. After fourteen days the patient died by progression of disease without recurrence of hiccup.

### **Case 3**

A 51-year-old man affected by small-cell lung cancer metastasised to the brain and liver was referred for pain, dyspnoea, anorexia and hiccup. Since the pain was classified as somatic and neuropathic, a therapy with oral morphine and gabapentin (300 mg tid) was started. We registered a prompt resolution of hiccup. Sporadic

episodes of hiccup were successfully treated with oral metoclopramide. After twenty days the patient died by progression of the disease.

## Discussion

Chronic hiccup is defined as hiccup lasting 48 hours continuously or in recurring attacks and is a very distressing symptom for patients with advanced cancer.<sup>3</sup> The literature is based largely on case reports and no definitive clinical evidence is available to define the standard treatment. To date, chlorpromazine, haloperidol, nifedipine, metoclopramide and baclofen are the drugs most commonly employed in clinical practice. In particular, baclofen seems to be the drug most commonly employed to treat hiccup, but with frequent side effects (sedation, insomnia, dizziness, weakness, ataxia, confusion).<sup>4,5</sup> Moreover, it should be used with caution in elderly patients.

Gabapentin is an anticonvulsant commonly administered to patients with advanced cancer for the treatment of neuropathic pain.<sup>6</sup>

It is not metabolised by the liver and not bound to plasma proteins. These characteristics make the drug particularly attractive for patients with advanced cancer who often exhibit a low level of plasma proteins and/or hepatic failure due to metastatic spread.

The mechanism of action is probably related to the increase of endogenous GABA release and, thus, to the modulation of the excitability of the diaphragm and the other inspiratory muscles.<sup>1</sup>

Gabapentin is well tolerated and negative interactions with other drugs should not be expected.

In our experience, gabapentin was effective either alone or in combination with other drugs to treat chronic hiccup; no side effects related to gabapentin were observed.

Trials with a larger number of patients are mandatory to establish the role of gabapentin for treatment of hiccup in patients with advanced cancer.

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