

**PALLIATIVE MANAGEMENT OF PERSISTENT HICCUPS IN A PATIENT WITH PROSTATE CANCER AFTER ROBOTIC PROSTATECTOMY**

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**ABSTRACT**

Persistent hiccups are an uncommon problem in terminally ill patients. We report our management of persistent hiccups in a 63-year-old man following a long robotic prostatectomy for advanced prostate cancer. Several measures and drugs were tried before introducing gabapentin and dexamethasone for the treatment of persistent hiccups.

**KEYWORDS:** Robotic prostatectomy, gabapentin, dexamethasone, persistent hiccups, palliative care.

**INTRODUCTION**

We report a case of 63-year-old male with locally advanced prostate cancer, who underwent robotic prostatectomy. Six hours after the operation he developed continuous persistent hiccups more than three days.

Hiccup is an involuntary contraction of the respiratory muscles of the chest and diaphragm, mediated by the phrenic and vagus nerves and a central (brainstem) reflex centre.<sup>[1]</sup> Based on the duration, hiccups can be divided into three categories: Acute (duration up to 48 hours), persistent or protracted (duration more than 48 hours) and intractable (duration over a month).<sup>[2]</sup> Intractable cases are rare but do occur. The causes of hiccups in palliative care settings include gastric stasis and distention (the most common causes), gastroesophageal reflux disease (GERD), metabolic disturbances (e.g., uremia, hypercalcemia or hyponatremia), infection, local factors causing irritation of the diaphragm or phrenic nerve, hepatic disease/ hepatomegaly and cerebral causes (e.g., tumors or metastases).<sup>[3]</sup>

The detailed pathophysiology of hiccups remains poorly understood. However, possible causes include irritation of the afferent or efferent nerves of the diaphragm (the phrenic or vagus nerves) or the medullary centres.<sup>[3]</sup>

Several neurotransmitter pathways of the brainstem and medulla, including those involving dopamine, serotonin, opioids, calcium channels and gamma-aminobutyric acid (GABA) are possibly involved in mediating hiccups.<sup>[4]</sup>

There are few reports on the treatment of intractable hiccups in patients with advanced malignancies and under palliative care. However; observational studies

have suggested that gabapentin may be useful for management of hiccups in patients with advanced malignancies.<sup>[5-7]</sup>

Here, we report on the successful use of gabapentin and short course of intravenous dexamethasone 4 mg for five days to treat persistent hiccups in a palliative care setting.

**CASE REPORT**

We report the case of a 63-year-old man with a 2-year history of TURP for BPH. Recently diagnosed locally advanced prostate cancer for which a robotic prostatectomy was done on the 25<sup>th</sup> of November 2019. The operation lasted for 8 hours in the trendelenburg position (causing diaphragmatic irritation). About 6 hours after the operation he developed continuous hiccups. The hiccups were frequent and irritating, which disturbed his sleep and caused severe distress to both him and his family. Simple breath holding and drinking cold water did not stop the hiccups.

The patient was on omeprazole 20 mg for three years due to GERD. He was started on metoclopramide 10 mg TID (three times per day) with no benefit. On the 26<sup>th</sup> of November, the patient also developed hydronephrosis with elevation in urea and creatinine, which were came back to the normal range after bilateral nephrostomy tubes were placed. On the third day (28/11/2019) we saw the patient as a palliative consultation and we started gabapentin 100 mg TID which was titrated up to 300 mg twice per day plus dexamethasone 4 mg intravenously once daily for five doses. The hiccups stopped completely on the first of December (4 days after starting gabapentin and dexamethasone). The five doses of dexamethasone completed and the gabapentin tapered

down over one week and he didn't suffer any more hiccups.

## DISCUSSION

Hiccups are frequent in general populations and are usually benign and transient. Intractable hiccups point to a possible organic cause that is usually serious. The pathogenesis of hiccups remains a mystery. A hiccup occurs due to an involuntary, intermittent, spasmodic contraction of the diaphragm and intercostal muscles. This causes sudden inspiration that ends with abrupt closure of the glottis, generating the "hic" sound. The left hemidiaphragm is involved in approximately 80 percent of cases.<sup>[8]</sup> It involves a spinal and central reflex arc. Sufferers may take over-the-counter medicines or home remedies, or simply wait until symptoms resolve spontaneously. Most sufferers will not seek medical attention. Persistent hiccups can have unpleasant effects including fatigue, dehydration, weight loss, wound dehiscence and death (in extreme cases).<sup>[9]</sup> Our patient experienced sleep deprivation and social embarrassment, fatigue and anxiety attributable to his persistent hiccups. The palliative care team aimed to control his symptoms quickly, while performing the minimal number of investigative procedures and minimizing the possible side effects of medications. The focus was on improving his quality of life. The patient was satisfied, and his hiccups were fully controlled. He was discharged home and was able to return to his usual activities. No side effects were reported by him or his family. He was followed up in the palliative care clinic and over the telephone. Gabapentin, an anti-epileptic drug commonly used for neuropathic pain management in patients with cancer and under palliative care, may effectively treat hiccups by increasing endogenous GABA-mediated inhibition of inspiratory muscle action,<sup>[10,11]</sup> reducing calcium influx by inhibiting voltage-operated calcium channels in the presynaptic terminals of respiratory muscles or both of these mechanisms. Furthermore, it also increases the levels of serotonin.

Gabapentin should thus be considered a treatment for persistent and intractable hiccups in palliative care settings, particularly if central causes are suspected. The drug is associated with minimal adverse effects and is safe, inexpensive and readily available in several formulations. Small dose of dexamethasone for short duration will fasten the treatment of hiccups. However; large doses of steroids may bring hiccups.

## CONCLUSION

This case report reinforces previous reports on the efficacy of gabapentin used to treat established hiccups that are resistant to other drugs. Furthermore, small and short course of dexamethasone will fasten hiccups resolution. Gabapentin may be particularly useful if the hiccups are caused by brain tumors. Further work is needed to establish treatment guidelines for the management of persistent hiccups.

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## Conflicts of interest

There are no conflicts of interest.

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