

# Olanzapine in the Treatment of Refractory Nausea and Vomiting in Palliative Care Settings

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## Abstract

The patients often present to palliative care with intractable nausea and vomiting. This may reduce the effectiveness of oral drugs and significantly affects the quality of life of these patients. Despite multiple drugs available for treatment, it is often difficult to control the symptoms. Olanzapine is an atypical antipsychotic and acts on multiple receptors and may help in treating vomiting in a patient with advanced malignancy. We report a case of gallbladder carcinoma who presented to us with intractable vomiting which was not relieved with a combination of traditional antiemetics but showed marked improvement with olanzapine.

**Keywords:** Gallbladder carcinoma, intractable vomiting, olanzapine

## INTRODUCTION

Nausea and vomiting is a common occurrence in patients with advanced cancer. The prevalence of nausea in the palliative population has been estimated to range from 16% to 68%.<sup>[1]</sup> Persistent nausea and vomiting in patients with palliative conditions can lead to unplanned hospital visits. Reasons can be multifactorial comprising metabolic issues, vestibular problems, central nervous system disorders, or metastasis.<sup>[2,3]</sup> In some cases, the cause remains unknown.

Various classes of antiemetics (phenothiazines, butyrophenones, benzamides, corticosteroids, serotonin (5HT<sub>3</sub>) receptor antagonists, anticholinergics, antihistamines, and cannabinoids) are used to control nausea and vomiting depending on the mechanism. Often, a combination therapy may be required to control vomiting.<sup>[4]</sup>

Olanzapine is an atypical antipsychotic agent of the thienobenzodiazepine class which acts as antagonist on multiple receptors including dopaminergic (D<sub>1</sub>, D<sub>2</sub>, D<sub>3</sub>, and D<sub>4</sub>), serotonergic (5-HT<sub>2A</sub>, 5-HT<sub>2C</sub>, 5-HT<sub>3</sub>, and 5-HT<sub>6</sub>), adrenergic (α<sub>1</sub>), histaminic (H<sub>1</sub>), and muscarinic (M<sub>1</sub>, M<sub>2</sub>, M<sub>3</sub>, and M<sub>4</sub>) receptors. Olanzapine has few extrapyramidal side effects because it has five times more affinity for 5HT<sub>2</sub> receptors than for D<sub>2</sub> receptors.<sup>[5]</sup>

Reports on the use of olanzapine in refractory nausea and vomiting in palliative care setting are limited.

## CASE REPORT

A 65-year-old female with gallbladder carcinoma presented to our palliative care unit (PCU) with a history of pain abdomen and vomiting. Patient had pain in the right upper quadrant of abdomen, which had increased over the past 15 days. Pain was associated with vomiting for the past 3 days. The patient was taking tablet hyoscine butyl bromide 10 mg tds and tablet metoclopramide 10 mg tds without any improvement.

A contrast-enhanced computed tomography abdomen revealed gallbladder mass with liver and periportal nodal metastasis. An ultrasound-guided fine-needle aspiration cytology from gallbladder mass was suggestive of adenocarcinoma. Since patient had an Eastern Cooperative Oncology Group 4 status, she was deemed unsuitable for chemotherapy and referred to PCU.

In the PCU, she was started on morphine-based analgesic titration. After 3 mg bolus of injection morphine, an infusion

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of injection morphine 0.5 mg/h was started. She was started on injection metoclopramide 10 mg thrice a day for nausea and vomiting. Her abdominal pain was reduced in intensity, but nausea and vomiting persisted and was severe in nature. Considering liver metastasis, she was started on injection dexamethasone 8 mg twice a day.

Pain was settled but vomiting still uncontrolled. Addition of ondansetron also did not relieve the symptoms. Her vomiting persisted and adversely affected her quality of life (QOL). Hence, injection haloperidol 0.5 mg twice a day was added. Even with the use of a combination of different classes of antiemetics, her nausea and vomiting was not controlled.

A diagnosis of functional small bowel obstruction was made, and patient was kept on nasogastric tube decompression along with nil per oral for 24 h as per surgical oncology opinion. After 24 h of fasting, intermittent feeds were started with Ryle's tube clamping, but patient symptoms of nausea and vomiting persisted. We decided to start tablet olanzapine 2.5 mg once daily Ryle's tube. There was a dramatic response after the first dose of olanzapine; her nausea and vomiting had reduced both in intensity and frequency. Ryle's tube was removed and she started accepting feed without symptoms. She was discharged with tablet olanzapine 2.5 mg *hora somni* and metoclopramide on as on required basis. In the follow-up period after 1 week, she had no complaints of nausea and vomiting.

## DISCUSSION

Nausea and vomiting is distressing symptoms that decrease the QOL of a cancer patient.

Emesis is controlled in our brain by chemoreceptor trigger zone (CTZ), the reticular formation in the medulla oblongata, and the central pattern generator (CPG). The CPG is an interconnected neural network that receives afferents from the cerebral cortex and higher brainstem, thalamus, hypothalamus, the vestibular system, and through the vagus and splanchnic nerves. The main receptors present within the CTZ are dopamine Type 2 (D2) and serotonin (5HT2 and 5HT3), whereas in CPG, the principal receptors are serotonin muscarinic cholinergic (ACh), 5-HT3, and histamine Type 1 (H1) receptors. Various antiemetics act on different receptors.<sup>[1,6,7]</sup> Haloperidol has its action on D2 receptors, whereas metoclopramide also acts peripherally to block D2 within the gastrointestinal tract and stimulates prokinesis through 5-HT4 receptors. Phenothiazines are mainly anticholinergic and antihistaminic as compared to antihistamines which act on H1 receptors in the CPG and on vestibular afferents. Anticholinergics drugs like hyoscine act on peripheral acetylcholine receptors located in the CPG. 5-HT3 receptor antagonists such as ondansetron act on receptors located both centrally at the CTZ and CPG and on the terminals of vagal afferents in the gut.<sup>[1-3]</sup>

Olanzapine is a broad-spectrum antiemetic with potential action of multiple receptors (D2, H1, ACh, and 5-HT3). Olanzapine has been suggested as a second-line antiemetic

for patients with chemotherapy-induced nausea refractory to butyrophenones or phenothiazines or who have extrapyramidal reactions to usual antiemetics.<sup>[8,9]</sup> In addition, a decreased cost and improved compliance have added advantage over other classes of antiemetic drugs.<sup>[10]</sup> There is not enough literature to suggest its use for intractable nausea and vomiting in advanced palliative care settings.

An open-label pilot study explored the antiemetic activity of olanzapine in patients with advanced cancer requiring opioid analgesics for pain. Olanzapine in three doses (2.5, 5, and 10 mg) was associated with significant reductions in nausea without extrapyramidal symptoms.<sup>[11]</sup>

It is also associated with weight gain and improved appetite which might also be helpful in cachectic patient.<sup>[12]</sup> It is associated with few drug–drug interactions, has a wide therapeutic index, and can be used safely in renal and liver dysfunction.<sup>[13]</sup>

In palliative care settings, the patients commonly present late with intractable nausea vomiting. The etiology is often multifactorial, and it is difficult to localize the emetogenic source. A mechanism-based treatment of vomiting has been suggested, but it may not be easy to recognize the cause of vomiting. A combination antiemetic therapy consisting of different classes of antiemetic drugs is one approach that can successfully treat refractory nausea and vomiting in some patients. However, it not only adds the cost but also the side effects. Furthermore, despite this, some patients do not have desired response. Our patient also had intractable vomiting which was refractory to multiple standard medications including metoclopramide, butyrophenones, corticosteroids, and 5HT3 antagonists. She subsequently showed improvement in symptoms after starting olanzapine. By virtue of acting on a number of key receptor sites, olanzapine as a single agent has a distinct advantage over combinations of various antiemetics by improving compliance and reducing drug interactions.

Olanzapine, in our experience, is an effective antiemetic drug in the treatment of refractory nausea and vomiting in advanced cancer patients. It should be started as a first-line drug initially in palliative care patients with intractable nausea and vomiting where it is often difficult to delineate the cause.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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