

Journal Watch

Olanzapine for the Relief of Nausea in Patients with Advanced Cancer and Incomplete Bowel Obstruction.”

Prepared by Dr. Jakub Hruczkowski (FMR2) for Oct 16, 2013.

Article: Keisuke et al. “Journal of Pain and Symptom Management 2012: 44(4): 604-607.

Background: Bowel obstruction is one of the most common complications in patients with advanced cancer. The compression of bowels due to cancer is gradual and often remains partial resulting in incomplete bowel obstruction, which is one of the leading causes of nausea and vomiting. Various standard pharmacologic therapies exist for the treatment of nausea and vomiting many of which result in adverse reactions such as extrapyramidal symptoms. Thus, it would be desirable to identify medications for nausea and vomiting that are safer to use and have a better therapeutic efficacy.

Olanzapine, an antipsychotic agent, has an affinity for multiple neurotransmitter receptors giving it potentially broad antiemetic properties. Previous studies in the treatment of chemotherapy-related nausea and vomiting have suggested olanzapine to be an efficacious agent with relatively few side effects.

Objective: The authors explore the antiemetic activity of olanzapine against nausea and vomiting in cancer patients with incomplete bowel obstruction.

Methods: The authors performed a retrospective study at a palliative care unit in Tokyo. 338 patient electronic medical records from 2007 to 2009 were reviewed. Patients had to fulfill the following inclusion criteria: 1) had advanced cancer and 2) received olanzapine for the relief of nausea and vomiting from incomplete bowel obstruction. Incomplete obstruction was diagnosed on the basis of physical and/or radiological examinations. The medical indications for olanzapine in these patients were: insufficient management with previous antiemetic treatment (metoclopramide, steroids, haloperidol, domperidone, chlorpromazine or prochlorperazine). The exclusion criteria for this study were: 1) any indication for palliative surgery, 2) presence of diabetes mellitus and 3) need for a nasogastric tube. Two palliative care specialists reviewed all the medical records. Data for demographic variables, disease site, dosage and dosing period and adverse effects were collected. Nausea and side effects were assessed daily by nurses. The intensity of each symptom was evaluated retrospectively and translated into four scores: none (0), mild (1), moderate (2), and severe (3). The frequency of vomiting was also recorded.

Results: During the study 20 patients met the inclusion criteria, with an average age being 65. Primary tumor sites included the stomach, colon/rectum, uterus/ovary, lung, urinary tract, esophagus, pancreas, and peritoneum. The average dose of

olanzapine was 4.9 +/- 1.2 mg (median 5.0; range 2.5 to 7.5), and the average treatment duration was 23.4 to 16.2 days (median 21; range 2 to 60). During the same period, a steroid (betamethasone) had been administered before olanzapine treatment to 12 patients and no other antiemetic drugs were used.

Olanzapine treatment led to a significant decrease in the average intensity score of nausea from 2.4 +/- 0.7 to 0.2 +/- 0.4 ($P < 0.001$). The percentage of patients with none or mild nausea was 10% before olanzapine treatment; 100% of the patients experienced no or mild nausea after the treatment. Of the 20 patients, 18 (90%) experienced a reduction in the intensity of nausea; no patient experienced worsening of the symptom.

The average frequency of vomiting significantly decreased with olanzapine treatment from 1.1 +/- 1.3 times/day (median 0.5; range 0 to 4) before the treatment to 0.3 +/- 0.5 times/day (median 0; range 0 to 1) after the treatment ($P < 0.01$). Before the treatment, 10 patients experienced vomiting; eight (80%) of these patients experienced a decrease in the frequency of vomiting after the treatment. Adverse effects of olanzapine treatment included drowsiness and dizziness. However, none of these patients chose to stop taking olanzapine.

Conclusion: The study results suggest the potential efficacy of olanzapine for nausea relief in incomplete bowel obstruction but that further prospective trials, including RCTs with a placebo-controlled design and comparison with an established antiemetic are required to validate these results.

Strengths:

- Hypothesis generating for future studies
- Shows olanzapine has little side effects

Weaknesses:

- No comparator group/arm
- Patients not blinded
- Observers not blinded
- Did not control for confounding variables
- Nausea and vomiting intensity scale applied retrospectively
- Inclusion criteria were not very strict
- Heterogeneous group of patients

Relevance to palliative care:

- Overall patients in this study were very heterogeneous, there was no comparator group and the study was not blinded. As a result is difficult to ascertain, based on this study, whether or not olanzapine had obvious beneficial effects for nausea and vomiting in patients with partial bowel obstruction. A prospective study should be done to validate the results of this study. If other antiemetic medications fail to control symptoms of nausea and vomiting secondary to partial bowel obstruction it may be reasonable to try olanzapine, as it seems to have few side effects based on this study.