UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

TODAY'S TOPIC:

UPMC Research: Description of Olanzapine Use in UPMC Palliative Care Population

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Results presented at American College of Clinical Pharmacy (ACCP) Global Conference 2022 and American Society of Health-System Pharmacists (ASHP) Midyear Meeting 2022

Background:

Olanzapine is an atypical (second-generation) antipsychotic that has shown off-label efficacy for the treatment of nausea, delirium, anxiety, insomnia and cachexia in adults. It has a unique receptor profile. It is an antagonist for dopamine, serotonin, muscarinic, alpha, histamine receptors which plays into the roles for its use as well as side effect profile. Olanzapine is sedating and anticholinergic, although has less risk for extrapyramidal symptoms and QTc prolongation.

Importance:

Olanzapine is being used by our palliative care teams for off-label indications. It is important to review our internal data and compare to what external data says about efficacy as well as side effects.

The Research:

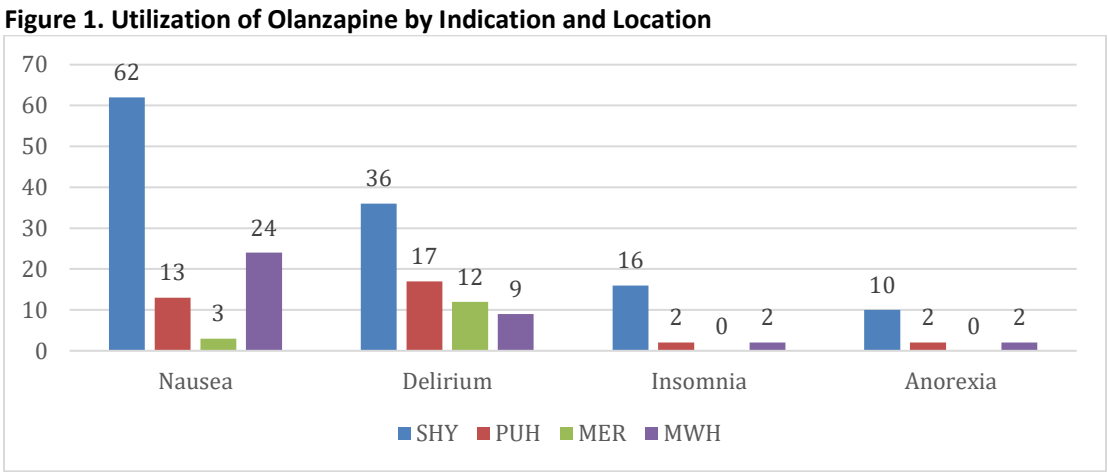
Objective: To describe prescribing patterns, effectiveness, and safety outcomes of olanzapine for off label use.

Methods:

- Retrospective Chart Review of Cerner data from July 1, 2020 through June 30, 2021
- Utilized Edmonton Symptom Assessment Scale (ESAS) documented in palliative care clinical notes to track improvement in outcomes. If symptom not included in ESAS, notes were subjectively evaluated for improvement within the assessment/plan section of the clinical notes
- Inclusion Criteria:
  - Patient admitted to Shadyside (SHY), Presbyterian (PUH), Magee-Womens (MWH), or Mercy (MER)
  - Seen by palliative care team during admission
  - Received **new start, scheduled** olanzapine for documented reason of nausea, delirium, insomnia, or anorexia during the time of palliative care involvement
- Exclusion Criteria:
  - Home olanzapine prescription prior to admission
  - Died during admission

Results:

Figure 1. Utilization of Olanzapine by Indication and Location



*olanzapine was documented for use in ≥ 1 indication
^location not recorded for one patient who received olanzapine for delirium

Table 1. Olanzapine Doses Utilized by Indication

Indication	Olanzapine Starting Dose, mean (standard deviation, SD)	Olanzapine Discharge Dose* mean (SD)
Nausea (N = 102)	3.9mg (1.4)	4.1mg (1.6)
Delirium (N = 75)	3.7mg (2.1)	4.7mg (1.7)
Insomnia (N = 20)	3.6mg (1.3)	3.9mg (1.2)
Anorexia (N = 14)	4.1mg (1.5)	5mg (3.7)

*if olanzapine was continued through discharge

Nausea (N = 102)

- N = 46 (45.1%) had reduction in ESAS score while receiving olanzapine therapy
- Antiemetics prescribed prior to initiating olanzapine:
  - 82.4% ondansetron/granisetron
  - 38.2% prochlorperazine
  - 17.6% metoclopramide

Delirium (N = 75)

- N = 10 (13.3%) had reduction in ESAS score while receiving olanzapine therapy
- N = 31 (41.3%) had "unobtainable" ESAS score
- 22 patients had another antipsychotic prescribed for delirium prior to olanzapine therapy
- 36 patients received benzodiazepine prior to olanzapine for delirium

Insomnia (N = 20)

- N = 6 (30%) had documented improvement in insomnia in clinical notes while receiving olanzapine therapy
- Sleep aids prescribed prior to initiating olanzapine:
  - 35% benzodiazepine
  - 20% melatonin
  - 5% different antipsychotic
  - 5% zolpidem

Anorexia (N = 14)

- N = 7 (50%) had reduction in ESAS score while receiving olanzapine therapy
- No effect on weight during hospital admission

CLINICAL PEARL: Olanzapine appears to be safe within the palliative care population at low, oral doses utilized in the short-term

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Safety (N = 178)

- No serious arrythmias or cardiac-related events documented
- Coadministration of other QTc-prolonging agents was common. Antiemetic co-administration most common (n=137)
- Mean dose of olanzapine initiated across indications = 3.8mg (+/- 1.7mg)
- Mean dose of olanzapine continued at discharge = 4.5mg (+/- 2.0mg)

Safety Outcome	N	Value*
QTc	28	+ 34.5 msec
Blood glucose	59	+ 22.4
Sedation score	12	+ 1.17

*mean change during olanzapine administration

Discussion:

- Utilization:
  - Shadyside is the highest utilizer of olanzapine, likely related to patient population
  - Nausea is most common indication for which we use olanzapine
    - On a (likely) related note… Olanzapine is now part of the ASCO Guidelines for treating chemo-induced nausea and vomiting
- Dosing:
  - Starting doses within our practice seem to average between 2.5-5mg
    - Effective doses for nausea have been around 5mg in the literature, between 2.5-10mg for delirium, as low as 2.5mg for insomnia and 2.5-20mg for anorexia
  - If not having a response with 2.5mg, would have a low threshold to increase to 5mg since that's where the data is (especially with nausea)
- Efficacy:
  - Olanzapine seems to have greatest impact for nausea in our population based on the data that we have
  - ESAS scores are not likely the most reliable way to track efficacy outcomes
  - Very small sample size for insomnia and anorexia make it difficult to generalize these findings
- Safety:
  - For 28 patients with QTc data, QTc increased by an average of 34.5 msec. It is not possible to conclude a relationship between the administration of olanzapine and QTc with a retrospective study
    - Olanzapine has a generally low QTc risk when used in low, oral doses
    - Keep in mind other patient-specific QTc prolonging risk factors or medications
  - There were no documented arrhythmias during olanzapine therapy.
  - Clinically significant difference not found in blood glucose during olanzapine treatment
    - Short-term use is not likely to pose a risk for hyperglycemia, like you would see with steroid administration
  - As we know, olanzapine may be sedating
  - For low oral doses utilized short-term, it is unlikely that we would see metabolic changes occur with olanzapine

CLINICAL PEARL: Olanzapine appears to be safe within the palliative care population at low, oral doses utilized in the short-term