Olanzapine for Nausea and Vomiting

Introduction:

Olanzapine is an atypical antipsychotic, which is increasingly being utilized off-label to treat nausea. Olanzapine was found to be an effective nausea treatment in palliative care patients with opioid-induced nausea in 2003[1] and is the only atypical antipsychotic medication that has been shown to have antiemetic properties.[2]

There is less evidence supporting the efficacy of olanzapine as an antiemetic medication in hospice and palliative care patients, despite strong evidence supporting its efficacy for chemotherapy-induced nausea and vomiting (CINV).[3] While the evidence is limited, it is positive, overall, in support of the safety and antiemetic efficacy of olanzapine in palliative care and hospice patients.

Mechanism of Action:

Olanzapine shows activity at multiple receptors, including serotonergic, dopaminergic, muscarinic, histaminergic, and adrenergic receptors.[4] It is theorized that the activity of olanzapine on D_2, 5-HT_{2C}, and 5-HT_3 may explain the antiemetic properties of the medication.[5]

Dosing:

The National Comprehensive Cancer Network® (NCCN®) guidelines for antiemesis recommend dosing olanzapine at 5-10 mg daily (in combination with other antiemetic medications).[6] The guidelines also note that patients who experience excessive sedation with 5 mg dosing may be given 2.5 mg daily.

While guidelines for olanzapine dosing for nausea and vomiting in hospice and palliative care patients do not currently exist, most studies and case-reports mirror the CINV dosing of 2.5-10 mg daily.[2] It would be reasonable to consider a starting dose of 2.5 mg daily in frail elderly patients.[2] Doses can be titrated up in 2.5 mg increments based on tolerability and symptom control.[2]

Adverse Effects:

Many of the adverse effects from olanzapine are related to its anticholinergic effect. Drowsiness is the most common, as noted in studies in hospice and palliative care patients.[2] For once daily dosing, olanzapine is recommended at bedtime due to this increased risk of sedation. Postural hypotension is also common and attributed to its alpha-adrenergic antagonism.[7]

Long-term use of olanzapine can lead to metabolic disturbances, such as dyslipidemia, hyperglycemia, hyperprolactinemia, increased appetite, and weight gain. Olanzapine can also cause extrapyramidal symptoms (EPS) due to its antagonism of dopaminergic D_2 receptors. EPS is less common with olanzapine than with haloperidol.[8] QT prolongation has been reported, although rare.

Drug Interactions:

- Olanzapine is a substrate of CYP1A2 (major) and CYP2D6 (minor).[8]
- Use with metoclopramide is listed as contraindicated due to the increased risk of dyskinesia, although some sources recommend close monitoring if these medications are used together.[8]
- The concomitant use of anticholinergic/sedating medications, such as antihistamines, benzodiazepines and opioids should be monitored closely and used with caution due to the risk of excessive sedation.
- Antihypertensive medications can increase the risk of orthostatic hypotension.
- Medications that can prolong the QT/QTc interval and increase the risk of TdP, such as amiodarone, buprenorphine, ketoconazole, and ondansetron, should also be used cautiously and monitored appropriately.

Summary:

While there is limited evidence regarding the use of olanzapine for nausea in hospice and palliative care patients, existing evidence is positive overall. It would be reasonable to use olanzapine as an option for patients who have not achieved symptom relief with standard antiemetics. Olanzapine is well-tolerated for short-term use, with drowsiness being the most common adverse effect. Olanzapine can be used in combination with non-antipsychotic antiemetic treatments.

References:

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