Olanzapine for the Prevention of Chemotherapy-Induced Nausea and Vomiting

Chemotherapy-induced nausea and vomiting (chemotherapy-induced emesis) is a common treatment-related side effect that has a detrimental effect on the quality of life of patients with cancer and may lead to dose reductions in or discontinuation of chemotherapy. Several neurotransmitters, including dopamine, serotonin, and substance P, have been identified as important mediators of chemotherapy-induced emesis. The development of new antiemetic agents has dramatically changed the landscape of chemotherapy-induced emesis. [(1)] Olanzapine, an atypical antipsychotic agent of the thiobenzodiazepine class, has the ability to target many different receptors, making it an attractive antiemetic agent. [(2)]

In a study conducted in 2016 they evaluated the use of olanzapine for the prevention of chemotherapy induced nausea and vomiting in patients receiving highly emetoginic chemotherapy. They found that olanzapine significantly improved nausea prevention, as well as the complete-response rate, among previously untreated patients who were receiving highly emetogenic chemotherapy.

A randomized double blind control trial was performed to compare olanzapine with placebo, in combination with dexamethasone, aprepitant or fosaprepitant, and 5-hydroxytryptamine type 3 receptor antagonist, in patients with no previous chemotherapy history who were receiving cisplatin (≥70 mg per square meter of body-surface area) or cyclophosphomide-doxorubicin.

380 patients were included in the trial (192 assigned to olanzapine, and 188 to placebo). The two groups received either 10 mg of olanzapine orally or matching placebo daily on days 1 through 4. The primary end point was nausea prevention, and the secondary end point was a complete remission with no emesis and no use of rescue medications. The proportion of patients with no chemotherapy-induced nausea was significantly greater with olanzapine than with placebo in the first 24 hours after chemotherapy (74% vs. 45%, P=0.002), the period from 25 to 120 hours after chemotherapy (42% vs. 25%, P=0.002), and the overall 120-hour period (37% vs. 22%, P=0.002). The complete-response rate was also significantly increased with olanzapine during the three periods: 86% versus 65% (P<0.001), 67% versus 52% (P=0.007), and 64% versus 41% (P<0.001), respectively. There were no grade 5 toxic effects; however some patients who received olanzapine had increased sedation on day 2. [(3)]

The mechanism of action of olanzapine involves the blocking of multiple neurotransmitter receptors including dopaminergic at D_1, D_2, D_3, and D_4 brain receptors, serotonergic at 5-HT_{2a}, 5-HT_{2c}, 5-HT_3, and 5-HT_6receptors, catecholamines at alpha$_1$ adrenergic receptors, acetylcholine at muscarinic receptors, and histamine at H_1 receptors.[(4)]

In a conclusion, olanzapine significantly improved nausea prevention, as well as the complete-response rate, among previously untreated patients who were receiving highly emetogenic chemotherapy.

Based on its effectiveness for the prophylaxis of chemotherapy-induced nausea and vomiting and relatively mild adverse effects; we are looking forward to start implementing it in the prophylaxis regimen.

References

(1) Rudolph M. Navari, M.D.,Ph.D, Matti Aapro,M.D. Antiemetic Prophylaxis for Chemotherapy-Induced Nausea and Vomiting.NEJM.2016 April 7.

(2) Megan V. Brafford, Pharm.D, BCOP, Ashley Glob, Pharm.D, BCOP. Olanzapine: An Antiemetic Option for Chemotherapy-Induced Nausea and Vomiting.JADPRO.2014 JAN 1.

(3) Rudolph M.Navari, M.D., Rui Qin, Ph.D., Kathryn J.Ruddy, M.D., et.al. Olanzapine for the Prevention of Chemotherapy-Induced Nausea and Vomiting.NEJM. 2016 july 14.

(4) Rudolph M.Navari. Treatment of Breakthrough and Refractory Chemotherapy-Induced Nausea and Vomiting.NEJM. 2014 Nov 18.

Done by Pharm D: Seveel AlSakran

Supervised by Pharm D: Eshraq Alabweeny