Addition of Olanzapine to Ondansetron and Dexamethasone for Prevention of Chemotherapy-induced Nausea and Vomiting: A Randomized, Double-blind, Placebo-controlled, Crossover Study

Veerisa Vimolchalao¹
Virote Siriuranpong¹
Napa Parinyanitikut¹
Sutima Luangdilok¹
Shama Sukprakun²
Seubpong Tanasanvimon¹
Chanida Vinayanzattikul¹
Nattaya Poovorawan¹
Ploytuangporn Wongchanapai¹

¹Division of Oncology, Department of Medicine, Chulalongkorn University, Bangkok 10330, Thailand,
²Division of Production Oncology Section, Department of Pharmacy, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand

Background: Currently, the anti-emetic regimen consisting of dexamethasone and palonosetron plus a neurokinin-1 (NK-1) antagonist or olanzapine is widely recommended in prevention of chemotherapy induced nausea and vomiting (CINV) for highly emetogenic chemotherapy (HEC). However, palonosetron and NK-1 antagonist are costly and not accessible for all Thai patients. We sought to evaluate efficacy and safety of the addition of olanzapine to ondansetron and dexamethasone, the commonly used regimen in Thailand, for CINV prevention in patients receiving HEC.

Objective: To determine the efficacy and safety of addition olanzapine to ondansetron and dexamethasone for prevention of chemotherapy-induced nausea and vomiting in HEC.

Methods: In this randomized, double-blind, placebo-controlled, crossover study, we randomly assigned chemotherapy-naïve patients receiving HEC, either anthracycline-cyclophosphamide or high dose cisplatin (>50 mg/m2) regimen, to receive olanzapine or placebo in addition to ondansetron and dexamethasone. All subjects were crossed over to another treatment arm on second-cycle chemotherapy. The primary endpoint was complete response (CR) rate defined as no vomiting and no use of rescue drugs.

Results: At first cycle, CR was 69% among the 32 patients receiving olanzapine and 25% among 32 patients receiving placebo, p<0.001. CR was significantly better with olanzapine than placebo in acute-phase (0-24 h) (75% vs 31%, p<0.001) and delayed-phase (24-120 h) (69% vs 43%, p=0.038). In analysis after two crossover antiemetic regimens, CR was significantly improved in olanzapine group compared to placebo group in acute phase (72% vs 33%, p<0.001), delayed-phase (67% vs 38%, p<0.001) and overall period (67% vs 25, p<0.001). In crossover analysis using visual analog score (VAS), the patients with olanzapine had significantly lower mean VAS in nausea (1.28 vs 3.05, p<0.001) and fatigue (3.5 vs 4.58, p<0.001) but higher mean VAS in appetite (2.5 vs 1.55, p=0.003) and sleepiness (3.26 vs 2.2, p<0.001). There were no grade 3 and 4 antiemetic-drug-related toxicities. Mean QT interval change did not different between the two groups (-4.30 ms vs -1.86 ms, p=0.69). The olanzapine combination was preferable to placebo in 52 of 60 patients, p<0.001.

Conclusion: Without NK-1 antagonists, the addition of olanzapine to ondansetron and dexamethasone significantly improves CINV prevention and is safe in patients receiving HEC.

Keywords: Olanzapine, Dexamethasone, Ondansetron, Chemotherapy induced nausea vomiting, Anthracycline and Cyclophosphamide Regimen (AC), High dose cisplatin Regimen