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Objective: Currently, the anti-emetic regimen consisting of dexamethasone and palonosetron plus a 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 additional olanzapine to ondansetron and dexamethasone for CINV prevention in patients receiving HEC.

Method: In this randomized, double-blind, placebo-controlled, crossover study, we randomly assigned chemotherapy-naïve patients receiving HEC, either AC regimen or high dose cisplatin (>50 mg/m2) regimen, to receive olanzapine(O) or placebo(P) 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 in O arm and 25% among the 32 patients in P arm, p<0.001. CR was significantly better with O in acute phase(75% vs. 31%, p<0.001) and delayed-phase(69% vs. 43%, p=0.038). No nausea rates in O group were also lower in all periods (24h; 78% vs. 44%, p=0.01, 24-120h; 68% vs. 44%, p=0.044, overall; 65% vs. 38%, p=0.024). In analysis after two crossover antiemetic regimens, CR was significantly improved in patients receiving O compared to P 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). No nausea rates were better with O in all periods(24h; 73% vs. 45%, p=0.001, 24-120h; 59% vs. 37%, p=0.001, overall; 56% vs. 31%, p<0.001). In crossover analysis using visual analog score(VAS), the patients with O had significantly lower mean VAS in nausea and fatigue but higher mean VAS in appetite and sleepiness. There were no grade 3 and 4 antiemetic-drug-related toxicities. Mean QT interval change did not differ between two drugs(-4.30 ms vs. -1.86 ms, p=0.69). The O combination was preferable to P in 52 of 60 patients, p<0.001.

Conclusions: Without the NK-1 antagonists, the additional olanzapine to ondansetron and dexamethasone significantly improved CINV prevention and was safe in Pt receiving HEC.