A Meta-Analysis of Palonosetron for the Prevention of Postoperative Nausea and Vomiting in Adults

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Purpose: *The aim of this meta-analysis was to evaluate the effectiveness and adverse effects of palonosetron in the prevention of postoperative nausea and vomiting (PONV).*

Design: *A meta-analysis using a systematic search strategy was performed.*

Methods: *A meta-analysis of randomized controlled clinical trials was performed to compare palonosetron with first-generation 5-hydroxytryptamine 3 receptor antagonist (5-HT3RA) or placebo to prevent PONV. Fixed or random effect models were used to combine homogenous data.*

Findings: *A total of 10 randomized controlled clinical trials including 1,827 patients were identified. The data showed statistically significant differences in favor of palonosetron (0.075 mg) in the prevention of acute PONV (*P *< .00001) and delayed PONV (*P *< .002), reducing the risk of PONV by 49% and 51%, respectively. Subgroup analyses indicated significant differences in favor of palonosetron compared with placebo (*P *< .00001) or first-generation 5-HT3RA (*P *= .002). There were no significant differences in the occurrence of headache, dizziness, and constipation between palonosetron and control groups (*P *= .85,* P *= .22, and* P *= .30, respectively).*

Conclusions: *The results of this meta-analysis suggest that intravenous palonosetron could become a prophylactic antiemetic 5-HT3RA in the prevention of PONV compared with first-generation 5-HT3RAs or placebo. No increased risk of side effects with palonosetron were found.*

Keywords: *palonosetron, prophylaxis, PONV, 5-HT3RA, meta-analysis.*

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Conflicts of interest: None to report.

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POSTOPERATIVE NAUSEA AND VOMITING (PONV), defined as nausea or vomiting within 24 hours of surgery, has an incidence rate ranging between 20% and 30%.[1,2] Four primary risk predictors have been reported as female gender, history of motion sickness, nonsmoking, and the use of postoperative opioids.[3] The simplified score by Apfel et al[1,3] suggests that patients with at least two of the four previously mentioned risk factors should be considered to receive a prophylactic antiemetic strategy. If untreated, PONV occurs in 20% to 30% of general surgical strategy. Among high-risk patients, the incidence of PONV will rise to as frequent as 70% to 80%.[1,4] Evidence-based guidelines have been established to identify the primary risk factors for PONV and give optimal approaches for PONV prophylaxis.[5]

Several first-generation 5-hydroxytryptamine 3 receptor antagonists (5-HT3RAs), such as ondansetron (recommended dose is 4 mg), dolasetron (12.5 mg), granisetron (0.35 to 1.5 mg), and tropisetron (2 mg), have been marketed and frequently used. Ondansetron was suggested to be more effective than others for preventing PONV in a meta-analysis.[6] However, the short life of the first-generation 5-HT3RAs limits their utilization as prophylactic antiemetics.[7,8] Palonosetron is a second-generation 5-HT3RA with a unique pharmacodynamic mechanism of allosteric binding with higher binding affinity and longer half-life and duration of action compared to standard 5-HT3RAs.[9] As of this publication, the US Food and Drug Administration has approved a single injection of a 0.075 mg dose for PONV prevention for up to 24 hours after surgery.[10] Numerous randomized controlled clinical trials (RCTs) have been performed to assess the efficacy and safety of palonosetron for preventing PONV as compared to other first-generation 5-HT3RAs or placebo after different kinds of surgery.[10–19]

In an effort to seek supportive evidence for the prophylactic use of palonosetron, this systemic review was performed to evaluate the effectiveness of prophylaxis and adverse effects associated with the use of palonosetron in different time periods.

Materials and Methods

Data Sources

PubMed (1966-April 2014), Cochrane Library, Google Scholar, Wanfang Data (Chinese 1998-April 2014), and China National Knowledge infrastructure electronic databases (1994-April 2014) were searched for RCTs. Search terms included "postoperative nausea and vomiting," "post-operative nausea and vomiting," and "PONV." We excluded unpublished data and RCTs of pediatric patients with PONV.

Selection Criteria and Outcomes

Primary outcomes of interest included complete response (CR) of acute (0 to 24 hours) and delayed (24 to 72 hours) periods of PONV by palonosetron. CR was defined as no emesis and no rescue medication during the different phases mentioned previously. The adverse effects of palonosetron were also investigated.

Methodological Quality and Statistical Analysis

Included studies were evaluated for methodological quality by the methods of randomization, allocation, and blinding. The meta-analysis was performed on the nonheterogenerous trials with Review Manager (RevMan 5.0; Nordic Cochrane Centre, Rigshospitalet, Denmark) using fixed or random effect models. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. The heterogeneity test ($P > .05$) was considered as the low level of heterogeneity. Funnel plots were used to assess for possible publication bias. Statistical significance was considered as P value less than .05.

Subgroup Analyses

We performed subgroup analyses using two different control criteria versus palonosetron during first 24 hours as follows: first-generation 5-HT3RA and placebo, respectively.

Results

Ten RCTs including 1,827 patients were considered, with eight studies in English and two in