**INTRODUCTION**

**Review question / Objective:** This meta-analysis intends to compare the effects of ondansetron and droperidol, the most commonly used antiemetics, on cardiac repolarization.

**Condition being studied:** The butyrophenone droperidol and 5-hydroxytryptamine type 3 receptor antagonists (ondansetron, dolasetron, Granisetron, tropisetron, palonosetron) are the most effective antiemetics for prevention or treatment of postoperative nausea and vomiting. However, relevant studies have shown that all of those drugs prolong QT interval, a circumstance that raise some concerns regarding the possibility of inducing torsades de pointes (TdP). Which one is safer still lacks evidence-based data.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 January 2022 and was last updated on 13 January 2022 (registration number INPLASY202210063).

**Conflicts of interest:** None declared.
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METHODS

Search strategy: Pubmed #1 Droperidol [TIAB] OR Holoperidol [TIAB] #2 Ondansetron [TIAB] #3 Repolarization [TIAB] OR QT interval [TIAB] OR QTc interval [TIAB] #4 #1 AND #2 AND #3 Medline #1 TS=(Droperidol) OR TS=(Holoperidol) #2 TS=(Ondansetron) #3 TS=(Repolarization) OR TS=(QT interval) OR TS=(QTc interval) #4 #1 AND #2 AND #3 Embase and Cochrane Library #1 Droperidol [ti,ab,kw] OR Holoperidol [ti,ab,kw] #2 Ondansetron [ti,ab,kw] #3 Repolarization [ti,ab,kw] OR QT interval [ti,ab,kw] OR QTc interval [ti,ab,kw] #4 #1 AND #2 AND #3.

Participant or population: Participants received ondansetron or droperidol injection.

Intervention: Ondansetron injection.

Comparator: Droperidol injection.

Study designs to be included: Randomized controlled trials (RCTs).

Eligibility criteria: All studies met the following criteria. (1) Participants were patients or volunteers that received ondansetron or droperidol injection. (2) Compared the effects of ondansetron versus droperidol. (3) Reported data to calculate the QTc prolongation (ΔQTcF) after drug administration. (4) Study design was randomized controlled trials (RCTs).

Information sources: Embase, PubMed, Medline and the Cochrane Library from inception to March 2022.

Main outcome(s): The maximal QTc prolongation (ΔQTc) after drug injection. The heart rate adjusted QT (QTc) interval was calculated according to the formula of Bazett (QTcB = QT √R R) or Framingham (QTcF = QT + [1-RR] × 0.154). The maximal ΔQTc = the maximal QTc after drug injection - QTc before drug injection.

Additional outcome(s): 1. The maximal Tp–e prolongation (ΔTp–e). Transmural dispersion of repolarization (TDR), which indicates the time elapsed between the peak of the T wave and the end of the T wave (Tp–e). The maximal ΔTp–e = the maximal Tp–e after drug injection - Tp–e before drug injection. 2. The incidence of the participants had QTc prolongation greater than 60 ms or over 500 ms. 3. The incidence of cardiac dysrhythmias. 4. The incidence of PONV. 5. The use of rescue antiemetics during the 24 h postoperatively. 6. Other drug-related side effect, such as headache or extrapyramidal symptoms.

Quality assessment / Risk of bias analysis: The quality of RCTs will be assessed according to the guidelines in the Cochrane Handbook for Systematic Reviews of Interventions to create a “risk of bias” table that included the following contents: details on methods of random sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other bias. The overall quality of each study will be evaluated as “low risk of bias”, “high risk of bias”, or “unclear risk of bias”.

Strategy of data synthesis: The meta-analysis will be conducted by Review Manager software 5.4. Mean differences (MDs) with 95% confidence intervals (CIs) will be used to assess continuous outcomes. Odds ratios (ORs) with 95% CIs will be used to assess dichotomous outcomes. Statistical heterogeneity will be assessed by P and I2. When I2 < 50% and P > 0.1, a fixed-effects model will be applied; otherwise, a random-effects model will be applied. The Mantel–Haenszel methods will be used to combine separate statistics. P values less than 0.05 will be considered statistically significant. Trial sequential analysis (TSA) software 0.9.5.10 will be
used to examine the reliability and conclusiveness of the available evidence.

**Subgroup analysis:** Subgroup analysis will be performed according to the sample situation in the included study: (1) quality of studies; (2) adults or children; (3) different types of anesthesia; (4) different types of surgery.

**Sensitivity analysis:** We will conduct sensitivity analysis by eliminating studies one by one and repeating meta-analysis.

**Country(ies) involved:** China.

**Keywords:** ondansetron; droperidol; meta-analysis; QT interval; QTc interval.

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