Efficacy of Ramosetron in Preventing Postoperative Nausea and Vomiting: An Updated Meta-analysis with Trial Sequential Analysis

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BACKGROUND

In 2013, we reported a meta-analysis on efficacy of ramosetron in preventing postoperative nausea and vomiting (PONV). Since then, several randomized controlled trials (RCTs) on the effects of ramosetron have been published. The aim of this study was to update the meta-analysis by using trial sequential analysis (TSA).

METHODS

Search target :

MEDLINE, CENTRAL, Embase, Web of Science

Inclusion criteria :

RCTs that reported the efficacy of ramosetron for preventing PONV compared with placebo

Outcome:

early PON, POV, late PON, POV
(early = 0-6 hours / late = 6-24 hours, PON = postoperative nausea / POV = postoperative vomiting)

① Summary :

Calculating risk ratio (RR) and 95% confidence interval (95%CI) using random-effects model to combine result
Significant heterogeneity : $I^2 \geq 50\%$

② Sensitivity analysis :

Restricting to only double-blind RCTs

③ TSA :

Calculating the required sample size for meta-analysis to determine whether more trials are needed or not

RESULTS

Out of 352 articles initially searched, 20 articles (2003 patients) had met the eligible criteria.

	① Summary			② Sensitivity analysis			③ TSA
	N	RR [95%CI]	I^2	N	RR [95%CI]	I^2	zone
early PON	1419	0.53 [0.41; 0.68]	55%	814	0.58 [0.46; 0.72]	10%	Evidence of effect
early POV	1481	0.49 [0.32; 0.74]	36%	878	0.39 [0.25; 0.62]	23%	Evidence of effect
late PON	1419	0.47 [0.34; 0.66]	67%	814	0.61 [0.46; 0.82]	36%	Evidence of effect
late POV	1481	0.50 [0.36; 0.69]	0%	878	0.46 [0.29; 0.72]	16%	Evidence of effect

Fig.1 TSA of early PON

- Conventional random-effects meta-analysis showed that ramosetron was more effective than placebo for preventing PON and POV in both early and late periods.
- Heterogeneity ($I^2 > 50\%$) observed in the early and late PON was reduced when restricted to double-blind RCTs.
- In all outcomes, the Z curve crossed the TSA monitoring boundary and reached the target sample size. It means that no additional trials are needed.

CONCLUSION

The efficacy of ramosetron is strong enough to lead to the conclusion that ramosetron reduces PONV compared with placebo, and thus there is no need for additional RCTs.

Fig.2 Explanation of TSA diagram

- **Conventional boundary for significance (green)** : $p=0.05$, $Z=1.96$
- **TSA monitoring boundary (red)** : adjust the p-value that is required for obtaining a statistical significance according to the number of patients
- **Z curve** : constructed with each cumulative Z-score calculated after including a new trial according to publication date

If the Z curve crosses the TSA monitoring boundary, it means that it is a reliable evidence, adjusting false positive error risk.