Dose-ranging study of ramosetron for the prevention of nausea and vomiting after gynecologic laparoscopic surgery: a prospective randomized study

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BACKGROUND

- Patients undergoing laparoscopic gynecological surgery are at high risk of postoperative nausea and vomiting (PONV).
- The aim of this study was to determine the effective dose of ramosetron, a 5-hydroxytryptamine type 3 receptor antagonist, for prophylaxis of PONV in this patient population.

METHODS

- In this prospective, randomized, double-blinded study, 174 patients received a single administration of either IV ramosetron 0.3 mg (R0.3 group), 0.45 mg (R0.45 group), or 0.6 mg (R0.6 group) immediately after the end of surgery.
 - R0.3 group(n=58) : IV ramosetron 0.3mg group
 - R0.45 group(n=58) : IV ramosetron 0.45mg group
 - R0.6 group(n=58) : IV ramosetron 0.6mg group
- In all groups, ondansetron 8mg was added to an intravenous patient-controlled analgesia (IV-PCA) fentanyl solution.
- The primary outcome was the incidence of PONV during the first 48h after surgery.
 - The severity of nausea
 - Pain score
 - Adverse events

RESULTS

Table 1. Patient Characteristics

	R0.3 group (n = 58)	R0.45 group (n = 58)	R0.6 group (n = 58)	P value
Age (yr)	42.2 (22-64)	41.0 (21-62)	41.2 (20-70)	0.809
Body mass index (kg/m ²)	23.9 ± 4.2	22.9 ± 3.5	22.8 ± 3.4	0.178
ASA classification (I/II/III)	4/ 2	6/ 3	8/ 2	0.774
Motion sickness (n)	14 (24%)	15 (26%)	14 (24%)	0.970
Previous PONV (n)	2 (3%)	3 (5%)	0	0.237
Nonsmoker (n)	56 (97%)	56 (97%)	56 (97%)	> 0.999
Apfel's score				0.996
2 (n)	2 (3%)	2 (3%)	2 (3%)	
3 (n)	41 (71%)	40 (69%)	42 (72%)	
4 (n)	15 (26%)	16 (28%)	14 (24%)	
Operation duration (min)	69.0 [52.0, 100.5]	69.0 [40.0, 104.8]	77.0 [58.5, 111.8]	0.221
Anesthesia duration (min)	95.0 [75.0, 131.3]	95.0 [69.8, 132.5]	100.0 [80.0, 140.0]	0.239
Type of surgery				0.585
salpingo-oophorectomy	18	15	10	
ovarian cyst enucleation	15	22	20	
myomectomy	9	7	10	
hysterectomy	16	14	18	

Values are mean (ranges), mean ± standard deviation, number of patients (%), or median [IQR].

Table 4. Adverse events

	R0.3 group (n = 58)	R0.45 group (n = 58)	R0.6 group (n = 58)	P value
Dizziness	16 (28%)	14 (24%)	13 (22%)	0.806
Headache	10 (17%)	6 (10%)	9 (16%)	0.545
Sedation	0	0	0	
Early discontinuation of patient-controlled analgesia	14 (24%)	5 (9%)	3 (5%)	0.005

Values are number of patients (%).

Table 2. Incidence of nausea and vomiting, and use of rescue antiemetics

	R0.3 group (n = 58)	R0.45 group (n = 58)	R0.6 group (n = 58)	P value
Nausea incidence				
30 min	8 (14%)	9 (16%)	9 (16%)	0.956
30 min to 6 h	5 (9%)	3 (5%)	4 (7%)	0.765
6 to 24 h	14 (24%)	11 (19%)	11 (19%)	0.730
24 to 48 h	14 (24%)	10 (17%)	8 (12%)	0.342
Severity of nausea				
30 min (mild/moderate/severe/intractable)	0/ 7/ 0/ 1	1/ 8/ 0/ 0	4/ 5/ 0/ 0	0.245
30 min to 6 h (mild/moderate/severe/intractable)	0/ 2/ 3/ 0	0/ 1/ 2/ 0	0/ 3/ 1/ 0	0.729
6 to 24 h (mild/moderate/severe/intractable)	2/ 4/ 8/ 0	0/ 8/ 3/ 0	1/ 8/ 2/ 0	0.204
24 to 48 h (mild/moderate/severe/intractable)	2/ 10/ 2/ 0	0/ 5/ 5/ 0	1/ 6/ 1/ 0	0.265
Emetic episodes				
30 min	1 (2%)	1 (2%)	3 (5%)	0.439
30 min to 6 h	0	1 (2%)	1 (2%)	0.603
6 to 24 h	0	0	2 (3%)	0.132
24 to 48 h	0	1 (2%)	1 (2%)	0.603
PONV				
30 min	8 (14%)	9 (16%)	10 (17%)	0.877
30 min to 6 h	5 (9%)	3 (5%)	4 (7%)	0.765
6 to 24 h	14 (24%)	11 (19%)	10 (17%)	0.628
24 to 48 h	14 (24%)	10 (17%)	7 (12%)	0.234
overall	20 (35%)	22 (38%)	20 (35%)	0.905

Values are number of patients (%).

Table 3. Postoperative pain score and use of rescue analgesics

	R0.3 group (n = 58)	R0.45 group (n = 58)	R0.6 group (n = 58)	P value
Worst pain score				
during 30 min after surgery	3.8 ± 1.3	3.5 ± 1.1	3.4 ± 1.4	0.342
during 30 min to 6 h after surgery	4.6 ± 1.7	4.7 ± 1.5	4.5 ± 1.6	0.816
during 6 to 24 h after surgery	2.7 ± 0.9	2.7 ± 1.0	2.6 ± 0.9	0.928
during 24 to 48 h after surgery	3.3 ± 1.6	3.0 ± 1.4	2.7 ± 1.3	0.102
Patients requiring additional analgesics				
during 30 min after surgery (n)	20	16	15	0.559
during 30min to 6h after surgery (n)	5	4	5	0.925
during 6 to 24 h after surgery (n)	3	6	2	0.283
during 24 to 48 h after surgery (n)	14	11	7	0.242

Values are mean ± standard deviation or number of patients.

Pain scores were assessed using an 11-point numerical rating scale (0, no pain, to 10, worst imaginable pain).

- The incidences of PONV were not different among three groups (35%, 38%, vs. 35%, $P = 0.905$).
- The severities of nausea, pain scores, and additional analgesic requirements were similar among the groups.
- The incidence of adverse events including dizziness, headache, and sedation were not different among the groups.
- However, more patients in R0.3 group required early IV-PCA discontinuation compared to those in R0.45 and R0.5 groups, primarily because of PONV and/or dizziness (24% vs. 9% and 5%, $P = 0.038$).

CONCLUSIONS

- Increased dose of ramosetron was not found to reduce the incidence of PONV in high risk patients undergoing laparoscopic gynecological surgery.