Postoperative Gastrointestinal Dysfunction After Neuromuscular Blockade Reversal With Sugammadex Versus Cholinesterase Inhibitors in Patients Undergoing Gastrointestinal Surgery: A Systematic Review and Meta-Analysis

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Background

•Postoperative gastrointestinal dysfunction (POGD) is common after GI surgery, often associated with specific anesthetic agents.
•Cholinesterase inhibitors used for reversing neuromuscular blockade are implicated in POGD development.
•Sugammadex, a novel reversal agent, shows promise in reducing POGD, but comprehensive comparative reviews are lacking.
•This study aims to systematically review sugammadex's impact on POGD compared to cholinesterase inhibitors following GI surgery.

Introduction

•Postoperative gastrointestinal dysfunction (POGD) after GI surgery involves symptoms like prolonged postoperative ileus (PPOI) and postoperative nausea and vomiting (PONV).
•Traditional NMB reversal methods with cholinesterase inhibitors (CI) and anticholinergics (AC) may worsen POGD due to AC effects.
•Sugammadex, a newer reversal agent without muscarinic activity, is hypothesized to reduce POGD. Studies on its effectiveness after abdominal surgery show mixed results, prompting the need for a systematic review comparing it to CI agents.

Methods

•**Search Strategy:**
- Databases searched: Medline, EMBASE, CENTRAL
- Terms used: "Sugammadex," "Ileus," "Bridion," "Neostigmine," etc.
- Grey literature and published studies manually surveyed
- Adherence to PRISMA and Meta-Analysis of Observational Studies in Epidemiology guidelines

•**Inclusion/Exclusion Criteria:**
- Included prospective and retrospective studies comparing sugammadex with CI in GI surgery patients
- Excluded commentaries, opinion articles, case reports, pediatric population, animal studies, <10 patients, non-GI surgery studies

•**Outcomes Assessed:**
- Primary: Incidence of PPOI (≥4 days) and PONV (within 24 hours postoperatively)
- Secondary: LOS, readmission rates within 30 days, pulmonary complications, postoperative morbidity

•**Data Extraction:**
- Search strategy executed by author SS
- Title/abstract screening, followed by full-text screening
- Data abstraction by 2 independent reviewers using standardized excel sheet

•**Risk of Bias Assessment and Certainty of Evidence:**
- Evaluated using Cochrane Risk of Bias Tool for RCTs 2.0 or ROBINS-I
- GRADE assessment for meta-analysis estimates

•**Statistical Analysis:**
- Analyses conducted using STATA version 14 and Cochrane Review Manager 5.3
- Pairwise meta-analysis using inverse variance, random effects model
- Heterogeneity assessed with I2 statistic (>50% indicates considerable heterogeneity)
- Publication bias assessed with funnel plot (>10 studies)
- Sensitivity analysis conducted for gastrointestinal organ system and surgical approach
- Systematic narrative summary provided for outcomes with <3 studies reported

Table 1. Study, Patient, and Operative Characteristics. BMI: Body Mass Index; ASA: American Society of Anesthesiologists Classification.

Author, Year	Intervention Arm	N	Female (%)	Age (y)	BMI	Surgery Type	Laparoscopic Surgery (%)	Anesthetic Duration (min)	ASA Class (%)
An, 2020	Sugammadex	49	33 (67.3)	51.2±12.9	25.4[a]	Laparoscopic cholecystectomy	49 (100)	57.1±15.6	I: 82 II: 91.8
	Pyridostigmine	53	29 (54.7)	46.8±13.9	25.3[a]		53 (100)	58.8±15.1	I: 75 II:92.5
Chae, 2019	Sugammadex	157	71 (45.2)	62.5±11.5	23.8±3.3	Laparoscopic or open colorectal surgery	32 (20)	176.0±46.7	I: 43 II: 57
	Pyridostigmine	157	74 (47.1)	63.1±11.8	23.4±3.4		34 (22)	175.1±41.0	I: 49 II: 51
Cho, 2021	Sugammadex	309	-	-	-	Pancreaticoduodenectomy	215 (29.8)	-	
	Neostigmine	429	-	-	-			-	
Brueckmann, 2015	Sugammadex	74	27 (36)	56.4±12.8	32.9[a]	Abdominal surgery	-	-	I: 1 II: 80 III: 19
	Neostigmine	77	34 (44)	57.0±12.7	30.2[a]		-	-	II: 82 III: 18
Hunt, 2020	Sugammadex	128	60 (62.5)	60.7±14.7	29.3±6.1	Laparoscopic colorectal surgery	128 (100)	229[b]	
	Neostigmine	96	70 (54.7)	60.3±14.1	29.6±6.2		96 (100)	214.2[b]	

[a]Calculated from average weight and height
[b]Missing standard deviation

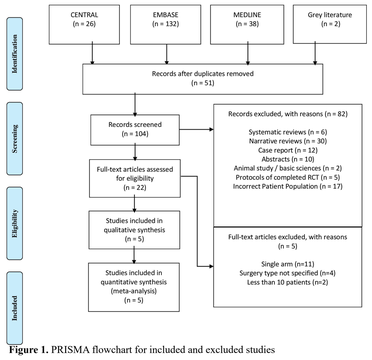

Figure 1. PRISMA flowchart for included and excluded studies

Table 2. Postoperative Complications. PPOI: Prolonged Postoperative Ileus; PONV: Postoperative Nausea/Vomiting; LOS: Length of Stay.

Author, Year	Intervention Arm	N	PPOI (%)	PONV (%)	LOS (days)	Readmission (%)	Pulmonary Complications (%)
An, 2020	Sugammadex	49	-	12 (24.5)	-	-	-
	Pyridostigmine	53	-	11 (20.8)	-	-	-
Chae, 2019	Sugammadex	157	9 (5.7)	-	10.1±12.9	12 (8.0)	4 (2.5)
	Pyridostigmine	157	36(22.9)	-	10.1±4.0	15 (10.0)	1 (.6)
Cho, 2021	Sugammadex	309	60 (19.3)	48 (15.5)	11[a] [9-17][b]	19 (6.3)	5 (1.6)
	Neostigmine	429	121 (28.3)	81 (18.8)	11[a] [9-16][b]	26 (6.1)	7 (1.6)
Brueckmann, 2015	Sugammadex	74	4 (5.4)	2 (2.7)	-	-	1 (1.4)
	Neostigmine	77	6 (7.8)	10 (13)	-	-	5 (6.5)
Hunt, 2020	Sugammadex	128	10 (10.4)	50 (52.1)	76.7±44.2	-	-
	Neostigmine	96	15 (11.7)	61 (47.7)	79.2±36.2	-	-

[a]Median.
[b]Interquartile range.

Figure 7. Risk of bias tool for randomized controlled trials 2.0 (RoB 2.0).

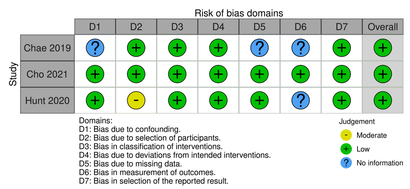

Figure 8. Risk of bias in non-randomized studies—of interventions (ROBINS-I).

Postoperative Nausea/Vomiting

Study	Sugammadex	(%)	Cholinesterase Inhibitors	(%)	Weight	OR [95% CI]
Brueckmann et al. 2015	2/74	(3%)	10/77	(13%)	11.7%	0.19 [0.04, 0.88]
An et al. 2020	12/49	(24%)	11/53	(21%)	21.6%	1.24 [0.49, 3.14]
Hunt et al. 2020	50/128	(39%)	61/96	(64%)	31.3%	0.37 [0.21, 0.64]
Cho et al. 2021	48/309	(16%)	81/429	(19%)	35.3%	0.79 [0.53, 1.17]
Pooled Estimate	112/560	(20%)	163/655	(25%)	I^2: 68%	0.58 [0.31, 1.09]

Mantel-Haenszel, DerSimonian-Laird Random Effects — *p=0.09, z=1.70, τ²=0.25*
OR: Odds Ratio; CI: Confidence Interval

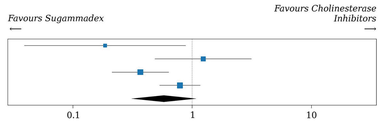

Figure 2. Overall odds ratio for development of postoperative nausea or vomiting in patients undergoing anesthetic reversal with Sugammadex vs Cholinesterase inhibitors

Prolonged Postoperative Ileus

Study	Sugammadex	(%)	Cholinesterase Inhibitor	(%)	Weight	OR [95% CI]
Brueckmann et al. 2015	4/74	(5%)	6/77	(8%)	13.1%	0.68 [0.18, 2.5]
Chae et al. 2019	9/157	(6%)	36/157	(23%)	24.8%	0.2 [0.09, 0.44]
Hunt et al. 2020	10/128	(8%)	15/96	(16%)	22.5%	0.46 [0.2, 1.07]
Cho et al. 2021	60/309	(19%)	121/429	(28%)	39.7%	0.61 [0.43, 0.87]
Pooled Estimate	83/668	(12%)	178/759	(23%)	I^2: 56%	0.44 [0.25, 0.77]

Mantel-Haenszel, DerSimonian-Laird Random Effects — *p=0.00, z=2.87, τ²=0.17*
OR: Odds Ratio; CI: Confidence Interval

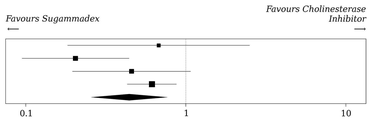

Figure 3. Overall odds ratio for development of prolonged postoperative ileus in patients undergoing anesthetic reversal with Sugammadex vs Cholinesterase inhibitors.

Length of Stay

Study	Sugammadex	(N)	Cholinesterase Inhibitor	(N)	Weight	MD [95% CI]
Chae et al. 2019	10.1 ± 12.9	(157)	10.0 ± 4.0	(157)	3.2%	0.1 [-2.01, 2.21]
Hunt et al. 2020	3.2 ± 1.8	(128)	3.3 ± 1.5	(96)	75.4%	-0.1 [-0.53, 0.33]
Cho et al. 2021	12.3 ± 6.0	(429)	12.0 ± 5.2	(309)	21.4%	0.3 [-0.51, 1.11]
Pooled Estimate					I^2: 0%	-0.01 [-0.38, 0.37]

Inverse Variance, DerSimonian-Laird Random Effects — *p=0.97, z=0.04, τ²=0.00*
MD: Mean Difference; CI: Confidence Interval

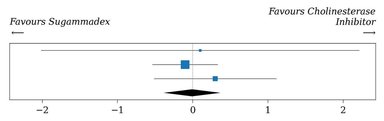

Figure 4. Overall mean difference in length of stay in patients undergoing anesthetic reversal with Sugammadex vs Cholinesterase inhibitors.

Postoperative Morbidity

Study	Sugammadex	(%)	Cholinesterase Inhibitor	(%)	Weight	OR [95% CI]
Brueckmann et al. 2015	39/74	(53%)	41/77	(53%)	23.6%	0.98 [0.52, 1.85]
Chae et al. 2019	23/157	(15%)	40/157	(25%)	24.6%	0.5 [0.28, 0.89]
Hunt et al. 2020	60/128	(47%)	76/96	(79%)	24.1%	0.23 [0.13, 0.42]
Cho et al. 2021	101/309	(33%)	134/429	(31%)	27.8%	1.27 [0.78, 1.46]
Pooled Estimate	223/668	(33%)	291/759	(38%)	I^2: 86%	0.6 [0.3, 1.21]

Mantel-Haenszel, DerSimonian-Laird Random Effects — *p=0.15, z=1.43, τ²=0.43*
OR: Odds Ratio; CI: Confidence Interval

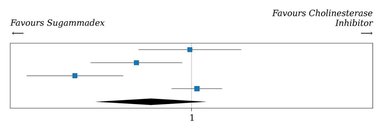

Figure 5. Overall odds ratio of postoperative morbidity in patients undergoing anesthetic reversal with Sugammadex vs Cholinesterase inhibitors.

Pulmonary Complications

Study	Sugamadex	(%)	Cholinesterase Inhibitors	(%)	Weight	OR [95% CI]
Chae et al. 2019	4/157	(3%)	1/157	(1%)	25.8%	4.08 [0.45, 36.91]
Cho et al. 2021	5/309	(2%)	7/429	(2%)	47.8%	0.99 [0.31, 3.15]
Brueckmann et al. 2015	1/74	(1%)	5/77	(6%)	26.3%	0.2 [0.02, 1.73]
Pooled Estimate	10/540	(2%)	13/663	(2%)	I^2: 46%	0.93 [0.23, 3.81]

Mantel-Haenszel, DerSimonian-Laird Random Effects — *p=0.92, z=0.09, τ²=0.71*
OR: Odds Ratio; CI: Confidence Interval

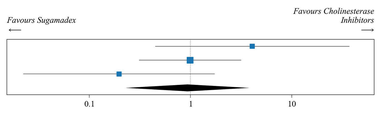

Figure 6. Overall odds ratio for development of pulmonary complications in patients undergoing anesthetic reversal with Sugammadex vs Cholinesterase inhibitors.

Log10 Optical Density at 600nm

Results and Conclusion

- 2 randomized trials and 3 retrospective cohorts included
- 717 patients in sugammadex group (mean age 59 +/- 13 years, 53.4% female)
- 812 patients in CI group (mean age 59 +/- 14 years, 50% female)
- Detailed Study, Patient, and Operative characteristics are presented in Table 1. Detailed postoperative complications are presented in Table 2.
- Sugammadex was associated with significantly lower rates of prolonged postoperative ileus compared to cholinesterase inhibitors (OR .44, 95% CI .25-.77, P < .05)
- No significant differences were observed in any other outcomes.
- Narrative review of readmission data showed no significant difference between the two groups.

Conclusions

In summary, this systematic review and meta-analysis demonstrated a potential benefit in terms of prolonged postoperative ileus (PPOI) for patients undergoing GI surgery receiving sugammadex compared to CI. However, there was no impact in terms of postoperative nausea and vomiting (PONV), length of stay (LOS), morbidity, or pulmonary complications. Large RCTs with standardization in measurement for clinically relevant outcomes, in addition to studies assessing cost effectiveness are required before routine use of sugammadex can be recommended.

Future Work

Large RCTs with standardization in measurement for clinically relevant outcomes, in addition to studies assessing cost effectiveness are required before routine use of sugammadex can be recommended.

References

*Please see attached document for full list of references used in this article. Below are the first 12 of 50

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