

## A Meta-Analysis of Dextrose Infusion as Perioperative Strategy on Preventing Postoperative Nausea and Vomiting



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### ABSTRAK

**Introduction:** Dextrose infusion was introduced as a non-pharmacological perioperative strategy to decrease the PONV incidence. However, current published studies reported remain inconsistent and debatable results regarding the efficacy. This research was conducted to improve the evidence-based perioperative strategies of administering dextrose infusion to prevent PONV.

**Method:** A literature search was conducted for randomized controlled trial studies (RCTs) in patients who administered dextrose infusion compared to other infusion fluid perioperatively. A quantitative analysis using Review Manager 5.4 was performed with a 95% confidence interval that was visualized in the forest plot graph using the fixed-effects or random-effects model based on the heterogeneity.

**Results:** A total of 18 RCTs studies analyzed demonstrated there were significant differences in composite PONV (RR, 0.66, 95%CI 0.60, 0.74;  $P < 0.00001$ ;  $I^2 = 46\%$ ), patients with postoperative antiemetic rescue requirements (RR, 0.67, 95%CI 0.53, 0.86;  $P < 0.001$ ;  $I^2 = 68\%$ ), and postoperative blood glucose levels (SMD, 2.63, 95%CI 1.76, 3.50;  $P < 0.00001$ ;  $I^2 = 97\%$ ). However, there were insignificant results in PONV severity (SMD, -0.94, 95%CI -2.20, 0.31;  $P = 0.14$ ;  $I^2 = 97\%$ ), patients with analgesic requirements (RR, 0.84, 95%CI 0.60, 1.19;  $P = 0.33$ ;  $I^2 = 81\%$ ), dose of analgesic requirements (SMD, -2.31, 95%CI -5.76, 1.14;  $P = 0.19$ ;  $I^2 = 99\%$ ), and PACU stay (MD, -24.73, 95%CI -66.07, 16.61;  $P < 0.24$ ;  $I^2 = 99\%$ )

**Conclusion:** This meta-analysis demonstrated that administering dextrose infusion perioperatively prevents both the PONV incidence and postoperative rescue antiemetic requirements, and also increase postoperative blood glucose levels. However, dextrose infusion is not associated with reducing the PONV severity, postoperative analgesic requirements, a dose of postoperative analgesic use, and PACU stay.

**Keywords:** Dextrose; PONV; Anaesthesia; Systematic Review; Meta-Analysis



## Meta-Analisis Infus Dekstrosa Sebagai Strategi Perioperatif dalam Mencegah PONV (Post Operative Nausea and Vomiting)

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### ABSTRAK

**Pendahuluan:** Infus dekstrosa diperkenalkan sebagai strategi perioperatif non-farmakologis untuk menurunkan kejadian Post Operative Nausea and Vomiting (PONV). Namun, penelitian yang dipublikasikan saat ini melaporkan hasil yang masih tidak konsisten dan diperdebatkan mengenai efikasinya. Penelitian ini dilakukan untuk meningkatkan strategi perioperatif berbasis bukti terkait pemberian infus dekstrosa untuk mencegah PONV.

**Metode:** Penelusuran literatur dilakukan untuk studi uji coba terkontrol secara acak (RCT) pada pasien yang diberikan infus dekstrosa dibandingkan dengan cairan infus lain secara perioperatif. Analisis kuantitatif menggunakan Review Manager 5.4 dilakukan dengan interval kepercayaan 95% yang divisualisasikan dalam grafik forest plot menggunakan fixed-effects atau random-effects berdasarkan heterogenitas.

**Hasil:** Sebanyak 18 penelitian RCT yang dianalisis menunjukkan terdapat perbedaan yang signifikan pada PONV komposit (RR, 0,66, 95%CI 0,60, 0,74;  $P < 0,00001$ ;  $I^2 = 46\%$ ), pasien dengan kebutuhan penyelamatan antiemetik pasca operasi (RR, 0.67, 95%CI 0.53, 0.86;  $P < 0.001$ ;  $I^2 = 68\%$ ), dan kadar glukosa darah pasca operasi (SMD, 2.63, 95%CI 1.76, 3.50;  $P < 00001$ ;  $I^2 = 97\%$ ). Namun, terdapat hasil yang tidak signifikan pada tingkat keparahan PONV (SMD, -0.94, 95%CI -2.20, 0.31;  $P = 0.14$ ;  $I^2 = 97\%$ ), pasien dengan kebutuhan analgesik (RR, 0.84, 95%CI 0.60, 1.19;  $P = 0.33$ ;  $I^2 = 81\%$ ), dosis kebutuhan analgetik (SMD, -2.31, 95%CI -5.76, 1.14;  $P = 0.19$ ;  $I^2 = 99\%$ ), dan lama tinggal di PACU (MD, -24.73, 95%CI -66,07, 16,61;  $P < 0,24$ ;  $I^2 = 99\%$ )

**Kesimpulan:** Meta-analisis ini menunjukkan bahwa pemberian infus dekstrosa perioperatif mencegah kejadian PONV dan kebutuhan antiemetik penyelamatan pasca operasi, serta meningkatkan kadar glukosa darah pasca operasi. Namun, infus dekstrosa tidak berhubungan dengan penurunan keparahan PONV, kebutuhan analgesik pasca operasi, dosis penggunaan analgesik pasca operasi, dan lama tinggal di PACU.

**Kata Kunci:** Dekstrosa; PONV; Anestesi; Systematic Review; Meta-Analysis

## INTRODUCTION

Postoperative nausea and vomiting (PONV) are still reported as common complications for both anesthesiology and surgery issue. The systematic review with a meta-analysis of 22,683 patients performed in eleven countries reported 31.4%, 16.8%, and 27.7% for the prevalence of nausea, vomiting, and PONV, respectively.<sup>1</sup> This undesirable complications still became a main complaint for postoperative patients, causing patient dissatisfaction, delayed discharge, and increasing treatment costs.<sup>2,3</sup> Even though several prophylactic strategies including pharmacology antiemetic have been used, this is still potentially associated with side effects and additional medical care costs.<sup>4</sup> Dextrose infusion was introduced by previous research as a non-pharmacological perioperative strategy to decrease the PONV incidence.<sup>5,6</sup> The mechanism of this clinical effect is unclearly understood, the current hypothesis is associated with the amelioration roles for gastric mucosal hypoperfusion due to prolonged preoperative fasting.<sup>7</sup> Although there have been many published studies to evaluate the clinical effects, however, current published studies reported remain inconsistent and debatable results, and the available randomized trials (RCTs) are not satisfactory enough to be applied to clinical practice. Therefore, we carried out this meta-analysis in order to improve the evidence-based perioperative strategies to provide the best answer is the administering of dextrose infusion perioperatively favorable on preventing PONV.

## METHOD

### *Database Search and Study Selection*

Ethical clearance was not required for this study. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) framework by Cochrane has guided the search and selection process of the studies.<sup>8</sup> Online databases specifically PubMed, ScienceDirect, and Google Scholar were used for systematic literature search using the following keywords: dextrose, perioperative, nausea, and vomiting. A review question was established for included studies following by PICOS framework: (i) Population: patients who underwent surgery; (ii)

Intervention: perioperative dextrose infusion; (iii) Comparator: other infusion fluid; (iv) Outcomes: the incidence of PONV, PONV severity, number of patients with postoperative antiemetic rescue requirements, number of patients with postoperative analgesic requirements, dose of postoperative analgesic requirements, postoperative blood glucose levels, and post-anesthesia care unit (PACU) stay; (v) Study design: Randomized controlled trials (RCTs).

We performed a systematic search of literature through online databases in June 2023 without any year restrictions. Then, all results were imported into Rayyan.ai for the selection process that was performed by two independent authors.<sup>9</sup> The selection process started with the title and abstract screening then eligibility selection by reading the full text of the selected studies. Any distinctions during study selection would be deliberated with all authors.

### *Data Extraction*

Two independent authors were responsible for data extraction when the final included studies were obtained. The PONV incidence was considered the primary outcome of this study. There were many secondary outcomes including PONV severity, number of patients with postoperative antiemetic rescue requirements, number of patients with postoperative analgesic requirements, a dose of postoperative analgesic requirements, postoperative blood glucose levels, and PACU length of stay. Detailed data extraction from the final included studies includes the authors' name and year of publication, type of surgery, number of patients, age, duration of anaesthesia, timing of administration, dose or volume of dextrose and fluid infusion, antiemetic prophylaxis, and anesthetic management. A discussion with all authors was required when the conflicts between the data extraction were present.

### *Risk of Bias Assessment*

The Risk of Bias 2 (ROB 2) framework by Cochrane was guided to judge the level of biases of the included studies.<sup>10</sup> This assessment tool reported the biases by several domains including selection or randomization of the sample, allocation concealment for the intervention, unawareness

between participants and personnel, blinding when measuring the outcomes, data complexity, selective reporting, and other sources of bias. Two authors independently assessed the biases to grade each domain into low, unclear, or high risk of bias. The essential conflicts during the assessment were resolved with other authors.

### Data Synthesis and Analysis

The final included studies were analyzed qualitatively, meanwhile, a we also performed a meta-analysis to present the data analysis quantitatively. The Review Manager 5.4 software was required to conduct the quantitative analysis with a 95% confidence of interval. The pooled risk ratio was chosen to estimate the PONV incidence as primary outcomes, and the secondary outcomes such as the number of patients with postoperative antiemetic rescue requirement and the number of patients with postoperative analgesic requirement. In addition, pooled standard mean difference (SMD) or mean difference (MD) were performed

to calculate continuous data such as PONV severity, dose of postoperative analgesic requirements, postoperative blood glucose level, and PACU length of stay. The forest plot graph was visualized for the quantitative analysis according the grade of heterogeneity to decided the fixed effects model for low heterogeneity ( $I^2 < 50\%$ ), meanwhile, the random effects model for the considerable heterogeneity ( $I^2 \geq 50\%$ ).<sup>10</sup>

## RESULTS

### Study Selection

We got 1228 articles from PubMed, ScienceDirect, and Google Scholar by systematic literature search. The duplicate elimination was done automatically using Rayyan.ai then 1097 articles were undergone for early elimination by title and abstract filtering. A total of 23 articles required eligibility assessment by full-text screening. Quantitative analysis was eligible for 18 final selected articles. Figure 1 shows the selection studies process by PRISMA Flow Diagram.

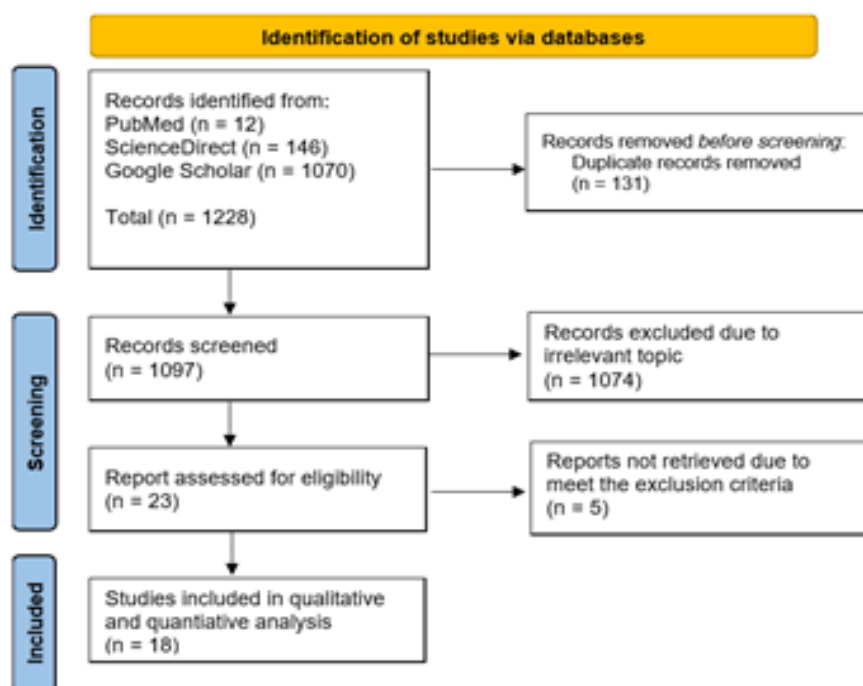


Figure 1. PRISMA Flow Diagram

### Study characteristics and Risk of Bias

Table 1 groups data extraction for included RCT studies. Two included studies were performed for general laparoscopy,<sup>11,12</sup> eight studies in specific gynecological patients,<sup>5,6,13-18</sup> five studies in laparoscopic cholecystectomy patient,<sup>19-23</sup> one study in tympanoplasty patients,<sup>24</sup> and two studies in varies type of surgery patients.<sup>25,26</sup>

The number of patients, age, duration of anaesthesia, timing of administration, dose or volume of dextrose and control fluid, antiemetic prophylaxis, and anesthetic management were presented in Table 1. Meanwhile, the graph judgement of risk of bias was visualized by Figure 2.



Figure 2. Risk of Bias Graph of Included Studies

### The incidence of PONV

The PONV incidence was reported by 11 studies. We analyzed for a subgroup analysis for the PONV incidence stratified by the time of evaluation including at PACU arrival, 15, 30, 45, 60, 120 minutes postoperatively, 3, 6, 12, and 24 hours postoperatively, within 0-2, 0-12, 2-24, and 0-24 hours postoperatively. The pooled effect size visualized at figure 3 and demonstrated significantly lower of PONV incidence in the dextrose group at PACU arrival (RR, 0.65, 95% CI 0.49, 0.87;  $P = 0.03$ ;  $I^2 = 3\%$ ), 60 min postoperatively (RR, 0.51, 95% CI 0.27, 0.99;  $P = 0.05$ ;  $I^2 = 0\%$ ), 120 min postoperatively (RR, 0.56, 95% CI 0.31, 0.99;  $P = 0.05$ ;  $I^2 = 40\%$ ), and 12 hours postoperatively (RR, 0.43, 95% CI 0.21, 0.88;  $P = 0.02$ ;  $I^2 = 0\%$ ). The subgroup analysis also revealed the significantly decreased at interval period within 0-2 hours postoperatively (RR, 0.72, 95% CI 0.59, 0.87;  $P = 0.0005$ ;  $I^2 = 87\%$ ), within 2-24 hours postoperatively (RR, 0.37, 95% CI 0.22, 0.62;  $P = 0.0001$ ;  $I^2 = 87\%$ ), and within 0-24 hours postoperatively (RR, 0.64, 95% CI 0.49, 0.84;  $P = 0.001$ ;  $I^2 = 65\%$ ). The composite PONV demonstrated by overall effect of the total subgroup also revealed significantly decreased in the dextrose group (RR, 0.66, 95% CI 0.60, 0.74;  $P < 0.00001$ ;  $I^2 = 46\%$ ). Figure 3 shows a

forest plot for the incidence of PONV between the dextrose and control groups.

### PONV severity

Four studies with a total of 267 and 269 participants in the dextrose and control group, respectively, reported that the severity of PONV assessed by different severity scale were no significantly different between groups (SMD, -0.94, 95% CI -2.20, 0.31;  $P = 0.14$ ;  $I^2 = 97\%$ ). The high heterogeneity was observed for this outcomes. Figure 4A shows a forest plot for PONV severity between the dextrose and control groups.

### Number of patients with postoperative rescue antiemetic requirements

Fourteen studies reported the number of patients with postoperative rescue antiemetic requirements was 234/722 and 364/722 in the dextrose and control groups. Pooling of outcomes revealed significantly decreased in the dextrose group and the analysis had considerable heterogeneity (RR, 0.67, 95% CI 0.53, 0.86;  $P < 0.001$ ;  $I^2 = 68\%$ ). Figure 4B shows a forest plot for the number of participants with postoperative rescue antiemetic requirements between the dextrose and control groups.

**Table 1.** Characteristics of Included Studies

Author	Type of surgery	Number of patient	Age	Duration of anaesthesia	Timing of administration	Dextrose fluid	Control fluid	Antiemetic prophylaxis	Anesthetic management
Cook et al., 1990	Laparoscopic examination of pelvic viscera	DG: 25 CG: 24	DG: 32.9 (6.5) CG: 31.4 (6.5)	Not available	Intraoperative, within 45 min	CSL 20 ml/kg with 1g/kg added dextrose	CSL 20 ml/kg	Not available	IA: Propofol (2.5 mg/kg), vecuronium (0.07 mg/kg), and fentanyl (1.5 µg/kg) MA: O <sub>2</sub> /NO (1:2) with enflurane 1%
Conan McCaul et al., 2003	Elective gynecologic laparoscopy	DG: 35 CG: 36	DG: 33.2 ± 4.9 CG: 32.3 ± 4.96	DG: 23 ± 7 CG: 22 ± 6	After induction of anesthesia, over approximately 20 min	CSL 1.5 ml/kg/h with 0.5 g/kg dextrose added in 50% formulation (CSL/dextrose)	CSL 1.5 mL/kg	Not administered	IA: Not available MA: O <sub>2</sub> /NO (1:2) with sevoflurane
Shin et al., 2007	General surgery, laparoscopy, and orthopaedic	DG <sup>a</sup> : 27 DG <sup>b</sup> : 26 CG <sup>a</sup> : 36 CG <sup>b</sup> : 35	DG <sup>a</sup> : 35.2 ± 14.4 DG <sup>b</sup> : 36.3 ± 11.7 CG <sup>a</sup> : 37.5 ± 14.7 CG <sup>b</sup> : 39.3 ± 13.5	DG <sup>a</sup> : 75.0 ± 34.1 DG <sup>b</sup> : 53.3 ± 21.3 CG <sup>a</sup> : 67.9 ± 32.5 CG <sup>b</sup> : 59.3 ± 36.2	Intraoperatively, within 30 min	5% dextrose water 2 ml /kg/h in DG <sup>a</sup> and 20 ml/kg/h in DG <sup>b</sup>	Hartmann's Solution 2 ml /kg in CG <sup>a</sup> and 20 ml/kg in CG <sup>b</sup>	Not available	IA: Lidocain 2% (40 mg), propofol 1% (2 mg/kg), rocuronium (0.6 mg/kg) MA: NO and O <sub>2</sub> with sevoflurane 2%
Dabu-Bondoc et al., 2013	Gynecologic laparoscopic and hysteroscopic procedures	DG: 30 CG: 32	DG: 37.9 (10.3) CG: 37.5 (9.8)	DG: 92.5 (75–130) CG: 107.5 (79–150)	At PACU arrival, over 30 min	5% dextrose in RL 1000 mL (D5LR)	1000 mL of RL solution	IV ondansetron 40 mg given a half befor emergence	IA: propofol (1.5–2 mg/kg), fentanyl (1–2 µg/kg) and vecuronium (0.05–0.1 mg/kg) MA: O <sub>2</sub> /air (1:2) with sevoflurane
Patel et al., 2013	Gynecologic, urologic, or breast surgery	DG: 87 CG: 75	DG: 46.3 (43.7 - 48.9) CG: 45.5 (43.0 - 47.9)	DG: 156, (133–176) CG: 151 (148–204)	Beginning with the start of surgical closure, within 2 hours by infusion pump	5% dextrose with a dose 125 mL/h iv	125 mL/h of RL solution	Not administered	IA: Propofol (2-2.5 mg/kg) MA: O <sub>2</sub> and air with sevoflurane

Irkal et al., 2016	Tympanoplasty	DG: 45 CG: 45	DG: 29.11±9.69 CG: 29.04±9.32	DG: 119.13±7.85 CG: 119.33±7.22	At PACU arrival, within 60 min	5% dextrose in RL solution 500 ml	500 mL of RL solution	Ondancetron 4 mg 30 min before emergence from general anaesthesia	IA: Thiopentone (5 mg/kg), vecuronium (0.1 mg/kg), fentanyl (2µg/kg) MA: O <sub>2</sub> /NO (1:2) with halothane 0.5–1%
Mishra et al., 2017	Laparoscopic cholecystectomy	DG: 50 CG: 50	DG: 37.42 ± 12.00 CG: 39.6 ± 11.54	DG: 65.2 ± 14.39 CG: 67.1 ± 17.41	At the time when gall bladder was taken out	5% dextrose with a dose 100 ml/h (total 250 mL)	250 ml of 0.9% NS solution	Dexamethason 4 mg	IA: Propofol, fentanyl, and atracurium MA: O <sub>2</sub> /air (1:1) with isoflurane
Firouzian et al., 2017	Laparoscopic cholecystectomy	DG: 60 CG: 61	DG: 41.2 (12.73) CG: 41.44 (12.75)	DG: 80 (70-90) CG: 75 (65-85)	30 min before induction anaesthesia, over a period of 30 min	5% dextrose in RL 500 mL	500 mL of RL solution	Not available	IA: Propofol 2–2.5 mg/kg, cisatracurium 0.15 mg/kg MA: O <sub>2</sub> /NO (1:1)w with isoflurane
Atashkhouei et al., 2018	Diagnostic gynecologic laparoscopy	DG: 35 CG: 35	DG: 30.49±0.91 CG: 32.09±1.02	DG: 54.57±2.47 CG: 61.34±3.10	5 min before the induction of anesthesia until the end of operation	RL 10 mL/kg/h with glucose 500 mg/kg (dextrose 5%)	RL 10 mL/kg/h with normal saline 0.9%	Not available	IA: Midazolam (0.05 mg/kg), fentanyl (2µg/kg), and propofol (1-2.5 mg/kg). MA: Propofol (50-150 mg/kg/min) and atracurium (0.2-0.3 mg/kg).
Pinon et al., 2018	Gynecologic laparoscopy	DG: 42 CG: 44	DG: 36.5±8.5 CG: 39.3±10.7	DG: 175.6±61.0 CG: 170.1±59.8	Intraoperative	5% D/NSS/2 at 2 mL/kg/hour	NS solution at 2 mL/kg/h	Not available	IA: Propofol 2 mg/kg and atracurium 0.6 mg/kg

										MA: O <sub>2</sub> /air (2:3) with sevoflurane 1.5-2%
Saleh et al., 2019	Laparoscopic cholecystectomy	DG: 65 CG: 65	DG: 31.40 ± 5.56 CG: 30.87 ± 5.42	DG: 97.50 ± 3.57 CG: 99.10 ± 3.69	Intraoperative, within 2 hours	10% dextrose, controlled by infusion pumps at 125 mL/h (total 250 mL)	250 mL of RL solution	Metoclopramide 10 mg		IA: Midazolam (0.02 mg/kg), propofol (2 mg/kg), fentanyl (2 µg/kg), and atracurium besylate (0.5 mg/kg) MA: Isoflurane 1-1.5%
Aasim et al., 2020	Laparoscopic Cholecystectomy	DG: 50 CG: 50	DG: 27.8±3.6 CG: 26.5±3.9	DG: 80±14.3 CG: 75±15.8	Before induction of anaesthesia, over 30 min	5% dextrose in RL solution	500 ml of RL solution	Not available		Not available
Zahid et al., 2021	Laprosopic Gynecological Procedures	DG: 125 CG: 125	DG: 43.14±9.532 CG: 41.38±10.031	Not available	Beginning with start of surgical procedure, over 2 hours	5% dextrose in RL with a dose 125 ml/h (total 250 mL)	125 ml/h RL (total 250 mL)	Not administered		IA: Propofol, atracurium MA: O <sub>2</sub> and air with sevoflurane
Ranjan et al., 2021	Elective laparoscopic surgery	DG: 30 CG: 30	DG: 37.16±12.01 CG: 35.3±11.89	Not available	Beginning with the start of surgical closure, within 2 hours	5% dextrose with a dose 125 ml/h (total 250 mL)	250 mL of 0.9% NS solution	Not administered		IA: Thiopentone (5 mg/kg), fentanyl (2 mcg/kg), atracurium (0.5 mg/kg) MA: O <sub>2</sub> /air (1:2) with isoflurane 0.5-1%
Nayak et al., 2022	Laparoscopic cholecystectomy	DG: 60 CG: 60	Not available	Not available	Before anaesthesia induction, over 30 min	500 mL of 5% dextrose in RL solution	500 ml of RL solution	Not available		IA: Midazolam (0.02 mg/kg), fentanyl (2µg/kg) MA: Not available
Kitsiripant et al., 2022	Abdominal hysterectomy	DG: 48 CG: 55	DG: 46.3±8.3 56.9 CG: 48.6±9	Not available	Arriving at the operating theatre	5% DNSS 2 mL/kg/h	0.9 % NS 2 mL/kg/h	Not administered		IA: Propofol 2(-3 mg/kg), cisatracurium (0.15 mg/kg), and fentanyl 2-3

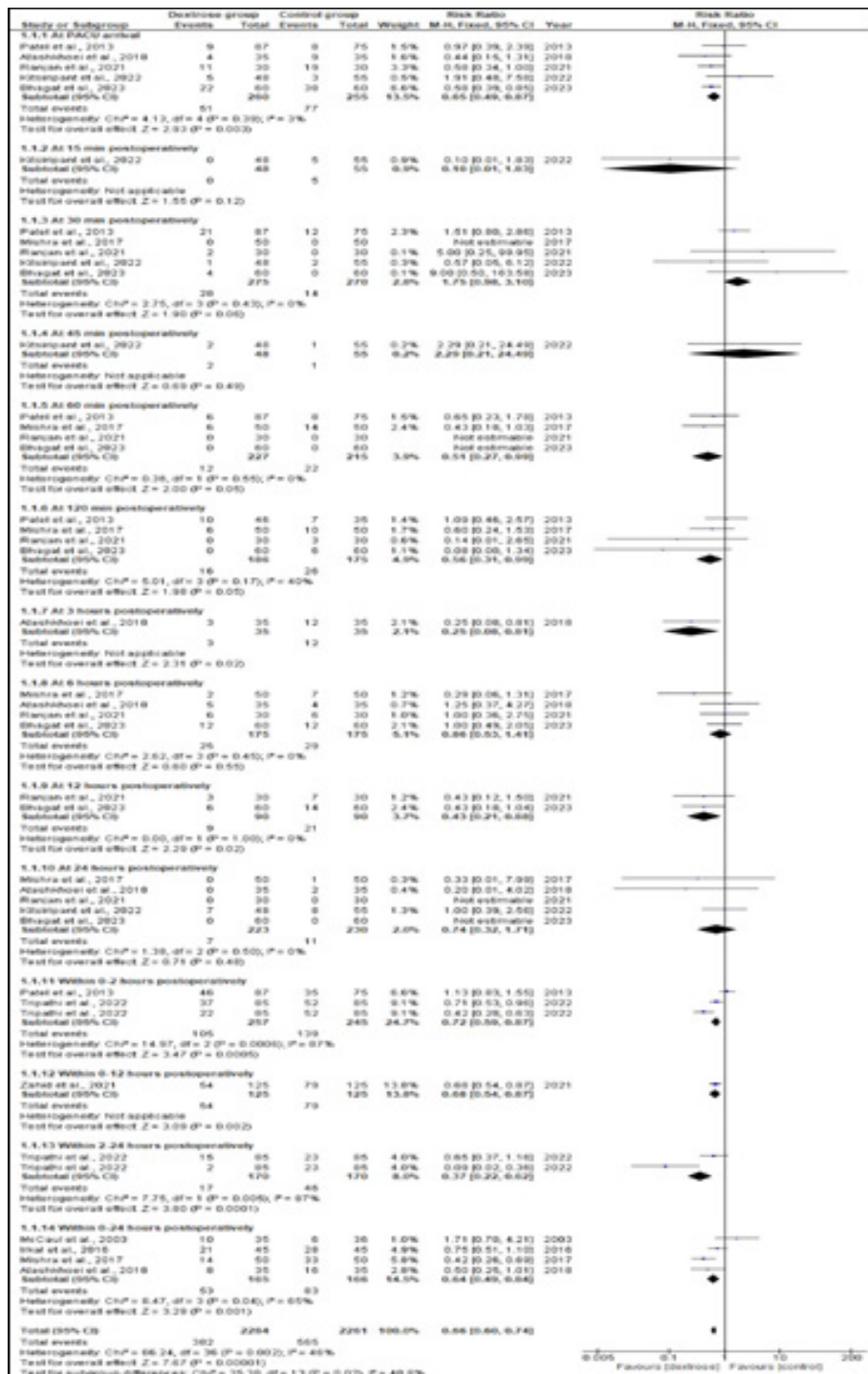
									(mcg/kg) MA: O <sub>2</sub> /air (1:1) with sevoflurane 0.8-1%
Tripathi et al., 2022	Laparoscopic cholecystectomy	DG <sup>a</sup> : 85 DG <sup>b</sup> : 85 CG: 85	DG <sup>a</sup> : 35.6±10.4 1.7 CG: 36.0±10.0	DG <sup>a</sup> :71.5±10.3 3 DG <sup>b</sup> : 70.3±10.2 CG: 71.9±11.9	At the time of gall bladder removal	5% and 10% dextrose with a volume 250 mL in DG <sup>a</sup> and DG <sup>b</sup>	250 mL of NS 0.9%	Dexamethason 4 mg	IA: Propofol (2–2.5 mg/kg), fentanyl (2 µg/kg), and vecuronium (0.1mg/kg) MA: O <sub>2</sub> /NO (1:2) with isoflurane 0.6-1%
Bhagat et al., 2023	Laparoscopic hysterectomy	DG: 60 CG: 60	DG: 37.14±12.03 CG: 35.1±11.91	Not available	Beginning of the surgical closure start, within 2 hours	5% dextrose with a dose 125ml/h (total 250 mL)	125 ml/h NS solution (total 250 mL)	Not administered	IA: Thiopentone (5 mg/kg), fentanyl (2 mcg/kg), and atracurium (0.5 mg/kg) MA: Thiopentone

DG, Dextrose group; CG, Control group; IA, Induction anesthetic; MA, management anesthetic; CSL, Compund sodium lactate; RL, Ringer's lactate; NS, Normal saline;

**Number of patients with postoperative analgesic requirements**

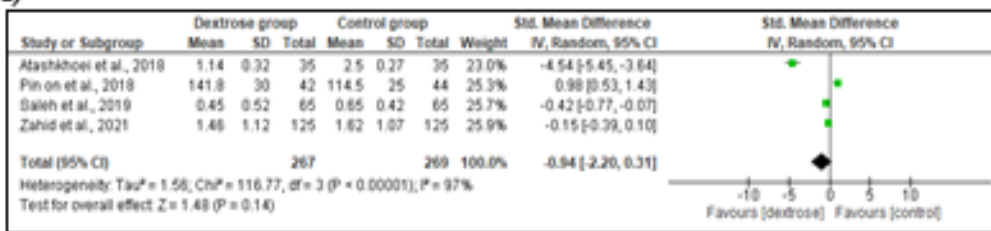
Three studies demonstrated the dextrose infusion perioperatively was not associated with a lower postoperative analgesics requirements for the total of opioid and non-opioid (RR, 0.84, 95% CI 0.60, 1.19; P = 0.33; I<sup>2</sup> = 81%). Analysis of subgroup also conducted for opioids

requirements and showed no significant difference (RR, 0.81, 95% CI 0.57, 1.16; P = 0.25; I<sup>2</sup> = 87%). The high heterogeneity was observed for these outcomes. Figure 5A shows the forest plot for the number of participants with postoperative analgesic requirements between the dextrose and control group.

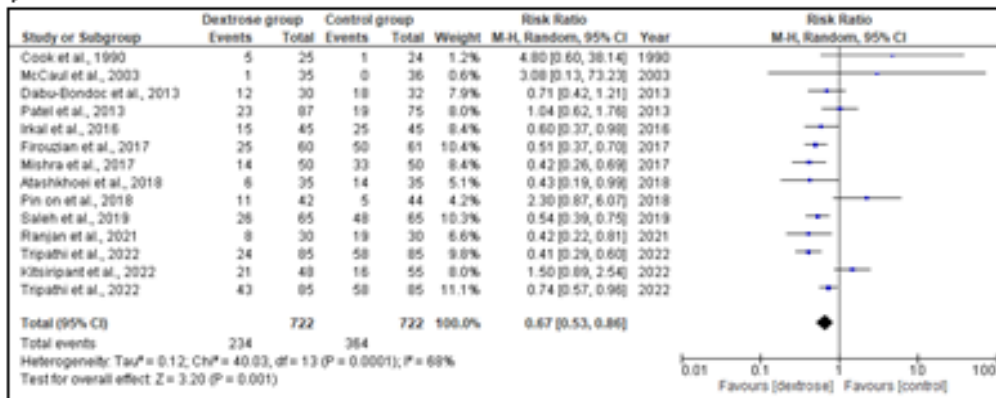


**Figure 3.** Forest Plot for the Primary Outcome in Terms of the Incidence of PONV Between the Dextrose and Control Groups

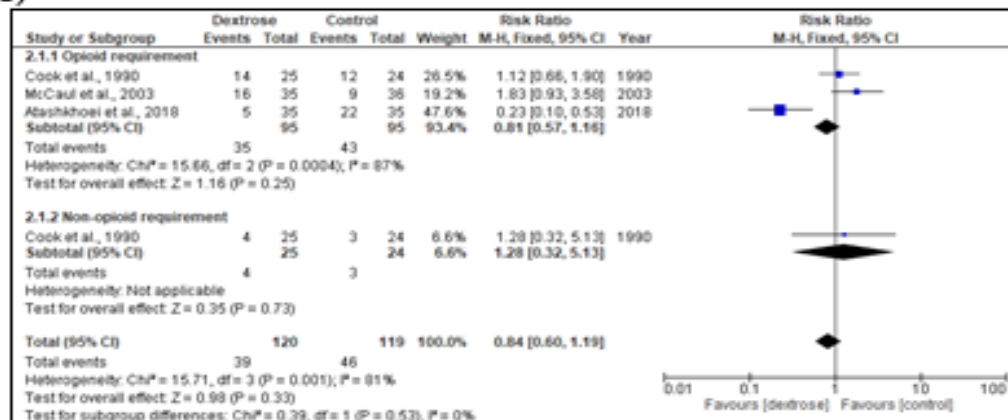
(A)



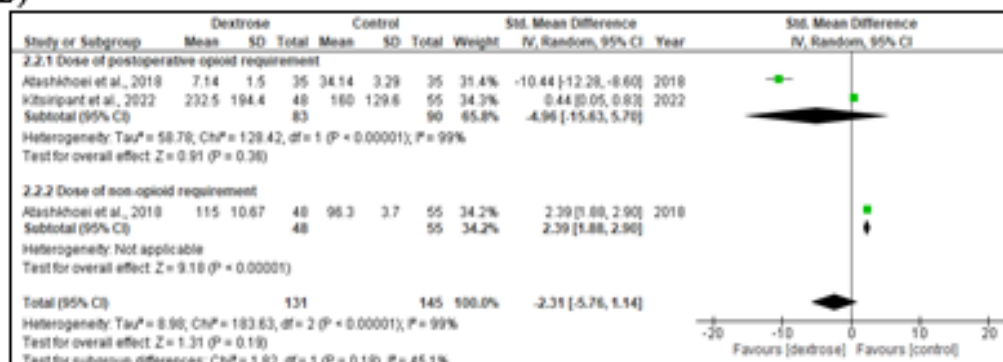
(B)

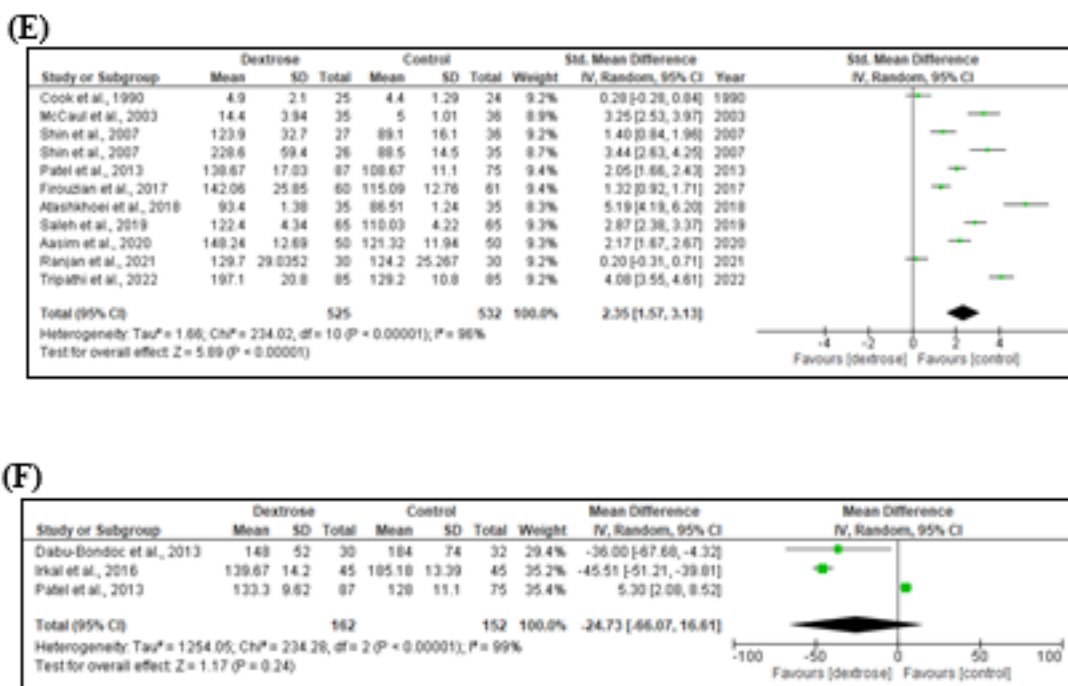


(C)



(D)





**Figure 4.** Forest Plot Comparing the Dextrose and Control groups for the Secondary Outcomes in Terms of the PONV Severity (A), Number of Patients with Postoperative Rescue Antiemetic Requirements (B), Patients with Postoperative Analgesic Requirements (C), Dose of Postoperative Analgesic Requirement (D), Postoperative Blood Glucose Level (E), and PACU Length of Stay (F)

**Dose of postoperative analgesic requirement**

The dose of postoperative analgesic requirement was conducted by two studies reported no significantly different between group (SMD, -2.31, 95% CI -5.76, 1.14; P = 0.19; I<sup>2</sup> = 99%). The subgroup analysis conducted for opioids also showed no significant difference (SMD, -4.96, 95% CI -15.63, 5.70; P = 0.36; I<sup>2</sup> = 99%). The heterogeneity was high for these analysis. The forest plot graph between dextrose and control group for this outcomes was visualized by figure 5B.

**Postoperative blood glucose level**

The postoperative blood glucose level was performed by ten selection studies with the parameter mg/dl and mmol/l. This analysis revealed the dextrose infusion significantly increase the postoperative glucose blood level than control (SMD, 2.63, 95% CI 1.76, 3.50; P < 0.0001; I<sup>2</sup> = 97%). The heterogeneity was high

for this outcomes. The forest plot graph between dextrose and control group for this outcomes was visualized by figure 5C.

**PACU length of stay**

PACU length of stay were analyzed for three included studies, whereas the results revealed no significant difference between the groups with high heterogeneity was observed (MD, -24.73, 95% CI -66.07, 16.61; P < 0.24; I<sup>2</sup> = 99%). The forest plot graph between dextrose and control group for this outcomes was visualized by figure 5D.

**DISCUSSION**

A meta-analysis including 18 RCTs with various surgery approaches was performed to present the evidence of the clinical effect of dextrose infusion as a perioperative strategy to prevent PONV. This study demonstrated evidence of the

benefit dextrose infusion compared to placebo to reduce the incidence of PONV at PACU arrival, 30 min, 120 min, and 12 hours postoperatively time of evaluation. The results also showed benefit for the interval period between 0-2, 2-24, and 0-24 hours postoperatively. The different time of evaluation of recent published studies is main reason to stratified the subgroup analysis in our researched, its hope to provide the best clinical answer regarding specific time period of how long the dextrose infusion give the best implication for postoperative patients.

Although the PONV incidence was reported to be favorable in the dextrose group, the severity score shows no significant difference even though the score was lower in dextrose group. Only one of four analyzed studies showed favorable in the control group, but this contradictory result highly impacted the result because of high standard mean difference was observed. This result should be interpreted with appropriate caution due to the high standard mean difference by Pin On et al., 2018 is affected by the outcomes of severity was reported using the total severity score rather than the average severity score.<sup>15</sup>

The significant favorable regarding the rescue antiemetic requirement in the dextrose group may be considered as a parameter to resolve this disappointment. Although a previous meta-analysis by Yokotama et al., 2020 reported no difference between the dextrose and control groups for the rescue antiemetic requirements, three previous meta-analysis reported in-line results with our study.<sup>27-30</sup> These previous meta-analysis and our favorable result hopefully empower the beneficial effect of dextrose in PONV cases.

The mechanism of dextrose infusion to resolve PONV remains unclear. Preoperative fasting was reported as an essential etiological factor for the incidence of PONV due to hypovolemic conditions that lead to gastric mucosal hypoperfusion. The role of dextrose infusion in resolving this problem may be associated with hypotheses that the increase of blood glucose levels due to dextrose infusion perioperatively leads to the decrease of gastric acid secretion by inhibiting the vagal cholinergic pathway.<sup>31</sup> Furthermore, glucose infusion during the perioperative period

could reduce insulin resistance after surgery. Insulin resistance is considered to play a role in the postoperative clinical outcomes, including PONV.<sup>32-34</sup> Our study analyzed postoperative blood glucose levels and found significantly higher results with the administration of dextrose infusion perioperatively. This result meaningfully shows that hyperglycemic conditions after dextrose infusion actually occur and are potentially in line with these hypotheses to contribute to the improvement of PONV.

Another hypothesis also stated hyperglycemia raises plasma cholecystokinin levels, which contributes to pain and anxiety regulation.<sup>35,36</sup> Postoperative pain was positively correlated as a risk factor of PONV, this mechanism was explained by the stimulation of a certain brain nucleus induces an interaction between nuclei in the thalamus. As a result, stimulation of the pain center induce PONV.<sup>37</sup> However, this study could not quantitative analyze postoperative pain due to unavailability of data in our study. The use of high doses of analgesics, especially opioids, also reported as a causative factor of PONV because of direct stimulation to the  $\mu$ -opioid receptors in the chemoreceptor trigger zone.<sup>37</sup>

This study assessed the number of patients with analgesic requirements as considerable outcomes to relay the postoperative pain assessment. Surprisingly, our results demonstrated no significant difference between groups although the number was lower in the dextrose group. The lower dose of analgesic is expected to reduce the incidence of PONV, and our dose analyzed for total analgesic requirement, including opioids demonstrated lower in the dextrose group but no significant difference. The insignificant results regarding analgesic requirement does not mean to disprove the hypothesis. This analysis must interpreted with caution because of the insignificant results may affected by the limited of included studies in the analysis.

The PACU stays demonstrated a shorter duration in the dextrose group without statistically significant. It is important to analyze that the decision for prolonged PACU stay is not only based on the PONV incidence or severity. The requirement for pain management, unavailability of beds in the ward, and both cardiovascular and respiratory adverse events are positively related

as risk factors for prolonged stay in PACU.<sup>38-40</sup>

The present systematic review and meta-analysis were conducted by the most up-to-date literature search, without language restriction, and assessed clinically important outcomes. We only included for RCT studies to provide a strict analysis. This is the first quantitative analysis which stratified by time of evaluation of the PONV incidence. However, the limitation of this systematic review and meta-analysis is the subgroup analysis for the dose administered was not carried out due to a limited number of studies. This study was restricted to patients judged ASA 1 and 2, with the results not applicable to patients with diabetes mellitus and other comorbidities. The majority of included studies were applied for abdominal surgeries, so cautious interpretation were needed when generalized to other surgeries. Furthermore, multicentre RCTs with a large population, various type of surgery and outcomes are required to enhance deeper insight.

## CONCLUSION

This meta-analysis demonstrated that administering dextrose infusion perioperatively prevents both the PONV incidence and postoperative rescue antiemetic requirements, and also increase postoperative blood glucose levels. However, dextrose infusion is not associated with reducing the PONV severity, postoperative analgesic requirements, a dose of postoperative analgesic use, and PACU stay.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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