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Original Article

Efficacy of Intravenous Glucose for Preventing Postoperative Nausea and Vomiting after Abdominal Hysterectomy under General Anesthesia

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ABSTRACT:

Objective: This study aimed to evaluate the ability of intravenous glucose administration during the maintenance of anesthesia as an alternative method for diminishing the incidence of postoperative nausea and vomiting (PONV) in patients undergoing total abdominal hysterectomy (TAH).

Material and Methods: This was a prospective, double-blind randomized placebo-controlled trial. One hundred and ten patients who were 18 - 65 years old, American Society of Anesthesiology (ASA) 1 or 2 and required general anesthesia for TAH, were divided randomly to receive 5% DNSS (Group D) or normal saline (Group N) as a maintenance fluid at a rate of 2 mL/kg/hr. The primary outcome was the incidence of PONV at the arrival time in post-anesthetic care unit (PACU). The secondary outcomes were severity of PONV, time to first dose of an antiemetic drug, amount of antiemetic dose, and length of stay in the hospital.

Results: The incidence of PONV in group N was 5.5% and in group D was 10.4% (p-value = 0.360). There were no statistically significant differences regarding the VRS scores, time to the first dose of antiemetic drug, the amount of antiemetic drug, and length of hospital stay between the 2 groups.

Conclusions: There was no significant difference in efficacy between intravenous glucose administration and placebo in the prevention of PONV in patients undergoing abdominal hysterectomy under general anesthesia.

Keywords: intravenous glucose; postoperative nausea and vomiting; total abdominal hysterectomy

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INTRODUCTION

Postoperative nausea and vomiting (PONV) remains a significant problem in many operations, leading to patient distress, delays in postoperative recovery and hospital discharge and even occasional surgical wound dehiscence or wound infection.[1-4] The prevention of PONV is a concern to all anesthesiologists and surgeons. No antiemetic can reduce the incidence of PONV to zero, but the use of multimodal techniques can help minimize PONV.[5] Over the past few decades, various options for reducing the incidence and severity of PONV have been tried, such as avoiding trigger factors or pharmacological therapy with antiemetic drugs or acupuncture.[6] Like other medicines, antiemetics also carry some risk of side effects which range from headache to QTc prolongation, which can occur even with low doses of droperidol or ondansetron.[7]

Recently, some studies on the influence of the enhanced recovery after surgery (ERAS) protocol have suggested that preoperative carbohydrate drinks might be effective in reducing PONV.[8,9] However, due to the risk of aspiration in patients with very large leiomyomas, this technique is not part of routine management in our institution. Other studies have reported that intravenous dextrose reduced the incidence of PONV.[2,3]

From a 3-year retrospective review in our institution, we found that the highest incidence of postoperative nausea and vomiting (PONV) occurred following gyneco logical surgery, especially in patients undergoing abdominal hysterectomy, even though antiemetics are administered as routine practice in our institution. Thus, this study aimed to evaluate the ability of intravenous (IV) glucose administration during maintenance anesthesia as an alternative method to diminish the incidence of PONV in patients undergoing abdominal hysterectomy under general anesthesia.

MATERIAL AND METHODS

This randomized control trial was approved by the Human Research Ethics Committee, Faculty of Medicine, Prince of Songkla University (REC. 61-024-8-4). One hundred and ten patients who required general anesthesia with an oroendotracheal tube for an abdominal hysterec-tomy from September 2018 to August 2019 were selected as the study group from the elective schedule of operations in our institute, Songklanagarind Hospital. The eligibility criteria were patients 18-65 years old with an American Society of Anesthesiologists (ASA) physical status 1 or 2. The exclusion criteria were patients with Type I or II dibetes mellitus or impaired fasting glucose or impaired glucose tolerance, pre-anesthetic blood glucose > 200 mg/dL or point-of-care testing (POCT) of blood glucose > 180 mg/dL, heart failure, acute coronary syndrome, moderate renal insufficiency or renal failure, recently received an antiemetic, steroid use, pregnancy, and/or abnormal EKG including any arrhythmia or patients on a cardiac pacemaker.

Our sample size was calculated by the two inde-pendent proportions formula, with a two-tailed significance of 0.05 and power of 0.95 based on previous data.[2] A drop-out of 10% was expected thus 110 patients were enrolled in the study. Patients were randomized by block randomization into N and D groups which received 0.9% NSS and 5% DNSS, respectively, as maintenance fluid **(Figure 1)**.

Informed consent was obtained from all participants in the study. The nausea level of the patients was assessed using a verbal rating score (VRS) by the research team on the day before the operation. All patients received the standard institute premedication including fasting from midnight before surgery, starting isotonic solution for fluid maintenance at 7 AM., and premedication with diazepam 1 hour (hr).

Upon arriving at the operating theatre, standard monitoring including non-invasive blood pressure, pulse oximeter, and electrocardiography were applied. A pre-anesthetic POCT of blood glucose was done using a blood glucose test strip (Accu-check® Performa, Roche,

USA) and repeated every hour. Anesthesia was induced with propofol 2–3 mg/kg, cisatracurium 0.15 mg/kg, and fentanyl 2–3 mcg/kg and maintained with 50% oxygen in air and 0.8 – 1 minimal alveolar concentration (MAC) of sevoflurane. Another IV line with a No. 20 catheter was established and connected with the research IV fluid at an infusion rate of 2 mL/kg/h. The attending anesthesiologist, anesthesiology resident, and nurse anesthetists were blinded to the intervention. Antiemetic drugs were not administered during the intraoperative period.

After surgery, the patients were taken to the post-anesthetic care unit (PACU). The anesthetic nurses, who were blinded from the study, evaluated nausea levels immediately by a verbal rating score (VRS) from 0 to 4, with 0 = no nausea/vomiting, 1 = mild nausea, 2 = moderate nausea, 3 = severe nausea, and 4 = vomiting, and then at postoperative times 15, 30, and 45 minutes and 24 hours. For patients who had a VRS ≥ 2 at any of the assessments, PONV was diagnosed and antiemetics were administered.[10,11] following the protocol as shown in **Figure 2**.

Patient characteristics, Apfel scores[12], PONV VRS scores, intraoperative opioid use, time to the first dose of antiemetic, doses of antiemetic, and length of hospital stay were recorded and analyzed. Statistical analyses were performed using R Studio version 2.13.0. Descriptive data were analyzed as numbers of patients and percentages. Categorical variables were compared by chi-square or Fisher's exact test, while continuous variables were compared by rank sum test and t-test. A p-value of less than 0.05 was considered statistically significant. Raw results confounded by covariates were adjusted by multivariable analysis. Confounders, when present, were extracted by multiple logistic regression. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were derived. Repeated measures data were analyzed using a linear mixed model.

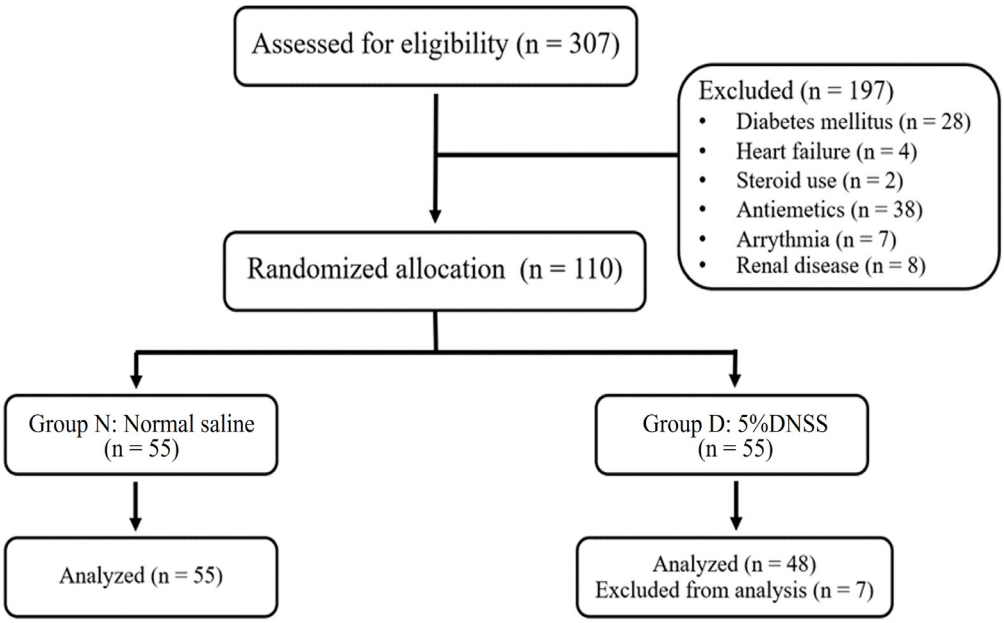
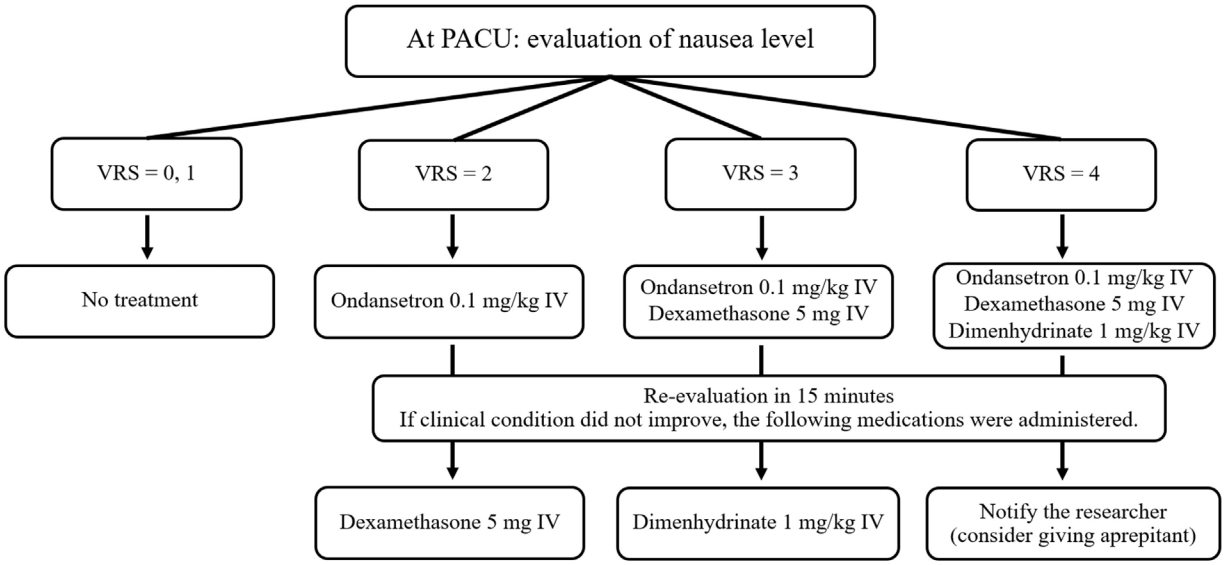


Figure 1 Number of subjects enrolled to the study, randomization and exclusion



PACU = post-anesthetic care unit; VRS = verbal rating score

Figure 2 Protocol of the study

RESULTS

Seven patients in group D were excluded from the analysis due to POCTs of blood glucose more than 180 mg/dL. Most patient characteristics were similar among the two groups. However, body weight, body mass index (BMI), operation time, estimated blood loss and intraoperative opioid consumption were significantly higher in group N than in group D (Table 1). The results were confounded by several covariates and multivariate analysis was used to determine the factors associated with PONV within the first 24 hours postoperatively. Nine variables, age, BMI, ASA classification, Apfel score, operation time, estimated blood loss, intraoperative IV fluid, intraoperative fentanyl use, and postoperative fentanyl use were verified to be correlated with PONV. Somewhat unexpectedly, we found that patients experiencing PONV had lower intraoperative fentanyl use (adjusted OR 5.78 (1.14, 29.24) (Table 2).

The incidence of PONV at the arrival time at the PACU was higher in group D (10.4%) than in group N (5.5%), but the difference was not significant (p-value = 0.360), nor were there significant differences in the incidences of PONV at the other postoperative times (Table 3). The baseline POCT of blood glucose in group N was significantly higher than in group D (p-value = 0.033). However, the patients in group D had significantly higher mean POCT levels of blood glucose at the recorded 1-hour intervals during the maintenance period than group N (p-value < 0.001), as shown in Figure 3.

There were no significant differences in the VRS scores at postoperative times 0, 15, 30, and 45 minutes and 24 hours between the 2 groups. The time to the first dose of antiemetic drug in group D was longer than in the control group, both in the PACU (p-value = 0.572) and postoperative period (p-value = 0.302) although the differences between the groups were not significant. Likewise, there was no statistically significant difference in respect of required rescue treatment within the first 24 hours after surgery (p-value = 0.154). The average length of hospital stay was 4 days. The number of patients who had a length of hospital stay exceeding 4 days was greater

Table 1 Patient characteristics

Parameter	Group N (N = 55)	Group D (N = 48)	p-value
Age, years, mean (S.D.)	48.6 (9)	46.3 (8.3)	0.190
Weight, kKg, mean (S.D.)	62.6 (13.3)	56.9 (10.1)	0.016
Height, cm, mean (S.D.)	155.9 (6.6)	154.5 (5.7)	0.262
BMI, kg/m2	25.1 (22.8,28.3)	22.6 (21,26.4)	0.016
ASA classification, n (%)			0.683
ASA I	4 (7.3)	2 (4.2)	
ASA II	51 (92.7)	46 (95.8)	
Risk factors according to Apfel score, n (%)			
Female	55 (100)	48 (100)	0.490
Nonsmoker			0.466
No	0 (0.0)	1 (2.1)	
Yes	55 (100)	47 (97.9)	
History of PONV			0.401
No	48 (87.3)	38 (79.2)	
Yes	7 (12.7)	10 (20.8)	
Opioid use	55 (100)	48 (100)	0.490
Operation time, min	195 (155, 247.5)	170 (120, 190)	0.002
Estimated blood loss, mL	300 (250, 575)	250 (150, 400)	0.012
Intraoperative IV fluid, mL	1900 (1425, 2325)	1600 (13,00, 2,000)	0.054
Fentanyl, mcg			
Intraoperative period	225 (175, 275)	200 (150, 225)	0.010
Postoperative 24 hours	160 (130, 305)	232.5 (120, 382.5)	0.330

Data are presented as median (IQR) unless otherwise indicated

S.D. = standard deviation; BMI = body mass index; kg = kilograms; m^2 = square meters; ASA = American Society of Anesthesiologists; PONV = postoperative nausea and vomiting; ml = milliliters; IQR = interquartile range

in group N than in group D, but the difference was not significant (group N 30.9%, group D 22.9%, p-value = 0.492) **(Table 4)**.

DISCUSSION

Antiemetics were given to no patients in the intra-operative period to avoid a potential confounding factor. Our study found that there were no differences between the NSS and 5% DNSS groups in the incidence and severity of PONV, time to first dose of antiemetic, total dose of antiemetic, or length of hospital stay. These results are similar to some recent studies. Patel et al.[13] reported that IV dextrose administration during emergence from anesthesia in outpatient gynecologic, urologic or breast surgeries was not associated with a difference in the incidence and severity of PONV. In the same way, the study of McCaul, et al.[14] found that administration of dextrose was associated with nausea, increased opioid requirement

and late thrist after gynecological laparoscopy. Pin-on, et al.[15] also found that the administration of dextrose in patients undergoing elective gynecologic laproscopic surgery did not decrease the incidence or severity of PONV and patients who received IV dextrose administration required more postoperative antiemetic medications. However, Mishra et al.[2] reported that perioperative administration of 5% dextrose in laparoscopic cholecystectomy patients decreased the incidence of PONV by 32%. The mechanism of how increased glucose reduces nausea and vomiting is still unclear. Some studies have hypothesized that the high osmotic pressure of dextrose has a direct local action on the gastrointestinal tract that may decrease smooth muscle contractions and slow gastric emptying time.[16-18] This mechanism would likely be a dose-dependent effect. We found that intraoperative blood glucose levels in both groups increased over time and the average blood glucose level of the patients in group D was significantly higher than in the N group.

We propose 2 explanations for this finding. First, the stress response to surgery is characterized by increased secretion of pituitary hormones and stimulated sympathoadrenergic activity.[19] The effect of various endocrine functions during general anesthesia increases catabolic activity which is caused by increased levels of catabolic hormones such as cortisol and glucagon. This stress response may increase the incidence of hyperglycemia.[20] The metabolic changes appear to be proportional to the severity of surgical trauma.[21] Cortisol and blood glucose concentrations increase significantly in intra-abdominal surgery. Secondly, hyperglycemia reduces the tone of the proximal stomach and increases the perception of fullness and nausea.[16]

The BMI, operation time, and estimated blood loss in group N were significantly higher than in group D. Therefore, group N received higher amounts of IV fluid infusion than group D. After the multivariate analysis was done, only less intraoperative fentanyl was associated

Table 2 Univariate and multivariate logistic regression of factory associating with postoperative nausea andvomiting

Factor	Crude OR (95%CI)	Adjusted OR (95%CI)
Age (years)	1.03 (0.96, 1.09)	1.02 (0.94,1.1)
BMI		
BMI < 23	1	1
BMI ≥ 23	0.41 (0.133, 1.25)	0.34 (0.09, 1.29)
ASA		
ASA 1	1	1
ASA 2	0.85 (0.09, 7.86)	0.86 (0.07, 10.91)
Operation time (hours)		
≤ 2	1	1
> 2	1.58 (0.33, 7.67)	1.91 (0.32, 11.36)
Blood loss (mL)		
≤ 200	1	1
> 200	1.2 (0.39, 3.7)	2.06 (0.4, 10.74)
Intraoperative fluid (mL)		
≤ 2000	1	1
> 2000	1.56 (0.51, 4.84)	2.02 (0.46, 8.96)
Intraoperative fentanyl use (mcg)		
> 200	1	1
≤ 200	2.96 (0.78, 11.24)	5.78 (1.14, 29.24)
Postoperative fentanyl use (mcg)		
> 150	1	1
≤ 150	1.62 (0.54, 4.87)	1.38 (0.4, 4.8)
Intravenous fluid		
D5% DNSS	1	1
NSS	0.97 (0.32, 2.92)	1.17 (0.32, 4.29)

OR = odds ratio; CI = confidence interval; BMI = body mass index; ASA = American Society of Anesthesiologists; mL = milliliters; mcg = micrograms; D5% DNSS = 5% dextrose in normal saline; NSS = normal saline solution

Table 3 Incidence and severity of postoperative nausea and vomiting at postoperative times 0, 15, 30, and 45 minutes and 24 hours

Postoperative time	Group N (N = 55)					Group D (N = 48)					p-value
	VRS=0	VRS=1	VRS=2	VRS=3	VRS=4	VRS=0	VRS=1	VRS=2	VRS=3	VRS=4	
0 minutes	46 (83.6)	6 (10.9)	3 (5.5)	0 (0)	0 (0)	41 (85.4)	2 (4.2)	4 (8.3)	1 (2.1)	0 (0.0)	0.357
15 minutes	44 (80.0)	6 (10.9)	4 (7.3)	0 (0)	1 (1.8)	41 (85.4)	7 (14.6)	0 (0.0)	0 (0.0)	0 (0.0)	0.191
30 minutes	48 (87.3)	5 (9.1)	2 (3.6)	0 (0)	0 (0)	43 (89.6)	4 (8.3)	1 (2.1)	0 (0.0)	0 (0.0)	1.000
45 minutes	48 (87.3)	6 (10.9)	1 (1.8)	0 (0)	0 (0)	44 (91.7)	2 (4.2)	1 (2.1)	1 (2.1)	0 (0.0)	0.486
24 hours	36 (65.5)	11 (20.0)	8 (14.5)	0 (0)	0 (0)	24 (50.0)	17 (35.4)	6 (12.5)	1 (2.1)	0 (0.0)	0.181

Data are presented as N (%)

VRS = verbal rating score; PONV = postoperative nausea and vomiting

Table 4 Secondary outcome measures

Parameter	Group N (N = 55)	Group D (N = 48)	p-value
Time to first dose of antiemetic			
PACU, min, mean (S.D.)		23.8 (20.9)	0.572
Postoperative 24 hours, hours, median (IQR)		8 (4,12)	0.302
Number of patients receiving antiemetics in 24 hours			0.108
No antiemetic	39 (70.9)	27 (56.2)	
At 1 – 6 hours	12 (21.8)	9 (18.8)	
At 7 – 12 hours	3 (5.5)	8 (16.7)	
After 12 hours	1 (1.8)	4 (8.3)	
Doses of ondansetron			0.154
0	38 (69.1)	27 (56.2)	
1	13 (23.6)	20 (41.7)	
2	1 (1.8)	0 (0.0)	
3	3 (5.5)	1 (2.1)	
Length of hospital stay, days			0.492
≤ 4 days	38 (69.1)	37 (77.1)	
> 4 days	17 (30.9)	11 (22.9)	

Data are presented as n (%) unless otherwise indicated

PACU = post-anesthesia care unit; S.D. = standard deviation; IQR = interquartile range

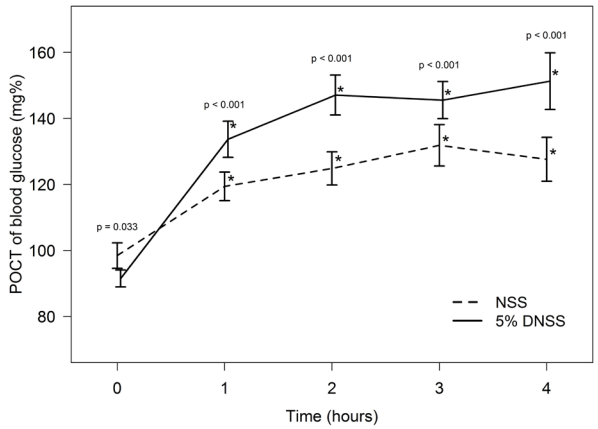


Figure 3 Post-operative point of care testing (POCT) of blod glucose, comparing between those who received NSS and 5% DNSS

with PONV. This finding was different from the review of Pierre and Whelan which found that PONV was associated with dose-dependent intraoperative and postoperative opioid use.[18]

There were two limitations to this study. First, seven patients in group D were excluded from the analysis, which might have had a confounding effect on the results. Secondly, the study was conducted only in female patients undergoing a specific operation, so the results might not be directly be applied to other patients or operations.

CONCLUSION

There was no significant difference in efficacy between intravenous glucose administration and placebo in the prevention of PONV in women undergoing abdominal hysterectomy under general anesthesia. The POCT glucose in the 5% DNSS group was statistically significantly higher, but there was no clinical significance.

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CONFLICTS OF INTEREST

There are no potential conflicts of interest to declare.

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