

Intraoperative intravenous dextrose administration and the incidence of nausea and vomiting after gynecologic laparoscopic surgery: a randomized double-blind controlled study

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Objective This study tested the hypothesis that administration of intravenous dextrose solution during gynecologic laparoscopic surgery would reduce the incidence and severity of postoperative nausea and vomiting (PONV) compared with an equal volume of normal saline solution

Methods A prospective randomized double blind controlled study was conducted. Eighty-six patients were randomized to receive either dextrose solution (n=42) or normal saline solution (n= 44). Bell-ville postoperative nausea and vomiting scores were recorded for the first 24 hours after surgery.

Results Fourteen of 44 patients (31.8%) in the normal saline solution group compared to 15 of 42 patients (35.7%) in the dextrose solution group developed postoperative nausea and vomiting ($p=0.09$). At each time point, the incidence and severity of PONV were similar. The patients in the dextrose solution group required more postoperative antiemetic medications ($p=0.04$). Blood glucose levels were significantly higher in the dextrose solution group during both the intraoperative and postoperative periods ($p \leq 0.01$).

Conclusions Intravenous dextrose administration does not reduce either the incidence or the severity of postoperative nausea and vomiting after laparoscopic gynecologic surgery but it does increase blood glucose level. **Chiang Mai Medical Journal 2018;57(2):61-9.**

Keywords: dextrose solution, normal saline solution, postoperative nausea and vomiting (PONV), laparoscopic gynecologic surgery

Introduction

Postoperative nausea and vomiting (PONV) is a major common complication after general anesthesia and after certain types of surgery like laparoscopic surgery. The incidence of nausea is slightly greater than the incidence of

vomiting (50% vs. 30%) (1-3). General anesthesia increases the likelihood of PONV by a factor of 11 compared with other types of anesthesia (1-2). Laparoscopic surgery combined with general anesthesia can further increase

the incidence of PONV to 80% (1-3). Identified risk factors for PONV included female gender, history of motion sickness, nonsmoking, younger age, general anesthesia, use of volatile anesthetics and nitrous oxide, use of opioids, duration of anesthesia, and type of surgery (cholecystectomy, laparoscopic, gynecological) (4).

The concept of routine pharmacologic PONV prophylaxis remains unconvincing. It can increase side effects and complications as well as reducing cost effectiveness (5). One non-pharmacologic strategy to minimize the risk of PONV is adequate intravenous fluid hydration (Evidence A2) (6-8). Dehydration and hypoglycemia have been proposed as risk factors for PONV (8-11). Reports on the results of using glucose for symptomatic relief of PONV have been variable (10-13). The mechanism of action of glucose is unclear. However, both peripheral effects acting through the wall of the gastrointestinal tract and central effects acting through the chemoreceptor trigger zone and effects of vasopressin secretion have been suggested (14-15).

In this study, we tested the hypothesis that intraoperative infusion of dextrose solution could reduce the incidence and severity of PONV. The aim of this study was to evaluate the effect of dextrose-containing crystalloid solution and dextrose-free crystalloid solution for intravenous fluid maintenance on PONV in patients scheduled for undergoing gynecologic laparoscopy.

Methods

A prospective randomized double-blind controlled study of the incidence and severity of PONV in female participants receiving different types of intravenous fluid solution during gynecologic laparoscopy was conducted. The study protocol was approved by the ethical committee (EC), Faculty of Medicine, Chiang Mai University. Participants were assigned to one of two groups: a normal saline solution (NSS group) and a 5% D/NSS/2 solution (dextrose group) using a computer-generated randomization process. The inclusion criteria included female gender, aged 18 to 65 years, ASA physical status I-II, and being scheduled for gynecologic laparoscopy under general anesthesia. Written informed consent was obtained from all

participants. Exclusion criteria were significant congestive heart failure, coagulopathy, severe respiratory disease, significant hepatic or renal disease, diabetes mellitus, blood glucose greater than 200 mg/dL on the morning of surgery, and withdrawal of consent.

During the pre-operative visit, all participants were informed about how they should describe nausea and vomiting symptoms that might occur postoperatively using the Bellville scoring system.

At the recovery room, the Bellville nausea vomiting score was assessed every 30 minutes for the first 2 hours after surgery. Patients who scored ≥ 2 received antiemetic drug, intravenously Metoclopramide (Plasil®) 10 mg. If the Bellville score was ≥ 2 at 30 minutes following Plasil® injection, Ondansetron (Onsia®) 4 mg was administered intravenously. After the 2-hour observation period in the recovery room, patients were transferred to the ward where the Bellville nausea vomiting scale score continued to be assessed postoperatively every 4 hours for a total of the next 24 hours.

Sample size calculation

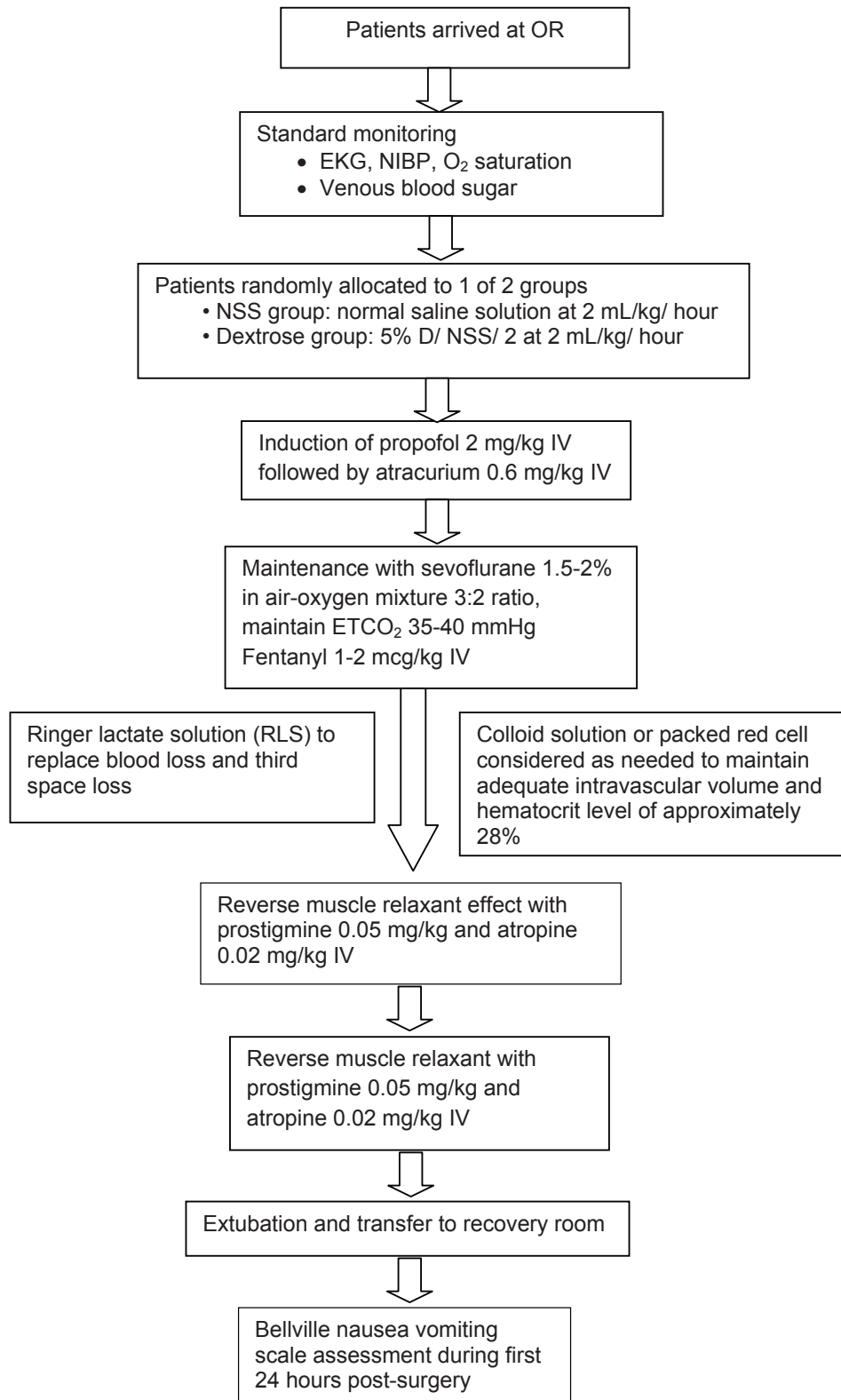
Bondoc *et al.* reported a 62% incidence of PONV in adult females undergoing gynecologic laparoscopy who received dextrose solution (11). We estimated that the incidence of PONV should be reduced by 30% in the dextrose group with a significance level of 95% ($\alpha \leq 0.05$) and a power of the study of 80 ($\beta \leq 0.2$). The calculated sample size was 37 participants per group. We added 20% to each group to compensate for potential incomplete data follow-up. We planned to include a total of 90 patients (45 per group).

Statistical analysis

The primary outcome measure was the intergroup difference in PONV incidence and severity at each time point, expressed as a number and a p-value. The secondary outcome measures were differences in blood glucose level and the requirement for antiemetic drugs. Statistical analysis was performed using SPSS version 14.0. All continuous data were tested for nor-

Table 1. Bellville postoperative nausea vomiting scale

Score	Clinical assessment
1	No symptoms
2	Nausea, subjective unpleasant sensation with awareness of urge to vomit
3	Retching, spasmodic contraction of abdominal wall and diaphragm muscles without expulsion of gastric contents
4	Vomiting, the same as retching but with forceful expulsion of gastric contents

**Figure 1.** Schematic of intraoperative anesthetic regimen

mal distribution prior to analysis. Values of $p < 0.05$ were considered statistically significant. Normally distributed data were analyzed using the independent t test. Data that were not normally distributed were analyzed using the Mann-Whitney U test. Ordinal data were compared using the Pearson Chi-Square or the Fisher exact test. The intention-to-treat method was used for all analyses.

Results

We enrolled 92 patients during January 2014 through June 2015. Figure 2 shows the CONSORT diagram of the study. Baseline characteristics of participants are shown in Table 2.

At each evaluation point, there was no significant difference in the incidence or severity of postoperative nausea and vomiting, as shown in Table 3.

In most of the patients who developed PONV, onset occurred during the first 4 hours after laparoscopic surgery. Five patients in the

NSS saline and 11 patients in the dextrose group required antiemetic drugs in the recovery room ($p = 0.04$).

Patients who received the dextrose solution had higher blood glucose levels during the recovery period and a larger increase in blood glucose level between the preoperative baseline and after the surgery, as shown in Table 4.

Discussion

Overall, 28% of the patients developed PONV within the first 4 hours after surgery. There was no association between intravenous dextrose administration and normal saline administration in either the incidence or time of onset of PONV. However, a significantly greater number of patients in the dextrose solution group required postoperative antiemetic drugs than in the normal saline group. Moreover, blood glucose levels were significantly higher in patients who received IV dextrose.

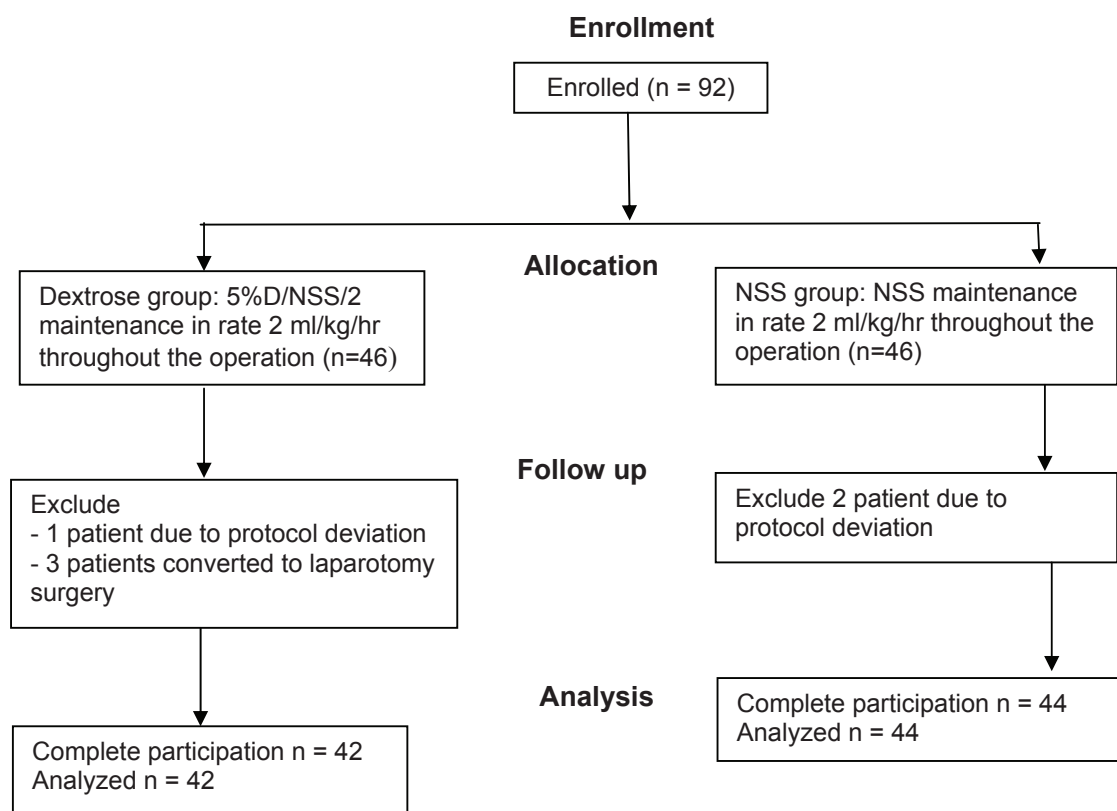


Figure 2. Consolidated Standards of Reporting Trials (CONSORT) diagram

Table 2. Demographic data and perioperative characteristics

Patient characteristic	NSS group (n=44)	Dextrose group (n=42)	<i>p</i>
Age (yrs)	39.3±10.7	36.5±8.5	0.18
Body weight (kg)	54.0±10.0	51.3±8.1	0.12
BMI (kg/m ²)	22.1±4.0	21.1±3.8	0.20
Duration of surgery (min)	141.9±54.3	148.6±59.9	0.62
Duration of anesthesia (min)	170.1±59.8	175.6±61.0	0.70
Blood loss (mL)	76.9±74.0	69.6±89.0	0.30
Fluid volume (mL)			
• Preoperative period	327.2±280.3	277.1±244.5	0.75
• Intra-operative period	677.7±299.5	634.3±327.8	0.31
• Postoperative period	245.1±114.9	247.7±107.0	0.42
Average end-tidal CO ₂ (mmHg)	36±3.0	35±3.0	0.34
Average intraoperative opioid (mcg/kg)	2.3	2.5	0.26
ASA physical status			
• I	35 (79.5)	35 (83%)	0.94
• II	9 (20.5)	7 (17%)	
Premedication			
• Diazepam	36 (81.8)	27 (64.3)	0.48
• Lorazepam	6 (13.6)	7 (16.7)	
• Aspiration prophylaxis	2 (4.6)	6 (14.3)	
• BDZ + Aspiration prophylaxis	0 (0)	2 (4.7)	

Table 3. Bellville postoperative nausea vomiting scale score

Fluid type	NSS group (n=44)				Dextrose group (n=42)				<i>p</i>
	0	1	2	3	0	1	2	3	
Preoperative	44	0	0	0	42	0	0	0	1
Postoperative									
0 min	43	0	0	1	40	1	1	0	0.46
30 min	43	0	1	0	41	1	0	0	0.47
60 min	41	1	1	1	39	1	1	1	0.86
90 min	42	1	1	0	40	0	1	1	1.00
120 min	42	2	0	0	42	0	0	0	0.49
4 hr	41	3	0	0	38	1	3	0	0.16
8 hr	43	1	0	0	39	0	1	2	0.15
12 hr	44	0	0	0	42	0	0	0	1.00
16 hr	43	1	0	0	42	0	0	0	1.00
20 hr	44	0	0	0	42	0	0	0	1.00
24 hr	44	0	0	0	42	0	0	0	1.00

Table 4. Bellville postoperative nausea vomiting scale score

	NSS group (n=44)	Dextrose group (n=42)	<i>p</i>
Preoperative	109.0±24.7	127.4±29.8	< 0.01
Arrival at the recovery room	114.5±25.0	141.8±30.0	< 0.01
120 minutes after surgery	106.8±22.8	127.9±36.1	< 0.01

The hypothesis of the present study originated from the apparent ability of carbohydrate or sugar-containing intravenous fluid to reduce the incidence and severity of PONV (16). We tested that hypothesis by studying a group of patients considered to have a high risk of PONV based on the nature of the surgical procedure. Previously, Bisgaard *et al.* had concluded that a preoperative carbohydrate beverage taken orally did not improve clinical outcome after laparoscopic cholecystectomy (13). A recent study by Raksakietisak *et al.* supported the findings of Bisgaard *et al.* that preoperative oral rehydration with carbohydrate drinks has no positive effect on PONV or the patients' comfort. That study reported the incidence rates of PONV with and without carbohydrate drinks of 81.2% and 72.0%, respectively ($p=0.536$) (10). Based on these methodological issues and the variation in results, we replaced the oral carbohydrate beverage with glucose-containing fluid administered as a maintenance fluid at a rate of 2 mL/kg/h. It is clearly understood that carbohydrates are broken down in the body into glucose, a simple sugar. Glucose-containing fluid provides the primary fuel for the brain and muscles, and also protects the brain from potential fuel shortages (17).

The results of this study were similar to the studies of Patel *et al.* and McCaul *et al.* Patel *et al.* studied 162 patients with normal baseline blood glucose and reported that the administration of dextrose during emergence from anesthesia was not associated with a difference in either incidence or severity of PONV during the first 2 hours after anesthesia (12). McCaul *et al.* compared IV fluid loading with and without supplementary dextrose for the prevention of PONV in 120 ASA I female patients undergoing elective gynecological laparoscopy. Their findings suggest that the administration of dextrose was associated with nausea, an increased opioid requirement, and latent thirst after elective gynecological laparoscopy. They concluded that dextrose-containing iv fluid did not decrease PONV (18). Patients who received dextrose containing IV fluid also developed early hyperglycemia, similar to the results of the present study. However, the results of this study are in contrast to those reported

by Bondoc *et al.* (11). That study tested the effect of postoperative dextrose administration on PONV rates in 62 non-diabetic, ASA class I or II non-smoking outpatients scheduled for gynecologic laparoscopic or hysteroscopy procedures. The researchers found that post-anesthesia IV dextrose administration resulted in reduction of antiemetic rescue medication requirements and length of post-anesthesia care unit (PACU) stay.

In addition to the type of intravenous fluid administered, the volume of fluid administered in previous studies is controversial and the results of those studies are inconsistent. In one study, the intravenous administration of compound sodium lactate (CSL) in 100 patients scheduled for thyroid surgery and the incidence of PONV was analyzed. The study found that CSL 30 mL kg⁻¹ did not reduce the incidence of PONV or the antiemetic requirement compared with CSL 10 mL kg⁻¹ (19). Those results do not support the findings of Maharaj *et al.*, who concluded that large amounts of fluid during laparoscopic surgery significantly decrease pain and PONV (6, 20). A study by Elgueta *et al.* of children undergoing tonsillectomy supports the use of super-hydration as an alternative means of decreasing the risk incidence of PONV (21). Chaudhary *et al.* reported that pre-operative intravenous fluid supplementation using crystalloids and colloids significantly decreased the incidence of PONV. They further stated that crystalloids and colloids were found to be equally effective in preventing PONV (22).

None of the participants in the present study received prophylactic antiemetic medication to avoid a potential confounding factor. The average end-tidal carbon dioxide level and amount of opioid used were comparable in both groups. During recovery period, a significantly larger number of patients in the dextrose group required antiemetic drugs than did patients in the normal saline group. That situation can be explained by the fact that hyperglycemia causes a reduction in gastric emptying time and potentiates the sensation of gastric fullness (23-24). All participants were anesthetized with Propofol which has been reported to reduce the incidence of PONV by 19% (23).

From a surgical aspect, Tseng *et al.* reported that a longer surgical period had a great impact on the incidence and severity of PONV in women undergoing gynecologic laparoscopic surgery (25). In the present study, the surgical duration was comparable between groups (141.9 ± 54.3 min vs. 148.6 ± 59.9 min, $p = 0.62$).

A limitation of the present study was that the start-up baseline level of blood glucose was different between the two groups which could have a confounding effect on the results of study. A second limitation was the lack of postoperative pain data reports by patients. Adequate analgesia may reduce PONV because of a complex interaction between nociception, emesis, and analgesia. It has been reported that hyperglycemia increases postoperative pain by stimulating cholecystokinin release and the N-methyl-D-aspartate-nitric oxide systems (26,27). A third limitation is that the results cannot be generalized to other types of surgical procedures or to male patients.

Conclusions

The administration of intravenous dextrose solution as a maintenance fluid in gynecologic laparoscopic surgery does not reduce the incidence of PONV. It does result in postoperative hyperglycemia and an increased antiemetic requirement. Further studies are needed to evaluate whether different intravenous fluids can reduce PONV.

Acknowledgements

An electronic poster version of an abstract of this study was presented at the World Congress of Anesthesiologists (WCA) meeting in Hong Kong, China, in August 2016. The research and presentation were supported by the Research Fund, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, 50200.

Conflicts of Interest

None

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การให้สารน้ำที่มีน้ำตาลกับอุบัติการณ์และความรุนแรงของอาการคลื่นไส้ อาเจียน หลังการผ่าตัดส่องกล้องทางสรีดุนรีเวช การศึกษาแบบสุ่ม เปรียบเทียบกับกลุ่มควบคุม

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โรงพยาบาลพุทธชินราช จังหวัดพิษณุโลก

วัตถุประสงค์ การศึกษาเพื่อทดสอบสมมติฐานว่าการให้สารน้ำที่มีน้ำตาลเด็กซ์โทรสทางหลอดเลือดดำในระหว่างการผ่าตัดส่องกล้องทางสรีดุนรีเวชจะช่วยลดอุบัติการณ์และความรุนแรงของอาการคลื่นไส้ อาเจียนหลังการผ่าตัดเมื่อเปรียบเทียบกับสารน้ำนอร์มัลเซลินในปริมาณที่เท่ากัน

วิธีการศึกษา การศึกษาไปข้างหน้าแบบสุ่ม เปรียบเทียบกับกลุ่มควบคุม ผู้ป่วยจำนวน 86 ราย ได้รับการสุ่มให้อยู่ในกลุ่มที่ได้รับสารน้ำที่มีน้ำตาลเด็กซ์โทรสจำนวน 42 ราย และอยู่ในกลุ่มที่ได้รับสารน้ำนอร์มัลเซลินจำนวน 44 ราย อาการคลื่นไส้ อาเจียนจะได้รับการประเมินด้วยเกณฑ์เบลล์วิลล์ เป็นระยะเวลา 24 ชั่วโมงแรกหลังการผ่าตัด

ผลการศึกษา ผู้ป่วย 14 รายจาก 44 ราย คิดเป็นร้อยละ 31.8 ในกลุ่มที่ได้รับสารน้ำนอร์มัลเซลินเปรียบเทียบกับผู้ป่วยจำนวน 15 รายจาก 42 ราย คิดเป็นร้อยละ 35.7 ในกลุ่มที่ได้รับสารน้ำที่มีน้ำตาลเด็กซ์โทรสเกิดอาการคลื่นไส้ อาเจียนหลังการผ่าตัด ($p = 0.09$) ในแต่ละจุดเวลาที่ทำการประเมิน พบว่าผู้ป่วยทั้ง 2 กลุ่มมีอุบัติการณ์และความรุนแรงของอาการคลื่นไส้ อาเจียนไม่แตกต่างกัน ในช่วงหลังการผ่าตัดผู้ป่วยในกลุ่มที่ได้รับสารน้ำที่มีน้ำตาลเด็กซ์โทรสต้องการยาแก้คลื่นไส้ อาเจียนมากกว่า ($p = 0.04$) และมีระดับน้ำตาลในเลือดสูงกว่าผู้ป่วยที่ได้รับสารน้ำนอร์มัลเซลิน ($p \leq 0.01$)

สรุปผลการศึกษา การให้สารน้ำที่มีน้ำตาลเด็กซ์โทรสทางหลอดเลือดดำในระหว่างการผ่าตัดส่องกล้องทางสรีดุนรีเวชไม่ช่วยลดอุบัติการณ์และความรุนแรงของการเกิดอาการคลื่นไส้ อาเจียนหลังการผ่าตัดแต่มีผลเพิ่มความต้องการยาแก้คลื่นไส้ อาเจียนและทำให้ระดับน้ำตาลในเลือดสูงขึ้น **เชียงใหม่เวชสาร 2561;57(2):61-9.**

คำสำคัญ: สารน้ำที่มีน้ำตาลเด็กซ์โทรส อาการคลื่นไส้ อาเจียนหลังการผ่าตัด การผ่าตัดส่องกล้องทางสรีดุนรีเวช

