South Afr J Anaesth Analg. 2025;31(2):47-51
https://doi.org/10.36303/SAJAA.3170

South Afr J Anaesth Analg
ISSN 2220-1181 EISSN 2220-1173

ORIGINAL RESEARCH

Evaluating the effect of perioperative carbohydrate loading on reducing the incidence of PONV in middle ear surgery: a multi-arm randomised controlled trial

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Background: This study aimed to assess the effect of perioperative carbohydrate loading on the incidence of postoperative nausea and vomiting (PONV) in patients undergoing middle ear surgery.

Methods: This randomised controlled trial included adult patients undergoing middle ear surgery. Patients in group D received 100 ml/hr apple juice until two hours before surgery, followed by 1 ml/kg/hr of 5% dextrose until the end of the procedure. Patients in group NS received 100 ml/hr water until two hours before the operation, then received 1 ml/kg/hr normal saline until the end of the procedure. Patients in group C fasted for six hours and received 500 ml Ringer's lactate followed by 1 ml/kg/hr intraoperatively. The primary outcome was the incidence of PONV in the first 24 hours (assessed using the Verbal Rating Scale [VRS]). Patients with a VRS score ≥ 5 received ondansetron and then metoclopramide as second-line treatment. Secondary outcomes included antiemetic consumption, nausea severity score, and patients' satisfaction.

Results: We analysed data from 105 patients (35 patients per group). The incidence of PONV was the least in group D (8, 23%) compared to groups NS (31, 89%) and C (31, 89%), $p < 0.001$. The severity of nausea was the least in group D compared to the other groups. The total antiemetic consumption was significantly less in group D than in the other groups. Patients' satisfaction levels were the highest in group D compared to the other groups.

Conclusion: Perioperative carbohydrate loading reduced the risk of PONV in patients undergoing middle ear surgery and improved patients' satisfaction.

Keywords: carbohydrate loading, middle ear surgery, postoperative nausea and vomiting

Introduction

Many patients experience PONV after surgical procedures. Multiple improvements have been used to reduce its risk. PONV can result in delayed discharge from the post-anaesthesia care unit (PACU), unexpected or prolonged hospitalisation, and increased medical costs.[1]

Middle ear surgery is among the surgeries that carry a high risk of PONV. The estimated risk of PONV in this procedure can reach up to 60% due to multiple factors, such as vestibular stimulation and the use of opioid and volatile agents.[2,3]

Several preoperative prophylactic antiemetics have been used to reduce the incidence of PONV. However, the risk is not entirely eliminated. Therefore, multimodal regimens have been recommended, including other non-pharmacological modalities such as acupuncture stimulation, adequate fluid hydration, and carbohydrate loading to control PONV.[4,5] Preoperative carbohydrate supplementation decreases gastric acid secretion and improves gastric emptying.[6,7] Consequently, it might aid in decreasing the incidence of PONV.

Studies investigating the impact of carbohydrate loading on PONV showed inconsistent results. The majority of studies included patients undergoing different abdominal and gynaecological surgeries.[8] However, there is a lack of data regarding the effect of carbohydrate loading on the risk of PONV in middle ear surgeries. Hence, we aimed to investigate the role of perioperative carbohydrate loading in the incidence of PONV after middle ear surgery.

We designed this study as three groups to compare carbohydrate loading to two different perioperative glucose-free hydration regimens. We hypothesise that perioperative carbohydrate loading will reduce the incidence of PONV more than other glucose-free hydration regimens.

Patients and methods

This randomised controlled trial was conducted at Cairo University Hospital between October 2023 and January 2024 after obtaining approval from the ethical committee (MS-206-2022), registration at ClinicalTrials.gov (NCT05947981), and informed consent. This manuscript complies with the Consolidated Standards of Reporting Trials (CONSORT) checklist.[9]

We included patients aged 20–60 years undergoing middle ear, day-case surgeries (such as cortical, modified radical, and radical mastoidectomy) with an American Society of Anesthesiologists (ASA) physical status I–II. Exclusion criteria included diabetes mellitus, a history of motion sickness, dependence on antiemetics, and pregnancy.

An online random sequence (simple randomisation) was used to produce three equal groups (37 patients in each group, https://www.graphpad.com/quickcalcs/randomize1) into which patients were allocated. The groups were assigned with drug preparation and enclosed in sequentially numbered, concealed envelopes. A researcher was responsible for opening the envelopes, group assignment, and fluid preparation without further involvement in the study.

The blood glucose level was measured immediately before starting study fluids using a point-of-care device. Six hours before surgery, patients in the dextrose group (group D) were allowed to drink 100 ml/hr of a clear carbohydrate-rich drink (apple juice containing 12 g carbohydrate per 100 ml) till two hours before surgery and then continued on a 5% dextrose infusion rate of 1 ml/kg/hr till the end of the operation.

In the control group (group C), nothing was allowed by mouth for six hours preoperatively. During the intraoperative period, Ringer's lactate solution was given intravenously (IV) as a 500 ml bolus followed by 1 ml/kg/hr as infusion fluid.

The normal saline group (group NS) of patients was instructed to take 100 ml/hr of water during fasting hours until two hours before the operation. They then received 0.9% normal saline at a rate of 1 ml/kg/hr IV for two hours before the operation until the end of surgery.

After arrival at the operating room, standard monitoring was applied (non-invasive blood pressure, 5-lead electrocardiogram [ECG], and pulse oximetry). Dexamethasone 8 mg IV was given before beginning the surgery. Anaesthesia was induced with propofol (1.5–2 mg/kg), fentanyl (2 mcg/kg), and atracurium (0.5 mg/kg), followed by endotracheal intubation. Anaesthesia maintenance was done with isoflurane in an oxygen and air (50:50) mixture. Morphine 0.1 mg/kg IV was given for analgesia. Incremental doses of fentanyl (0.5 mcg/kg) were given if the heart rate was > 75 or blood pressure > 110/70 to control the surgical field. Paracetamol (1 g IV) was given at the end of surgery for postoperative analgesia.

Four values of random blood sugar were recorded: six and two hours before surgery, one hour just after anaesthesia induction, and immediately after the operation. The patients were educated about rating their sense of nausea using a VRS ranging from 0 to 10 (no nausea = 0, worst imaginable nausea/retching = 10). The data collector was blinded to the group assignment and was responsible for recording episodes of PONV at prespecified time points (1, 6, 12, and 24 hours after operation). PONV was defined as either spontaneous complaints of nausea (VRS > 5) or vomiting. Patients with a VRS score ≥ 5 received ondansetron 4 mg IV as a first-line antiemetic treatment, followed by 10 mg metoclopramide as a second line.

The primary outcome of this study was the incidence of PONV, defined as either spontaneous complaint of nausea (nausea VRS > 5) or vomiting between the groups. Secondary outcomes included the total amount of rescue antiemetic (IV ondansetron in an incremental dose of 4 mg and a metoclopramide dose of 10 mg) 24 hours postoperatively, VRS for nausea, total amount of opioids, and random blood sugar. The patient satisfaction index was recorded 24 hours postoperatively on a VRS of 0–10, where 0 was strongly dissatisfied and 10 was strongly satisfied. The patients' demographic data and Apfel scores were also recorded.

Statistical analysis

In a pilot study of 10 patients in the control group, the incidence of PONV was 80%. The sample size was calculated using MedCalc Software version 14 (MedCalc Software bvba, Ostend, Belgium). A minimum sample of 102 patients was needed to detect a difference of 35% between the groups to achieve a study power

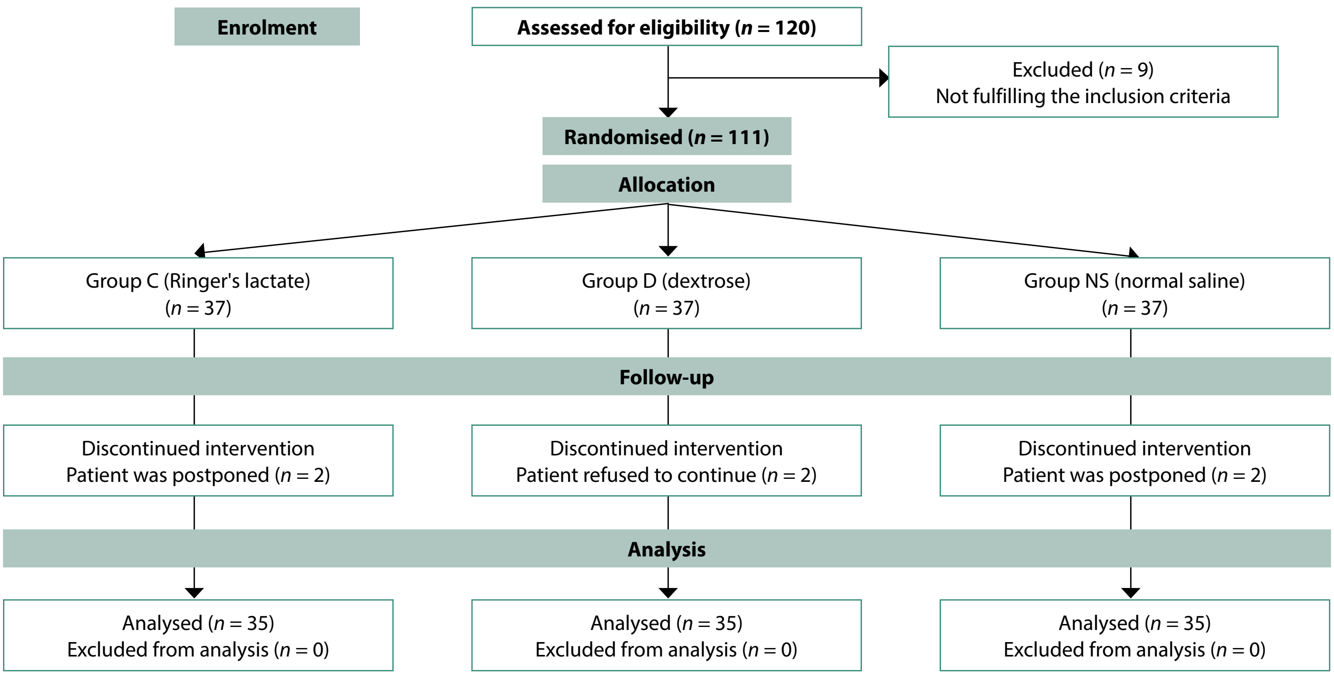

Figure 1

Table I: Demographic data and Apfel scores

	Group C (*n* = 35)	Group D (*n* = 35)	Group NS (*n* = 35)	*p*-value
Age (years)	35 ± 8	35 ± 9	34 ± 9	0.856
Male sex	18 (51%)	18 (51%)	19 (54%)	0.963
ASA classification				0.162
I	35 (100%)	32 (91%)	34 (97%)	
II	0 (0%)	3 (9%)	1 (3%)	
Apfel score	1 (0, 2)	1 (0, 2)	1 (0, 2)	0.940

Group C – control group, Group D – dextrose group, Group NS – normal saline group, ASA – American Society of Anesthesiologists
Data are presented as mean ± standard deviation, median (quartiles), and frequency (%).

of 90% with an alpha error of 0.025. The required sample size was increased to 111 patients (37 patients per group) to compensate for possible dropout. International Business Machines (IBM) Corporation Statistical Package for the Social Sciences (SPSS) software package version 20.0 (IBM Corporation, Armonk) was used for data analysis.

Categorical data are presented as frequency (%) and were analysed using the chi-square test or Fisher's exact test as appropriate. The Shapiro–Wilk test was used to check the distribution of continuous data. Continuous data are reported as mean ± standard deviation or median (quartiles) according to data distribution. Unpaired data were analysed using the one-way analysis of variance with the post-hoc Tukey test or Kruskal–Wallis test according to data distribution. Repeated measure analysis of variance was used to analyse repeated measured data.

For the primary outcome, the relative risk and its 98% confidence interval (Bonferroni corrected confidence interval) were calculated. The Bonferroni test was used to correct for multiple comparisons. A p-value < 0.05 was considered statistically significant. No subgroup analysis was done. A preplanned statistical analysis was described in the original protocol but not uploaded in the clinical trial registration.

Results

We screened 120 patients for eligibility; nine patients were excluded for not fulfilling the inclusion criteria, and 111 patients were included, but six patients were excluded, and 105 were available for the final analysis. The analysis was a modified intention-to-treat analysis (Figure 1). Patients' demographic data (including age and gender), ASA physical status classification, and Apfel scores were comparable between the three groups (Table I).

The incidence of PONV was lower in group D (8/35, 23%) compared to groups C (31/35, 89%) and NS (31/35, 89%), $p < 0.001$, and it was comparable between groups C and NS. The relative risk (98% confidence interval) for PONV in groups C and NS was 3.9 (1.8–8.3) compared to group D, and it was 1.0 (0.8–1.2) between groups C and NS.

The nausea severity was lowest in group D compared to groups C and NS ($p < 0.001$). Furthermore, the total antiemetic consumption was significantly less in group D than in the other groups. Conversely, there was no statistically significant difference among the groups regarding the incidence of vomiting (Table II).

Table II: PONV and antiemetic consumption

	Group C (*n* = 35)	Group D (*n* = 35)	Group NS (*n* = 35)	*p*-value
Incidence of PONV **Pairwise comparison**	31 (89%)* *p < 0.001	8 (23%)	31 (89%)* *p < 0.001	< 0.001
Incidence of vomiting	11 (31%)	3 (9%)	9 (26%)	0.055
Incidence of nausea with VRS ≥ 5 **Pairwise comparison**	31 (89%)* *p < 0.001	8 (23%)	31 (89%)* *p < 0.001	< 0.001
Antiemetic consumption				
Ondansetron (mg) Pairwise comparison	4 (4, 8)* *p < 0.001	0 (0, 0)	8 (4, 8)* *p < 0.001	< 0.001
Metoclopramide intake Pairwise comparison	16 (46%)* *p < 0.001	1 (3%)	16 (46%)* *p < 0.001	< 0.001
Metoclopramide (mg) Pairwise comparison	0 (0, 10)* *p < 0.001	0 (0, 0)	0 (0, 10)* *p < 0.001	< 0.001
VRS for postoperative nausea				
1 hr Pairwise comparison	3 (2, 4)* *p = 0.038	2.(0, 3)	3 (2, 4) p = 0.124	0.029
6 hr Pairwise comparison	6 (4, 8)* *p < 0.001	2 (0, 4)	6 (4, 8)* *p < 0.001	< 0.001
12 hr Pairwise comparison	4 (3, 7)* *p < 0.001	0 (0, 2)	7 (2, 8)* *p < 0.001	< 0.001
24 hr Pairwise comparison	2 (0, 2)* *p = 0.009	0 (0, 2)	2 (0, 2)* *p = 0.028	0.005

Group C – control group, Group D – dextrose group, Group NS – normal saline group, hr – hour, PONV – postoperative nausea and vomiting, VRS – Verbal Rating Scale
* Denotes statistical significance in relation to Group D.
Data presented as frequency (%) and median (quartiles).

Table III: Other outcomes

	Group C ($n = 35$)	Group D ($n = 35$)	Group NS ($n = 35$)	p-value
Blood glucose level (mg/dl)				
Baseline	91 ± 8*	102 ± 11	93 ± 10*	< 0.001
Pairwise comparison	*$p < 0.001$		*$p = 0.002$	
1 hr post-intervention	91 ± 7*	119± 15	90 ± 8*	< 0.001
Pairwise comparison	*$p < 0.001$		*$p < 0.001$	
After induction	96 ± 10*	135± 14	94 ± 11*	< 0.001
Pairwise comparison	*$p < 0.001$		*$p < 0.001$	
At the end of surgery	93 ± 11*	163 ± 22	93± 12*	< 0.001
Pairwise comparison	*$p < 0.001$		*$p < 0.001$	
Intraoperative opioid consumption				
Fentanyl (mcg)	200 (200, 200)	200 (200, 200)	200 (200, 200)	0.377
Morphine (mg)	5 (5, 5)	5 (5, 5)	5 (5, 5)	0.389
Time of first oral intake (hr)	3 (2, 3)	2 (2, 3)	3 (2, 3)	0.141
Satisfaction index	7 (7, 8)*	9 (8, 9)	7 (6, 8)*	< 0.001
Pairwise comparison	*$p < 0.001$		*$p < 0.001$	

Group C – control group, Group D – dextrose group, Group NS – normal saline group, hr – hour
* Indicates significance in relation to group D.
Data are presented as mean ± standard deviation and median (quartiles).

The blood glucose level was the highest in group D compared to the other groups. Other outcomes, including intraoperative opioid consumption and time to the first oral intake, were comparable among the groups. Patients' satisfaction levels in group D were the highest compared to the other groups (Table III).

Discussion

In this study, we report that carbohydrate loading reduced the incidence of PONV, antiemetic consumption, and the severity of nausea compared to fasting patients and those receiving normal saline. The exact mechanism by which carbohydrate loading affects PONV could be explained by glucose metabolism improvement and the metabolic stress resulting from preoperative fasting and surgical stress responses.[10] Also, carbohydrate loading directly affects the gastrointestinal tract, increasing gastric emptying and decreasing the psychological stress response.[11,12]

Previous studies have shown conflicting results regarding the effect of perioperative carbohydrate loading on PONV. Similar to our findings, previous studies in cholecystectomy and laparoscopic hysteroscopy showed the beneficial effect of carbohydrate loading in reducing PONV.[13-16] However, to the best of our knowledge, this is the first study to assess the effect of carbohydrate loading in middle ear surgery.

In contrast, studies involving major upper gastrointestinal surgeries, colorectal surgeries, and thyroidectomies demonstrated no effect of carbohydrate loading on PONV.[17-19] This conflicting evidence among the studies could result from including different types of surgical procedures, which might have different additional PONV risks, such as direct manipulation of the gastrointestinal tract in major upper gastrointestinal surgeries or colorectal surgeries.

PONV is an undesirable and distressing adverse event. PONV incidence can reach 80% in patients undergoing middle ear surgery. The use of antiemetics showed varied efficacy and side effect profiles. Consequently, the choice of an antiemetic should be balanced with the risk of adverse effects. Furthermore, proper PONV management requires a multimodal approach that tackles the different mechanisms of PONV.

Carbohydrate loading is a cheap and safe alternative to control PONV. Different doses and routes of carbohydrate loading were tried in different populations to assess its impact on patient satisfaction and its efficacy in reducing the incidence of PONV.[20-22] This study's findings support the use of carbohydrate loading in patients undergoing middle ear surgery to reduce the risk of PONV.

This study has several advantages, including being a randomised controlled trial and choosing the incidence of PONV as the primary outcome. However, the study has some limitations. It was conducted in a single centre. We evaluated a single carbohydrate loading regimen in ASA I–II patients. Therefore, future studies are needed to identify the optimal regimen for different population types.

Six patients were excluded from the analysis in this study due to the discontinuation of the intervention. However, the study was not affected as the sample size was fulfilled. The glucose level was increased in the carbohydrate loading group, which limits its role in diabetic patients. The protocol and datasets used/analysed during this study are available from the corresponding author upon reasonable request.

Conclusion

Perioperative carbohydrate loading reduced the risk of PONV in patients undergoing middle ear surgery and improved patients' satisfaction.

Conflict of interest

The authors declare no conflict of interest.

Funding source

None.

Ethical approval

Ethical approval was obtained from the Cairo University Faculty of Medicine, Research Ethics Committee (Ref: MS-206-2022), with clinical trial registration (NCT05947981).

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Supplementary file available online