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## Prevention of post-operative nausea and vomiting with honey as a pre-operative oral carbohydrate: A randomised controlled pilot trial

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## Prevention of post-operative nausea and vomiting with honey as a pre-operative oral carbohydrate: A randomised controlled pilot trial

### Cover Page Footnote

The confidentiality and anonymity of findings were preserved according to the Helsinki Declaration.  
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# Prevention of post-operative nausea and vomiting with honey as a pre-operative oral carbohydrate: A randomised controlled pilot trial

## Abstract

**Background:** Post-operative nausea and vomiting (PONV) is the second-most common post-operative complication. Prolonged pre-operative fasting is common in Australia despite guidelines recommending reduced fasting to improve patient outcomes, such as PONV. Commercially prepared pre-operative oral carbohydrate (OC) drinks may be used to reduce fasting time. In this study commercial products were replaced with honey, an inexpensive and common food item.

**Design:** Partially blinded, four parallel arms randomised controlled non-inferiority trial compared pre-operative OC loading with overnight fasting.

**Methods:** Adult elective laparoscopic cholecystectomy and thyroidectomy patients having two or more risk factors for PONV were allocated into intervention and control groups by simple randomisation. The intervention group ingested 60g of honey in 100 ml of water at least two hours before surgery as pre-operative OC loading to reduce PONV. Participants and assessors to the group assignment were blinded to the study outcomes. Early PONV (0–6 hours) was measured with Rhodes index of nausea, vomiting and retching (R-INVR) and a numeric rating scale (NRS).

**Results:** The four groups (N = 142) were control and intervention groups of thyroidectomy patients (n = 72: C = 37, I = 35), and control and intervention groups of laparoscopic cholecystectomy patients (n = 70: C = 37, I = 33) and had similar distributions of variables. The estimated effect size was 140 with a 95 percent confidence interval. The PONV incidence (Pearson  $\chi^2 = 4.54$ ; df = 1; p = 0.03) and severity were significantly lower in the laparoscopic cholecystectomy intervention group (R-INVR: Mann–Whitney U = 446.5; p = 0.01; NRS: Mann–Whitney U = 444.5; p = 0.01) and results were not conclusive in the thyroidectomy group (NRS: Mann–Whitney U = 629.5; p = 0.95; R-INVR: Mann–Whitney U = 629.5; p = 0.76).

**Conclusion:** Honey could be recommended as an inexpensive pre-operative OC to reduce PONV in adult patients receiving general anaesthesia.

**Keywords:** pre-operative, carbohydrate loading, honey, post-operative nausea and vomiting, prevention, randomised controlled trial

## Introduction

Overnight fasting of patients before surgery (no oral intake from midnight until surgery) is an outdated and harmful practice; however, it remains common in Australia. The fasting period is frequently prolonged – greater than 12 hours and up to 24 hours. Guidelines recommend reduced fasting and early post-operative oral intake to improve patient outcomes such as post-operative nausea and vomiting (PONV) and glycaemic balance. One strategy to reduce the fasting period is providing patients with oral carbohydrate (OC) drinks up to two hours before surgery. However, evidence-based guidelines on pre-operative fasting are poorly implemented and research is not being translated into reduced fasting times.<sup>1,2</sup>

Despite the improvement in anaesthesiology and surgical methods, PONV is the second-most common post-operative complication, experienced by approximately one third of all perioperative patients.<sup>3-5</sup> The aetiology and pathophysiology of PONV is multidimensional and not fully understood. The nausea and vomiting centre, located in the medulla oblongata of the brain, is thought to respond to chemoreceptor inputs from blood circulation, toxins or other stimulants received from the gastrointestinal tract, and other inputs from the cerebral cortex, thalamus and vestibular region.<sup>5</sup> PONV is considered to be a consequence of physiological stress, prolonged fasting time and anaesthetic agents.<sup>6,7</sup> Increased length of hospital stay and subsequent increased cost, discomfort, anxiety, incisional tension and pain can occur due to PONV.<sup>8-10</sup>

Recommendations for the prevention of PONV include reduced pre-operative fasting, early post-operative oral intake, determination of the risk groups and prophylactic interventions for those at high risk of developing PONV.<sup>1,7</sup> However, the best way to manage PONV has not yet been determined, although 5-HT<sub>3</sub> receptor antagonists, glucocorticoids or a combination of these are used with limited efficacy.<sup>1,11,12</sup> Many studies have investigated the best practice for pharmacological PONV management; however, many had suboptimal methodology resulting in a weak to moderate level of evidence for prevention.<sup>13-15</sup> The recommended approach for managing PONV is to determine patients at higher risk of developing PONV and focus on prevention for this population rather than the current practice of polypharmacological interventions for all surgery patients. Polypharmacological intervention for PONV poses a risk of adverse effects, such as drowsiness and hypotension, and increases the cost of care. Non-pharmacological interventions for PONV include reducing the fasting time and pre-operative OC loading.<sup>7,15,16</sup>

Current recommendations regarding non-pharmacological interventions for managing PONV include oral pre-operative carbohydrate.<sup>5,17,18</sup> The evidence remains moderate as PONV is a multifaceted issue and previous studies lack inclusion of all relevant variables. For instance, some reports did not present an anaesthesia protocol, some were unclear regarding the medical management of PONV and very few included data regarding PONV risk factors; thus, making comparisons to results in future studies is difficult.<sup>6,19,20</sup> We have not found any studies that used honey as an oral pre-operative carbohydrate for PONV or any other type of nausea prevention.

The evidence for the effectiveness of pre-operative OC loading in reducing PONV has not been conclusive; however, it was recommended as a simple and safe intervention to reduce fasting time (gastric emptying time for clear fluids was determined between 60 to 90 min).<sup>21-24</sup> OC loading is described as ingestion of 400–800 ml of OC the night before surgery and 200–400 ml up to two hours before elective surgery.<sup>1,6</sup>

Studies indicate that reducing pre-operative fasting time improves patients' comfort, insulin resistance and stress responses in the post-operative period.<sup>21,23</sup> Moreover, the pre-operative OC loading improved post-operative insulin resistance and return of bowel function,<sup>6,17</sup> and did not increase the risk of aspiration.<sup>22,25,26</sup> The recommendations from anaesthesiology professionals resulted in commercial pre-operative drinks emerging in the market and being promoted to health care institutions with an additional cost. The content of these commercial pre-operative drinks varies but is usually a hypo-osmolar solution including around 50 grams of complex glucose, sometimes with vitamins and minerals.<sup>22,27,28</sup> The economic and environmental impact of manufacturing, packaging, storing and distributing is assumed to be a significant consideration when developing a commercial OC preparation, whereas using honey, a common pantry item that can be ingested by patients as preferred, avoids these impacts. Honey has been used for gastric mucosal protection and healing, and its consumption has been shown to be just as effective as sucralfate or allopurinol<sup>29-31</sup> in reducing glycated hemoglobin, LDL cholesterol, and fasting triglycerides.<sup>32</sup>

Previous studies measured PONV as a gastric complication, as described in the design section. Therefore, the current study was planned as a pilot superiority randomised controlled trial to support or refute our hypothesis that a natural nutrient source, honey, would be beneficial to prevent or reduce PONV.

Pre-operative OC has been beneficial for reducing PONV in a number of studies<sup>5,33,34</sup> and was recommended in the Enhanced Recovery After Surgery (ERAS) guidelines.<sup>6</sup> As a natural carbohydrate source, honey has an antioxidant effect with tocopherol, ascorbic acid, flavonoids and other phenolic-enzyme compounds in its structure.<sup>35–37</sup> To date, there are no published studies investigating the effect of honey consumption on PONV or any other type of nausea, to our knowledge.

Perioperative nurses are patient advocates for improving surgical outcomes and reducing the cost of health care. This study presents evidence and recommendations for reducing the pre-operative fasting period by replacing commercial carbohydrate products with a common food item, informing practice regarding non-pharmacological interventions and introducing a new method for managing PONV.

## Aim

The aim of this randomised control trial (RCT) was to evaluate whether pre-operative oral honey and water intake is associated with a lower incidence and severity of PONV in adult participants, compared to overnight fasting.

## Hypotheses

Hypothesis 1: Pre-operative oral intake of 60 g of honey in 100 ml of water is associated with a lower incidence and severity of early PONV for laparoscopic cholecystectomy patients, compared with standard pre-operative overnight fasting.

Hypothesis 2: Pre-operative oral intake of 60 g of honey in 100 ml of water is associated with a lower incidence and severity of early PONV for thyroidectomy patients, compared with standard pre-operative overnight fasting.

## Methods

### Study design

The study was designed as a single-centred, open-label randomised control non-inferiority trial with a 1:1 allocation ratio. The impact on PONV incidence and severity of oral administration of honey in water as oral carbohydrate loading to reduce fasting time was compared with overnight fasting.

### PONV risk factors and the participants selection

The factors that affect incidence of PONV are: female gender, history of PONV or motion sickness, not smoking, younger age, general anaesthesia, use of volatile anaesthetics and nitrous oxide, use of post-operative opioids, longer duration of anaesthesia and type of surgery (cholecystectomy, laparoscopic, gynaecological).<sup>1,5</sup> We considered Koivuranta's five risk factors (female, age <50, non-smoking, duration of anaesthesia >60 min, history of PONV or motion sickness<sup>38</sup>) as they were indicated to be superior to Apfel's risk factors<sup>39</sup> (female, non-smoking, history of PONV or motion sickness, use of post-operative opioids<sup>5</sup>). To obtain

more robust results in smaller samples, we aimed to include patients with two or more of Koivuranta's risk factors.

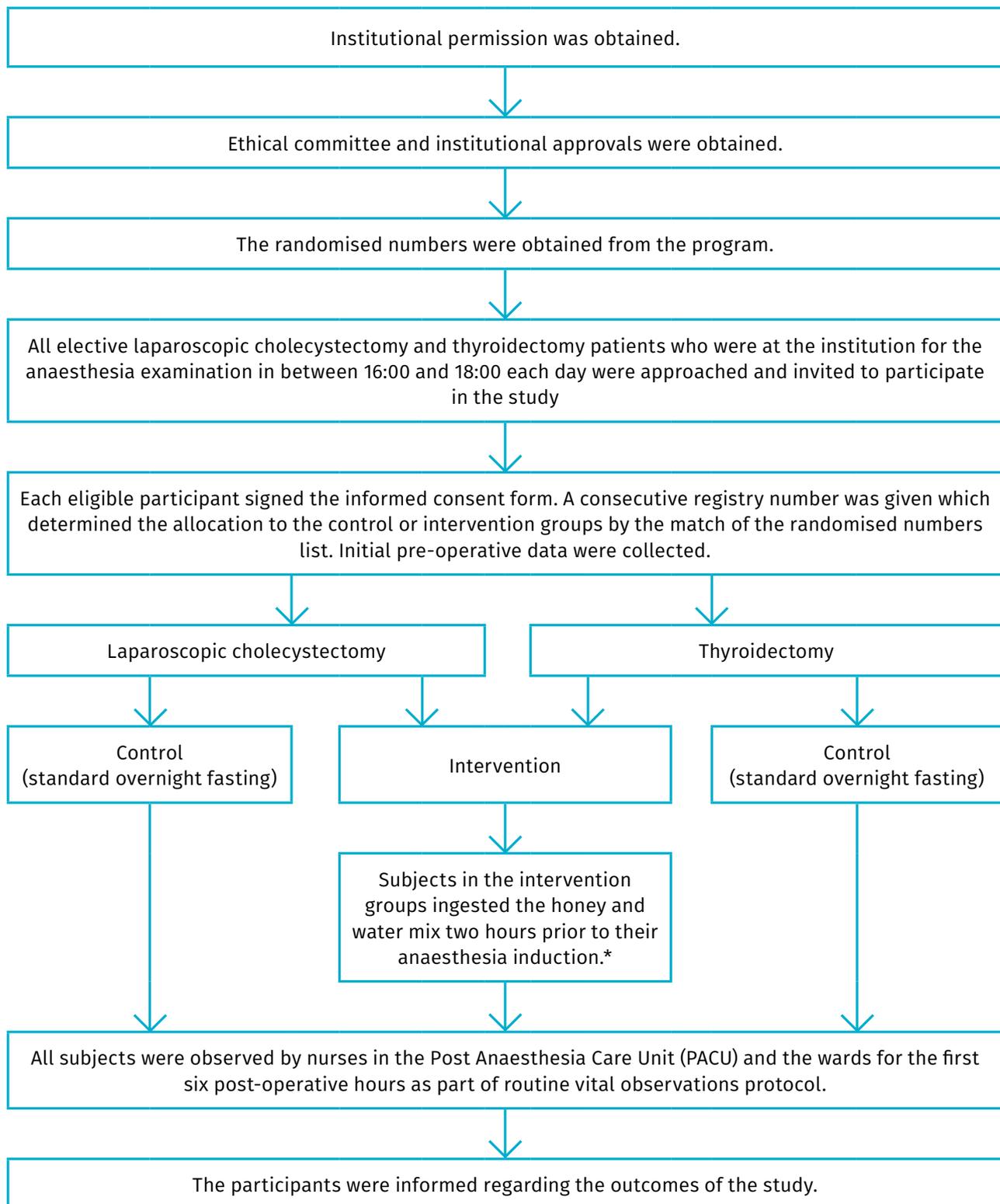
Elective laparoscopic cholecystectomy and thyroidectomy surgeries were targeted, to obtain consistent results with previous studies<sup>24</sup> and to reach a robust sample size for comparison, as these surgeries were frequent in the study setting.

Patients aged 18 to 79, having two or more Koivuranta risk factors for PONV<sup>38</sup> were approached between May 2017 and January 2018. Patients with diabetes, oral restrictions other than fasting, or pollen allergy were excluded (Figure 1).

### Intervention (description of study procedures and methods)

The intervention in this study was the oral intake of a honey and water mixture as a pre-operative carbohydrate source. We compared the impact on PONV incidence and severity of oral honey intake with overnight fasting. Previous studies used 50 g (200 kilocalories) of carbohydrate in 400 ml of water two hours pre-operatively. The anaesthesiology department where the study was conducted limited the oral fluid to 100 ml. Therefore, our intervention was 60 grams of honey (200 kilocalories approx.) in 100 ml of spring water at room temperature. The mixture was ingested by participants up to two hours pre-operatively.

The honey used in the study was purchased from a single producer, collected in the same season and in the same region for consistency of chemical and glycaemic properties. The honey samples were tested for quality and confirmed to meet the quality standards of international consumable honey.<sup>40</sup>



**Figure 1: Research process diagram**

\*Subjects whose surgery was planned as second, third and fourth cases of the day were given the honey and water mixture an estimated two hours before surgery.

The primary investigator prepared a food-grade jar with 60 g of honey, marked each jar to the top-up point of 100 ml for water to be added and mixed before consuming. The hospital where the study was conducted admits perioperative patients at 7.00 am, and the first case of each operating room commences at 8.00 am. Therefore, the first patients of each operating room list were instructed to consume the mixture at 6.00 am before coming to the hospital and two hours before the anaesthesia induction. The primary investigator phoned the participants a day before the operation and repeated the instructions. Confirmation of drinking the mixture was sought on hospital admission by the primary investigator. The same investigator observed the participants' intake at the hospital for the remainder of the cases on each operating room list of the day from 8.00 am onwards. Patients who did not follow these instructions were excluded from the study.

All participants received the same protocol (as follows) for a general inhalation (inh.) and intravenous (IV) anaesthesia: propofol 1-1.5 mg/kg (IV), midazolam 0.03-0.05 mg/kg (IV), fentanyl 0.5-1 mg/kg (IV), rocuronium bromide 0.3-0.6 mg/kg (inh.), sevoflurane %2-3/L (inh.), prophylactic antibiotic 1 g (IV), paracetamol 1 g (IV), atropine sulphate 1 mg (IV), neostigmine methyl sulphate 2 mg (IV), famotidine 20 mg (IV).

## Outcomes

There were two primary outcomes for this study:

1. the incidence of PONV per group over the early post-operative period (0-6 hours)
2. the severity of PONV per group over the early post-operative period (0-6 hours).

## Data collection

The data collection form consisted of three sections:

1. participant characteristics – age, gender, education, height, weight, BMI, general health condition and planned type of surgery
2. PONV risk factors – gender, age, smoking status, anaesthesia medications, duration of anaesthesia and history of PONV or motion sickness<sup>5,38</sup>
3. post-operative complications – pain, bleeding, antiemetic use, PONV incidence and severity (measured by the Rhodes index of nausea, vomiting and retching (R-INVR) and the numeric rating scale (NRS) at each routine post-operative assessment for the first six hours post-operatively.

The first part of the data collection form was completed by the primary investigator during the pre-operative anaesthesia examination of patients. Data for the second section was pulled from the institutional patient data, and data for the third section was collected by nurses who were trained by the primary investigator prior to data collection. The nurses in the Post Anaesthesia Care Unit (PACU) and general surgery departments collected the post-operative data by observation and patient reporting in the first post-operative hour, and by patient reporting in the next five post-operative hours.

The R-INVR and NRS were used for PONV measurement along with routine post-operative observations which were conducted, according to hospital protocol, every 15 minutes in the first hour, every 30 minutes in the second hour and hourly thereafter. PONV incidence and severity were measured by R-INVR

scores (eight items, 0-4 points; total of 0-32 points) and NRS (0 to 10 patient expression) in the early post-operative period, zero to six hours after surgery. The highest recorded scores of PONV within the observation period were used for the analysis; the intervention group was compared to the control group for each type of surgery.

## Description of instruments, including measurement reliability and validity evidence

The R-INR and NRS are validated scales and have been used in previous studies of PONV. The R-INVR was developed by Rhodes and McDaniel in 1999, validated for PONV in adult patients by Kim et al. in 2007 and Genc and Tan proved language validity of the scale in 2010. It is widely used in the literature for PONV.<sup>39,41-44</sup> Responses are recorded using a scale ranging from '0' for no discomfort to '4' for the highest discomfort, with a total of 32 points for eight scale items. The internal consistency coefficient of the scale was 0.91; sub-dimensions alpha internal consistency coefficients were 0.81 and 0.89 for 'symptom development' and 'symptom discomfort' respectively in this study.

The NRS is a widely used tool and has been used in several studies to measure PONV in similar populations, including adult laparoscopic cholecystectomy patients. Patients were asked by nurses to rate their discomfort, nausea, vomiting/retching and pain on an NRS ranging from '0' for no complaints to 10 for worst imaginable complaint, during the routine post-operative care intervals. The highest score of the repeated assessments was recorded.

Both scales were approved by a panel of experts.

## Sample size

The literature indicated the average incidence for PONV is around 30 per cent of patients. We aimed to reduce this by 50 per cent. For the power analysis, alpha was set at 0.05 and estimated power at 0.8. Estimated effect size of two independent groups was calculated at an average of 0.5 ( $d=0.50$ ).<sup>24</sup> In consideration of any data loss and non-parametric analysis, the power analysis determined the sample size at a minimum of 140 participants – 70 laparoscopic cholecystectomy participants (35 in each of the intervention and control groups) and 70 thyroidectomy participants (35 in each of the intervention and control groups).

## Simple stratified randomisation

The patients were assigned to the four groups – laparoscopic cholecystectomy control and intervention and thyroidectomy control and intervention – by simple randomisation using an online number randomisation service.<sup>45</sup> The primary investigator gave consecutive registration numbers to volunteering participants; these registration numbers were randomised and used to assign participants to a group (intervention or control). Allocation was marked only on the data collection forms, the patient records did not include any allocation information.

## Partial blinding

This study was an open-label RCT. The outcome measures of the intervention were not disclosed to participants – information provided to participants included the general statement ‘gastrointestinal system and other post-operative outcomes will be observed after surgery’. The nurses who collected the post-

operative data were blinded to the group allocation of participants. The external expert who supervised the statistical analysis was not blinded to the group allocations.

## Statistical analysis

Statistical analyses were performed with SPSS 21.0 (IBM Corp. released 2012, Armonk, NY, USA) package program. Descriptive statistics were mean, standard deviation, median, minimum–maximum, frequency, percentile and regression analysis.

We used Pearson’s chi-squared test and Fisher’s exact test in the comparison of discrete variables regarding the incidence of PONV. We performed Mann Whitney U test for comparisons between groups of continuous variables related to the severity of PONV with mean scores of the R-INVR and the NRS.  $P < 0.05$  value was accepted for statistical significance with a 95 per cent confidence interval.

## Ethical considerations

Following the institutional permits and ethical approval from Istanbul University, Cerrahpaşa Medical Faculty Ethical Board (03/05/2017-166977), health professionals in the relevant departments were informed. The primary investigator approached the patients at their pre-operative anaesthesia examination a few days before their surgery, provided verbal and written information about the study, and obtained written consent from voluntary participants.

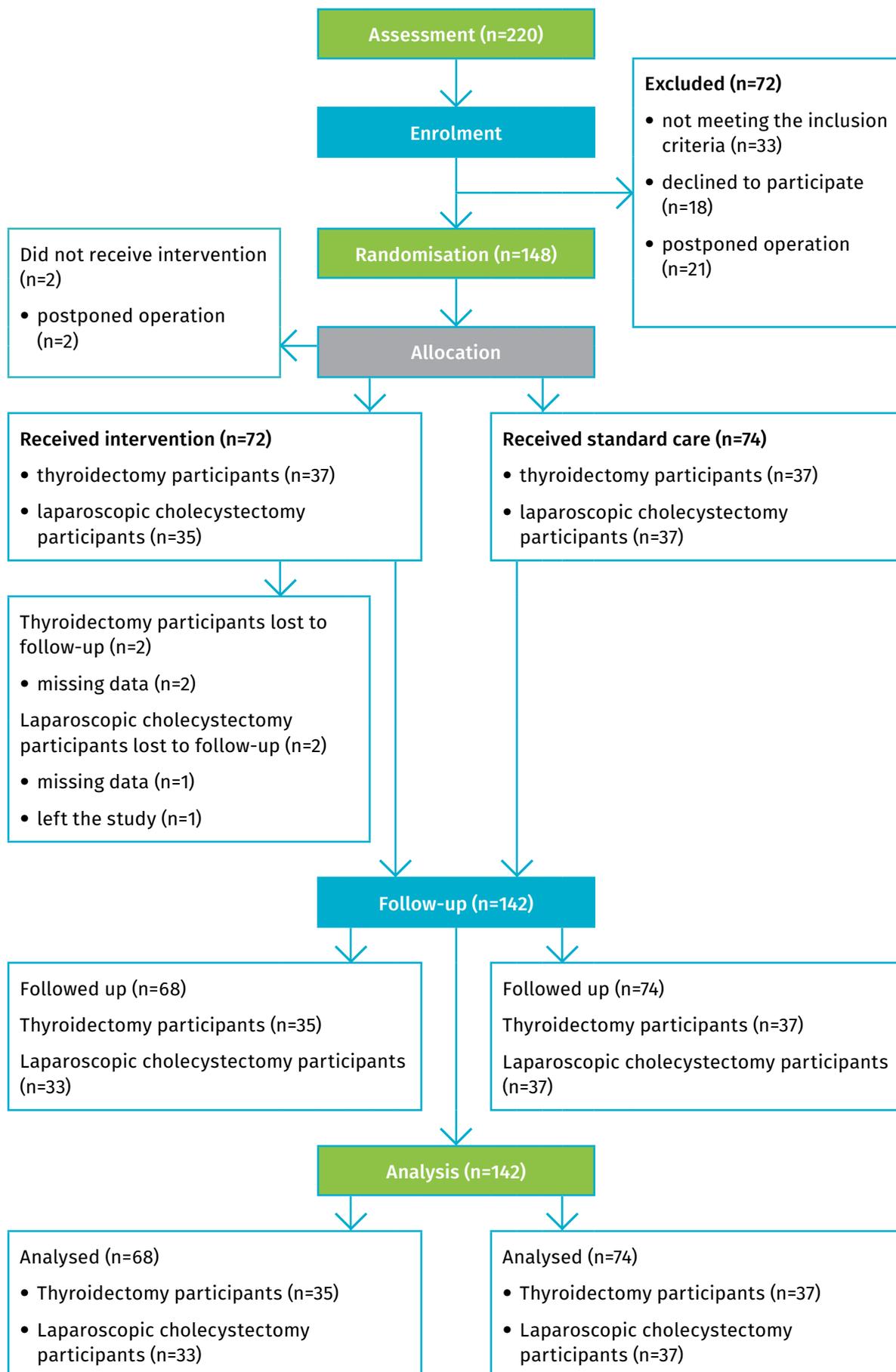
We censored the patient identification information in the data set prior to the analyses, archived all patient data collection forms safely, and stored and protected the electronic data in an offline device.

## Results

The study was conducted with a total of 142 participants in four groups; 72 of the participants underwent thyroidectomy – 37 were randomly assigned to the control group (T-control) and 35 to the intervention group (T-intervention); 70 patients underwent laparoscopic cholecystectomy – 37 were randomly assigned to the control group (LC-control) and 33 to the intervention group (LC-intervention). Table 1 shows the distribution of variables of the four groups.

The intervention and control groups were comparable in terms of type of surgery, age, gender, smoking status, PONV or motion sickness history and obesity. On the other hand, more participants in the intervention group had a history of gastric morbidity (presence of ulcer, gastritis, reflux, hiatal hernia, pain or gastric cancer), In addition, more patients received tramadol hydrochloride in the intervention groups of both types of surgery, and more patients in the thyroidectomy control group received dexamethasone compared to the intervention group.

Four of Koivuranta’s five PONV risk factors<sup>38</sup> – being female, being younger than 50, being a non-smoker (tobacco) and having a history of PONV and/or motion sickness were included in the data collection to facilitate comparisons to results in future studies. Other PONV risk factors indicated in the literature, including opioid, antiemetic, or tramadol hydrochloride administration (opioid analgesic), and body mass index<sup>1</sup> (recorded as obesity) were included for the same reasons.



**Figure 2: Modified Consolidated Standards of Reporting Trials (CONSORT) flow diagram for individual randomised controlled trials of nonpharmacologic treatments**

**Table 1: Distribution of variables between groups (N=142)**

Variable		Control (n=74)	Intervention (n=68)
Operation	Thyroidectomy	37 (50.0%)	35 (51.5%)
	Laparoscopic cholecystectomy	37 (50.0%)	33 (48.5%)
Gender <sup>α</sup>	Female	63 (85.1%)	52 (76.5%)
	Male	11 (14.9%)	16 (23.5%)
Age <sup>α</sup>	Mean ± standard deviation	47.1±14.4	45.7±12.3
	Median (min–max)	50.5 (19–79)	45 (22–79)
Smoking status <sup>α</sup>	Smoking	16 (21.6%)	19 (27.9%)
	Non-smoking	58 (78.4%)	49 (72.1%)
History of PONV and motion sickness <sup>**</sup>	No	60 (81.1%)	53 (77.9%)
	Yes	14 (18.9%)	15 (22.1%)
Obesity	No	47 (63.5%)	52 (76.5%)
	Yes	27 (36.5%)	16 (23.5%)
Gastric morbidity	No	47 (63.5%)	32 (47.1%)
	Yes	27 (36.5%)	36 (52.9%)
Use of tramadol hydrochloride	No	67 (90.5%)	48 (70.6%)
	Yes	7 (9.5%)	20 (29.4%)
Use of dexamethasone	Thyroidectomy	16 (43.2%)	6 (17.1%)
	Laparoscopic cholecystectomy	1 (2.7%)	3 (9.1%)

PONV = Post-operative nausea and vomiting; α = Koivuranta risk factor; Gastric morbidity = presence of ulcer, gastritis, reflux, hiatus hernia, pain or gastric cancer

\* All participants who had a history of PONV also had a history of motion sickness.

**Table 2: Incidence of PONV by R-INVR (N=142)**

Operation	R-INVR Score	Control n	Intervention n	Pearson $\chi^2$ / df	P *
Thyroidectomy	0	30 (81.1%)	29 (82.9%)	0.038 / 1	0.84
	>0	7 (18.9%)	6 (17.1%)		
Laparoscopic cholecystectomy	0	23 (62.2%)	28 (84.8%)	4.54 / 1	0.03
	>0	14 (37.8%)	5 (15.2%)		

R-INVR = Rhodes index of nausea, vomiting and retching (8 items of 0–4 points, total of 0–32 points); df = degrees of freedom

The time between the intervention (ingestion of honey and water mixture) and anaesthesia induction varied from two to five hours, as the daily operation lists were frequently updated; however, the difference in incidence of PONV was not significant (Spearman's correlation -0.085, P=0.49).

Table 2 shows the incidence of PONV in the four groups. There was no significant difference in incidence of PONV in the R-INVR mean score comparison between the thyroidectomy groups (Pearson  $\chi^2$  =0.038; p=0.84; df=1). However, a statistically significant lower severity of PONV was determined in the laparoscopic cholecystectomy intervention group than in the control group (Pearson  $\chi^2$  =4.54; p=0.03; df=1).

Table 3 shows the mean R-INVR and NRS scores for each group. The R-INVR and NRS scores were statistically lower in the laparoscopic cholecystectomy intervention group than in the control group; no statistical significance was calculated between thyroidectomy intervention and control groups (Table 3).

## Discussion

The intervention and control groups in the present study had a similar distribution of characteristics, including the PONV risk factors (gender, age, smoking status and

**Table 3: Mean R-INVR and NRS scores (N=142)**

Score	Operation	Group	n	Mean±SD	Median (min–max)	Mann-Whitney U	P
R-INVR	Thyroidectomy	Control	37	1.8±4.3	0 (0-17)	629.5	0.76
		Intervention	35	1.6±5.4	0 (0-30)		
	Laparoscopic cholecystectomy	Control	37	3.0±5.1	0 (0-23)	446.5	0.01
		Intervention	33	0.5±1.4	0 (0-6)		
NRS	Thyroidectomy	Control	37	1.1±2.5	0 (0-8)	629.5	0.95
		Intervention	35	1.1±2.4	0 (0-10)		
	Laparoscopic cholecystectomy	Control	37	2.0±2.7	0 (0-7)	444.5	0.01
		Intervention	33	0.4±1.4	0 (0-5)		

R-INVR = Rhodes index of nausea, vomiting and retching (8 items of 0–4 points, total of 0–32 points);

NRS = numeric rating scale (0–10)

history of PONV or motion sickness). The time between the intervention (ingestion of honey and water mixture) and anaesthesia induction varied from two to five hours, as the daily operation lists were frequently updated; however, the difference between PONV incidence and mean R-INVR was not significant. The incidence of PONV was significantly lower in the laparoscopic cholecystectomy intervention group; there was no significant difference between the thyroidectomy groups.

In line with the literature,<sup>5,38,46,47</sup> we believe the balanced distribution of factors affecting PONV among the groups strengthens the results of our study. Gastric morbidity can make a patient more prone to PONV<sup>48</sup> and history of gastric morbidity was more frequent in the intervention groups for both surgeries. Therefore, we considered the lower incidence of PONV to be another strength for the validity of the results.

Oral pre-operative carbohydrate solutions have been shown to be effective in reducing PONV in some studies. Yilmaz et al.<sup>34</sup> and Ayoğlu et al.<sup>24</sup> showed in their research that 200 kilocalories of carbohydrate

and 400 ml of fluid administered to participants two hours before laparoscopic cholecystectomy surgery reduced early PONV, Weledji et al.<sup>35</sup> showed positive effects of pre-operative oral carbohydrate intake on metabolic and endocrine surgical stress response and an RCT by Hausel et al.<sup>21</sup> showed that pre-operative carbohydrate solutions could reduce PONV.<sup>16</sup> In contrast, Poyraz<sup>49</sup> examined the effects of pre-operative oral carbohydrate solutions on surgical stress response and did not find any significant difference. A number of systematic reviews and guidelines stated the need for more robust RCTs that include an anaesthesia protocol, antiemetic treatment and rescue treatment.<sup>2,50,51</sup>

We observed a significantly lower occurrence of PONV in the intervention group compared to the control group of laparoscopic cholecystectomy participants. In thyroidectomy participants, significantly more patients received dexamethasone in the control group to prevent vocal cord oedema. The lack of significant differences between

the thyroidectomy groups may be associated with the antiemetic effect of dexamethasone.<sup>52,53</sup> Lauwick et al.<sup>54</sup> also reported no difference in PONV with oral carbohydrate administration with thyroidectomy participants. They indicated that factors such as pharynx and vagal nerve stimulation may have affected their results and that a more detailed examination was necessary to draw conclusions.<sup>54</sup>

Post-operative nausea and vomiting is one of the most common perioperative complications, and pre-operative oral carbohydrate administration is recommended for its prevention. Honey is a natural and available source of carbohydrate. Pre-operative oral honey and water administration can reduce the incidence and severity of PONV.

In-service or postgraduate education programs for perioperative health professionals could include up-to-date recommendations for improved patient care, such as ERAS protocols which involve reducing pre-operative fasting time and providing pre-operative oral carbohydrates.

Anaesthetists, surgeons and perioperative nurses should be informed of the consequences of prolonged fasting practices and recent evidence regarding the safety of pre-operative oral intake. Studies have shown no changes in gastric emptying time between individuals (including patients with obesity or diabetes, unless gastric reflux was present) or any risk of aspiration for fluids ingested up until two hours prior to surgery. These findings from oral carbohydrate loading were equal to overnight fasting.<sup>1,55</sup> The recommendations for all solid and liquid dietary intake have been present for quite some years; however, today's routine surgical practices still do not reflect those recommendations.

Despite the fact that general anaesthesia practices have been trending towards the reduction of volatile anaesthetics to reduce PONV, the issue seems to remain pertinent. Therefore, further studies to modify risk factors and reduce the incidence of PONV are recommended. Considering that the results for thyroidectomy participants in our study were not significant, covariate-adaptive randomisation is recommended in future studies to obtain definitive evidence for this type of surgery and the relation between the use of dexamethasone and PONV.

### Strengths and limitations

The R-INVR and NRS scales used in this study to measure outcomes and to define risk for PONV were previously validated, and the sample size was sufficient. Data was presented regarding the type and total dose of medications that impact emesis, such as anaesthetics, antiemetics, tramadol-HCl and dexamethasone. This will assist with replication of the study and applicability of the results. However,

PONV incidence in total intravenous anaesthesia should be further investigated as our study included combined inhalation and intravenous anaesthesia protocols.

Identified limitations are that the study was conducted in a single centre, and the primary investigator registered the participants and conducted randomised allocation. A potential bias could exist during the study's introduction; however, we prevented this by providing the same information to all participants and blinding the nurses collecting the data to the group allocation. The interrater reliability for the nurses' collection of the data was not analysed and this could present another limitation.

The use of dexamethasone and antiemetic treatment, tramadol hydrochloride, could not be standardised across groups. The total doses of each medication administered were analysed, and no influence on the primary outcomes was determined. The time between intervention (participants ingesting the honey and water mix) and anaesthesia induction also varied between participants, as the operation list of the day was frequently updated. The amount of time from the intervention to anaesthesia induction varied from two hours to five hours, and this was analysed against PONV outcomes using regression analysis; however, the difference appeared not to be statistically significant.

### Conclusion

In this RCT, it was discovered that honey could be recommended as a simple and inexpensive pre-operative oral carbohydrate to prevent or reduce PONV in adult participants receiving general anaesthesia (combined inhalation and intravenous administration)

undergoing laparoscopic cholecystectomy. Honey, which is a common and economical nutrient, is available as an effective intervention for PONV prevention and is an alternative to commercially prepared, processed carbohydrate which is less economical.

### Knowledge translation

- PONV is presently one of the most common perioperative complications. Pre-operative oral carbohydrate administration is recommended for PONV prevention.
- Honey is a natural, economical and readily available source of carbohydrate. Pre-operative oral honey and water administration can reduce the incidence and the severity of PONV in laparoscopic cholecystectomy.

### Conflict of interest and funding statement

The authors have declared no competing interests. No funding was used.

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