Chewing gum prophylaxis for postoperative nausea and vomiting in the intensive care unit: a pilot randomised controlled trial

Hussam Abdelkarim, Natasha Ciampoli, Lara Zwakman-Hessels, Jai N Darvall and Rinaldo Bellomo

ABSTRACT

Objective: To test the effectiveness of chewing gum in the prophylaxis of postoperative nausea and vomiting (PONV) in patients admitted to the intensive care unit (ICU) after surgery.

Design: Prospective, open label, pilot randomised controlled trial.

Setting: Two metropolitan ICUs.

Participants: Ninety postoperative adult patients admitted to the ICU.

Intervention: Patients administered chewing gum, who chewed for at least 15 minutes every 4 hours, were compared with a control group, who were administered a 20 mL sip of water orally every 4 hours.

Main outcome measures: The primary outcome was the number of patient-reported episodes of nausea in the first 24 hours after the operation. Secondary outcomes included vomiting or dry retching episodes, and duration and severity of nausea.

Results: Forty-six patients were randomly allocated to chewing gum and 44 patients to water. There was no difference between groups in the number of patients with nausea (10 [22%] chewing gum *v* 12 [27%] control patients; $P = 0.72$), nausea episodes (22 episodes; [median, 0; IQR, 0–0] *v* 21 episodes [median, 0; IQR, 0–1] per patient in each group respectively), vomiting/retching (2 [4%] chewing gum *v* 6 [14%] control patients; $P = 0.24$), or duration/severity of nausea.

Conclusion: Regular postoperative administration of chewing gum in a surgical ICU patient cohort did not reduce nausea, vomiting or retching. The prevalence of PONV is less than previously reported. Our findings can inform future studies of PONV prophylaxis in post-surgical ICU patients.

Trial registration: Australian New Zealand Clinical Trial Registry No. ACTRN12617001185358.

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Postoperative nausea and vomiting (PONV) is an important cause of distress for patients. Depending on the presence of known risk factors — female sex, non-smoking status, past history of PONV or motion sickness, or anticipated requirement for postoperative opioids (the Apfel criteria) — it can affect up to one-third of patients.[1,2] Patients rank PONV ahead of pain in the list of undesirable outcomes after an operation.[3] Moreover, PONV can lead to complications such as wound dehiscence, aspiration, hypovolaemia, and even oesophageal rupture.[4]

PONV is also common in the intensive care unit (ICU), particularly after cardiac surgery. In a study of 400 cardiac surgical patients, the baseline incidence of nausea was reported at 47% and retching/vomiting at 37%.[5] Both surgical-specific aspects (eg, longer operation duration, greater intraoperative opioid and volatile general anaesthetic agent exposure) as well as components of ICU management (ongoing opioid analgesia and sedation administration, as well as other emetic medications) combine to make ICU patients particularly prone to PONV.[6,7]

Chewing gum stimulates gastrointestinal motility by vagal activation through effects of sham feeding and perhaps a reduction in systemic inflammation,[8,9] with a good safety profile in resolving postoperative intestinal ileus in a number of surgical populations (including after gastrointestinal tract surgery, caesarean delivery and liver transplantation).[10-14] A meta-analysis of 26 randomised controlled trials involving 2214 colorectal surgical patients demonstrated a reduced time to recovery of intestinal function and shortened length of stay with chewing gum compared with standard postoperative care protocols.[15] More recently, chewing gum has been investigated as a novel treatment for PONV, demonstrating non-inferiority compared with ondansetron in a pilot randomised controlled study of 94 female patients undergoing breast and laparoscopic surgery.[16] No studies, however, have addressed its role in prophylaxis for PONV in postoperative patients in the ICU. It is unknown whether the unique factors to the ICU environment, such as the

greater requirement for sedation and analgesia after major surgery, patient drowsiness and challenges relating to gum chewing with ongoing mechanical ventilation, may affect its efficacy in this patient group.

In patients admitted to the ICU after surgery, we therefore performed a pilot randomised controlled trial of the prophylactic effectiveness of chewing gum on PONV compared with a control group administered 20 mL of oral water. We hypothesised that chewing gum would decrease the incidence, duration and severity of PONV in this patient group.

Methods

Study design

This was a prospective, open label, pilot randomised controlled trial conducted in two metropolitan ICUs. Ethics approvals from Austin Health (LNR/17/Austin/205) and Epworth Health (EH2017-288) were obtained. The trial was prospectively registered with the Australian New Zealand Clinical Trial Registry (No. ACTRN12617001185358).

This trial was conducted in compliance with the Consolidated Standards of Reporting Trials (CONSORT) statement.

Eligible patients were those aged 18 years or more; admitted to the ICU within 16 hours after non-oropharyngeal, maxillary or oesophageal surgery; and anticipated to stay in the ICU for more than 12 hours. Patients who remained mechanically ventilated, who were deemed too sedated (based on the judgement of attending clinical staff), or who had partial or full dentures were excluded.

Patients were enrolled after written informed consent was obtained, either before or after the surgery. Patients were randomly allocated to either the intervention chewing gum group (Falim [Kent Gida], lightly mint flavoured, sugarless gum; ingredients: gum base, flavouring, colouring [E171], antioxidants [E321, E320]), which was chewed for at least 15 minutes every 4 hours, or to a control group, who were administered a 20 mL sip of water orally every 4 hours. Randomisation was achieved using a computerised random number generator; allocation concealment was done via sequentially numbered envelopes. Participants were enrolled by the two investigators (HA and NC). All patients were allowed other oral intake as tolerated and permitted by the surgical team. We pre-determined a cardiac surgery subgroup.

All enrolled patients had access to a standardised antiemetic rescue protocol:

- first line — ondansetron 8 mg intravenous;
- second line — droperidol 0.625 mg intravenous;
- third line — metoclopramide 10 mg intravenous;
- fourth line — prochlorperazine 12.5 mg intravenous.

If nausea was rated greater than 5 points on a visual analogue scale from 0 to 10 points,[17] actual vomiting occurred or, at any time, if requested by the patient, rescue antiemetic was administered. After 30 minutes, PONV assessment was made by the attending ICU nurse to determine if further rescue antiemetic was needed. After randomisation, the attending ICU nurse collected data for 24 hours, divided into continuous 4-hour observation periods. Data collected included presence, duration and severity of nausea (measured on a ten-point Likert scale), number of retching/vomiting episodes, and antiemetic medication administered. If nausea was not self-reported, the frequency of querying the patient for nausea within each 4-hour period by the ICU nurse was not standardised. The number of episodes of gum chewing was recorded, with the underlying reason if not able to be chewed (eg, patient refusal or drowsiness). The ICU nurse attending the patient reconciled all gum administered and discarded, with any instances of swallowed or aspirated gum recorded.

The primary outcome was the number of patient-reported nausea episodes in the first 24 hours after the operation, with secondary outcomes including the combination of vomiting or dry retching episodes, duration of nausea episodes, use of rescue antiemetics in the two groups, and the severity of nausea as reported in a visual analogue scale from 0 to 10 every 4 hours.

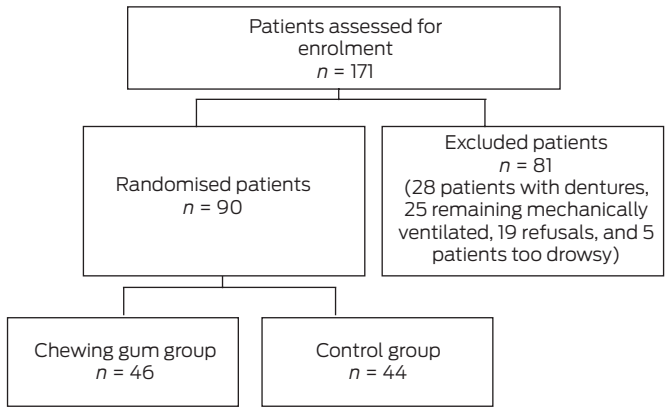
Sample size calculation

We based our power calculation on a pilot study comparing chewing gum with ondansetron, with a full resolution rate of PONV in the chewing gum group of 75% and in the ondansetron group of 39%.[16] We assumed that, in our prophylaxis study, a smaller effect would apply, with a decrease in combined nausea and vomiting/dry retching episode from 75% in the intervention group to 50% in the control group, which, at an 80% power and an $\alpha = 0.05$, would require 90 patients in total.

Statistical analysis

Data are expressed as means with standard deviation (SD), when normally distributed, or median and interquartile range (IQR), when non-parametric. The χ^2 or Fisher exact test was applied to categorical variables (including the primary outcome), with normally distributed continuous variables compared using the Student *t* test, and the Mann– Whitney U test used for non-parametric continuous variables. A $P < 0.05$ indicated statistical significance. All statistical analyses were performed using R, version 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria).

Figure 1. Patient enrolment flow chart



Results

Between October 2017 and January 2019, we screened a total of 171 patients, after exclusions (28 patients with dentures, 25 patients remaining mechanically ventilated, 19 refusals, and five patients too drowsy), 90 patients were enrolled. Forty-six patients were randomised to the chewing gum group and 44 patients to the control group (Figure 1).

The demographic features of enrolled patients are outlined in Table 1. Groups were similar in baseline characteristics, including Apfel PONV risk scores. Thirty-seven patients (41%) were admitted after cardiac surgery, 14 (15%) after bariatric surgery, and 16 (17%) after other gastrointestinal surgery, with the remainder undergoing other procedures.

Gum was chewed on 148 occasions by all patients randomised to the chewing gum group (median, 3 occasions; IQR, 2–4). It was not administered on 93 occasions (38%): 72 occasions because the patient was sleeping, 15 occasions because the patient refused, and six occasions due to patient drowsiness. No gum was swallowed or aspirated.

There was no difference between groups in the number of patients with nausea (10 [22%] chewing gum patients [95% CI, 4–15; 9–34%] *v* 12 [27%] control patients [95% CI, 5–18; 14–41%]; $P = 0.72$) or vomiting (2 [4%] chewing gum *v* 6 [14%] control patients; $P = 0.24$) with a combined incidence of these outcomes of 12 (16%) versus 18 (41%) (Table 2). There was no difference in the number of patient-reported nausea episodes (total 22 nausea episodes per patient in the chewing gum group [median, 0; IQR, 0–0] *v* 21 in the control group [median, 0; IQR, 0–1]; $P = 0.706$). There was also no difference in the degree, duration or severity of nausea; number of episodes of vomiting or retching; or the use of rescue antiemetics (Table 2). Thirty-seven patients were enrolled in the pre-determined cardiac surgical subgroup: 19 in the chewing gum group and 18 in the water group, with no differences in outcomes between groups.

Discussion

Key findings

In this prospective, open label, two-centre randomised controlled trial, we assessed the use of chewing gum for the prevention of postoperative nausea and vomiting in the ICU. We found chewing gum treatment feasible in the ICU, but we also found no difference between chewing gum and water administered orally every 4 hours in the number of patients with, or in the episodes of, nausea, vomiting or retching, nor in the severity or duration or in the use of rescue antiemetics. There was also no difference between the two groups in the subgroup of patients after cardiac surgery.

Relationship to previous studies

One prior randomised controlled pilot trial has demonstrated the non-inferiority of chewing gum compared with ondansetron for the treatment of established PONV in female patients undergoing breast and laparoscopic surgery.[17] A large, multicentre definitive trial is ongoing.[18] To date, chewing gum for the prevention of PONV has not been specifically studied, likely due to concerns about increased gastric residual volume if administered preoperatively.[19,20] These early studies, however, have given way to more recent acceptance of its safety profile when fasting, with major guidelines (including the Association of Anaesthetists of Great Britain and Ireland and the European Society of Anesthesiology) no longer prohibiting chewing gum before surgery.[21,22] Nevertheless, to our knowledge, no studies have explored the role of chewing gum as a prophylactic strategy for PONV prevention before surgery. Our study adds to the existing knowledge base by assessing chewing gum therapy in a prophylactic role after surgery; the major finding of no difference compared with orally administered water suggests that chewing gum may be more effective in a treatment role, perhaps related to mooted effects of increased gastric motility and vagal activity.[8,11] A further major finding of our study was the low incidence of PONV after cardiac surgery, with nausea and vomiting rates of 28% and 7% respectively. This rate is significantly less than the 47% and 36% reported in a 1996 study of 400 cardiac surgical patients[5] and is likely related to differences in modern cardiac anaesthetic techniques.

Implications of the study findings

Although feasible to deliver, chewing gum administered every 4 hours is likely not to be effective as a prophylactic

Table 1. Patient characteristics

	Chewing gum	Water
Total number of patients	46	44
Age (years), median (IQR)	65.0 (56.25–71.00)	63.0 (51.7–7.00)
Sex, male	26 (57%)	28 (64%)
BMI (kg/m^2), median (IQR)	29.4 (24.2–37.4)	27.6 (26.1–33.3)
ASA physical status, mean (SD)		
2	3 ± 6.5	5 ± 11.6
3	22 ± 47.8	16 ± 37.2
4	21 ± 45.7	21 ± 48.8
5	0 ± 0.0	1 ± 2.3
Smoking, mean (SD)		
Never	23 ± 50.0	24 ± 54.5
Ex-smoker	21 ± 45.7	17 ± 38.6
Current smoker	2 ± 4.3	3 ± 6.8
APACHE III score, median (IQR)	34.0 (28.5–44.0)	36.0 (29.0–44.7)
Post-operative nausea and vomiting, mean (SD)	2 ± 4.3	2 ± 4.5
Opioids		
Preoperative	11 (24%)	5 (11%)
Intraoperative	46 (100%)	44 (100%)
Postoperative	45 (98%)	36 (82%)
Apfel score		
1	2	5
2	25	28
3	18	9
4	1	2
Total intravenous anaesthesia	4 (9%)	4 (9%)
Volatile-based inhalation anaesthesia	42 (91%)	40 (91%)
Regular ondansetron use*	1 (2%)	3 (7%)
Regular metoclopramide use*	1 (2%)	1 (2%)
Type of surgery		
Cardiac	19 (41%)	18 (41%)
Bariatric	8 (17%)	6 (14%)
Other gastrointestinal	8 (17%)	8 (18%)
Other	12 (26%)	11 (25%)

APACHE = Acute Physiology and Chronic Health Evaluation; ASA = American Society of Anesthesiologists; BMI = body mass index; IQR = interquartile range; SD = standard deviation. * Prescribed prophylactically after the operation for postoperative nausea and vomiting by treating anaesthetist.

measure for PONV after an operation. Despite not demonstrating a difference attributable to chewing gum, our study provides a reasonable estimate of the incidence of PONV in a modern postoperative cohort in the ICU (24% of patients with nausea, 9% with vomiting). This prevalence rate can serve as a guide for future studies in PONV in the ICU.

Study strengths and limitations

The strengths of our study include the setting in two major metropolitan ICUs, with a broad spectrum of surgical patients. Inclusion of a pre-specified subgroup of cardiac surgical patients is also instructive, as this population represents a large proportion of surgical admissions to ICUs in our region. Our study had a number of limitations. No blinding was used in this study; although a methodological challenge in chewing gum trials, such blinding may be possible to achieve. Future studies of chewing gum in the ICU may improve on our study design by blinding data collectors and also standardising the questioning of patients for the presence of nausea. Furthermore, we did not use a validated measure of the patient alertness to assess readiness for chewing gum, instead relying on bedside nursing staff guidance. It is possible that our high rates of patient ability to chew gum may overestimate readiness to chew gum as assessed with an objective sedation score, although the pragmatic criterion chosen here mirrors real-world practice. Moreover, there were no instances of gum swallowed or aspirated in our cohort. In addition, we did not control for the potential confounding influence of concurrently administered regular antiemetic medications after an operation. The low rate of overall administration, however, combined with more patients in the control group prescribed regular metoclopramide or ondansetron (2 [4%] chewing gum patients *v* 4 [9%] water patients) is unlikely to have influenced our results. Finally, the dosing schedule chosen for our study (administration every 4 hours) may not represent an adequate dose for the antiemetic prophylactic effects of chewing gum to be

Table 2. Patient outcomes

	Chewing gum	Water	*P*
Total number of patients	46	44	
Study observation duration (h), median (IQR)	20 (16–24)	22 (16–24)	0.447
Time to enrolment (min), median (IQR)	345 (180–533)	348 (191–555)	0.594
Number of patient-reported nausea episodes, median (IQR)	0 (0–0)	0 (0–1)	0.706
Patients with nausea	10 (22%)	12 (27%)	0.715
Cardiac subgroup	5/19 (26%)	6/18 (33%)	0.836
Patients with vomiting/retching	2 (4%)	6 (14%)	0.239
Cardiac subgroup	1/19 (5%)	2/18 (11%)	0.924
Vomiting/retching episodes, median (IQR)	0 (0–0)	0 (0–1)	0.164
Total duration of nausea (min),* median (IQR)	35 (25–45)	40 (15–120)	0.620
Rescue antiemetic doses	12 (26%)	15 (34%)	0.550
Worst nausea score			0.421
0	37 (82%)	32 (73%)	
2	1 (2%)	2 (5%)	
3	2 (4%)	0 (0%)	
5	3 (7%)	3 (7%)	
6	1 (2%)	3 (7%)	
7	1 (2%)	2 (5%)	
10	0 (0%)	2 (5%)	
ICU LOS (days), median (IQR)	1.0 (1.0–2.0)	2.0 (1.0–2.3)	0.057
Hospital LOS (days), median (IQR)	8.0 (4.0–11.0)	9.0 (6.3–12.0)	0.602

ICU = intensive care unit; IQR = interquartile range; LOS = length of stay. * Duration of nausea for the ten chewing gum and 12 water group patients experiencing nausea.

realised. However, it was chosen to be logistically feasible and acceptable to both patients and nursing staff. Future research may investigate the impact of more frequent dosing on a similar cohort of patients.

Conclusion

Regular postoperative administration of chewing gum in a surgical ICU patient cohort did not confer any benefit in the prevention of PONV. Moreover, the prevalence of PONV is less than previously reported. Our findings can inform future studies of PONV prophylaxis in postoperative ICU patients.

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Competing interests

None declared.

Author details

Hussam Abdelkarim[1]
Natasha Ciampoli[2]
Lara Zwakman-Hessels[3,6]
Jai N Darvall[4,5]
Rinaldo Bellomo[4,5,6]

1 Department of Intensive Care, Ballarat Health Service, Ballarat, VIC, Australia.
2 Department of Intensive Care, Epworth Eastern, Melbourne, VIC, Australia.
3 Department of Critical Care, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.
4 Department of Intensive Care, Royal Melbourne Hospital, Melbourne, VIC, Australia.
5 Centre for Integrated Critical Care, School of Medicine, University of Melbourne, Melbourne, VIC, Australia.
6 Department of Intensive Care, Austin Hospital, Melbourne, VIC, Australia.

Correspondence: hussam.abdelkarim@bhs.org.au

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