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Clinical Practice

Chewing gum for the treatment of postoperative nausea and vomiting: a pilot randomized controlled trial

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Abstract

Background. A novel treatment, chewing gum, may be non-inferior to ondansetron in inhibiting postoperative nausea and vomiting (PONV) in female patients after laparoscopic or breast surgery. In this pilot study, we tested the feasibility of a large randomized controlled trial.

Methods. We randomized 94 female patients undergoing laparoscopic or breast surgery to ondansetron 4 mg i.v. or chewing gum if PONV was experienced in the postanaesthesia care unit (PACU). The primary outcome was full resolution of PONV, with non-inferiority defined as a difference between groups of <15% in a per protocol analysis. Secondary outcomes were PACU stay duration, anti-emetic rescue use, and acceptability of anti-emetic treatment. The feasibility of implementing the protocol in a larger trial was assessed.

Results. Postoperative nausea and vomiting in the PACU occurred in 13 (28%) ondansetron patients and 15 (31%) chewing gum patients ($P=0.75$). Three chewing gum patients could not chew gum when they developed PONV. On a per protocol basis, full resolution of PONV occurred in five of 13 (39%) ondansetron *vs* nine of 12 (75%) chewing gum patients [risk difference 37% (6.3–67%), $P=0.07$]. There was no difference in secondary outcomes between groups. Recruitment was satisfactory, the protocol was acceptable to anaesthetists and nurses, and data collection was complete.

Conclusions. In this pilot trial, chewing gum was not inferior to ondansetron for treatment of PONV after general anaesthesia for laparoscopic or breast surgery in female patients. Our findings demonstrate the feasibility of a larger, multicentred randomized controlled trial to investigate this novel therapy.

Clinical trial registration. Australian New Zealand Clinical Trials Registry: ACTRN12615001327572.

Key words: chewing gum; ondansetron; postanaesthesia nursing; postoperative nausea and vomiting

Postoperative nausea and vomiting (PONV) affects one-third of untreated patients after general anaesthesia.[1 2] It is a leading cause of admission after planned ambulatory surgery and may lead to dehydration, bleeding, surgical wound complications, and

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Editor's key points

- Chewing gum may be as effective as ondansetron in inhibiting postoperative nausea and vomiting (PONV).
- Either ondansetron 4 mg or chewing gum was randomly provided to female patients who had PONV after laparoscopic or breast surgery, to test the feasibility of a large randomized controlled trial.
- A large randomized controlled trial would be feasible, because recruitment was satisfactory, the protocol was acceptable to anaesthetists and nurses, and data collection was complete.

aspiration of gastric contents.[3 4] Well-established guidelines for the pharmacological prophylaxis and treatment of PONV exist; however, medications such as the 5-hydroxytryptamine type 3 (5-HT) receptor antagonists are only partly effective and have side-effects.[5] More recently, interest has emerged in non-pharmacological therapies, such as P6 stimulation with acupuncture modalities[6] and ginger,[7] which have advantages including low cost, favourable side-effect profile, and patient acceptability.

Chewing gum has been prospectively evaluated as a therapy to reduce postoperative paralytic ileus after gastrointestinal surgery. Postulated mechanisms of its effect surround the principle of 'sham feeding', with chewing resulting in increased gastrointestinal activity via cephalic vagal stimulation.[8] Recent meta-analyses (the largest involving 272 patients across seven randomized controlled trials) have demonstrated a reduced time to first flatus and bowel motion, and a non-significant trend towards earlier hospital discharge.[9–11] To date, however, no study has examined the effect of gum chewing on PONV.

We previously conducted a prospective cohort study to assess the safety and acceptability of chewing gum in the postanaesthesia care unit (PACU), enrolling 41 patients undergoing ambulatory gynaecological laparoscopy.[12] Thirty-one patients (76%) were awake enough to chew gum. Chewing gum was acceptable to patients and PACU nurses, with no identified safety concerns. Chewing gum has also been linked to lowered cortisol concentrations, improved stress and anxiety, and more positive mood in the research setting.[13 14]

We therefore conducted a pilot randomized controlled non-inferiority trial to test the hypothesis that chewing gum in the PACU would prove to be non-inferior to ondansetron for the treatment of PONV in female patients after laparoscopic or breast surgery and to test the feasibility of a large multicentre randomized controlled trial using this protocol. The primary outcome was full resolution of PONV after either ondansetron or chewing gum. Secondary outcomes were the duration of PACU stay, anti-emetic rescue use in the PACU, and patient acceptability of anti-emetic treatment. Feasibility outcomes were recruitment rate, protocol compliance, incidence of PONV, ability to chew gum, and the primary outcome.

Methods

This pilot randomized controlled non-inferiority trial was conducted in the Department of Anaesthesia and Pain Management, Royal Melbourne Hospital. Approval was gained from the hospital Human Research and Ethics Committee (21 December 2015, HREC number 2015.230), and the trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12615001327572; 3 December 2015).

Female patients aged ≥18 yr and of ASA physical status I–III undergoing laparoscopic or breast surgery were enrolled between January and June 2016, after being advised that the principal purpose of the study was to assess the feasibility of a larger randomized controlled trial and after written informed consent had been obtained. Patients were excluded if they had inadequate English comprehension, significant cardiorespiratory impairment, impaired pharyngeal or oesophageal function, phenylketonuria (contraindication to the sweetener aspartame in chewing gum), a full upper or lower denture (not feasible to chew gum), or a contraindication to any of the protocolized anti-emetic drugs. Patients were randomized to either chewing gum or ondansetron after written informed consent had been obtained and before surgery. The randomization schedule was created via a computerized random number generator, with sequentially numbered envelopes used for allocation concealment until PONV developed in the PACU. Patients, anaesthetists, PACU nurses, and observers therefore were blind to group allocation until PONV developed in the PACU.

Procedure

Induction of general anaesthesia was accomplished with either fentanyl or alfentanil, propofol, and a non-depolarizing neuromuscular blocker if indicated. Midazolam premedication was permitted at the discretion of the attending anaesthetist. Anaesthesia was maintained with sevoflurane without nitrous oxide. Patient monitoring was established in accordance with the standards published by the Australian and New Zealand College of Anaesthetists. At the conclusion of anaesthesia, antagonism of neuromuscular block was accomplished with neostigmine and glycopyrrolate, or if the train of four count was zero with sugammadex 200 mg. Non-opioid analgesics and additional fentanyl or morphine were given at the discretion of the attending anaesthetist.

Anti-emetic prophylaxis

Intraoperative anti-emetic prophylaxis was protocolized according to simplified Apfel risk factors, commensurate with the Consensus Guidelines for the Management of Postoperative Nausea and Vomiting published by the Society for Ambulatory Anesthesia.[5] Risk factors were female gender, non-smoking status, past history of PONV or motion sickness, or anticipated requirement for postoperative opioids (defined as estimated requirement of at least 20 mg oral oxycodone equivalent in the first 24 h after surgery, consistent with the initial validation trials of the Apfel scoring system).[15] Patients with one risk factor ('low risk') received no prophylaxis; patients with two or three risk factors ('medium risk') received dexamethasone 4 mg i.v.; and patients with four risk factors ('high risk') received dexamethasone 4 mg i.v. and droperidol 0.625 mg.

Treatment of postoperative nausea and vomiting

Patients randomized to chewing gum and experiencing PONV in the PACU, with an Observer's Assessment of Alertness/Sedation (OAA/S) rating scale of 5[16] ('responding readily to name spoken in normal tone') and with the PACU nurse satisfied that the patient was not sleeping between observations, commenced gum chewing (Wrigley's Extra Sugarfree Gum®, peppermint flavour), aiming for a period of 15 min. Patients randomized to ondansetron, or those randomized to chewing gum who either refused it or were too drowsy, received ondansetron 4 mg i.v. in the event of PONV. The feasibility of chewing gum was recorded (able; unable because of refusal; unable because of drowsiness). Rescue