Chewing Gum for Prevention of Nausea and Vomiting After Elective Caesarean Section: a Pilot Randomised Controlled Trial

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Abstract
Nausea and vomiting are common complications in patients undergoing caesarean delivery under regional anaesthesia. When experienced after surgery, they may delay recovery, reduce patient satisfaction and affect the bonding between mother and baby. Various pharmacological and non-pharmacological approaches for prophylaxis and treatment of postoperative nausea and vomiting (PONV) have been employed with different degree of efficacy. In this pilot randomised controlled trial, we aimed to determine the possible preventative effects of chewing gum on the rate of PONV in expectant mothers undergoing neuraxial anaesthesia for elective lower segment caesarean section. All participants underwent spinal anaesthesia with administration of 10–11.5 mg of intrathecal heavy Bupivacaine 0.5% according to anaesthetists’ preference, Morphine 100 μg and Fentanyl 25 μg. Postoperative analgesia regimen was also standardised. Two hundred ninety-six patients were randomised to an intervention arm to receive chewing gum in addition to standard therapy and to a non-intervention arm to receive standard therapy. After exclusions, 258 patients were followed up 24 h postoperatively. Standard therapy is defined as Ondansetron 4 mg IV intra-operatively. The primary outcomes were the incidences of nausea and vomiting in the first 24 h postoperatively. Secondary outcomes were the number of episodes of nausea or vomiting in the recovery room and on the ward 24 h postoperatively, use of anti-emetics postoperatively, severity of nausea and patient satisfaction with the intervention. Our study revealed no significant differences in rates of postoperative nausea and vomiting between the intervention and standard therapy groups (41.4% v 36.9% p = 0.461). There were no significant differences in secondary outcomes between groups. Chewing gum does not reduce the incidence of PONV after elective LSCS under spinal anaesthesia. Our trial was registered with clinicaltrials.org (NCT04191694).

Keywords Chewing · Gum · Caesarean · LSCS · PONV · Nausea · Vomiting · Spinal · Morphine

Introduction
Postoperative nausea and vomiting (PONV) is a common complication following lower segment caesarean section (LSCS). PONV reduces patient satisfaction and is outranked only by intra- and postoperative pain as a side effect to be avoided by obstetric patients [1]. It prolongs recovery by delaying eating, drinking and mobilisation and prolongs hospital discharge [2]. It can also interrupt maternal bonding with the newborn. Patients undergoing caesarean delivery have a number of procedure-specific risk factors that increase the incidence of PONV in this cohort. Neuraxial anaesthesia is generally considered the standard of care in most countries [3]. However, neuraxial anaesthesia with the use of intrathecal opioids is an established risk factors for PONV [4]. Others are related to the caesarean section itself including being female, blood loss, vagal stimulation,
uterine exteriorisation and uterotonics. The incidence of PONV in patients undergoing caesarean delivery under regional anaesthesia varies between 23 and 79% [5]. With caesarean section representing 7.3% of surgeries worldwide and current rates of caesarean delivery exceeding 28% in most OECD countries, PONV poses a significant burden to patients, staff and resources [6, 7].

Comprehensive guidelines and systematic reviews exist for the risk stratification, prophylaxis and treatment of PONV [8]. Risk assessment tools, such as the Apfel score, are widely used in practice despite recent evidence that it is unhelpful in this population [9, 10]. However, prophylactic measures to date are only partially effective. Thus, the incidence and impact of PONV remain high despite our best efforts. The body of evidence for the role of non-pharmacological measures such as acupuncture and carbohydrate drinks remains limited.

Chewing gum has previously being shown to improve recovery of gastrointestinal function after abdominal surgery, with a shorter time to flatus, reduced postoperative ileus and early feeding [11]. In one pilot trial, chewing gum was not inferior to Ondansetron for treatment of PONV after general anaesthesia for laparoscopic and breast surgery in female patients [12]. However, we are uncertain of its role in the prophylaxis and prevention of PONV.

In this pilot randomised controlled trial, we investigated whether the addition of regular chewing gum in addition to standard anti-emetic prophylaxis reduced the incidence of PONV after caesarean delivery. We hypothesised that chewing gum’s effects on gastrointestinal function outlined above may reduce the incidence of PONV.

Methods

This pilot randomised controlled trial was performed at the Coombe Women and Infants University Hospital, Dublin, Ireland, which is a university-affiliated, tertiary referral centre.

Our study received ethical approval from the Research Ethics Committee (Study no 17–2019), Coombe Women and Infant’s University Hospital, Dublin, Ireland (Chairman Professor Jan Miletin) on 25th November 2019. Our trial was registered with clinicaltrials.org (NCT04191694). The study was an investigator-led, single-centre, randomised, unblind double-arm comparator study. It took place between 10th December 2019 and 30th June 2020 with temporary suspension (28th March 2020–20th of April 2020) due to COVID-19 restrictions.

The primary outcome measures were the difference in the incidence of self-reported nausea and/or vomiting in the 24-h post-elective caesarean section under spinal anaesthesia.

Secondary outcome measures included:

- Number of episodes of self-reported nausea, vomiting or both in recovery room and at 24 h after caesarean section;
- Severity of nausea, based on the worst episode in the last 24 h reported as a number between 0 and 10, 0 being none, 10 being most severe;
- Anti-emetic use in the first 24 h following surgery, as recorded in the medical notes;
- Patient satisfaction with the intervention on a scale of 0–10, 0 being not satisfied, 10 being extremely satisfied.

Inclusion criteria:

- Undergoing elective caesarean section under spinal anaesthesia
- Minimum age 18 years
- Able and agreeable to chew chewing gum in recovery room and in the first 24 h
- Received Ondansetron 4 mg i.v intra-operatively

Exclusion criteria:

- Type 1 diabetes mellitus
- Nausea and/or vomiting on arrival to recovery room
- Received supplementary anti-emetic medication to the standard therapy intra-operatively
- Post-partum haemorrhage > 1000 ml
- Ergometrine or Misoprostol intra-operatively
- Intravenous opioid intra-operatively

The incidence of nausea and vomiting after caesarean section in our institution, recorded at daily pain rounds as part of data collection for audit and quality improvement, is 28%. A sample size calculation, using G*Power 3.1.9.2. [13], showed that 129 patients in each group would give 80% power to detect a 50% reduction in nausea and vomiting ($a=0.05$, power 80%). Allowing for a 10% dropout rate, we aimed to recruit 142 participants in each group.

The trial was discussed with potential participants by anaesthetists, and they were provided with a patient information leaflet, in the pre-assessment clinic. Consent was sought and obtained by the investigator at admission, prior to arrival in the operating theatre and after all questions or concerns were addressed. All patients were informed of the objectives of the study as well as benefits, risks, obligations and option to withdraw consent at any time.

At the onset of the trial, an internet-based randomisation tool (www.sealedenvelope.com) generated random codes into two groups—intervention and standard therapy. The codes were then written on sealed opaque envelopes, containing the corresponding randomly assigned group. After consent and before arriving in theatre, an envelope was given...
to each participant by the investigator and opened in front of them, and the investigator informed them which group they were assigned to.

All participants underwent spinal anaesthesia with administration of 10–11.5 mg of intrathecal heavy Bupivacaine 0.5% according to anaesthetists’ preference. Morphine 100 μg and Fentanyl 25 μg. The level of sensory block was checked with Ethyl Chloride spray to ensure satisfactory surgical conditions. No patients in our trial required repeat spinal anaesthetic.

Intra-operative hypotension, recorded on the electronic anaesthetic records, was treated as per hospital/international standards—Ephedrine boluses or Phenylephrine as a bolus or infusion was used with a target systolic blood pressure above 100 mmHg. If further anti-emetic medication was administered to treat intra-operative nausea and vomiting, patients were excluded from the trial as outlined above. Patients adhered to ESAIC standard pre-operative fasting guidelines. Resumption of oral intake was permitted 6 h postoperatively if the patient so wished.

The intervention arm received standard intra-operative anti-emetic therapy of Ondansetron 4 mg i.v.—timing of administration was not standardised. On arrival to the recovery room, investigators informed midwives which arm of the trial the participant had been assigned. A pack of 10 pieces of sugar-free, mint-flavoured chewing gum (Wrigley’s Extra Sugarfree, peppermint) was given to the participants by the midwives. They were asked to chew at their leisure over the subsequent 24 h. The interval and duration of chewing were not protocolised and every patient chewed the gum at their own discretion. Preset chewing time was considered but did not become part of the protocol so as to allow for maximal simulation of real-life conditions. As much as chewing gum is an intervention, it is also a familiar product and patients would have had established patterns of chewing before enrolment.

The standard therapy arm received Ondansetron 4 mg i.v intra-operatively which is routine protocol in our institution.

Both arms of the trial were charted anti-emetic medication postoperatively and this was not to be with-held if it was required, regardless of which arm the participant was in.

No patients received additional regional anaesthesia such as quadratus lumborum block or TAP (Transversus Abdominis Plain) block. Patients were prescribed postoperative analgesia according to the standard protocol in our institution—Paracetamol 1 g QDS IV/PO, Diclofenac 75 mg BD PO or Ibuprofen 400 mg TDS PO and Oxycodone IR 5–10 mg 4–6 hourly PO provided there were no contraindications.

Patients were followed up twice, initially at discharge from recovery room and at 24 h after their procedure in the post-natal wards. Data related to primary and secondary outcomes were collected from investigator during patient reviews and from review of the medical notes. The intervention arm was also asked how long they chewed chewing gum for in the first 24 h and times were recorded. We conducted interviews postoperatively to assess the self-reported incidence of nausea and vomiting as this is common in studies related to PONV [14–16].

Statistical analysis was performed using SPSS v24 (IBM Corp, Armonk, NY, USA). The Shapiro–Wilk test was used to test for normality of distribution. Comparisons between groups were performed using Pearson’s chi-squared test. Continuous data were compared using independent t-test or Mann–Whitney U test as appropriate. Differences were considered significant for p values < 0.05.

Results

We asked 297 patients who met the inclusion criteria to participate in the study. One patient refused. From the recruited 296 patients, 38 were excluded or lost to follow-up. Twenty-six patients were excluded after giving consent—one patient was not assigned to a group, 12 patients had > 1000 ml post-partum haemorrhage, four patients were excluded after receiving Dexamethasone intra-operatively and five patients received Ergometrine intra-operatively, one patient received Misoprostol intra-operatively, one patient underwent induction of labour for vaginal delivery and two patients returned to theatre for general anaesthetic. Three patients in the chewing gum group did not chew the chewing gum. The data sheets for nine patients could not be located.

Two hundred and fifty-eight patients were followed up after 24 h. One hundred and twenty-eight patients received chewing gum postoperatively and 130 patients received standard therapy (Fig. 1).

There were no significant differences in age, BMI or pre-operatives fasting times between the two arms of the study (Table 1).

Chewing times in the chewing gum group are outlined in Table 2.

Fifty-three (41.4%) patients in the chewing gum group experienced PONV in the 24-h postoperatively. Forty-eight (36.9%) patients in the standard therapy arm experienced PONV in the 24-h postoperatively (p = 0.461).

Secondary outcomes are outlined in Table 3.

The mean score of severity of nausea on a scale of 1–10 among both groups are similar with a mean score of 6.20 (SD 2.12) in the standard therapy group and 5.7 (SD 4.95) in the chewing gum group.

Participants reported a high degree of satisfaction with the intervention with a mean satisfaction score of 7.29 (SD 2.30) on a scale of 1–10. Thirteen patients in the chewing gum arm reported satisfaction scores below five out of 10.

Participants reported a high degree of satisfaction with the intervention with a mean satisfaction score of 7.29 (SD 2.30) on a scale of 1–10. Thirteen patients in the chewing gum arm reported satisfaction scores below five out of 10.
There were no complications or deleterious effects attributable to chewing gum in our trial.

**Discussion**

Chewing gum has been postulated as a non-pharmacological treatment for PONV in laparoscopic and breast surgery in female patients [13]. It may therefore have a role in other surgical settings such as the prevention of PONV. It is relatively cheap and patients are familiar with its use. The high percentage (99.66%) of patients who, when offered, consented to take part in our study suggests patients are well receptive of this intervention.

Patients who took part in the chewing gum arm reported a high degree of satisfaction with the intervention due to its effects on promoting saliva secretion and freshening breath after a period of fasting.

While other studies have shown non-inferiority of chewing gum compared to Ondansetron 4 mg in treatment of PONV after laparoscopic and breast surgery [13], in our study, we reasoned that expectant mothers undergoing LSCS
under spinal anaesthesia should receive Ondansetron 4 mg i.v as standard as not receiving a standard anti-emetic intra-operatively as part of their care would be unconscionable for investigators and unpalatable for many expectant mothers at such an important event in their lives, particularly given the relative paucity of evidence of an anti-emetic effect of chewing.

Our study found no significant difference in rates of PONV 24-h post-LSCS between patients receiving standard care in our facility and patients receiving supplementary chewing gum postoperatively. These results suggest that recovery of gastric function associated with chewing gum postoperatively [12] may not be a significant contributor to reducing the incidence of PONV or perhaps that other factors play a bigger role in PONV in the population we studied.

The incidence of PONV in this trial was found to be higher than the recorded incidence in our institution. This may be due to recall bias of patients participating in a trial specifically assessing the incidence of PONV. It may also be due to various anaesthetists’ preference for administering Dexamethasone intra-operatively in conjunction with Ondansetron, which may contribute to the lower institutional incidence.

Our results contrast with the results presented by Darvall et al. in their trial where chewing gum was shown to be non-inferior to Ondansetron in the treatment of PONV after laparoscopic and breast surgery. While that trial was

### Table 1 Patient characteristics

|                         | Chewing gum group | Standard therapy group |
|-------------------------|-------------------|------------------------|
| Age (years)             | 35.27 (4.941)     | 34.75 (5.015)          |
|                         | n=128             | n=130                  |
| BMI (kg.m²)             | 27.57 (5.230)     | 27.61 (5.580)          |
|                         | n=122             | n=119                  |
| LSCS duration (minutes) | 44.29 (14.520)    | 45.69 (18.168)         |
|                         | n=125             | n=128                  |
| Time fasted pre-operatively food (hours) | 13.22 (3.497) | 12.76 (3.742) |
|                         | n=126             | n=127                  |
| Time fasted pre-operatively fluids (hours) | 5.27 (3.316) | 5.45 (3.441) |
|                         | n=125             | n=127                  |
| QoR11                   | 83.43 (13.826)    | 80.69 (18.139)         |
|                         | n=114             | n=123                  |
| Oxycodone in 24 h (mg)  | 8.76 (7.072)      | 9.86 (7.838)           |
|                         | n=127             | n=128                  |

Characteristics of patients receiving either standard therapy and chewing gum or standard therapy. Values, unless otherwise stated, are mean (standard deviation) number, standard error of the mean (σx̄).

### Table 2 Chewing time

| Hours | Frequency |
|-------|-----------|
| < 1   | 29 (22.6%)|
| 1–3   | 72 (56.3%)|
| 3–5   | 19 (14.8%)|
| > 5   | 6 (4.7%)  |
| Not recorded | 2 (1.6%) |

Chewing time in chewing gum group. Values are number (proportion).

### Table 3 Secondary outcomes

|                        | Chewing gum group (n = 128) | Standard therapy group (n = 130) | p value |
|------------------------|-----------------------------|----------------------------------|---------|
| Anti-emetic in recovery| 11 (8.6%)                   | 9 (6.9%)                         | 0.616   |
| Nausea in recovery     | 18 (14%)                    | 17 (13%)                         | 0.817   |
| Vomiting in recovery   | 9 (7%)                      | 7 (7.07%)                        | 0.583   |
| Anti-emetic in ward    | 22 (17.2%)                  | 19 (14.6%)                       | 0.572   |
| Nausea in ward         | 48 (37.5%)                  | 43 (33%)                         | 0.457   |
| Vomiting in ward       | 34 (26.6%)                  | 27 (20.8%)                       | 0.274   |
| Vomiting intra-op      | 11 (8.6%)                   | 5 (3.8%)                         | 0.117   |
| Vomiting 24 h          | 35 (27.3%)                  | 30 (23%)                         | 0.430   |
| Nausea intra-op        | 45 (35.2%)                  | 39 (30%)                         | 0.369   |
| Nausea 24 h            | 51 (39.8%)                  | 48 (36.9%)                       | 0.630   |

Values are number (proportion)
a non-inferiority study and tested treatment rather than prophylaxis, it did demonstrate that chewing may have an anti-emetic effect. Our trial failed to show chewing gum having an additional or synergistic anti-emetic effect when used in conjunction with Ondansetron for prophylaxis of PONV. This is perhaps due to chewing gum having no supplementary anti-emetic effect or perhaps neuraxial anaesthesia with spinal morphine playing a significant role in the incidence of PONV compared to general anaesthetic. Patients undergoing lower limb surgery under spinal anaesthesia combined with intrathecal Morphine had a similar incidence of PONV to that in our study [17]. Trials assessing the non-inferiority of chewing gum compared to Ondansetron in treatment of PONV after LSCS may shed more light on this subject.

The patient population may also have influenced the outcome of this trial. Pregnant women often experience nausea and vomiting throughout their pregnancy [18] and this perhaps impacts the incidence of PONV in this population. Trials assessing the impact of chewing gum on the incidence of PONV after lower limb surgery under spinal anaesthesia may be of benefit in this regard in order to determine if there is a role for chewing gum in other populations undergoing similar anaesthetic techniques.

There were no significant differences in secondary outcomes with postoperative anti-emetic use similar between groups. The severity of nausea was also similar between groups.

The strengths of our trial include the high recruitment rate with 99.6% of patients agreeing to take part. The simplicity of the protocol, coupled with the familiarity with this low-cost, self-applicable intervention, may have contributed to the high participation rate. There was near complete follow-up of participants.

There are several limitations to our study. We did not quantify blood loss if it was less than 1000 ml and the volume of intravenous fluid administered was not recorded as part of follow-up. Intra-operative and postoperative blood pressure values were also not recorded as part of follow-up. Intra-operative circulatory management is thought to be a mainstay of the prevention of postoperative nausea and vomiting [19]. No data were collected on uterine exteriorisation. Our study also did not record the administration of medications intra-operatively other than those which were included in the exclusion criteria. There was no standard chewing time and interval between chewing. It is thus unclear whether the results would have been different if patients were asked to chew the ten pieces of chewing gum for a set, protocolised period of time.

A significant limitation of our study was the lack of blinding. This would of course prove impossible for the participants, as there is no possibility of blinding chewing gum as an intervention. Investigators were not blinded as owing to a small anaesthetic department this would have complicated follow-up and may have impacted on the ability to deliver timely service. With the onset of the COVID-19 pandemic, this would have also meant increased exposure to different personnel where this was undesirable given the circumstances. Furthermore, multi-centre studies may allow for the possibility of blinding of some elements of the protocol and follow-up.

A further limitation to this study is the sample size calculation. Based on the LSCS rate in our institution and aiming to complete this pilot study within reasonable time frame, we planned to demonstrate a 50% reduction in PONV. A larger follow-up study aiming for PONV reduction at 10%, and corresponding larger sample size, might be considered.

Conclusion

The results from our study indicate that chewing gum does not significantly reduce the rate of PONV in the 24 h following LSCS under spinal anaesthetic. Further studies are warranted on non-pharmacological agents, alone or in combinations, that may be of benefit in reducing the incidence of PONV after LSCS as the burden remains relatively high.

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Author Contribution Ross Bowe contributed to formulating the trial protocol, acquiring data and writing the manuscript. Petar Popivanov contributed to formulating the trial protocol, acquiring data and made a substantial contribution to writing/revision of the manuscript as well as data interpretation. Ruairí Irwin I contributed to protocol formulation, data analysis/interpretation and revision of the manuscript. Terry Tan made substantial contributions to protocol formulation, data analysis and interpretation as well as revisions of the manuscript. Gerard Browne conducted data acquisition and contributed to protocol formulation. Meghan Harbison conducted data acquisition in the recovery room and post-natal wards and contributed to protocol formulation. Shauna Gallen conducted data acquisition in the recovery room and post-natal wards. Patrick Yore conducted data acquisition in the recovery room and post-natal wards. Eanna MacGearailt conducted data acquisition in the recovery room and post-natal wards. Gerard Browne conducted data acquisition in the recovery room and post-natal wards. Eanna MacGearailt conducted data acquisition in the recovery room and post-natal wards. Eanna MacGearailt conducted data acquisition in the recovery room and post-natal wards.

All authors have approved the submitted version.

All authors have agreed both to be personally accountable for the author’s own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated and resolved and the resolution documented in the literature.

Data Availability The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Code Availability Statistical analysis was performed using SPSS v24 (IBM Corp. Armonk, NY, USA). Available at https://www.ibm.com/spss as a subscription service.
Declarations

Ethics Approval Our study received ethical approval from the Research Ethics Committee (Study no 17–2019), Coombe Women and Infant’s University Hospital, Dublin, Ireland (Chairman Professor Jan Miletin) on 25th November 2019. Our trial was registered with clinicaltrials.org (NCT04191694). The study was an investigator-led, single-centre, randomised, unblind double-arm comparator study. It took place between 10th December 2019 and 30th June 2020 with temporary suspension (28th March 2020–20th of April 2020) due to COVID-19 restrictions.

Consent to Participate Consent was sought and obtained by the investigator at admission, prior to arrival in the operating theatre and after all questions or concerns were addressed. All patients were informed of the objectives of the study as well as benefits, risks, obligations and option to withdraw consent at any time.

Consent for Publication Not applicable.

Conflict of Interest The authors declare no competing interests.

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