

CLINICAL INVESTIGATION

Fentanyl-induced cough is a risk factor for postoperative nausea and vomiting

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Abstract

Background: Postoperative nausea and vomiting (PONV) and fentanyl-induced cough (FIC) are two common anaesthesia-related events, which seem to have common risk factors. In this prospective cohort study, we investigate whether patients who have FIC during induction of anaesthesia have an increased incidence of PONV.

Methods: We studied adult non-smoking gynaecological surgical patients enrolled between July 1, 2011 and July 30, 2012. The presence of FIC during induction and the occurrence of PONV were recorded. Fentanyl-induced cough and other perioperative variables were subjected to multivariate analysis to determine the association between FIC and PONV.

Results: All 502 patients enrolled in this study had at least two risk factors for PONV, and 154 (31%) developed FIC. The incidence of PONV in the FIC group was higher than in the non-FIC group (56.5 vs 38.2%; $P < 0.0001$). Multivariate logistic regression analysis found FIC to be a predictive risk factor for the development of PONV (adjusted odds ratio 2.08, 95% confidence interval 1.41–3.07).

Conclusions: Non-smoking women undergoing gynaecological surgery who develop FIC during induction of anaesthesia have a higher incidence of PONV.

Key words: analgesics opioid, fentanyl; cough; postoperative nausea and vomiting

Postoperative nausea and vomiting (PONV), defined as nausea, vomiting, or both within 24 h after operation, is a long-standing concern for anaesthetists.¹ The incidence after general anaesthesia with an inhalational agent, opioid, and no antiemetic prophylaxis is ~10% in the recovery room² and 30% during the first 24 h,^{3,4}

this increases up to 70–80% in high-risk populations.³ Postoperative nausea and vomiting not only limits patient mobility,⁵ delays discharge from the postanesthesia care unit (PACU), and increases care cost,^{6,7} but was also ranked as the most common postoperative complaint in a recent report.⁸ Several predictive

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Editor's key points

- More accurate prediction of which patients are most likely to experience postoperative nausea and vomiting (PONV) would be helpful.
- Fentanyl-induced cough immediately before induction of anaesthesia occurs in about 30% of patients.
- Fentanyl-induced cough may be attributable to histamine release, a pathway shared by PONV.
- Antihistamines might decrease the risk of PONV in patients with fentanyl-induced cough.

models have been developed to stratify the risk for PONV. However, a simplified scoring system by Apfel and colleagues^{9,10} compares favourably against other scoring systems. The Apfel score included four predictive risk factors for PONV (female gender, history of motion sickness or PONV, non-smoking status, and use of postoperative opioids) and if none, one, two, three, or four risk factors were present, the incidences of PONV were 10, 21, 39, 61 and 79%, respectively.³

Fentanyl is one of the most commonly administered parenteral opioid analgesics for balanced anaesthesia. Fentanyl-induced cough (FIC), first reported more than two decades ago, has an incidence between 18 and 65%.^{11,12} The range of incidence is attributable to differences in the dose and speed of fentanyl injection and the presence or absence of effective pretreatment. Fentanyl-induced cough is usually transient and self-limiting in most patients. Several severe complications have been reported.^{13,14}

In our experience, FIC is more common in young female non-smokers, which is also the high-risk population for PONV. This suggests that FIC and PONV may share some common mechanisms. Therefore, we designed this prospective cohort study to assess whether FIC is a risk factor for PONV.

Methods

The National Taiwan University Hospital Committee Review Board approved the study protocol. As the study did not require a deviation from standard clinical care, the ethics committee waived the requirement for written consent from the patients. The study was performed in female patients undergoing elective, inpatient, non-malignant uterine or ovarian surgery via laparotomy from July 1, 2011 to July 30, 2012. Inclusion criteria were age between 18 and 60 yr and ASA physical status classification I and II. Patients with pre-existing lung or cardiac disease, impaired kidney or liver function, obesity (body mass index $>30 \text{ kg m}^{-2}$), pregnancy, history of bronchial asthma or chronic obstructive pulmonary disease, history of smoking, respiratory, or gastrointestinal tract infection in the previous 2 weeks, preoperative use of an angiotensin-converting enzyme inhibitor, an antiemetic, a bronchodilator, or a steroid, a history of PONV or motion sickness, and postoperative intensive care unit admission were excluded from the study.

Estimation of sample size was based on a 60% incidence of PONV in our patient group, assuming that patients without FIC would have a 30% relative reduction rate in the incidence of PONV. With $\alpha=0.05$ and $\beta=0.20$, a minimum of 131 patients in each group was required. We assumed a 30% incidence of FIC.^{12,15}

All patients fasted overnight and received no premedication. Before being taken to the operating room, venous access was established using a 22-gauge cannula on the dorsum of the hand, connected to a T-connector. On arrival in the operating room,

continuous ECG lead II, non-invasive arterial pressure and pulse oximetry monitoring were instituted. A fentanyl bolus ($2 \mu\text{g kg}^{-1}$) was then injected via the T-connector over 5 s. An anaesthetist recorded the occurrence of cough up to 1 min after the bolus. General anaesthesia was induced with propofol $2\text{--}2.5 \text{ mg kg}^{-1}$ after cough cessation or 1 min after fentanyl injection. Cisatracurium, 0.2 mg kg^{-1} , was used to facilitate tracheal intubation. Maintenance of anaesthesia consisted of desflurane or sevoflurane in an air-oxygen mixture. Intermittent bolus doses of $50 \mu\text{g}$ fentanyl were administered as needed for intraoperative analgesia. The total dose of intraoperative fentanyl used varied between 150 and 250 μg . Upon completion of the procedure, residual muscle relaxant effect was antagonized with neostigmine 2.5 mg and atropine 1 mg , and the volatile anaesthetic was discontinued. The tracheal tube was removed upon resumption of spontaneous ventilation, and the patient was then transferred to the PACU.

All postoperative assessments were made by observers blinded to whether the patient experienced FIC. The incidence of patient complaints of nausea or vomiting was recorded by a trained nurse in the PACU. The need for postoperative opioid and antiemetics was assessed by the on-duty anaesthetist in the PACU and the consulting anaesthetist on the ward. No prophylactic antiemetics were administered. All patients who received a postoperative antiemetic were given prochlorperazine 5 mg i.m. The National Health Insurance of Taiwan does not pay for postoperative i.v. patient-controlled analgesia; therefore, most patients received ketorolac 30 mg i.v. at the first complaint of postoperative pain and i.v. morphine boluses for subsequent pain complaints. Some patients chose to pay for morphine i.v. patient-controlled analgesia and received this form of postoperative analgesia.

Another group of trained nurse anaesthetists assessed the incidence and severity of PONV 24 h after surgery. The severity of nausea and vomiting was recorded as a score of 0, 1, or 2 (0=no nausea or vomiting, 1=tolerable nausea or vomiting, and 2=intractable nausea or vomiting requiring prochlorperazine 5 mg i.m.). Patients who experienced any degree of nausea or vomiting within the first 24 h after surgery were classified as having PONV.

Statistical analysis

In this analysis, patient-related variables were age, BMI, ASA class, FIC and postoperative use of opioid. The anaesthesia-related variable was the duration of anaesthesia. Patient data were analysed with Student's unpaired t-test for continuous variables and the χ^2 test for categorical variables.

The joint contribution of these factors on the incidence of PONV was evaluated by logistic regression. Given that the postoperative use of opioid is the only established modifiable risk factor, we further analysed patients who did and did not receive postoperative morphine separately using the above-mentioned statistics. As all study patients were female non-smokers, those who did and did not receive postoperative morphine corresponded to an Apfel score 3 and 2, respectively. All statistical tests were two sided, and $P<0.05$ were considered statistically significant. Analyses were performed with SAS version 9.1 (SAS Institute, Cary, NC, USA) and Stata version 9.1 (StataCorp LP, College Station, TX, USA).

Results

Of 502 patients enrolled in the study, 154 (31%) had FIC. There were no significant differences between those with and without FIC in terms of patient characteristics or anaesthetic duration

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