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Original Article

Omitting fentanyl reduces nausea and vomiting, without increasing pain, after sevoflurane for day surgery*

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Summary

Background and objective: Despite advantages of induction and maintenance of anaesthesia with sevoflurane, postoperative nausea and vomiting occurs frequently. Fentanyl is a commonly used supplement that may contribute to this, although it may also improve analgesia. *Methods:* This double-blind study examined the incidence and severity of postoperative nausea and vomiting and pain in the first 24 h after sevoflurane anaesthesia in 216 adult day surgery patients. Patients were randomly allocated to either receive or not receive 1 $\mu g\,kg^{-1}$ fentanyl, while a third group received dexamethasone in addition to fentanyl. *Results:* Omission of fentanyl did not reduce the overall incidence of postoperative nausea and vomiting, but did reduce the incidence of vomiting and/or moderate to severe nausea prior to discharge from 20% and 17% with fentanyl and fentanyl-dexamethasone, respectively, to 5% ($P = 0.013$). Antiemetic requirements were reduced from 24% and 31% to 7% ($P = 0.0012$). Dexamethasone had no significant effect on the incidence or severity of postoperative nausea and vomiting. Combining the two fentanyl groups revealed further significant benefits from the avoidance of opioids, reducing postoperative nausea and vomiting and nausea prior to discharge from 35% and 33% to 22% and 19% ($P = 0.049$ and $P = 0.035$), respectively, while nausea in the first 24 h was decreased from 42% to 27% ($P = 0.034$). Pain severity and analgesic requirements were unaffected by the omission of fentanyl. Fentanyl did reduce minor intraoperative movement but had no sevoflurane-sparing effect and increased respiratory depression, hypotension and bradycardia. *Conclusion:* As fentanyl exacerbated postoperative nausea and vomiting without an improvement in postoperative pain and also had adverse cardiorespiratory effects, it appears to be an unnecessary and possibly detrimental supplement to sevoflurane in day surgery.

Keywords: SURGERY AMBULATORY; POSTOPERATIVE NAUSEA AND VOMITING; SEVOFLURANE; ANAESTHESIA INHALATIONAL; FENTANYL; PAIN ACUTE AND POSTOPERATIVE.

Introduction

Volatile induction and maintenance of anaesthesia (VIMA) with sevoflurane confers several benefits to day case patients [1]. These include smooth transition from induction to maintenance, minimal apnoea following induction, minimal hypotension and rapid emergence [2–6]. One potentially important drawback with the technique is postoperative nausea and vomiting (PONV), which appears to occur to an unacceptable degree [1,7].

In most cases, these high rates of PONV were an incidental finding in randomized studies primarily comparing VIMA with alternative anaesthetic techniques. The protocols invariably included the

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administration of opioid analgesia (usually fentanyl) at, or prior to, induction of anaesthesia [5,6,8–11]. Opioid analgesics are a recognized cause of PONV [12–14]. They are usually required in association with intravenous (i.v.) anaesthesia, since propofol is a relatively pure hypnotic with no demonstrable analgesic properties [15], but their adverse effects are probably offset by the antiemetic effect of propofol [16]. In contrast, inhaled anaesthetic agents, such as sevoflurane, are able to modify responses to noxious stimuli to a greater degree than propofol [17,18] and, in combination with nitrous oxide (N_2O), it may be unnecessary to deliver intraoperative opioids, provided adequate measures are taken to prevent postoperative pain. One retrospective clinical audit suggested that omission of opioid analgesia from a VIMA technique resulted in a substantially lower incidence of PONV [19]. There did not appear to be any clinically noticeable detriment to this omission, although intraoperative anaesthetic requirements and postoperative pain were not examined in detail and the audit included patients having procedures (such as cystoscopy) where postoperative pain would not be expected. Rates of PONV following discharge from the day surgery unit were also not investigated [19].

We therefore designed this prospective, randomized, double-blind trial to examine whether omitting opioid analgesia could reduce PONV associated with VIMA without adversely affecting intraoperative conditions or increasing postoperative pain. In anticipation that omission of fentanyl might have both advantages and adverse consequences, our secondary objective was to see whether the addition of a prophylactic antiemetic might be protective against PONV when fentanyl is used with VIMA. For this purpose, we chose to use dexamethasone, since it appears to be effective, long lasting and is not particularly expensive [20].

Methods

Adult patients (aged over 16) undergoing elective, non-endoscopic day case surgery were invited to participate in this protocol approved by the local ethics committee. Patients were initially sent written information about the proposed trial and informed consent was confirmed on the morning of surgery and recorded in writing. Patients with known or suspected adverse reaction to sevoflurane or any of the other study medications, as well as any patients in whom tracheal intubation and/or controlled ventilation were required, were excluded. The patient's potential for PONV was assessed according to Apfel's simplified risk score [14], by recording patient gender, smoking status, previous history of PONV and history of motion sickness. Perioperative opioid use was excluded as a risk factor, as this was fundamental to the study design. Patients were then randomly allocated to receive VIMA supplemented by fentanyl (Group 1), or supplemented by fentanyl and dexamethasone (Group 2) or without i.v. supplement (Group 3). To ensure the even distribution of other causes of PONV, randomization was performed in two strata according to whether patients had either zero or one risk factor or two or more risk factors.

All patients received prophylactic analgesia with our standard regimen of slow-release ibuprofen, 1600 mg, given by mouth about an hour before surgery. No other sedative or anxiolytic premedication was administered. Following the attachment of routine monitors, anaesthesia was induced in the operating theatre by inhalation of sevoflurane. We used a tidal breathing technique in which 8% sevoflurane was inhaled from the outset [2] in a total fresh gas flow comprising $2\,L\,min^{-1}$ of oxygen and $4\,L\,min^{-1}$ of N_2O, delivered from a circle absorber system. Ventilation was gently assisted following the loss of consciousness and a laryngeal mask airway (LMA) was inserted following the achievement of adequate jaw relaxation. At this time, patients also received two i.v. supplements determined by the randomization sequence. These study medications were prepared in two syringes by an anaesthetist not involved with the clinical care of the patient using the sealed opaque envelope technique and were identified only by study number. The first syringe contained 2 mL (100 μg) of fentanyl in Groups 1 and 2 and 2 mL of saline in Group 3, while the second syringe contained 1 mL of dexamethasone (4 mg) in Group 2 and 1 mL of saline in the other groups. Patients received $0.02\,mL\,kg^{-1}$ from the first syringe (equivalent to a fentanyl dose of $1\,\mu g\,kg^{-1}$, limited to a maximum of 100 μg) and the whole contents of the second syringe. The injection from the first syringe was given in small increments over a period of about 3 min in an attempt to minimize any possible respiratory effects of fentanyl and therefore compromise the blinding of the anaesthetist.

Immediately after LMA insertion, the fresh gas flow was reduced to $0.3\,L\,min^{-1}$ of oxygen and $0.4\,L\,min^{-1}$ of N_2O and the sevoflurane vapourizer was turned off until the end-tidal sevoflurane concentration (ET_{sevo}) had decreased towards 1.3–1.5% and/or the patient demonstrated signs of inadequate anaesthesia. Anaesthesia was subsequently titrated according to standard clinical signs (heart rate, blood pressure, respiratory rate and somatic response) and guided by ET_{sevo}. All anaesthetics were delivered by the senior author (IS) who was unaware of the group allocation. Minor adjustments to the level of anaesthesia were made by adjusting the vapourizer setting

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without altering the fresh gas flow. For any episodes of patient movement or other signs of inadequate anaesthesia, the ET_{sevo} concentration was rapidly increased using the 'inhaled bolus' technique [21], whereby the vapourizer setting was increased to 8% and the fresh gas flow increased to $6\,L\,min^{-1}$ for a period of up to 1 min, after which low fresh gas flow and lower vapourizer settings were restored. Patients who failed to respond to this manoeuvre, or in whom inadequate anaesthesia occurred despite an already high ET_{sevo} concentration (e.g., >1.5 MAC (minimum alveolar concentration)), received an i.v. bolus of alfentanil, 0.25 mg. Episodes of hypotension or bradycardia that were persistent and judged by the anaesthetist to be severe were treated with ephedrine and atropine, respectively.

Heart rate (HR), systolic, diastolic and mean arterial pressure (MAP) and haemoglobin oxygen saturation (S_PO_2) were recorded before induction of anaesthesia, every minute during the first 5 min of the induction phase and after skin incision and at 5 min intervals at other times. Respiratory rate and end-tidal carbon dioxide ($ETCO_2$) and sevoflurane concentrations were recorded following LMA insertion at the same time points. The exact time of all changes to vapourizer setting and/or fresh gas flow was accurately recorded to allow total sevoflurane concentration to be calculated as has been described previously [5,22].

Ventilation was manually assisted during any periods of apnoea to prevent serious hypoxia and to obtain end-tidal data, but patients breathed spontaneously at all other times. In the longer and more invasive surgical procedures, patients received 1 L of i.v. saline intraoperatively, but fluids were not given during more minor procedures. At the end of surgery, wounds were infiltrated, by the surgeon, with 10–20 mL of 0.5% *levo*bupivacaine, depending upon the wound size. Anaesthesia (sevoflurane and N_2O) was discontinued at the last suture, the breathing circuit was flushed using the high-flow oxygen button and the fresh gas flow was set to $10\,L\,min^{-1}$ of oxygen. The times from discontinuation of anaesthesia until patients expelled the LMA or had it removed by the recovery nurse, and until they could open their eyes to command were recorded by the lead author. Once the patient was communicative, they were also asked whether they had any pain or sickness. These symptoms were graded as none, mild, moderate or severe. The occurrence of any vomiting was also recorded.

Subsequent patient management was standardized according to the usual practices of the recovery room and the day unit. Patients were assessed by a dedicated research nurse (who was unaware of intraoperative events or group allocation) at 1 and 2 h after the end of surgery and at discharge from the day unit. At each of these times, the nurse recorded the incidence and worst severity of pain, nausea and emesis since the last evaluation using the same criteria as before. Any medication given for pain or nausea (administered for moderate–severe symptoms, or at patient request) was also recorded, as was the time of discharge. Patients were discharged with our standard take-home medication comprising slow-release ibuprofen and co-codamol.

The following day, the research nurse telephoned the patient to assess the incidence and worst severity of pain, nausea and emesis since discharge and whether any analgesia or antiemetics had been taken. Patients were also asked to record their satisfaction with the control of pain, the control of sickness and their overall day surgery experience on 11-point (0–10) verbal rating scales.

We calculated that a sample size of 72 patients per group would have 80% power to detect a clinically significant decrease in PONV from 30%, a typical value derived from previous studies [5,6], to 10%, assuming that two between-group comparisons would be made. Combining the two groups that received fentanyl further increased the power to 91%. Data were entered into a custom-designed database (FileMaker Pro 6; FileMaker Inc, USA), with all perioperative data entered in real time. Subsequent data analysis was performed using StatView (version 4.02 for Macintosh, Abacus Concepts) using analysis of variance or non-paired *t*-tests for continuous data, *U*-tests for respiratory parameters that may not have always have been distributed normally and χ^2 or Fisher's exact test for categorical data, as appropriate. In all cases, a P value of <0.05 was taken as significant. Values are presented as the median and interquartile range or mean ± SD in the text and mean ± SEM in figures.

Results

There were no differences in the patient characteristics and risk factors for PONV of the three treatment groups (Table 1). The incidence of PONV prior to discharge from the day unit (Table 2) was not significantly different between the three groups ($P = 0.55$); however, the proportion of patients experiencing either vomiting or nausea of moderate to severe intensity was significantly lower in Group 3 compared to either of the two groups receiving fentanyl ($P = 0.02$; Table 2). Similarly, the requirement for antiemetic therapy was considerably increased by the use of fentanyl ($P = 0.001$), irrespective of the addition of prophylactic dexamethasone. Prophylactic dexamethasone had no significant effect on either the incidence of severity of PONV at any time point;

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Table 1. Patient characteristics in the three study groups and in the combination of the two groups that received fentanyl.

	Group 1 (fentanyl) $n = 71$	Group 2 (fentanyl-dexamethasone) $n = 72$	Groups 1 and 2 combined $n = 143$	Group 3 (no supplement) $n = 73$
Age (yr)	44.5 ± 16.2	42.3 ± 13.5	43.4 ± 14.9	43.0 ± 15.5
Weight (kg)	78.9 ± 16.3	80.5 ± 16.4	79.7 ± 16.3	79.9 ± 16.2
ASA (I/II)	37/34	41/31	78/65	38/35
Received i.v. fluids	39	45	84	42
Surgical procedure				
Breast surgery	24	14	38	19
Hernia repair	17	19	36	20
Open urology	14	19	33	11
Circumcision	10	13	23	14
Other	6	7	13	9
Anaesthesia time (min)	40.5 ± 17.6	39.7 ± 17.4	40.1 ± 17.4	39.2 ± 17.3
Risk factors for PONV				
Female gender	23	21	44	26
Non-smoker	55	50	105	54
Previous PONV	11	13	24	17
Motion sickness	15	16	31	13
0 or 1 risk factors	42	43	85	44
2 or more risk factors	29	29	58	29

Values are mean ± SD or number of occurrences.
PONV: postoperative nausea and vomiting.

Table 2. Incidence, severity and requirement for treatment of postoperative nausea and vomiting in the three study groups and in the combination of the two groups that received fentanyl up to discharge from the day unit and during the entire first 24 h following surgery and patients' verbal rating of their satisfaction with the control of sickness assessed at 24 h.

	Group 1 (fentanyl) $n = 71$	Group 2 (fentanyl-dexamethasone) $n = 72$	Groups 1 and 2 combined $n = 143$	Group 3 (no supplement) $n = 73$
PONV before discharge	21	29	50*	16
Nausea	21	26	47*	14
Vomiting	10	9	19	4
Moderate–severe nausea or vomiting	14*	12*	26*	4
Required antiemetics	17†	22†	39†	5
PONV within 24 h	31	32	63	23
Nausea	31	29	60*	20
Vomiting	14	10	24	11
Moderate–severe nausea or vomiting	20	13	33	12
Satisfaction with control of PONV	10 (9–10)	10 (9–10)	10 (9–10)	10 (10–10)
Satisfaction <8 out of 10	12	12	24	6

Values are number of occurrences or median (IQR).
PONV: postoperative nausea and vomiting; *$P < 0.05$, †$P < 0.01$, from Group 3.

hence, the two fentanyl groups were combined to increase the power of the study. When this was done, the incidence of PONV and nausea prior to discharge and nausea during the entire first 24 h were all shown to be significantly reduced by the omission of fentanyl (Table 2). There were no other differences in the incidence or severity of PONV after hospital discharge between any of the groups.

PONV was successfully managed in all groups prior to discharge from the day unit and no patient required admission for persistent symptoms. A small number of patients in each group experienced PONV for the first time after hospital discharge (Table 2), but no patient required antiemetic therapy at home or readmission to hospital. The majority of patients were very satisfied with the control of their PONV and the median satisfaction scores did not differ between the groups ($P = 0.58$). Low satisfaction scores (7 out of 10 or less) appeared to be more common in the fentanyl groups, but this did not achieve statistical significance even when the groups were combined ($P = 0.085$).

Only two patients, both in the fentanyl-dexamethasone group, awoke in severe pain. In contrast,

Table 3. Incidence, severity and requirement for treatment of postoperative pain in the three study groups up to discharge from the day unit and during the entire first 24 h following surgery and patients' verbal rating of their satisfaction with the control of pain and their overall day surgery experience assessed at 24 h.

	Group 1 (fentanyl) $n = 71$	Group 2 (fentanyl-dexamethasone) $n = 72$	Group 3 (no supplement) $n = 73$
Worst pain up to discharge			
None	28	27	32
Mild	31	26	29
Moderate	12	16	9
Severe	0	3	3
Analgesia before discharge			
None	45	39	42
Simple oral	3	6	8
Compound oral	22	25	22
Systemic opioid	1	2	1
Worst pain in first 24 h			
None	18	16	18
Mild	35	28	32
Moderate	15	23	17
Severe	3	5	6
Satisfaction with control of pain	10 (9–10)	10 (8–10)	10 (8–10)
Overall satisfaction	10 (10–10)	10 (9–10)	10 (9–10)

Values are number of occurrences or median (IQR).

89%, 78% and 90% in Groups 1, 2 and 3, respectively, were initially pain free, the remaining patients reporting only minor pain. Up to the point of discharge from the day unit, there were no differences between the three groups in the incidence or severity of pain, nor in the requirement for postoperative analgesia (Table 3). Although pain severity increased slightly in all groups after discharge from the day unit, pain remained manageable with the supplied oral analgesia. Patients were highly satisfied with the control of their pain and with their overall day case experience. Two patients, one each from Groups 1 and 3, were admitted overnight for observation of a wound haematoma; both were discharged early the following day with no further treatment. A third patient, in Group 2, underwent inguinal hernia repair combined with orchidectomy and vasectomy and was admitted overnight for observation and because of drowsiness following postoperative morphine analgesia. He was also discharged uneventfully the following morning. None of these three admissions was related to the anaesthetic technique, to the study drugs or to PONV, and these patients were not excluded from data analysis.

The addition of dexamethasone to fentanyl made no significant difference to intraoperative conditions or haemodynamic parameters (data not shown). Therefore, to simplify analysis and interpretation of intraoperative data, the two groups that received fentanyl (Groups 1 and 2) were combined into a single 'fentanyl' group for comparison with the unsupplemented or 'pure VIMA' group (Group 3). During induction of anaesthesia, there was a modest decrease in MAP and increase in HR in both groups. After administration of the study drugs and by the time of skin incision, MAP and HR had both decreased further in the fentanyl group and were significantly lower compared to the pure VIMA group (Fig. 1). Both MAP and HR steadily increased following skin incision and by 20 min were similar to values in the pure VIMA group, which had remained closer to baseline values (Fig. 1). MAP and HR did not differ between the groups for the remainder of the procedure. Clinically significant hypotension, defined as a MAP less than 60% of the baseline value, was significantly more common in the fentanyl group, occurring in 36 (25%) patients compared with 9 (12%) in the pure VIMA group ($P = 0.0279$). Only three patients, all in the fentanyl group, required treatment with ephedrine, however. Clinically significant bradycardia, defined as an HR $\leqslant 40$ beats per minute, was also significantly more common in the fentanyl group, occurring in 16 (11%) patients compared with 2 (3%) in the pure VIMA group ($P = 0.0336$). Atropine was required in just four patients, all in the fentanyl group. No patient in either group required treatment for either tachycardia or hypertension.

Apnoea occurred following induction of anaesthesia and injection of the i.v. supplements in exactly half of the fentanyl group compared to just one patient in the pure VIMA group ($P < 0.001$). The median duration of apnoea in the fentanyl

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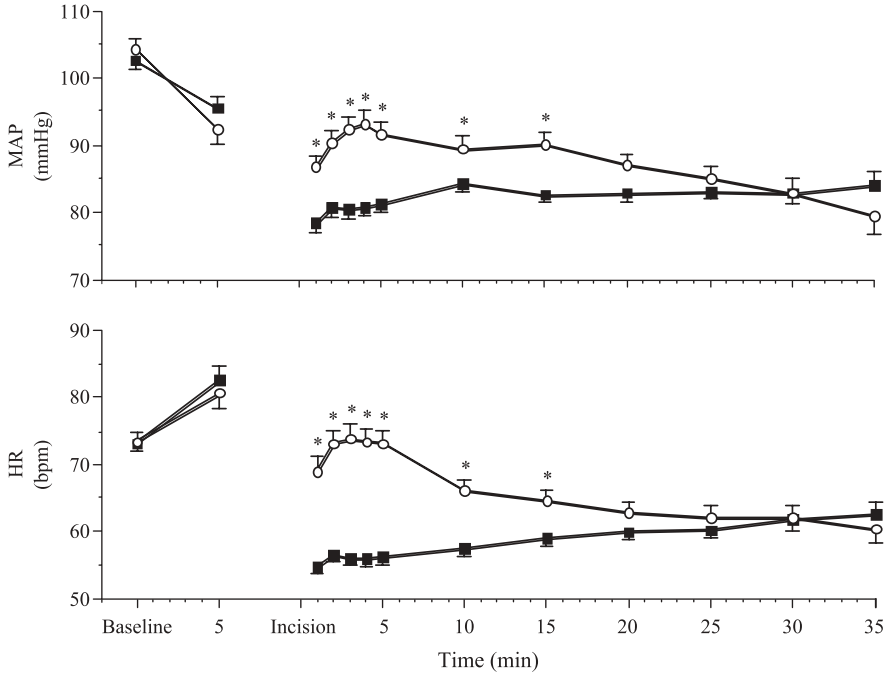

Figure 1.
Mean arterial pressure (MAP; upper panel) and heart rate (HR; lower panel) immediately before induction of anaesthesia (baseline), at skin incision (incision) and at the indicated number of minutes after induction or incision in the fentanyl (Groups 1 and 2 combined) group (solid squares) and Group 3 (open circles). Values are mean ± SEM; $^{*}P < 0.05$*, from the fentanyl group.*

group was 5 min (range 1–20) and the apnoea in the single pure VIMA patient lasted approximately 5 min. By the time of skin incision, mean respiratory rate in the fentanyl group was 9 ± 9 breaths per minute (bpm), which was significantly lower than the rate of 25 ± 7 bpm in the pure VIMA group ($P < 0.001$). Mean respiratory rate increased only transiently in the next few minutes following incision in the pure VIMA group and remained relatively constant for the remainder of the procedure (Fig. 2), whereas respiratory rate increased progressively in the fentanyl group. In parallel with ventilatory changes, S_PO_2 was significantly lower in the fentanyl group for the first 20 min after incision and $ETCO_2$ was significantly higher for the first 30 min after incision compared to the pure VIMA group (Fig. 2). Although statistically significant, these differences of approximately 1% were not considered clinically significant. However, decrease in S_PO_2 to below 92% occurred in 27 (19%) patients in the fentanyl group compared to 4 (5.5%) in the pure VIMA group ($P = 0.008$).

Intraoperative conditions were acceptable in the majority of patients in both groups; however, significantly more episodes of minor movement occurred in the pure VIMA group ($P < 0.001$). Seventeen episodes of movement occurred in 14 (19%) patients in the pure VIMA group (three patients moved twice), compared to five episodes in 4 (3%) patients (one patient moved twice) in the fentanyl group. Movements occurred within a few minutes of skin incision or an increase in intensity of surgical stimulus. Most episodes were treated by an increase in vapour concentration, but five patients, all in the pure VIMA group, required a bolus of alfentanil. Surgery was delayed for approximately 10 s by movement in one patient in the fentanyl group and in five patients (median 30 s, range 10–45) in the pure VIMA group. Surgery was not delayed in the other patients who moved and no patient had recall of postoperative events. Surgery was also delayed, for about a minute in each case, by one episode of laryngospasm in the fentanyl group and one episode of coughing in the pure VIMA group. A further two episodes of mild laryngospasm or stridor in the fentanyl group and one of coughing in the pure VIMA group did not cause any interruption to surgery.

Average values of ET_{sevo} were similar between the groups at most time points. There was no difference in the calculated consumption of sevoflurane during the maintenance phase, which was 2.2 ± 1.6 mL in the pure VIMA group and 2.0 ± 1.6 mL in the fentanyl group, or in the total sevoflurane consumption, which was 10.8 ± 2.3 and 10.9 ± 2.6 mL, respectively. Patients in the pure VIMA group rejected the LMA significantly earlier than those in the fentanyl group (3.3 ± 1.9 vs. 4.1 ± 1.6 min; $P = 0.003$), but neither the time of eye opening to command (4.6 ± 2.0 and 4.7 ± 1.7 min, respectively) nor the overall length of

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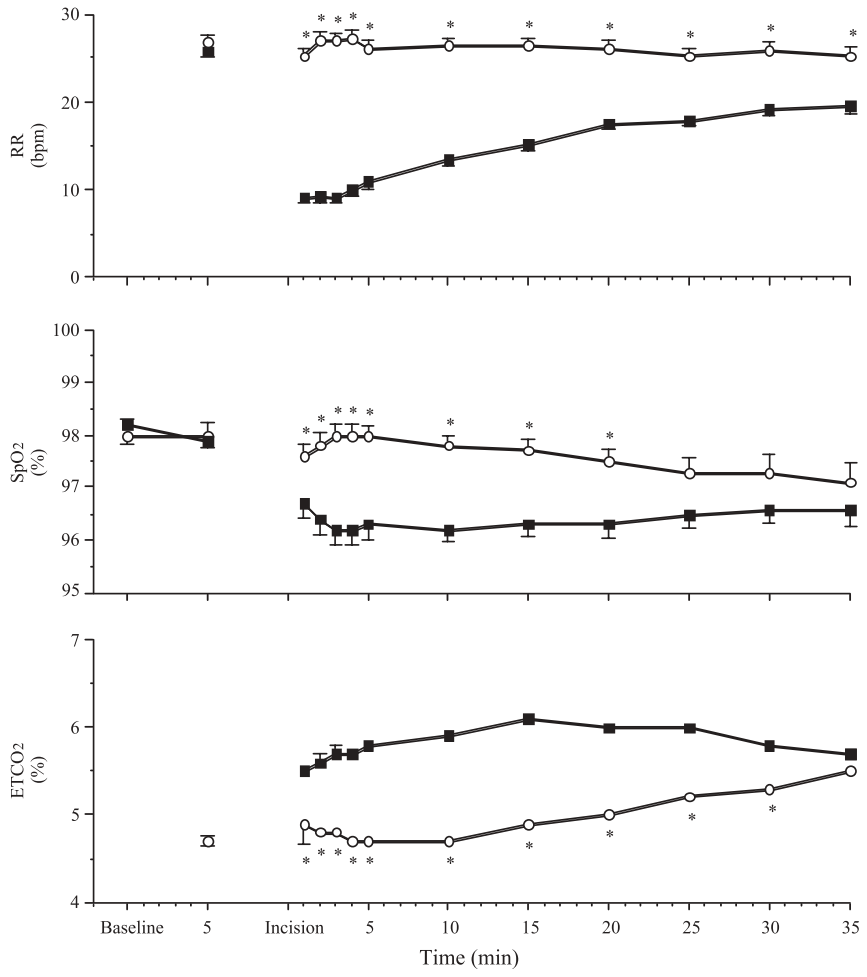

Figure 2.
Respiratory rate (RR; upper panel), haemoglobin oxygen saturation from pulse oximeter (S_PO_2; middle panel) and end-tidal carbon dioxide concentration ($_{ET}CO_2$; lower panel) immediately before induction of anaesthesia (baseline), at skin incision (incision) and at the indicated number of minutes after induction or incision in the fentanyl (Groups 1 and 2 combined) group (solid squares) and Group 3 (open circles). Values are mean ± SEM; $^*P < 0.05$, *from the fentanyl group (by the* U*-test).*

stay (3.5 ± 1.3 and 3.6 ± 1.1 h, respectively) differed between the two groups.

Discussion

The omission of fentanyl from a sevoflurane VIMA technique significantly reduced the severity and requirement for treatment of PONV before discharge from the day unit without any increase in postoperative pain or analgesic requirements. When the use of prophylactic dexamethasone was discounted, omission of opioids was also shown to significantly reduce the overall incidence of PONV within the day unit and the incidence of nausea within the first 24 h. The only obvious detriment was a small increase in intraoperative movement, although this did not result in any clinically significant delays or recall of intraoperative events. Patient movement is relatively common in spontaneously breathing patients and has been reported in 30–60% of patients receiving i.v. anaesthesia [6,23,24], an incidence far higher than that observed in the current study. Movement is usually seen as an early warning of inadequate anaesthesia and ceases, as it generally did in this study, with an increase in anaesthetic concentration. In the very small number of cases where movement could not be easily controlled by an increase in sevoflurane concentration, it responded rapidly to a small bolus of alfentanil. We chose alfentanil due to its rapid onset of action and brief duration of effect, both of which appeared well-suited to the context in which it was used. Of the five patients who required an alfentanil bolus, only one experienced mild nausea within the day unit, while another patient experienced an episode of vomiting after discharge. Since this

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intervention did not appear to cause a significant increase in PONV, we analysed our results on an intention to treat basis. However, the numbers were too small to confirm that the selective use of alfentanil was entirely benign. Even the ultra-short-acting opioid remifentanil increases the incidence of PONV compared with the complete avoidance of opioids [25].

Supplementing VIMA with fentanyl had no significant sevoflurane-sparing effect, but appeared to produce other detrimental effects. In particular, it resulted in greater cardiorespiratory depression, which was more likely to require intervention by the anaesthetist. While bradycardia and respiratory depression are known and predictable effects of fentanyl, their magnitude may have been exacerbated by our chosen method of sevoflurane delivery. During inhalation induction with sevoflurane, a high end-tidal (and hence blood) concentration of sevoflurane is achieved but the concentration in the effect site will be somewhat lower. If the fresh gas flow is reduced to low levels immediately after LMA insertion, the drug already in the patient's blood is not washed-out through the lungs but will continue to diffuse into the effect site, further deepening the level of anaesthesia, even in the absence of further drug delivery [1]. We chose this technique as it is the most efficient way in which to use sevoflurane [1] and also minimizes the likelihood of inadequate anaesthesia in the early surgical period. This technique helped to make fentanyl unnecessary for achieving acceptable intraoperative conditions, but probably also exacerbated its adverse effects, since it would have been administered at a time of relatively deep anaesthesia.

We thought that omission of fentanyl might have both positive and negative consequences and had therefore tried to counter its emetogenic properties by the use of prophylactic dexamethasone. In the event, this proved unnecessary, due to the lack of significant benefit from fentanyl. It was nevertheless surprising that dexamethasone caused no obvious reduction in PONV. Several other studies have shown prophylactic dexamethasone to be beneficial [20] and our chosen dose of 4 mg is commonly used [26] and comfortably above the minimum effective dose of 2.5 mg [27]. One possible explanation is the relatively slow onset of the antiemetic effect of dexamethasone, which may have had insufficient time to have much impact on PONV during early recovery from these short day surgery procedures, the time at which most cases of PONV occurred. Dexamethasone does have a prolonged effect and may be more useful at preventing late PONV. Our data showed that there was less of an increase in PONV from the time of hospital discharge until the follow-up telephone call in the fentanyl-dexamethasone group compared to the fentanyl group, although the overall incidence of PONV within the first 24 h was 44% in both groups. We also observed a moderate increase in PONV between discharge and the follow-up call in the pure VIMA group and it is possible that this might have been reduced by dexamethasone prophylaxis, although this was not studied. It is possible that an alternative antiemetic might have reduced PONV associated with fentanyl.

The overall incidence of PONV associated with VIMA in this study was quite high, even when perioperative opioids were avoided. Because we wanted to ensure that omission of fentanyl did not increase postoperative pain, we only included patients having procedures with a significant surgical incision. This excluded minor procedures, such as cystoscopy, where the incidence of PONV is very low and may have exaggerated the overall incidence. Conversely, we also excluded laparoscopic surgery, where the incidence of PONV may be higher. It must also be remembered that patients knew they were participating in a trial where PONV was the focus of study. They were specifically questioned about nausea at several time points, which, with their heightened awareness, could have revealed minor symptoms that would go unrecorded in routine practice. This is supported by the small number of patients requesting antiemetics for mild symptoms.

It has been suggested that the overall incidence of PONV is really a surrogate measure of patient outcome and that delayed recovery, economic differences and the patient's satisfaction are all more important end-points [28,29]. Interestingly, patient satisfaction and specifically satisfaction with the control of nausea and vomiting did not differ between the groups, even if only those patients with PONV were considered. No patient in any group required hospitalization for PONV, although this should be a rare event if appropriate treatment is provided for severe symptoms. We also did not observe any difference in length of stay between the groups, although patients with PONV had a longer postoperative stay than those without in the fentanyl groups combined, but not in the pure VIMA group. Finally, the significantly reduced requirement for treatment of PONV in the pure VIMA group was a clear advantage with an additional economic benefit that was achieved at no extra cost.

It is possible that the overall incidence of PONV could have been further reduced by the omission of N_2O, as this is known to increase the incidence of vomiting and, to a lesser extent, nausea [30]. The effect is relatively weak, however, and postoperative vomiting was not as common as nausea in our study.

Detecting even a halving of the overall incidence of vomiting in our study would require almost 300 patients per group, whereas a reduction of 50% in the need for antiemetic therapy would require group sizes of 650 patients. It is also quite likely that the omission of both N_2O and opioids would make it very difficult to achieve acceptable intraoperative conditions.

Our study could be criticized in that the respiratory depression caused by fentanyl partially negated the blinding of the study. However, fentanyl only caused apnoea in half of the patients and the lower respiratory rate was most evident when all the results were combined, making it unclear what many individual patients had received. Partial unblinding could have biased the collection of intraoperative data, although most of the data were from objective physiological monitors. Assessment of pain and PONV on awakening may also have been compromised. However, the prime objective of this early assessment was to ensure that transient episodes of pain or PONV on awakening, which a patient might fail to remember when more fully recovered, were not missed. All subsequent assessments were made by the dedicated research nurse who was deliberately kept well away from the operating theatre environment to preserve her blinding.

The study could also be criticized in that i.v. fluids were given to some but not all patients. Intravenous fluids have been shown to be beneficial in reducing postoperative nausea [31], although their routine use in UK day surgery is still uncommon [32]. We administered fluids to patients having longer procedures, predominantly herniae and open urological operations, primarily to reduce the postoperative dizziness that we previously found problematic in these patients. Intravenous fluids have a far greater preventative effect on postoperative dizziness than they do on PONV; the latter symptoms only being significantly reduced on the first postoperative day [31]. However, the administration of fluids was equally distributed between the groups, as were all other recognized risk factors for PONV.

In conclusion, when sevoflurane is used for the induction and maintenance of anaesthesia for day case surgery, the addition of supplemental fentanyl results in a significant increase in the incidence of moderate to severe nausea and in the requirement for antiemetic therapy. Avoidance of fentanyl does result in an increase in minor intraoperative movement, but this is easily managed and appears to have no serious consequences. Fentanyl also has adverse cardiorespiratory effects, has no demonstrable sevoflurane-sparing effects, causes a small delay to initial awakening and does not improve postoperative pain when appropriate day surgery analgesia is provided. Fentanyl appears to be an unnecessary and possibly detrimental supplement to sevoflurane VIMA in day surgery.

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