The menstrual cycle and nausea or vomiting after wisdom teeth extraction

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We have investigated 195 pre-menopausal women undergoing third molar extractions, in a prospective study, to assess the influence of the day of the menstrual cycle on the incidence of postoperative nausea or vomiting. In the 95 patients taking the oral contraceptive pill the incidence of postoperative nausea or vomiting was higher on days 9 to 15 of the menstrual cycle ($P < 0.05$) than on days one to eight and days 16 to the end of cycle. In the 100 patients who were not taking the oral contraceptive pill the incidence of postoperative nausea or vomiting was not higher on days 9 to 15. The strongest predictor for postoperative nausea or vomiting in our study was a previous episode of postoperative nausea or vomiting ($P < 0.005$). Patients with a tendency to motion sickness did not have a higher incidence of postoperative nausea or vomiting.

Pour évaluer l'influence de la journée du cycle menstruel sur les nausées ou les vomissements postopératoires, nous avons étudié prospectivement 195 femmes postménopausiques soumises à une extraction de la troisième molaire. Pour 95 patientes sous contraceptifs oraux, l'incidence des nausées ou des vomissements postopératoires est plus élevée aux jours 9 à 15 du cycle menstruel ($P < 0,05$) comparativement aux jours un à huit et au jour 16 jusqu'au dernier jour du cycle menstruel. Chez les 100 patientes qui ne prennent pas de contraceptifs oraux, l'incidence des nausées ou des vomissements postopératoires n'est pas plus élevée aux jours 9 à 15. Dans notre étude, le facteur de prédiction le plus important consiste en un épisode antérieur de vomissements ou nausées postopératoires ($P < 0,005$). Les patientes ayant déjà une tendance au mal des transports n'ont pas une incidence plus élevée de nausées ou vomissements postopératoires.

Key words

ANAESTHESIA: outpatient;

VOMITING: postoperative, nausea, incidence.

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The prevention of postoperative nausea or vomiting is an important aspect of anaesthesia for outpatient surgery. The incidence of nausea or vomiting is high in young adult women¹⁻⁴ who make up the majority of the patients presenting for third molar extractions. Other factors associated with an increased incidence include the use of perioperative opioid analgesics,¹ previous nausea or vomiting after anaesthesia¹ and possibly motion sickness.^{5,6}

In two studies of women undergoing gynaecological laparoscopy,^{7,8} the incidence of nausea or vomiting was seen to vary markedly with the time in the woman's menstrual cycle, with a greater risk during menses. Laparoscopic surgery is associated with a particularly high rate of postoperative nausea or vomiting³ and these findings may not apply to other surgical procedures. Consequently, we undertook a prospective study of pre-menopausal women presenting to our institution for third molar extraction under general anaesthesia to examine further this phenomenon. We also assessed the influence of other risk factors that may influence the incidence of postoperative nausea or vomiting.

Methods

The study was approved by the Hospital Ethics Committee. Informed written consent was obtained from each patient who agreed to take part in the study.

We studied 195 women, aged between 16 yr and the menopause, who presented to the Perth Dental Hospital to undergo third molar extractions. Patients were excluded if they were amenorrhoeic, had an irregular menstrual cycle, had undergone hysterectomy or may have been pregnant. Those who had stopped or commenced taking oral contraceptive medication in the last month were excluded, but those established on oral contraceptives were studied to assess difference between women with ovulatory and anovulatory cycles.

Preoperatively, patients supplied information on the date of their last menstrual period, length of cycle and its regularity. Their previous anaesthetic history was taken with reference to associated nausea or vomiting, and any tendency to travel sickness of any kind was noted.

Premedication of papaveretum 0.2 mg · kg⁻¹ and hyos-

cine $0.04 \mu\text{g} \cdot \text{kg}^{-1} \text{ min}^{-1}$ was administered one hour before anaesthesia. Induction was with thiopentone $4\text{--}6 \text{ mg} \cdot \text{kg}^{-1}$ followed by succinylcholine or a non-depolarizing muscle relaxant to facilitate nasotracheal intubation. Patients received nitrous oxide in oxygen and supplementation with either enflurane or isoflurane as required. Their lungs were ventilated or they were allowed to breathe spontaneously according to the anaesthetist's preference. No opioids were given during anaesthesia. Each patient received prochlorperazine $0.17 \text{ mg} \cdot \text{kg}^{-1} \text{ iv}$ at induction of anaesthesia. One litre of compound sodium lactate was infused over the first hour after induction and thereafter dextrose 5% was infused at $2 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$ until full ambulation and return of the ability to take oral fluids.

On recovery and at one, two and four hours after waking the patients were questioned by trained recovery room nurses who did not know the purpose of the study. The patients were asked whether they had felt any nausea or had retched or vomited during the previous time period. The administration of any simple or opioid analgesics and antiemetics was noted, the decision to give any particular agent being at the recovery nurse's discretion. Full ambulation was encouraged between the third and fourth hour and discharge home was approximately 4.5 hr after awakening.

The patients were categorised by day of menstrual cycle into three groups: days one to eight (pre-ovulatory), days 9 to 15 (ovulatory) and days 16 to the end of cycle (post-ovulatory). Chi-squared analysis was used to compare the incidence of nausea or vomiting between the groups. Stepwise multiple logistic regression analysis was used to identify factors independently related to postoperative nausea or vomiting. Statistical significance was set at the 5% level.

Results

Two hundred and three patients were recruited into the survey of whom 195 had complete data and in whom the protocol had been followed. Mean age was 22.4 yr (SD = 5.14) and mean weight 62.33 kg (SD = 13.16). The menstrual history revealed that 95 (48.7%) patients were taking oral contraceptives. Mean length of menstrual cycle was 27.9 d (SD = 2.47).

The overall incidence of nausea or vomiting was 18.5%. The incidence of postoperative nausea or vomiting was higher on days 9 to 15 ($P < 0.05$) (Table). When the 95 patients taking the oral contraceptive pill were analysed independently, the incidence of nausea or vomiting was higher in those patients on days 9 to 15. Seventy-eight of the 95 patients on the oral contraceptive pill knew which preparation they were taking. Fifty-five (70%) of these 78 patients were taking the triphasic oral contra-

TABLE The incidence of postoperative nausea or vomiting (%) by day of menstrual cycle

	Day of menstrual cycle		
	1-8	9-15	16+
All patients	10/52 (19)	15/51 (29)*	11/92 (12)
Patients on OCP	4/18 (22)	9/25 (36)*	6/52 (12)
Patients not on OCP	6/34 (18)	6/26 (23)	5/40 (13)

* $P < 0.05$ compared with days 1-8 and days 16 to the end of cycle.

ceptive pill and the remainder taking a standard combined preparation. In those patients who were not taking the oral contraceptive pill the incidence of postoperative nausea or vomiting was not higher in the ovulatory group (Table).

Forty of the 119 patients who had undergone previous general anaesthesia had a history of postoperative emesis. The incidence of nausea or vomiting was 15/40 (37.5%) in these patients, compared with 11/79 (13.9%) in patients with no previous history of postoperative emesis ($P < 0.005$).

Seventy of the 195 patients claimed to have suffered from motion sickness. The incidence of nausea or vomiting was 12/70 (17.1%) in these patients, compared with 24/125 (19.2%) in patients who did not suffer from motion sickness ($P: \text{NS}$). In this study motion sickness was not a risk factor for postoperative nausea or vomiting.

The incidence of nausea or vomiting in the patients who breathed spontaneously was 8/48 (16.7%), compared with 28/147 (19%) in the patients whose lungs were mechanically ventilated ($P: \text{NS}$). The incidence of nausea or vomiting in the patients who received succinylcholine to facilitate intubation was 8/53 (17%) compared with 28/142 (19.7%) in the patients who received only non-depolarising relaxants ($P: \text{NS}$).

One patient required an intramuscular antiemetic postoperatively but had recovered sufficiently to be discharged on the same day. No patient required opioid analgesia postoperatively.

Stepwise multiple logistic regression analysis of the data showed that there were three independent risk factors that increased the incidence of postoperative nausea or vomiting in our study. These factors were previous postoperative nausea or vomiting ($P < 0.005$, risk ratio = 2.80, confidence interval 1.56-5.03), presenting for surgery on day 9 to 15 of the menstrual cycle ($P < 0.05$, risk ratio = 1.70, confidence interval 0.99-2.94) and increased weight ($P < 0.05$, risk ratio = 1.03 (for each kg greater than the mean), confidence interval 1.00-1.06).

Discussion

The overall incidence of nausea or vomiting in this study

compares favourably with previous studies.⁹ Although the relative risk of nausea or vomiting is not high after third molar extractions,^{1,2} the patients in this study were all young adult women and all received opioid analgesics. Forrest *et al.* suggest a risk ratio for nausea of 2.3 for females and 1.3 for those <40 yr in their survey of 17,201 patients.³ The use of opioid analgesics further increases the likelihood of emetic sequelae. Our low incidence may be attributable to the maintenance of adequate hydration with intravenous fluid therapy which has been shown to reduce the incidence of postoperative dizziness and nausea,¹⁰ or to the use of a prophylactic antiemetic. Prochlorperazine is a useful agent in the treatment of established nausea or vomiting¹¹ and also when given prophylactically in the recovery room¹² and is used as a standard therapy for comparisons among antiemetics. Although it would be expected to be protective if given prior to awakening it has proved disappointing when used in this way.¹³ However, our patients also received hyoscine and it is possible that the combination may have been more effective.

The increased incidence of nausea or vomiting in patients near the time of ovulation is at odds with the results of Beattie *et al.*^{7,8} They found an increase in risk of nausea or vomiting in patients undergoing laparoscopy during menses compared with the remainder of the cycle, whereas our patients had a low incidence during menses similar to that seen in the postovulatory period. Beattie postulated that changing concentrations of FSH and/or oestrogen may sensitize the chemoreceptive trigger zone and/or the vomiting centre.⁷ Endogenous oestrogen concentrations increase rapidly around day eight of the menstrual cycle, decreasing to intermediate levels for the remainder of the cycle after day 16.¹⁴ This period of high oestrogen secretion corresponds with the period of highest incidence of nausea or vomiting in our study, the ovulatory period. We postulate that oestrogen may sensitize the chemoreceptive trigger zone and/or the vomiting centre to effect this cyclical variation in female's susceptibility to postoperative nausea or vomiting.

In the group of women taking the oral contraceptive pill we have shown a variation in the incidence of postoperative nausea or vomiting in different phases of the menstrual cycle. The majority of those participants were on a triphasic preparation which has a higher oestrogen content on those days corresponding to our ovulatory group. If higher levels of oestrogen are responsible for the increase in postoperative nausea or vomiting, we suggest that it is the varying levels of exogenous oestrogens that may have influenced the cyclical changes in susceptibility in our study. Further work comparing high and low oestrogen dose contraceptives will be needed to confirm this hypothesis.

A history of motion or travel sickness did not increase the likelihood for postoperative emetic sequelae. This has been shown in another recent study¹³ and calls into question the association between the two. The use of hyoscine preoperatively in our patients may have been effective in preventing any differences from becoming apparent. The stimuli for motion sickness arise from conflict between the vestibular apparatus and the visual cortex and higher centres.¹⁵ Those for postoperative emesis arise from the action of anaesthetics and opioids on the chemoreceptive trigger zone, from pain and hypotension on the vomiting centre and miscellaneous gut and pharyngeal reflexes.¹ Although the final common pathway is the same, we suggest that the susceptibility of an individual to one set of stimuli may not reflect their susceptibility to the others.

Nausea or vomiting after previous general anaesthesia has again been shown in this study to be an important predictor of an individual's risk of postoperative nausea or vomiting. Our finding of a positive correlation between the incidence of postoperative nausea or vomiting and increasing weight is in keeping with previous reports.^{2,16} Explanations for this include increased oesophageal reflux with larger residual gastric volumes, and a greater risk of inflation of the stomach as a result of more difficult airway management.¹ Alternatively, the larger reservoir of inhaled agent in the adipose tissues may contribute to greater postoperative side effects.¹ We propose that an additional factor in obese patients may be that the increased production of oestrogen by adipose tissue sensitizes the vomiting centre.

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