Does smoking have an influence on postoperative nausea and vomiting?

Ionescu D[1], Bãdescu C[2], Maican D[2], Acalovschi I[3]
1. Senior lecturer, Anaesthesia and Intensive Care Department, University of medicine and Pharmacy, Cluj-Napoca, Romania
2. Registrars in Anaesthesia and Intensive Care, Clinica ATI, Spitalul Clinic de Adulti, Cluj-Napoca, Romania
3. Professor in Anaesthesia and Intensive Care, Clinica ATI, Spitalul Clinic de Adulti, Cluj-Napoca, Romania

Correspondence to: Dr D Ionescu, e-mail: dionescuati@yahoo.com

SAJAA 2007; 13(4): 29-32

ABSTRACT

Background
Smoking is considered a risk factor not only for anaesthesia, but for general health. On the other hand, it was demonstrated that smoking reduces postoperative nausea and vomiting. In our study, we have investigated this effect in patients undergoing laparoscopic cholecystectomy. Moreover, we have looked to see if there is a relationship between the number of cigarettes smoked daily and the antiemetic effect.

Methods
71 patients scheduled for elective laparoscopic cholecystectomy under general anaesthesia were divided into 2 groups: group 1 (n=40) included non-smokers and group 2 (n=31) included the smokers. Each group was randomized for propofol and thiopentone as an induction agent. In addition, the smokers were further divided into heavy smokers, for patients smoking more than 20 cigarettes daily and smokers for patients smoking less than 20 cigarettes daily. The incidence of postoperative nausea and vomiting and the severity of pain (on Visual Analogue Score) were both assessed for the first 24 hours postoperatively.

Results
Postoperative nausea and vomiting occurred in 31 patients (77.5%) in the non-smokers' group, as compared with 12 patients (38.7%) in smokers' group ($p<0.05$). The mean maximum degree of pain (5,82) was significantly lower in the smokers' group as compared with non-smokers where this was 2.8 ($p<0.05$).

Conclusions
A history of current smoking significantly reduces postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. Smoking also reduced the incidence of postoperative pain. Despite these favorable effects, we would like to emphasize that our study is not intended to promote smoking.

Introduction

There are numerous studies in the literature detailing the serious side effects and complications of smoking, many of which represent perioperative risk. However there is also a favorable effect of smoking in the perioperative period. Cohen M *et al* [1], Koivuranta M *et al* [2], and Hugh MB *et al* [3], identified smoking as a protective factor against postoperative nausea and vomiting (PONV), and Apfel *et al* [4] found that non-smoking represents one of the four most important risk factors for PONV, together with female gender, history of PONV, or motion sickness and the use of opioids postoperatively. Chimbira and Sweeney[5] confirmed the anti-emetic effect of smoking in a study on 327 consecutive patients undergoing arthroscopic day-case knee surgery and this has also been demonstrated by other groups.[6-9] Our study was designed to investigate the effects of smoking on postoperative nausea and vomiting as well as on postoperative pain. Furthermore we investigated if there is a relationship between the number of cigarettes smoked daily and the incidence of PONV, considering that such a relationship has not yet been reported.

Methods

Seventy one patients (ASA I/II) undergoing laparoscopic cholecystectomy (between Jan 1999 - Jan 2000) under general anaesthesia were enrolled in the study after obtaining the approval of the Ethics Committee of the University of Medicine from Cluj-Napoca, and written informed consent from the patients the evening before operation.

Patients aged 20-73 (48 ± 11.93) years, body weight range of 55-120 (42.87 ± 13.44) kg were divided into 2 groups: group 1(n=40) NS was non-smoking patients and group 2 (n=31) was current smokers. In the smokers group 8 patients were "heavy smokers" (i.e. patients smoking more than 20 cigarettes daily) and 23 patients were "smokers" (i.e. patients smoking less then 20 cigarettes daily) for at least one year. None of the patients included in the study have had any concomitant medication that may influence the study results. The groups were further randomized to thiopentone or propofol as the anaesthetic induction agent.

Patients were premedicated with diazepam 10 mg and meperidine 100 mg i.m. one hour before surgery. They were brought into the operating theatre 30 min before induction, when a peripheral cannula was inserted and 500 ml Ringer's solution was administered in all patients.

General anaesthesia was induced with 1.25 mg droperidol, midazolam 1 mg, fentanyl 2 $\mu g.kg^{-1}$, and thiopentone 2-3 $mg.kg^{-1}$

or propofol 1.5-2 mg.kg^{-1}. Tracheal intubation was facilitated with 0.5-0.6 mg.kg^{-1} atracurium. Anaesthesia was maintained with halothane (Ethal 1-1.5 MAC) in 100% oxygen, and 100 μg fentanyl was given when the HR and BP were increased 20% above the patient's preoperative reference level. During anaesthesia patients were mechanically ventilated to maintain EtCO2 between 4.5 –5.5 kPa. After intubation, a nasogastric tube was introduced to empty the stomach of fluid and air. The tube was removed at the end of surgery. During the operation, patients were placed in a reverse Trendelenburg position and 25° - 35° left lateral decubitus. Intraoperatively, pneumoperitoneum with CO_2 was maintained at a pressure of 12-15 mmHg. At the end of surgery, halothane was discontinued after skin closure and muscle relaxation was reversed with 2.5 mg neostigmine and 1 mg atropine.

During anaesthesia BP, HR, ECG, inspiratory and expiratory O_2 and halothame concentration and CO_2 were monitored. Postoperatively all 71 patients were monitored for PONV and pain for the first 24 hours by a blinded observer, who was unaware of the patient's smoking habit. The need for rescue antiemetic medication (mg.kg^{-1}) was also recorded. Rescue antiemetic medication consisted of 10 mg metoclopramide i.v. administered for severe nausea and/or vomiting. The intensity of postoperative pain was evaluated on a visual analogue scale (VAS) ranging from 0 – 10, where: 0 – no pain, 10 – most severe pain. The mean of maximum score in each study group during the first 24 h was recorded. For postoperative analgesia, the protocol was 2 g metamizol i.m. for a VAS < 4 and meperidine 1 mg.kg^{-1} i.m. for a VAS ≥ 4.

The statistical pack SPSS for Windows was used to analyze the results. Nominal data were reported as incidences and analyzed using the chi-square test or the Fisher's exact test. Continuous and discrete data are reported as mean (± standard deviation) and analyzed using the two-sided t-test for independent samples, assuming equal variances (the F-test for variances) if the data were normally distributed (the Kolmogorov-Smirnov Liliefors test). Alternatively the the Mann-Whitney U test was used. A $p < 0.05$ was considered significant.

Results

The study groups were comparable in terms of age, weight, gender, anaesthetic risk, duration of anaesthesia and intraoperative opioid consumption (Table I).

Table I: Demographic data of the study groups (mean ± SD)

	Group 1 (n = 40)	Group 2 (n = 31)
Age (yr)	48.6 (± 12.3)	42.96 (± 13.08)*
Weight (kg)	72.7 (± 12.5)	75.29 (± 15.62) *
Gender (M/F)	13/27	8/23
ASA I/II	22/18	17/14
Fentanyl consumption (μg/kg)	5.9 (± 0.17)	5.7 (± 0.16) *
Anaesthesia time (min)	62 (± 17.28)	59.67 (± 14.14) *

*p>0.05

The average amount of crystalloids given during anaesthesia was 750-1000 ml.

As can be seen from Table II, the incidence of PONV was significantly lower in group 2 (smokers) as compared with group 1 (non-smokers).

Table II: The overall incidence of PONV in study groups.

	Group 1 (n = 40)	Group 2 (n = 31)	p
Nausea (only)	16 (40%)	4 (12.9%)	$p < 0.05$
Vomiting	15 (37.5%)	8 (25.8%)	$p > 0.05$
PONV	31 (77.5%)	12 (38.7%)	$p < 0.001$

With regard to the influence of anaesthetic induction agent on perioperative outcomes, the incidence of PONV was significantly increased ($p < 0.05$) in the non-smoking group, regardless of which induction agent was used. Insert Tables III and IV.

Table III: The incidence of PONV in study groups using thiopentone as induction agent

	Group 1 (n = 20)	Group 2 (n = 16)	p
Nausea (only)	7 (35%)	0	p < 0.01
Vomiting	10 (50%)	7 (43.75%)	p > 0.05
PONV	17 (85%)	7 (43.75%)	p < 0.01

Table IV: The incidence of PONV in study groups using propofol as induction agent

	Group 1 (n = 20)	Group 2 (n = 15)	p
Nausea (only)	9 (45%)	4 (26.66%)	p > 0.05
Vomiting	5 (25%)	1 (6.66%)	p > 0.05
PONV	14 (70%)	5 (33.33%)	p < 0.05

As was expected, the overall incidence of PONV is lower in the propofol group in both smokers and non-smokers. The results regarding the relationships between the number of the cigarettes smoked daily and the incidence of PONV are listed in Table V.

Table V: The incidence of PONV in smokers group

	Heavy smokers (n = 8)	Smokers (n = 23)	p
Nausea (only)	2 (25%)	2 (8.7 %)	p > 0.05
Vomiting	0	8 (34.7%)	p > 0.05
PONV	2 (25%)	10 (43.4%)	p > 0.05

The incidence of PONV was found to be lower in heavy smokers, although the difference was not statistically significant. This is likely due to the sample size being too small to show any differences.

Regarding the severity of pain, the greatest postoperative score was registered in the non-smoking group, and there was a significant difference between this group and the smoking group (Table VI).

Table VI: Postoperative maximum pain score in study groups

	Group 1 (n = 40)	Group 2 (n = 31)
VAS (mean ± SD)	1.81 (± 2.1)	2.8 (± 2.3)*

*p< 0.05

Discussion

Until a few years ago, it was generally accepted that tobacco, and nicotine, in particular, have an emetogenic effect.[10] It was only recently demonstrated that smoking has, in fact, an antiemetic effect.[1,4] Assigned with these opinions, in this study we have demonstrated that smoking significantly reduced the incidence of PONV after laparoscopic cholecystectomy, when both thiopentone and propofol have been used as induction agents. Moreover our results demonstrate that this antiemetic effect may be related to the number of cigarettes smoked, but our sample of heavy smokers is too small to allow a statistical conclusion. Also, the upper limit for a definition of heavy

smoking was determined arbitrarily at 20 cigarettes per day. It is thus conceivable that a cut-off level of 10 per day may have shown a significant difference, but this awaits confirmation in another study.

Numerous substances in the cigarette smoke could be responsible for these postoperative effects. The exact mechanism of the antiemetic effect of nicotine and/or other substances in the cigarette smoke is not completely understood. It is known that cigarette smoke is a mixture of approximately 4000 substances (carbon monoxide, nor nicotine, antabine, anabasine, ketones, nitrosamines, polyaromatic hydrocarbons),[11] so it is difficult to say at this moment whether this effect is produced by nicotine only or by other substances.

One explanation for such an effect would be the presence of one or more antiemetic substances in tobacco smoke. The pharmacological receptors that mediate PONV are known to act at the dopamine (D_2), cholinergic, histamine (H_1), 5-HT_3 and (neurokinin 1) NK_1 receptors[12] and if there were an antiemetic in cigarette smoke it would have to belong to one of these classes of receptor-blocking drugs. Presumably, if this were the case, then other dopaminergic, cholinergic or histaminergic effects would be seen occasionally. Alternatively, the reduction in PONV may be seen as an adaptive response to a repeated emetic stimulus, although it is known that only those who have smoked too much or are uninitiated find tobacco emetogenic.[13]

These substances and many more included in cigarette smoke condensate (naphtalene, phenanthrene, anthracene and others) are toxic, and their detoxification occurs via cytochrome P450 (CYP) enzyme pathways. Cigarette smoke can result in as much as a 3-fold increase in CYP1A2 activity, in common with polycyclic aromatic hydrocarbons.[13] This can lead to increased drug metabolism including that of morphine, meperidine and other analgesics.[13-17] Volatile anaesthetics, on the other hand, are metabolized by CYP2E1[18,19] which is also induced by nicotine and aromatic hydrocarbons.[20] These changes in enzyme pathways would suggest a quicker and smoother emergence in smokers, but may also have implications for increased intraoperative opioid requirements. Previous data have demonstrated an increased requirement for meperidine and morphine in smokers.[14]

However, our results have not shown a significant difference in intraoperative opioid requirements between smokers and non-smokers, although there was a significant difference in the severity of postoperative pain scores between the groups. In the mean time nicotine-induced analgesia was documented in experimental studies on mice and rats.[21, 22] This nicotine-induced analgesia was non-competitively antagonized by naloxone, leading to the hypothesis that nicotine as well as smoking releases endogenous opioids in the brain that are responsible for the analgesic effects. At the same time the nicotine-induced antinociception effect was antagonized by EDTA and abolished by $CaCl_2$, leading to the hypothesis that Ca^{2+} channels are involved in mediating nicotine-induced analgesia.[22] Besides nicotine, there could be other substances from cigarette smoke (such as polycyclic aromatic hydrocarbons, antabine, anabasine and others) that may contribute to the antiemetic and analgesic effects.

Conclusion

We conclude that in our study smoking significantly reduced the incidence of PONV as well as the severity of postoperative pain after laparoscopic cholecystectomy. SAJAA

References:

1. Cohen MM, Duncan PG, De Boer DP, Tweed WA. The postoperative interview: assessing risk factors for nausea and vomiting. Anaesth Analg 1994;78:7-16
2. Koivuranta M, Laara E, Snare L, Alahunta S. A survey of postoperative nausea and vomiting. Anaesthesia 1997;52:443-449
3. Hough MB, Sweeney BP. The influence of smoking on postoperative nausea and vomiting. Anaesthesia 1998;53:932-3
4. Apfel CC, Laara E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting. Conclusion from cross validation between two centers. Anasthesiology 1999;91:693-700
5. Chimbira W, Sweeney BP. The influence of smoking on postoperative nausea and vomiting. Anaesthesia 2000;55:540-545
6. Apfel CC, Kortilla , Abdalla M, *et al.* A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. N Engl J Med 2004;350:2441-51
7. Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? Anaesthesiology 1999;91:109-118
8. Apfel CC, Kranke P, Berhart LHJ, Roos Y A, Roewer N. A comparison of predicting models for postoperative nausea and vomiting. Br J Anaesth 2002;88:234-240
9. Pierre S, Benais H, Pouymayou J. Apfel's simplified score may favourably predict the risk of postoperative nausea and vomiting. Can J Anesth 2002;49:237-42
10. Greenland S, Satterfield MH, Lanes SF. A meta-analysis to assess the incidence of adverse effects associated with the transdermal nicotine patch. Drug Saf 1998;18:297-308
11. Seversons RF, Snook ME, Arrendale RF, Chortyk OT. Gas chromatographic quantitation of polynuclear hydrocarbons in cigarette smoke. Analyt Chem 1976;48:1866-72
12. Hefferman AM, Rowbotham DJ. Postoperative nausea and vomiting-time for balanced antiemesis? Br J Anaesth 2000; 5:675-7
13. Sweeney BP. Why does smoking protect against PONV? Br J Anaesth 2002;89:810-813
14. Miller LG. Cigarettes and drug therapy: pharmacokinetic and pharmacodynamic considerations, Thor Rev 1990;9:125-35
15. Ali B, Kumar A, Bhargova KP. Comparative evolution of stimulatory effects of oral tobacco on nicotine consumption on hepatic microsomal N-demethylation. Biochem Pharma 1980;29:3087-92
16. Kerri-Szanto M, Pomeroy JR. Atmospheric pollution and pentazocine metabolism. Lancet 1971;1:947-9
17. Schein JR. Cigarette smoking and clinically significant drug interactions. Annal Pharmacother 1995;29:1139-47
18. Spracklin DK, Hankins DC, Fisher JM, Thummel KE, Kharasch ED. Cytochrome P4502E1 is the principle catalyst of human oxidative isoflurane metabolism in vitro. J Parmacol Exp Ther 1997; 281:400-11
19. Kharasch ED, Thummel KE. Identification of cytochrome P4502E1 as the predominant enzyme catalyzing human liver microsomal defluorination of sevoflurane, isoflurane and methoxyflurane. Anaesthesiology 1993;79:795-807
20. Zevin S, Benowitz NL. Drug interactions with tobacco smoking. Clin Pharm 1999;36:425-38
21. Carstens E, Anderson KA, Simons CT, Carstens MI, Jinks SF. Analgesia induced by chronic nicotine infusion in rats: differences by gender and pain test. Psychopharmacol 2001;157:40-45
22. Block RC, Chin CW, Wu W, Zbuzek VK. Nicotine-induced analgesia in rats: the role of calcium and the diversity of responders and nonresponders. Life Sci 1993;53:195-200