

Original

Postoperative Analgesic Requirement in Abstaining Smokers and Non-smokers

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Objectives: This study was designed to test the hypothesis that smoking patients who abruptly discontinue smoking require more postoperative analgesics than nonsmokers. **Methods:** The data of all patients who had received intravenous fentanyl via a patient-controlled analgesia (PCA) device for a year were reviewed. Smokers (n = 44) were compared with non-smokers (n = 102) with regard to analgesic use during the 24 hours after surgery. **Results:** No significant differences were observed in the weight-adjusted fentanyl use, the incidence of adverse effects and the pain visual analog scale at the initiation and 24 hours after starting PCA. However, the percentage of patients who received NSAIDs and intravenous morphine was significantly higher in the smokers than in the non-smokers (p = 0.01 and 0.03, respectively). **Conclusion:** Despite the fact that no significant difference in fentanyl consumption was observed, the percentage of patients for whom other analgesics were prescribed was significantly higher in smokers than non-smokers. This result might support the hypothesis that abstaining smokers require more analgesics than non-smokers after surgery.

Key Words: smokers, intravenous patient-controlled analgesia (PCA), postoperative pain

Introduction

Approximately 25 million Japanese smoke cigarettes and many of them undergo surgery in their lifetime¹⁾. While hospitalized, surgical patients are forced to abstain from smoking and could develop nicotine withdrawal syndrome. An animal study demonstrated analgesic properties of nicotine through the endogenous opioid system²⁾. Although the mechanism of the nicotine-related analgesic effect is not fully understood in humans, several human studies suggested an analgesic effect of nicotine in humans^{3)~5)}. Furthermore, it was shown that chronic administration followed by abrupt discontinuation of nicotine develops a tolerance to nicotine-induced analgesia and an increased nociception in an animal model⁶⁾. This finding is supported by a preliminary study showing that nicotine abstinence during hospitalization resulted in greater uses of morphine for postoperative analgesia compared to non-smokers⁷⁾.

This study was designed to study effects of smoking abstinence on postoperative analgesia of patients receiving patient-controlled analgesia (PCA) with intravenous fentanyl. Because the intensity of postoperative pain varies widely among surgical procedure, the many previous studies investigating postoperative pain restricted subject populations undergoing a single surgical procedure. In the present study, however, we investigated patients who underwent a variety of surgical procedures, since we considered limiting surgical procedures is not clinically realistic.

Material and Methods

This retrospective study was performed to conform with the World Medical Association Declaration of Helsinki⁸⁾. The protocol was approved by the institutional ethics committee for human studies of the Tokyo Women's Medical University, Tokyo, Japan.

All patients who were treated with intravenous

PCA fentanyl for postoperative analgesia admitted to the Intensive Care Unit (ICU) of Tokyo Women's Medical University Hospital for the first one or more days at the study period from January to December in 2005. Patients were divided into two groups according to their smoking status. Smokers were defined as those smoking one or more cigarettes every day for at least one year immediately before surgery. We reviewed the postoperative ICU records of all subjects. Preoperative factors, such as smoking history, gender, age, weight, and medical history, were collected. Patients with any of the following criteria were excluded from the study: (1) insufficient information on the medical record; (2) smoking history for less than one year before surgery; (3) preoperative use of analgesics such as non-steroidal anti-inflammatory drugs on a regular basis; and (4) PCA use for less than 24 hours.

The main characteristics of surgery were compared between groups including the type of surgery, and duration of surgery. Intraoperative analgesia was provided by intravenous fentanyl with doses determined by each anesthesiologist. A microcomputer-controlled PCA pump device (CAPD Legacy[®] PCA pump; Smiths Medical Japan, Tokyo, Japan) containing fentanyl solution was connected at the end of the surgical procedure. Two dosing regimens were employed to deliver intravenous fentanyl: 15 µg bolus at lockout intervals of 5 min; and a 30 µg/h continuous infusion supplemented by 15 µg bolus with a lockout interval of 5 min. In both regimens, dose limits were set at 150 µg in one hour. The attending anesthesiologists decided which regimen to be used judging the risk of respiratory depression. After patients were admitted to the ICU, PCA was initiated following instructions to patients of the use of the PCA device. ICU nurses examined the levels of analgesia and sedation using the visual analog scale (VAS) and Ramsay scores, respectively, every four or five hours. At the same time, they checked the amount of fentanyl left in the PCA pump and the occurrence of fentanyl-derived side effects, including respiratory depression (breathing rate below 10 min⁻¹), nausea and vomiting, and pruritus. When ICU physicians

determined insufficient analgesia produced by the PCA fentanyl, either suppository NSAIDs or intravenous morphine was administered.

Above data were collected for 24 hours after starting the PCA fentanyl administration and compared between the two groups of smokers and non-smokers. When the 24th hours data were missing, the means of the values of immediately before and after 24th hours were adopted as the 24th hours value.

Statistical Analysis

Data are presented as the mean ± SD or the median (25-75 percentiles) where appropriate. A one-way analysis of variance (ANOVA) followed by the Bonferonni's post hoc test was used to compare the clinical characteristics of the two groups. The Mann-Whitney test was used to compare two medians. The chi-square test was used for categorical variables. A two-way ANOVA for repeated measures was used to analyze the differences between values recorded at 0 hours and at 24 hours after the start of PCA. All probability values were 2-tailed. A value of $p < 0.05$ was considered statistically significant. All the statistical analyses were performed using SPSS software, version 11.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 264 patients were reviewed in this study. After excluding patients who did not satisfy the analysis criteria, 44 smokers and 102 non-smokers were analyzed. None of the smokers had used any form of nicotine replacement therapy.

Patient profile, types of surgery and anesthesia of the groups are listed in Table 1. The two groups were similar in age, weight, duration of surgery, and anesthetic dose of fentanyl, but not in gender. Postoperative analgesic requirement, adverse effects, and pain and sedation scores are listed in Table 2. None of the patients consumed the maximum amount of fentanyl available via PCA. In each group, both the VAS and the Ramsay score were significantly decreased at 24 hours after the start of PCA. No significant differences between the groups were observed in the weight-adjusted fentanyl use, the incidence of fentanyl-related adverse effects, the VAS, and the Ramsay score both at the begin-

Table 1 Main characteristics of patients, surgery and anesthesia in the two groups

	Smokers	Non-smokers	p value
Number	44	102	
Age (y)	59.3 ± 13.7	58.7 ± 17.4	0.65
Weight (kg)	59.4 ± 11.8	56.3 ± 12.0	0.18
Gender (male/female)	39/5	59/43	<0.01
Dose of fentanyl (µg/kg/hr)	3.1 ± 1.6	3.2 ± 1.6	0.97
Duration of surgery (min)	223.8 ± 79.0	211.4 ± 79.7	0.35
Type of surgery			
Number of patients (%)			0.06
Abdominal	16 (36.3%)	50 (49.0%)	
Orthopedics	5 (11.4%)	16 (15.7%)	
Thoracic	14 (31.8%)	13 (12.9%)	
Urologic	9 (20.5%)	23 (22.5%)	

Data are shown as the mean ± SD.

Table 2 Postoperative analgesic requirement, adverse effects, behavioral measures of pain and sedation

	Smokers (n = 44)	Non-smokers (n = 102)	p value
Fentanyl use (total µg 24 hr)	664.8 (374-948)	650.4 (357-1003)	0.78
Weight-adjusted fentanyl use (µg/kg/24 hr)	0.54 (0.28-0.72)	0.42 (0.22-0.73)	0.86
Background infusion (with/without)	9/35	23/79	0.78
Adverse events			
Nausea or vomiting	1 (2.2%)	3 (2.9%)	
Ventilatory depression	0	0	
Use of other analgesics			
NSAIDs	7 (15.9%)	4 (3.9%)	0.01
IV morphine	7 (15.9%)	5 (4.9%)	0.03
VAS (cm)			
Baseline	3.1 ± 3.1	3.1 ± 2.8	
24 th hours	1.9 ± 1.6*	2.1 ± 2.1*	
Ramsay score			
Baseline	2.4 ± 0.5	2.3 ± 0.7	
24 th hours	2.0 ± 0.1*	2.0 ± 0.3*	

The data of postoperative analgesic requirement are shown as the median (25-75 percentiles). The data of behavioral measures of pain and sedation are shown as the mean ± SD. NSAIDs, nonsteroidal anti-inflammatory drugs; IV, intravenous; VAS, visual analog scale.

*p < .01 vs baseline (ANOVA).

ning and the end of PCA. On the other hand, the percentage of patients who received supplemental analgesics other than PCA fentanyl was significantly higher in smokers than in non-smokers.

Discussion

We demonstrated that the smokers required supplemental analgesics, such as an intravenous bolus of morphine or non-steroidal anti-inflammatory drugs, more frequently than the non-smokers during the first 24 hours after the start of PCA, although no significant difference was observed in

the amount of PCA fentanyl consumed. It supports the hypothesis that abrupt discontinuation of smoking shortly before surgery increases the use of postoperative analgesia.

These results are consistent with previous studies^{7,9}. Alan et al analyzed seven female patients who underwent cesarean section⁷. They demonstrated that smoking patients required more frequent bolus administrations as well as a greater amount of PCA morphine than non-smoking patients for postoperative analgesia. Freddy et al presented that smokers

required 23% more morphine equivalents than non-smokers during the first 24 hours after coronary bypass graft⁹. To our knowledge, the postoperative analgesia requirement in a large population of abstaining smokers and non-smokers based on intravenous fentanyl PCA use has not been previously described.

Although the VAS was significantly lower at 24th hours than that at the start of PCA in both groups, there were patients who expressed 24th hours values greater than 30 mm indicating moderate pain or more. Nevertheless, none of the patients consumed the maximum amount of fentanyl deliverable by the PCA device. Several studies indicated that patients using PCA are often reluctant to medicate themselves to obtain complete pain relief^{10,11}. Moreover an insufficient understanding on PCA usage and pharmacological effects of fentanyl might be let the patients prefer to request other analgesics rather than to give themselves fentanyl boluses. In addition, fear for opioid side effects might make them willing to remain painful.

Although mechanisms by which smoking abstinence might modify postoperative analgesic requirement are unclear, several speculations have been made. First, smoking and its abstinence could alter the sensitivity to pain^{3,9}. Ingestion of nicotine stimulates the hypothalamo-pituitary adrenal (HPA) axis, producing an increased secretion of the β -endorphin and cortisol^{12,13} which then modify the transduction of pain. An increased level of endogenous opioids induces cross-tolerance against exogenous opioids¹⁴ and might increase the opioid requirement for postoperative analgesia. Chronic activation of the endogenous opioid system is known to down-regulate the HPA axis function, which might further augment the above responses¹⁵.

Second, it has been established that smoking can acutely reduce stress, and that withdrawal from tobacco is distressing to many smokers¹⁶. Supplemental analgesics, especially morphine which has a sedative effect might have helped suppress tobacco withdrawal in smokers, which resulted in the smoker's Ramsay scores similar to nonsmoker. The Ramsay score is considered to partially reflect irri-

tability and anxiety¹⁷ which may be a part of the nicotine withdrawal symptoms.

This study has several limitations besides its retrospective design. First, each cohort contained both patients who received background infusions and who did not. Previous studies have failed to show the advantage of continuous background infusions of opioids¹⁸, despite greater amount of opioids used compared with no-background administration. However, the proportion of patients receiving PCA with to without continuous infusion was not significantly different between the two groups. Second, the ratio of men to women in the smoking group was higher than that in the non-smoking group. Morin et al indicated that women may be less tolerant to pain than men¹⁹. Thus, the difference in supplemental analgesic use between the two groups may have been minimized. Third, we did not confirm of the duration of preoperative abstinence from smoking. Variations in the period of preoperative abstinence could have affected the result.

Conclusion

When intravenous PCA fentanyl is employed for postoperative analgesia, abstaining smokers tended to require more supplemental analgesics than non-smokers during the first 24 hours of the postoperative period. It should be reasonable to consider an additional analgesic requirement when managing postoperative pain in patients who smoke.

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喫煙患者における術後鎮痛剤使用量

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ニコチンは内因性オピオイド系に作用し、鎮痛作用を生じるが、入院期間中は禁煙の必要があり、急激なニコチン断絶により疼痛閾値の低下が予測される。そこで、喫煙者と非喫煙者との術後鎮痛剤使用量を測定するため、術後 Intravenous Patient-Controlled Analgesia (IV-PCA) フェンタニル使用量を後ろ向きに比較検討した。対象は、2005年1月から12月までの1年間で東京女子医科大学病院にて手術し、術後にIV-PCAを使用した者で、診療記録の不備、喫煙期間が1年未満、術前に鎮痛剤使用、PCA使用が24時間に満たない者を除外した。そして、たばこ1日1本を1年以上継続している喫煙群44例と禁煙期間が3ヵ月以上の非喫煙群102例の2群において、ICU入室時から24時間のフェンタニル使用量、鎮痛度 Visual Analog Scale (VAS)、鎮静度 Ramsay Score、呼吸抑制、嘔気・嘔吐といった副作用を比較した。その結果、体重当たりの術後フェンタニル使用量、副作用出現率、ICU入室時と24時間後のVAS、Ramsay Scoreは2群間で有意差がなかったが、フェンタニル以外の補助鎮痛剤使用率は喫煙群で有意に高かった。また、VAS値が高い症例でもフェンタニルを最大量まで使用せず、疼痛が軽減するまでPCAを有効に使用しない傾向にあった。本研究で補助鎮痛剤使用率が喫煙群で有意に高かった機序として、喫煙患者は外因性オピオイドに耐性があり、疼痛閾値が禁煙により低下し、禁煙による禁断症状を緩和させるなどを考える。