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ORIGINAL ARTICLE

EFFECTS OF DIFFERENT CONCENTRATION OF FENTANYL ON THE INCIDENCE AND SEVERITY OF FENTANYL-INDUCED COUGH DURING ANESTHESIA INDUCTION: A DOUBLE-BLIND CONTROLLED STUDY

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ABSTRACT:fentanyl induced cough is commonly occur during anesthesia, which should be prevented in these patients. The aim of this study was to assess different concentration of fentanyl on the incidence and severity of fentanyl-induced cough during anesthesia induction.This double blind randomized clinical trial was carried out in Shahid Mohammadi Hospital of Bandar Abbas on 150 patients aged between 18 and 50 who were candidates for elective surgery. All the 150 patients were allocated into three groups of 50 patients. Two minutes after different concentration of fentanyl injection, the intensity and number of coughs were assessed. Data were entered SPSS v. 19 and was analyzed using descriptive statistics, chi square and independents sample t test. The mean age of the patients of the first, second and third group was 24.4 ± 6.8, 25.3 ± 6.8 and 24.6 ± 6.6 years, respectively. The difference of age, gender, weight, body mass index (BMI), O_2 saturation level, systolic and diastolic blood pressure of the patients of the three groups were not significant. The incidence of cough was 22%, 6% and 10% among the patients of the first, second and third group, respectively. The difference between cough incidence was significant (P=0.031) and there was a significant relationship between cough intensity and fentanyl concentration (p=0.044). the results of this study indicates low dose fentanyl may be effective method for reducing incidence and severity of fentanyl induced cough during anesthesia induction.

Key words: fentanyl, cough, anesthesia induction

INTRODUCTION

Opioids act as agonist in surface of three-dimensional receptors in the central nervous system and other tissues.The opioids to mimic the actions of endogenous opioid peptide ligands and leading to pain relief (1-7).

Fentanyl is a synthetic opioid agonist analgesic being 75 to 125 times more potent than morphine. Administration of a single dose of Fentanyl faster onset and shorter duration of action is to morphine. Higher power and faster onset of action of fentanyl versus morphine represents a higher solubility in lipids that it passes through the membrane to facilitate blooded brain (8-12).

The most serious side effect of opioids is respiratory depression. Although drug-induced respiratory depression of opioids are predictable, but its incidence is about 0.1 - 1 percent. Observations show that both μ and δ receptors are involved in these complications (13, 14).

Cough after Fentanyl administration is common and numerous studies that have reported (15-23). Fentanyl because lack of cardiovascular depression and histamine release used for analgesia during anesthesia commonly (19, 21).

Although fentanyl-induced cough is not a serious side effect in anesthesia but is unpleasant and can cause increased intracranial pressure, intra-abdominal pressure and intra ocular pressure, especially in patients with intracranial space-occupying lesions or glaucoma is be dangerous (19-23).

Slower injection of fentanyl and the use of drugs such as propofol (15, 58), ketamine (22, 58), lidocaine (13, 58), dexamethasone, clonidine before of fentanyl injection including various methods that have been used to prevent or minimize fentanyl-induced cough (58).

Given that the drug concentration is a simple and uncomplicated, the goal of this study was assess the effects of different concentration of fentanylon

the incidence and severity of fentanyl-induced cough during anesthesia.

METHODS

In this double blind clinical trial study, 150 patients that aged from 14 to 50 years old, according to physical classification of American society ofanesthesiology ranged in ASA class I were evaluated. This study is approved in ethic committee of Bandar AbbasUniversity of medical science. Initial vital signs and demographic characteristics of the patients were recorded.

Patient with positive history of asthma, smoking, chronic pulmonary disease, respiratory infection in recent two weeks or using steroid drugs, bronchodilators and ACE inhibitors, were excluded.

As the surgery begins routine monitoring including electrocardiogram, non invasive blood pressure calf, pulse oximetery, and capnograph was connected to patient and an intravenous cannula 18-20 was inserted in posterior vein of right arm, and serum was injected through a triode with maximum rate. Fentanyl in 50, 25 and 10 microgram per ml was prepared in three syringe labeled as A, B and C,then Fentanyl were injected 2 microgram per kg.

In first group (50 patients) Fentanyl with 50 microgram per ml concentration were injected in 5 seconds and in second and third groups containing 50 patients respectively with 25 and 10 micro gram per ml concentration. Then all patient were monitored for 2 minutes, and cough onset and its severity (mild: 1or 2 cough, moderate: 3-5 cough, and severe more than 5 cough) by the anesthetist who was blindto thestudy design and drug concentration were evaluated. Anesthesia induction in all groups, by the same method and by injection of 0.03mg midazolam and 1.5-2mg propophol per kg, was done. And if intubation and muscle relaxant were needed, we used 0.5 mg terbocurarin per kg. The information was analyzed by SPSS-19 statistical software and statistical tests including: t test and chi square, and $P<0.05$ was considered significant.

RESULTS

In this study 150 patient were included, containing 112 male (74.7%) and 38 female (25.3%). Mean age of these patients was 24.8± 6.6 years old. Average weight for the patients was 64.96 kg and average height was 170.66±9.01 cm.averaged oxygen saturation percentage was 98.90±1.20, mean systolic blood pressure was 123.40±8.3, mean diastolic blood pressure was 74.69 ±5.09, and heart rate was 83.96±12.5 beat per minute. Table 1 showed basic characteristic for participant and these variables are shown separately for each group in table 2.

Table 1: Some variables in the study participants.

	mean	Standard deviation	min	max
Age	24.8	6.66	14	50
Weight	64.96	13.06	38	104
Height	170.66	9.01	148	195
BMI	3.72	22.27	15.2	37.7
Oxygen saturation	98.90	1.20	95	100
Systolic blood pressure	123.40	8.33	92	140
Diastolic blood pressure	74.69	5.09	59	85
Heart rate	83.96	12.59	52	108

Average baseline oxygen saturation before anesthesia for the first, second and third group was respectively 98.7±1.2, 98.8±1.2 and 99.1±1.1, and this difference wasn't significant.

Mean systolic blood pressure before anesthesia for patient in group 1, 2 and 3 was 124.5±7.45, 122.6±8.61, 123.04±8.907 respectively.That was no statistical differences seen.

Table 2: Basic characteristics of the patients before anesthesia.

		Group A (50 µg/ml)	Group B (25 µg/ml)	Group C (10 µg/ml)	P-value
Age		24.4±6.8	25.3±6.5	24.46±6.6	0.777
Sex	Male	34(74%)	33(66%)	42(84%)	0.116
	Female	13(26%)	17(34%)	8(16%)	
Weight		64.2±12.9	65.4±14.1	0.887	0.887
Height		170.1±9.8	169.8±8.8	172.04±8.32	0.418
BMI		22.21±3.8	22.58±4.06	22.05±3.2	0.776
Oxygen saturation		98.7±1.2	98.8±1.2	99.1±1.1	0.246
Systolic blood pressure		124.5±7.4	122.6±8.6	123.04±8.9	0.502
Diastolic blood pressure		73.5±5.5	74.96±4.6	123.4±8.3	0.112
Heart rate		85.6±11.9	85.54±12.09	80.7±13.32	0.079

Mean diastolic blood pressure before anesthesia for patient in first, second and third group was 73.5±5.599, 74.96±4.695 and 73.4_±4.33 respectively, and their difference wasn't statistically significant.

Average heart rate before anesthesia for patient in first, second and third group was 85.6±11.9, 85.54±12.09 and 80.7±13.3 and this difference wasn't statistically significant too.

No patient in three groups was smoker. No patient suffered from underlying disease such as asthma, cough before surgery, common cold, upper respiratory tract infection, and chronic pulmonary disease and also no body used corticosteroids, bronchodilators and ACE inhibitors.

As shown in table 3, in first group 11 patient coughed, 3patients have mild cough, 3 have moderate cough and 3 have severe cough. In second group, 3 patientscoughed and all coughs were mild. In third group 5 patientscoughed, and among them 4patients have mild cough and one patient have moderate cough.

Table 3: Incidence and severity of cough in study participants.

	No cough	Mild	Moderate	Severe	P-value
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	
Group A (50 µg/ml)	39(78)	3(6)	3(6)	5(10)	0.031
Group B (25 µg/ml)	46(92)	3(6)	0(0)	0(0)	
Group C (10 µg/ml)	45(90)	4(8)	1(2)	0(0)	

There were a significant correlation between cough severity and Fentanyl concentration.Also there were a significant correlation between cough incidence and Fentanyl concentration.

There were no reported nausea, vomiting, itching, apnea, and muscle spasm among patient in all groups.

DISCUSSION

In overall cough incidence after Fentanyl injection varies in a large scale from 1 to 56 percent. That maybe depends on Fentanyl dose, drug injection rate, and time of drug injection (24). In or to minimizing this reflex, several steps including:ketamine,dextromethorphan, lidocaine and clonidineprescription was done (25, 26, 27).

In this study we evaluated the effect of Fentanyl concentration on cough incidence and its severity. There were no significant differences about baseline oxygen saturation and demographic characteristic, among patient in three groups but cough occurrence, 2 minute after Fentanyl injection with 50, 25, and 10 microgram per ml was 22, 6 and 10 percent respectively.

In oshimaet alstudy showed that, smoking, chronic lung disease, history of asthma, gender, and ACE inhibitors are disturbing factors of Fentanyl

induced cough. In our study no patient suffers from mentioned disease and no one smokes (28). But inLin et al study observed that cough occurrence rate in smokers who use less than 10 cigarettesper day,is less than nonsmoker patient (29).

In our study, in the first group 11 patient coughed, 3 had mild cough, 3 had moderate cough and 3 had severe cough. In second group 3 patients coughed and all of them had mild cough. In the third group 5 patientscoughed, that 4 of them had mild cough and 1 had moderate cough.There were a significant correlation between cough severity (P=0.031) and incidence (P=0.044) with Fentanyl concentration. it means that when Fentanyl concentration become less than 50 micro gram ,cough incidence and cough severity decline too.

Hunt and assistants reported that patients was treated with 25 microgram Fentanyl,coughed just 3.5 percent ,while patient was treated with 150 micro gram Fentanyl coughed by 18.5 percent. They considered this differencewas significant(P<0.001) (30) and this result is consistent with our study. It has been shown in Yu et al study that Fentanyl in 10 microgram per ml concentration lead to more depletion in cough incidence and severity compared to 50 microgram per ml concentration (31). They showed that this difference is significant and this finding is consistent with our study.

Most studies in this area show that lower dose of fentanyl before induction of anesthesia can significantly help fentanyl-induced cough symptoms (22, 32, 33). But Jung et al study showed that a lower dose of fentanyl before induction significant impact on the incidence and severity of fentanyl-induced cough (34).

In Schäpermeieret alstudy, average age for the first, second and third groups were 54±16, 54±14 and 52±15respectively (35). InHorng study average age for patient in group 1, 2 and 3 was 44.8±3.17, 40.5 ±17.5 and 44.2±18 respectively (26).While according to our results,average age for first, second and third group was 24.4±6.8, 25.3±6.5 and 24.6±6.6 respectively. It means that there was not any significant difference about age in our study. Another hand patientsin our study were younger (35). its seems that selecting archetype from younger age is suitablefor removing disturbing factor,and can be justified by increase activity of motivation receptor in young people. Finally analysis of all data about patientage didn'tshowedsignificant correlation between age and cough incidence.

In our study average body weight for patient in first, second and third groups was 64.2±12.9, 65.4±14.1 and 65.2 ±12.2 kg respectively and there were no significant difference for weight in three groups.In Schäpermeieret al study average body weight for the first, second and third group was 81±15, 78±15 and 81±17 kg respectively, and no significant difference about weight was seen.InHornget alstudy, average body weight for the first, second and third group was 62.9±5.11, 63.7±10.4 and 62.8 ±11.7 kg respectively. Patient participating in our and Horng study had same weight but had lower weight than patient in Schäpermeier study (26, 35).

In our study,mean systolic blood pressure was 123.40±8.3 mmHg, mean diastolic blood pressure was 74.693±5.097 mmHg, and patient pulse rate was 83.996±12.595 per minute.Therewas no significant difference between about systolic and diastolic blood pressure and heart rate of patient in all groups. It was shown in Hung study that mean systolic blood pressure, mean diastolic blood pressure, andaveraged pulse rate was 136.6±19.1, 77.9 ±11.2 mmHg and 76.4±14.6 per minute respectively and no significant difference was seen (30, 36).This result was consistent with our results too.

Conclusion

This study shows that decreased concentration of Fentanyl lead to considerable depletion of cough incidence.We suggest more studies with larger sample size for verification of this study and it seems that systemic review all studies are needed to evaluation of appropriate concentration of Fentanyl.

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