ScienceForecast
A digital science library

Research Article
Published: 26 Jan, 2018

Journal of Anesthesia Forecast

Investigating the Effects of Premedication with Low-Dose Fentanyl, Lidocaine and Ketamine on Fentanyl-Induced Cough

*Hatami M[1], Hobab H[1], Ayatollahi V[1] and Vaziribozorg S[2]**

[1]Departments of Anesthesiology, Pain Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[2]Department of Otolaryngology-Head and Neck Surgery, Otorhinolaryngology Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Abstract

Objective: This study was designed to investigate whether premedication with low-dose fentanyl, lidocaine and ketamine can decrease the incidence of FIC efficiently.

Design: A randomized double-blind clinical trial study.

Setting: Shahid Sadoughi hospital, Shahid Sadoughi University of medical sciences, Yazd, Iran.

Patients or Subjects: 200 patients undergoing surgery were randomly allocated into four groups (F, L, K, N; n = 50).

Interventions: The patients in all groups were given 5mL fentanyl (25μg) or lidocaine (1mg/kg) or ketamine (0.15mg/kg) or normal saline, respectively, (IV) over 5 seconds. After 1 minute, a fentanyl bolus (2μg/kg) was injected into all patients over 2 to 3 seconds. The incidence of cough and hemodynamic alterations were then investigated among the four groups.

Measurements and Main Results: The incidence of FIC was 16% in group F, 14% in group L, 24%in group K, and 46% in group N. The incidence of FIC in group N (the control) was significantly more than other groups. The SBP and MAP in lidocaine group were significantly higher than other groups. There was no significant difference regarding onset time of cough among the four groups.

Conclusions: Our study suggests that premedication with low-dose fentanyl (25μg), lidocaine (1mg/kg), and ketamine (0.15mg/kg) 1 min prior to the higher bolus dose of fentanyl can efficiently reduce cough and can be a simple and cost-effective technique for prevention of fentanyl-induced coughing, without any harmful effects on the patient's hemodynamic status.

Keywords: Fentanyl; Lidocaine; Ketamine; Fentanyl-induced cough

Introduction

During anesthesia induction for surgery, most patients may experience some sympathetic and psychological adverse effects [1]. Opioids are applied to allay anxiety and pain associated with surgery [2]. Fentanyl is one of the most broadly used opioids for analgesia due to its fast onset of action, cardiovascular stability and strong analgesic effect [3,4]. Fentanyl is also often applied in general anesthesia (GA), since it can facilitate tracheal intubation and prevent tube-induced cough [5,6]. Fentanyl itself can lead to cough [7] and the incidence of fentanyl-induced cough (FIC) differs from 28 to 46% according to prior reports [8]. An intravenous bolus of fentanyl can often induce a cough reflex [9]. To date, fentanyl-induced cough has received low attention because it rarely causes serious effects in most ASA I-II patients under surgery [7]. FIC is not an unusual phenomenon during the induction of GA [10]. The vast majority of FIC are benign, with scarce events of spasmodic and explosive coughing [11,12]. Of course, FIC is accompanied by great intrathoracic pressure and can increase intraocular, intracranial, and intra abdominal pressures, so it should be efficiently prevented in patients needing a steady induction at the beginning of GA, especially in those with elevated intracranial pressure, acute glaucoma, penetrating eye injury, dissecting aneurysm, serious airway responsiveness, full stomach, pneumothorax and so on. Additionally, severe FIC can cause fatal upper airway obstruction and aspiration pneumonia, which need immediate intervention [7]. The mechanism of FIC is unknown, and various agents and techniques are used to decrease its

OPEN ACCESS

*Correspondence:
Vaziribozorg S, Department of Otolaryngology-Head and Neck Surgery, Otorhinolaryngology Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
Tel: +983538113368
E-mail: s.vaziribozorg1408@gmail.com

Received Date: 02 Oct 2017
Accepted Date: 15 Jan 2018
Published Date: 26 Jan 2018

Citation: Hatami M, Hobab H, Ayatollahi V, Vaziribozorg S. Investigating the Effects of Premedication with Low-Dose Fentanyl, Lidocaine and Ketamine on Fentanyl-Induced Cough. J Anesthesia Forecast. 2018; 1(1): 1001.

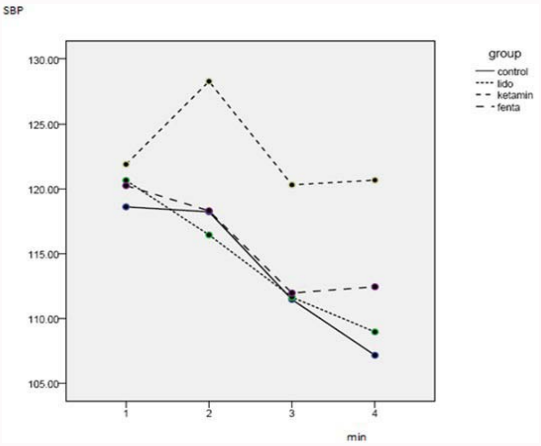

Figure 1: Systolic blood pressure (SBP) alterations during anesthesia.

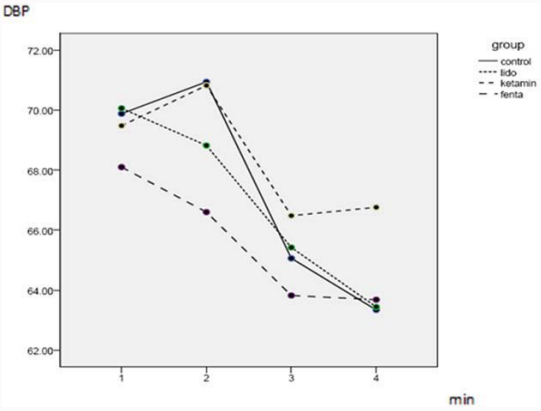

Figure 2: Diastolic blood pressure (DBP) alterations during anesthesia.

incidence [13]. Some studies have found that premedication with certain agents (e.g. clonidine, dexmedetomidine, lidocaine, dezocine, ketamine and so on) could decrease the incidence of FIC [7]. All these agents have bronchorelaxant effects on airway smooth muscle [14]; however, these methods are not uniformly effective [15].

Given that prevention of fentanyl-induced cough (FIC) is a significant clinical implication [16], the present study was designed to investigate whether premedication with low-dose fentanyl, lidocaine, and ketamine can decrease the incidence of FIC efficiently.

Materials and Methods

After approval by ethics committee and obtaining written informed consent, in this double-blinded randomized placebo-controlled study, 200 patients aged between 18 to 50 years old, with ASA I or II underwent surgery under general anesthesia involved. Patients with BMI<30, history of asthma, smoking, upper respiratory tract infection in recent two weeks, chronic cough, and history of using steroids drugs or bronchodilators were excluded. Patients were randomly allocated in four groups (I, II, III, IV; n = 50 for each group) using a computer-generated table of random numbers. Patients were pretreated with IV midazolam 0.02mg/kg 10min before Induction of anesthesia in the operating room. The patients in groups I, II, III and IV were given 5mL fentanyl (25μg), lidocaine (1mg/kg), ketamine (0.15mg/kg) or normal saline (as the control group), respectively, intravenously (IV) over 5 seconds. After 1 minute, a fentanyl bolus (2μg/kg) was then injected into all patients over 2 to 3 seconds.

Table 1: The incidence of fentanyl-induced cough (FIC) in four groups.

Groups	fentanyl-induced cough			P.value[a]
	Mild cough, N (%)	Moderate cough, N (%)	Sever cough, N (%)	
Group I (fentanyl)	5 (62.5)	3 (37.5)	0	0.03
Group II (lidocaine)	4 (57.1)	3 (42.9)	0	
Group III (ketamine)	7 (58.3)	4 (33.3)	1 (8.3)	
Group IV (saline)	3 (13)	13 (56.5)	7 (30.4)	

[a] Chi-square test

Table 2: Onset time of cough after fentanyl injection.

Groups	Onset time of cough [a]	p-value [b]
Group I (fentanyl)	13.12±5.9	> 0.05
Group II (lidocaine)	20.18±18.13	
Group III (ketamine)	14.57±6.29	
Group IV (saline)	16.25±12.58	

[a] Mean ± SD
[b] Kruskal-Wallis Test

Immediately, an observer, blinded to the groups, noted the incidence and severity of cough during the next 1 min. Any episodes of cough within 1 min of fentanyl administration was classified as FIC, and the severity was graded based on the number of coughs (mild, 1–2; moderate, 3–5; and severe, >5). The patient's vital signs such as systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded 1 min before primary drug injection, before fentanyl bolus injection, and 1 and 3 minutes after fentanyl bolus injection. SPSS (version 15) was used for statistical analysis. P<0.05 was considered as significant.

Results

The mean age of participants in group I (fentanyl), II (lidocaine), III (ketamine) and IV (normal saline) was 30.58±11.3, 29.60±11.7, 31.20±11.20 and 31.52±12.70, respectively. Four groups had no significant difference in terms of mean age (p=0.89). The incidence of FIC was 16% in group I, 14% in group II, 24%in group III, and 46% in group IV (Table 1). The incidence of FIC in group IV (the control) was significantly more than the other groups (p<0.05). The incidence of FIC in group II (lidocaine) and I (fentanyle) were significantly lower than other groups (p<0.05). There was no significant difference considering the onset time of cough among the four groups (p=0.97) (Table 2). The patient's hemodynamics data (SBP, DBP, MAP) were recorded 1 min before primary drug injection, before fentanyl bolus injection, and 1and 3 min after fentanyl bolus injection (Figure 1 and 2). The chi-square test showed that SBP and MAP in group II (lidocaine) were significantly more than other groups (p=0.005 and 0.028, respectively). There was no significant difference regarding DBP among the four groups (p=0.474).

Discussion

Fentanyl itself can lead to cough [7] and the incidence of fentanyl-induced cough (FIC) differs from 28 to 46% according to prior reports [8]. Various efforts have been made to decrease the incidence of FIC during induction of anesthesia [10]. A number of studies have been designed to decrease the incidence of FIC using available anesthetic agents (eg, lidocaine, propofol, ephedrine, midazolam, and atropine with varying success) [16]. In our study, antitussive effect of premedication with Intravenous lidocaine and low-dose fentanyl was more than ketamine. There was no significant difference in the onset

time of cough among the four groups. Pandey et al. suggested that Intravenous lidocaine 1.5mg/kg, when administered 1 min before bolus fentanyl, is considerably effective in preventing FIC compared to placebo (0.9% saline), without affecting the severity of cough [17]. In another study, Pandey et al. showed that IV lidocaine 0.5mg/kg is the least dose required to prevent FIC when administered 1min prior to fentanyl [18]. It is recognized that IV ketamine, an NMDA antagonist, has well-known effective analgesic and bronchodilatory effects [16]. Yeh et al. represented that Low-dose ketamine (0.15mg/kg IV) effectively decreases FIC and delays the onset time of cough [16]. Guler et al. demonstrated that IV ketamine (0.5mg/kg) considerably reduced the FIC with lidocaine and placebo [19]. Shrestha et al. found that pre-emptive use of least dose fentanyl 25μg administered 1 min before a higher bolus dose of fentanyl (125 or 150μg) can efficiently prevent cough [2]. Gu C et al. reported that a primary dose of fentanyl 0.5μg/kg prevented FIC during induction of anesthesia in clinical practice. FIC was positively associated with the dose of fentanyl [10]. In our study, the incidence of FIC was lower in group I (pretreated with low-dose fentanyl) than placebo group which was in line with previous findings. Our hemodynamics data showed that SBP and MAP in group II (lidocaine) were significantly more than other groups (p=0.005 and 0.028, respectively). However, these hemodynamic changes were not serious and harmful for the patients. There was no significant difference in DBP among the four groups.

Conclusion

Our study suggests that premedication with low dose fentanyl (25μg), lidocaine (1mg/kg), and or ketamine (0.15mg/kg) 1min previous to the higher bolus dose of fentanyl can efficiently prevent cough and can be a simple and cost effective process for prevention of FIC, without any harmful effects on the patient's hemodynamic status. These agents caused no delay in onset time of fentanyl induced coughing.

Acknowledgment

*Authors have no conflicts of interest.

*Study protocol was in accordance with the latest Declaration of Helsinki for medical research involving human subjects and was approved by ethics committee of Shahid Sadoughi University of medical sciences.

This article does not contain any studies with animals performed by any of the authors

*Informed consent was obtained from all participants of the study.

References

1. Saleh AJ, Zhang L, Hadi SM, Ouyang W. A priming dose of intravenous ketamine-dexmedetomidine suppresses fentanyl-induced coughing: A double-blind, randomized, controlled study. Upsala journal of medical sciences. 2014; 119: 333-337.
2. Shrestha S, Bhattarai B, Shah R. Preemptive use of small dose fentanyl suppresses fentanyl induced cough. Kathmandu University Medical Journal. 2012; 10: 16-19.
3. Smith H. A comprehensive review of rapid-onset opioids for breakthrough pain. CNS drugs. 2012; 26: 509-535.
4. Mireskandari SM, Abulahrar N, Darabi ME, Rahimi I, Haji-Mohamadi F. Comparison of the effect of fentanyl, sufentanil, alfentanil and remifentanil on cardiovascular response to tracheal intubation in children. Iranian journal of pediatrics. 2011; 21: 173-180.
5. Inomata S, Maeda T, Shimizu T, Satsumae T, Tanaka M. Effects of fentanyl infusion on tracheal intubation and emergence agitation in preschool children anaesthetized with sevoflurane. British journal of anaesthesia. 2010; 105: 361-367.
6. Yoo YC, Na S, Jeong JJ, Choi EM, Moon BE, Lee JR. Dose-dependent attenuation by fentanyl on cough during emergence from general anesthesia. Acta Anaesthesiologica Scandinavica. 2011; 55: 1215-1220.
7. Du BX, Cao L, Zhao WL, Xu ZH, Song J, Shi XY. Pre-emptive small dose of fentanyl suppresses fentanyl-induced cough: a meta-analysis of randomized controlled trials. Int J Clin Exp Med. 2014; 7: 826-836.
8. Lin CS, Sun WZ, Chan WH, Lin CJ, Yeh HM, Mok MS. Intravenous lidocaine and ephedrine, but not propofol, suppress fentanyl-induced cough. Canadian Journal of Anesthesia. 2004; 51: 654-659.
9. Horng HC, Lin BF, Wang TC, Lin SL, Liaw WJ, Wang HJ, et al. Priming dose of intravenous rocuronium suppresses fentanyl-induced coughing. Acta anaesthesiologica Taiwanica: official journal of the Taiwan Society of Anesthesiologists. 2012; 50: 147-149.
10. Gu C, Zhou M, Wu H, Li F, Tang Q. Effects of different priming doses of fentanyl on fentanyl-induced cough: a double-blind, randomized, controlled study. Pharmacological reports: PR. 2012; 64: 321-325.
11. Ambesh S, Singh N, Srivastava K. Fentanyl induced coughing caused life-threatening airway obstruction in a patient with arteriovenous malformation of tongue and hypopharynx. Int J Anesthesiol. 2009; 20.
12. Tweed WA, Dakin D. Explosive coughing after bolus fentanyl injection. Anesthesia & Analgesia. 2001; 92: 1442-1443.
13. He L, Xu J-M, Dai R-P. Dexmedetomidine reduces the incidence of fentanyl-induced cough: a double-blind, randomized, and placebo-controlled study. Upsala journal of medical sciences. 2012; 117: 18-21.
14. Tang Q, Qian Y, Zhang Q, Yang J, Wang Z. Effects of different priming doses of propofol on fentanyl-induced cough during anesthesia induction: a preliminary randomized controlled study. Upsala journal of medical sciences. 2010; 115: 121-124.
15. Ai Q, Hu Y, Wang Y, Wu S, Qin Z, Wang J, et al. Pentazocine pretreatment suppresses fentanyl-induced cough. Pharmacological reports. 2010; 62: 747-750.
16. Yeh CC, Wu CT, Huh BK, Lee MS, Lin SL, Sheen MJ, et al. Premedication with intravenous low-dose ketamine suppresses fentanyl-induced cough. Journal of clinical anesthesia. 2007; 19: 53-56.
17. Pandey CK, Raza M, Ranjan R, Lakra A, Agarwal A, Singh U, et al. Intravenous lidocaine suppresses fentanyl-induced coughing: a double-blind, prospective, randomized placebo-controlled study. Anesthesia and analgesia. 2004; 99: 1696-1698.
18. Pandey CK, Raza M, Ranjan R, Singhal V, Kumar M, Lakra A, et al. Intravenous lidocaine 0.5mg.kg^{-1} effectively suppresses fentanyl-induced cough. Canadian journal of anaesthesia = Journal canadien d'anesthesie. 2005; 52: 172-175.
19. Guler G, Aksu R, Bicer C, Tosun Z, Boyaci A. Comparison of the effects of ketamine or lidocaine on fentanyl-induced cough in patients undergoing surgery: A prospective, double-blind, randomized, placebo-controlled study. Current therapeutic research, clinical and experimental. 2010; 71: 289-297.