WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 8, Issue 3, 255-267. Research Article ISSN 2277– 7105

THE EFFICACY OF FENTANYL AND FENTANYL PLUS LIDOCAINE IN HYPERTENSION

Basim Abed Kassim* and Ashwaq Basim Hamed

Ministry of Health - Baghdad Medical Office - Al-Karkh, - Al-Kadhimiya Teaching Hospital, Baghdad, Iraq.

Department of Anesthesia and Intensive Care

Specialist of Anesthesia and Intensive Care

Article Received on
08 Jan. 2019,

Revised on 29 Jan. 2019,
Accepted on 18 Feb. 2019

DOI: 10.20959/wjpr20193-14345

***Corresponding Author**
Basim Abed Kassim
Ministry of Health - Baghdad Medical Office - Al-Karkh, - Al-Kadhimiya Teaching Hospital, Baghdad, Iraq.

ABSTRACT

This trial aimed to evaluate and to compare the efficacy of fentanyl and fentanyl plus lidocaine in hypertension. We conducted a prospective, randomized, doubleblind trial in 40 patients with hypertension in the alkark Hospital, Iraq, from March to December 2018. T. Including criteria comprised; elective surgery with general anesthesia, 65 > age > 20, ASA class II patients (hypertensive patients). Excluding criteria; patients undergoing heart surgery, ASA III or above, CHF (congestive heart failure, arrhythmia, 20 > age > 65 years, problems with intubation, intubation time greater than 15 seconds, contraindications to lidocaine use, and no control of hypertension and/or asthma. We found that fentanyl and fentanyl plus lidocaine are effective medications on hemodynamic responses (HR, SBP and DBP) decreasing before induction, three minutes before intubation and 1, 3 and 5 minutes after intubation.

KEYWORDS: fentanyl, fentanyl plus lidocaine, hypertension.

INTRODUCTION

Tracheal intubation may induce; hypertension, tachycardia, and/or arrhythmia. These tracheal responses are mediated by sympathetic responses and are normally well tolerated by normotensive patients. However, induction of anesthesia and endotracheal intubation often produces a period of hemodynamic instability for hypertensive patients and regardless of the level of preoperative blood pressure control, many patients with hypertension display an accentuated hypotensive response to induction of anesthesia, followed by an exaggerated

hypertensive response to endotracheal intubation. Endotracheal intubation of the trachea stimulates laryngeal and tracheal sensory receptors, resulting in a marked increase in the elaboration of sympathetic amines (adrenaline and noradrenaline), this sympathetic stimulation results in tachycardia and elevation of blood pressure.[1]

Thus diverse classes of drugs and different techniques such as; local anesthetics, opioids, calcium channel blockers, short acting β-adrenergic blockers, and their combinations have been used to prevent hemodynamic responses induced by laryngoscopy and endotracheal intubation[2]. The hypothetical background for the use of these methods for laryngoscopy and tracheal intubation is that these adjuvant measures may be able to decrease hemodynamic responses by blocking intense sympathetic discharge caused by stimulation of the upper airway. Fentanyl is a frequently used opioid that joins with hypnotic agents to diminish hemodynamic responses to tracheal intubation.[3]

Furthermore, lidocaine has a suppressive effect on the circulatory responses in patients undergoing laryngoscopy and tracheal intubation.[4]

The poor physical condition of the patient, emergency intubation and use of drugs to induce anesthesia during intubation, cause complications. one of these complications is the stimulation of the sympathetic system as hypertension and tachycardia. These complications can increase mortality and morbidity.[5]

In order to relieve these stress-induced responses of the various drugs different methods have been proposed. Lidocaine is one of those drugs. Lidocaine is a local anesthetic and an anti-arrhythmic drug that can suppress this complication.[6]

Lidocaine was used for spinal anesthesia and also injected around the dura-mater. Lidocaine intravenously was used in cardiac arrhythmias, ventricular arrhythmias, in particular applications. It is a Class Ib anti-arrhythmic drug and is effective on the zero phases of the cardiac cells action potential.[7]

OBJECTIVES

This trial aimed to evaluate and to compare the efficacy of fentanyl and fentanyl plus lidocaine in hypertension.

BACK GROUND

High blood pressure (hypertension) is often called a silent killer because you can have it for years without knowing it. In fact, about 50 million Americans have high blood pressure, but about 30 percent of them don't know it. Blood pressure is determined by the amount of blood your heart pumps and the amount of resistance to blood flow in your arteries. Your blood pressure normally varies during the day. It can even vary slightly with each beat of your heart. It increases during activity and decreases with rest.[8]

Many people may not view high blood pressure as life-threatening. But uncontrolled high blood pressure can increase your risk of serious health problems. Fortunately, high blood pressure can be detected with a simple test — and once you know you have high blood pressure, you can work with your doctor to control it.

Signs and symptoms

Most people with high blood pressure have no signs or symptoms, but people often think that headaches, dizziness or nosebleeds are common warning signs and symptoms of high blood pressure. It's true that a few people with early-stage high blood pressure have a dull ache in the back of their heads when they wake in the morning. Or perhaps they have a few more nosebleeds than normal.[9]

Headaches, dizziness or nosebleeds typically don't occur until high blood pressure has reached a more advanced stage — one that's possibly life-threatening. Even so, most people with the highest blood pressure readings don't experience any of these symptoms. Other signs and symptoms sometimes associated with high blood pressure generally are caused by other conditions that can lead to high blood pressure. Such signs and symptoms include:

- Excessive perspiration
- Muscle cramps
- Weakness
- Frequent urination
- Rapid or irregular heartbeat (palpitations).

Causes

The more blood your heart pumps and the narrower your arteries, the higher your blood pressure. A blood pressure reading consists of two numbers:

- **The top number indicates systolic pressure.** This is the amount of pressure your heart generates when pumping blood out through your arteries.
- **The bottom number indicates diastolic pressure.** This is the amount of pressure in your arteries when your heart is at rest between beats.[10]

The most recent guidelines for high blood pressure were issued in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC) and published in the *Journal of the American Medical Association* in May 2003. The JNC represents a coalition of leaders from 46 professional, public, voluntary and federal health care agencies, including the American College of Cardiology, the American Diabetes Association, the American Heart Association, the American Public Health Association, the American Society of Hypertension, and the National Heart, Lung, and Blood Institute. According to these guidelines, blood pressure for adults is classified as follows:

- **Normal blood pressure.** Your blood pressure is normal only if it's below 120/80 millimeters of mercury (mm Hg), but some data indicate that 115/75 mm Hg should be the new gold standard. Once your blood pressure rises above that threshold, your risk of cardiovascular disease may begin to increase.
- **Prehypertension.** Prehypertension is a systolic pressure ranging from 120 to 139 or a diastolic pressure ranging from 80 to 89. If your blood pressure is right at 120/80, you have prehypertension — your blood pressure isn't normal or optimal.
- **Stage 1 hypertension.** This includes a systolic pressure ranging from 140 to 159 or a diastolic pressure ranging from 90 to 99.
- **Stage 2 hypertension.** The most severe hypertension, this includes a systolic pressure of 160 or higher or a diastolic pressure of 100 or higher[11].

Only one of the numbers — the top or the bottom — needs to be high for you to have prehypertension or hypertension. In 90 percent to 95 percent of high blood pressure cases, there's no identifiable cause. This type of high blood pressure is called essential hypertension or primary hypertension. It differs from secondary hypertension, in which the increased pressure results from another underlying condition, such as:

- Kidney disease

- Adrenal disease
- Thyroid disease
- Abnormal blood vessels
- Preeclampsia — high blood pressure and protein in the urine after the 20th week of pregnancy
- Sleep apnea

Certain medications, including birth control pills, cold remedies, decongestants, over-the-counter pain relievers and some prescription drugs, may also cause secondary hypertension.

Although acetaminophen (Tylenol, others) was once considered very safe, researchers reported in September 2005 that regular use of higher doses may increase the risk of secondary hypertension. Researchers studied 5,000 women who didn't have high blood pressure when the studies began. Women who took an average of 500 milligrams or more of acetaminophen daily over several years were more likely to develop high blood pressure than were women who didn't take any acetaminophen. It's not known if the same holds true for men since they weren't included in this study. The women were part of two phases of the Nurses' Health Study, a study of more than 200,000 nurses that began in 1976 and still continues.[12] Illegal drugs, such as cocaine and amphetamines, can also increase blood pressure. Secondary hypertension may have a more rapid onset and cause higher blood pressure than does primary hypertension, which tends to develop gradually over many years.[13]

Risk factors

There are four major risk factors for high blood pressure that you can't control. They are[14]:

- **Age.** Your risk of high blood pressure increases as you get older.
- **Race.** High blood pressure occurs far more frequently in blacks than in any other racial group in the United States. High blood pressure in blacks generally develops at an earlier age than it does in whites. Plus, it's more likely to lead to serious complications such as stroke or heart attack.
- **Sex.** In young adulthood and early middle age, high blood pressure is more common in men than in women, but the opposite is true for men and women age 60 and older.[15]
- **Family history.** High blood pressure tends to run in families.

The risk factors you can control or manage include:

- **Obesity.** The greater the body mass you have, the more blood you need to supply oxygen and nutrients to your tissues. The volume of blood circulated through your blood vessels increases and creates an extra force on your artery walls. In addition, fat cells produce chemicals that circulate and affect your blood vessels and heart.[16]
- **Inactivity.** Lack of physical activity increases your risk of high blood pressure by increasing your risk of being overweight. Inactive people also tend to have higher heart rates. Their heart muscles have to work harder with each contraction, increasing the force on the arteries.
- **Tobacco use.** The chemicals in tobacco can damage the lining of your artery walls, causing the arteries to accumulate fatty deposits that contain cholesterol (plaques). Nicotine also constricts your blood vessels and forces your heart to work harder.
- **Sodium sensitivity and salt intake.** People who are sodium sensitive retain sodium more easily, leading to fluid retention and increased blood pressure.
- **Low potassium intake.** Potassium is a mineral that helps balance the amount of sodium in your cells. If you don't consume or retain enough potassium, you can accumulate too much sodium.
- **Excessive alcohol.** Exactly how or why alcohol increases blood pressure isn't understood. But over time, heavy drinking can damage your heart muscle.[17]
- **Stress.** High levels of stress can lead to a temporary but dramatic increase in blood pressure. Stress also can promote high blood pressure if you then try to relax by eating more, using more nicotine or drinking more alcohol.

You may also be at increased risk of high blood pressure if you have certain chronic conditions. Examples include high blood cholesterol, diabetes and sleep apnea.[18] High blood pressure in children, more often than in adults, indicates that something else is wrong, and the increase in blood pressure is a sign of an underlying condition. In general, high blood pressure in children is uncommon. However, as an increasing number of children become less physically active and more obese, a greater percentage of them are developing high blood pressure.

Screening and diagnosis

Blood pressure is measured with a medical device called a sphygmomanometer, which consists of an inflatable arm cuff and a pressure-measuring gauge. High blood pressure is

most often discovered during a routine physical examination. However, a single high blood pressure reading usually isn't enough for a diagnosis. You have high blood pressure only if your blood pressure readings are persistently high at two or more office visits over several weeks or months.

Everyone's blood pressure normally varies throughout the day. And some people have a rise in blood pressure especially during visits to a doctor — a phenomenon known as white-coat hypertension. That's why it's important to take more than one reading and on more than one occasion. Your doctor may ask you to record your blood pressure at home and at work to provide additional information.[19]

For years health professionals tended to focus on diastolic pressure, which is the bottom number. The theory was this: The body can tolerate occasional increases in systolic pressure, but diastolic pressure that stays consistently high can lead to organ damage. However, this theory has been revised. A high systolic reading is now considered an equally important value and a more important number for people older than 50. In fact, many people, particularly older Americans, have a normal diastolic level but an elevated systolic level. This type of high blood pressure is called isolated systolic hypertension (ISH). In people older than 55, the pulse pressure — the difference between the systolic and diastolic pressures — is an important predictor of health risks as well.[20]

If you have any type of high blood pressure, your doctor is likely to do the following:

- Ask you questions about your health and your family's health (a health history).
- Do a physical examination.
- Ask you to have routine tests such as a urine test (urinalysis), a blood test and an electrocardiogram (ECG), which measures your heart's electrical activity.[21]
- Consider the need for more specialized tests to examine blood flow. These tests may include ultrasonography, magnetic resonance angiography, angiography, computerized tomography (CT), magnetic resonance imaging (MRI) or nuclear scanning. They're especially important if your doctor is looking for secondary causes of hypertension.

METHODS

We conducted a prospective, randomized, double-blind trial in 40 patients with hypertension in the alkark Hospital, Iraq, from March to December 2018. T. Including criteria comprised;

elective surgery with general anesthesia, 65 > age > 20, ASA class II patients (hypertensive patients).

Excluding criteria; patients undergoing heart surgery, ASA III or above, CHF (congestive heart failure, arrhythmia, 20 > age > 65 years, problems with intubation, intubation time greater than 15 seconds, contraindications to lidocaine use, and no control of hypertension and/or asthma. The patients' demographic data such as sex and age were recorded, and then patients were randomly divided into two groups (fentanyl group and fentanyl plus lidocaine group). The fentanyl group received 2 mcg/kg and the fentanyl plus lidocaine group received 1.5mg lidocaine and 2mcg/kg fentanyl. Patients received their morning dose of anti-hypertensive medication before surgery. A routine pre-operative check-up was done in all patients and baseline vitals were noted, next patients received normal saline or ringer 5ml/kg in the admission operation room, and then they were oxygenation for three minutes. In the operating room, an intravenous line was started. Patients were attached to the following monitors; ECG, noninvasive blood pressure monitor, pulse oximetery. The baseline values (pre-anesthetic reading) for; mean arterial pressure, systolic blood pressure (SBP), diastolic blood pressure (DBP), and heartrate (HR) were recorded. Anesthesia was induced by thiopental given in a 3-5 mg/kg dose with fentanyl, orlidocaine plus fentanyl, next succinylcholine was given in a dose of 1-1.5 mg/kg succinylcholine given approximately 30-60 seconds before endotracheal intubation and induction were confirmed by loss of eyelash reflexes. Fentanyl or lidocaine plus fentanyl was administered three minutes prior to intubation. The hemodynamic variables; MAP), SBP, DBP, and HR were recorded after giving inductive anesthetic agents and trial drugs (before performing endotracheal intubation). Then a laryngoscopy was performed by a professional anesthetist with a standard Macintosh laryngoscope blade and the trachea was intubated with an appropriate size cuffed endotracheal tube and the patient was ventilated with oxygen. Hemodynamic variables; MAP, SBP, DBP, and HR were recorded 3 and 5 minutes after performing endotracheal intubation. We also recorded any possible complications such as; bradycardia (HR < 50), hypotension (SBP < 90), bronchospasm, seizure and rigidity.

All results were expressed as mean ± SD. Hemodynamic variables in the present study were analyzed statistically by using a t-test. P values ≤ 0.05were consideredsignificant.

Inclusion criteria

1. Patients aged 25 to 40 years for elective surgery and general anesthesia.
2. Patients without underlying disease such as diabetes, hypertension, cardiovascular disease, kidney and liver diseases, and respiratory diseases and patients except for 1 or 2 ASA classification.
3. Patients who filled consent from

Exclusion criteria

1. Patients with a history of allergic reaction to treatment with lidocaine and labetalol (and other beta-blockers) or cardiac pulmonary disease, heart failure, asthma and insulin-dependent diabetes, angina were and hyper thyroid, there were excluded because of complications with β-blocker.
2. Patients with cardiogenic shock, severe bradycardia and CHF uncontrolled.
3. Trauma patients and patients with unstable hemodynamics.
4. Patient with life-threatening drug reactions.
5. Breastfeeding and Pregnant women.
6. Patient with concomitant use of monoamine oxidase inhibitors or TCA.

RESULTS

Table 1: Mean Standard Deviation and a P value of Heart Rate in Fentanyl and Fentanyl Plus Lidocaine Groups.

Heart Rate	Fentanyl	Fentanyl+lidocaine	P value
Befor Induction	84.38±13.38	80.25 ± 84	
3 minutes before intubation	**8-+11**	**7-+12**	**0,000**
1 minutes after intubation	**7-+11**	**7-+12**	**0,04**
3 minutes after intubation	**7-+9**	**7-+12**	**0,000**
5 minutes after intubation	**6-+11**	**6-+9**	**0,86**

Table 2: Mean Standard Deviation and a P value of Systolic Blood Pressure in Fentanyl and Fentanyl Plus Lidocaine Groups.

Systolic Blood Pressure Groups	Fentanyl	Fentanyl+lidocaine	P value
Befor Induction	129.54± 21.	21.54 162.00 ± 26.61	
3 minutes before intubation	118.77±15.15	125.04 ± 24.11	**0,110**
1 minutes after intubation	124.38 ± 20	121.08 ± 14.84	**0,245**
3 minutes after intubation	116.62 ± 24	113.88 ± 24.29	**0,124**
5 minutes after intubation	107.31 ± 21	113.42 ± 29.96	**0,86**

Table 3: Mean Standard Deviation and a P value of Diastolic Blood Pressure in Fentanyl and Fentanyl Plus Lidocaine Groups.

Systolic Blood Pressure Groups	Fentanyl	Fentanyl+lidocaine	P value	
Befor Induction	86.30±10.57	95.41 ± 12.78		
3 minutes before intubation	78.53±11.60	79.45 ± 19.05	**0,110**	**0,76**
1 minutes after intubation	73.46±11.34	78.20 ± 13.49	**0,245**	**0,34**
3 minutes after intubation	73.23±14.76	73.83 ± 17.13	**0,124**	**0,88**

DISCUSSION

We found that fentanyl and fentanyl plus lidocaine are effective medications on hemodynamic responses (HR, SBP and DBP) decreasing before induction, three minutes before intubation and 1, 3 and 5 minutes after intubation. However, we did not discern any significant difference between the efficacy of the two kinds of medication (fentanyl and fentanyl plus lidocaine). Endotracheal intubation is a stressful noxious force stimulus, it stimulates laryngeal and tracheal sensory receptors, resulting in a marked increase in the expansion of sympathetic amines (adrenaline and noradrenaline), and this increase in the sympathetic amines leads to complications especially in a patient with cardiovascular diseases. Responses to endotracheal intubation arise essentially due to sympathetic stimulation causing increases in blood pressure, increases in heart rate and tachyarrhythmia. In normal patients, these responses are significantly high, but they are generally well tolerated, whereas in patients with cardiovascular diseases, many complications may occur like; increases in systolic and diastolic blood pressure, increases in heart rate, tachyarrhythmia, cerebral hemorrhage, left ventricular failure, and in rare conditions, myocardial ischemia.[22]

These hemodynamic responses to intubation in our patients were controlled effectively in the two groups, but adding lidocaine to fentanyl did not increase the hemodynamic stability more than fentanyl alone. In contrast with our study, several previous studies have verified that lidocaine improves intraoperative and postoperative hemodynamic stability by stabilizing the changes in arterial pressure, heart rate and cardiac output. The mechanism behind these beneficial effects of lidocaine on hemodynamic stability is possibly due to; the direct myocardial depressant effect, peripheral vasodilating effect and the effect on synaptic transmissions.[23]

Moreover, another study by Ali et al. in 2010 revealed that pre-treatment with xylocard improves intra- and postoperative hemodynamic stability during laparoscopic surgery without

prolonging recovery. Our study was in line with some previous studies such as Shin et al. that compared the effects of lidocaine, fentanyl, Nicardipine and Esmolol, on the hemodynamic response during intubation and that study revealed that all of these agents are effective in producing hemodynamic stability.[24]

Were matched appropriately. Nevertheless, our results were possibly limited by the fact that we did not monitor the depth of anesthesia. Doses that are entirely based on mcg/ kg probably produce different depths of anesthesia in a given population, which may have affected our results. In addition, we firmly declare, that a more profound induction of anesthesia before tracheal tube insertion may also have influenced the results of this study. Fentanyl and fentanyl plus lidocaine are effective in decreasing the hemodynamic response to tracheal intubation, however, neither fentanyl nor fentanyl plus lidocaine could inhibit all hemodynamic responses, furthermore fentanyl plus lidocaine was not more effective than fentanyl alone.

REFERENCES

1. Kimura A, Yamakage M, Chen X, Kamada Y, Namiki A. Use of the fibreoptic stylet scope (Styletscope) reduces the hemodynamic response to intubation in normotensive and hypertensive patients. Can J Anaesth, 2001; 48(9): 919-23.
2. Abrams JT, Horrow JC, Bennett JA, Van Riper DF, Storella RJ. Upper airway closure: a primary source of difficult ventilation with sufentanil induction of anesthesia. Anesth Analg, 1996; 83(3): 629-32.
3. del Rio Vellosillo M, Gallego Garcia J, Soliveres Ripoll J, Abengochea Cotaina A, Barbera Alacreu M. [Bolus administration of fentanyl vs continuous perfusion of remifentanil for control of hemodynamic response to laryngoscopy and orotracheal intubation: a randomized double-blind trial]. Rev Esp Anestesiol Reanim, 2009; 56(5): 287-91.
4. Aouad MT, Sayyid SS, Zalaket MI, Baraka AS. Intravenous lidocaine as adjuvant to sevoflurane anesthesia for endotracheal intubation in children. Anesth Analg, 2003; 96(5): 1325-7. table of contents
5. Arasu M, Al-Dhabi N, Rejiniemon T, Lee K, Huxley V, Kim D, Duraipandiyan V, Karuppiah P and Choi K. Identification and characterization of Lactobacillus brevisP68 with antifungal, antioxidant and -probiotic functional properties. Indian Journal of Microbiology, 2015; 55(1): 19-28.

6. Min JH, Chai HS, Kum YH, Chae YK, Choi SS, Lee A, et al. Attenuation of hemodynamic responses to laryngoscopy and tracheal intubation during rapid sequence induction: remifentanil vs. lidocaine with esmolol. Minerva Anesthesiol, 2010; 76: 188-92.
7. Mann D. Zipes D, Libby P, BonowR. Braunwald's Heart disease, tenth edition, ELSEVIER, 2015; 35(693).
8. Higgins JP, Thompson SG: Controlling the risk of spurious findings from meta-regression. Stat Med., 2004; 23: 1663–1682.
9. Simon KC, Chen H, Schwarzschild M, Ascherio A: Hypertension, hypercholesterolemia, diabetes, and risk of Parkinson disease. Neurology, 2007; 69: 1688–1695.
10. Miao G: A Case-Control Study on the Risk of Hypertension, Hyperuricemia, Lifestyle and Parkinson's Disease. Suzhou, Soochow University, 2015; 1–36.
11. McCann SJ, LeCouteur DG, Green AC, Brayne C, Johnson AG, Chan D, McManus ME, Pond SM: The epidemiology of Parkinson's disease in an Australian population. Neuroepidemiology, 1998; 17: 310–317.
12. Iadecola C: Hypertension and dementia. Hypertension, 2014; 64: 3–5.
13. Chan SL, Sweet JG, Cipolla MJ: Treatment for cerebral small vessel disease: effect of relaxin on the function and structure of cerebral parenchymal arterioles during hypertension. FASEB J., 2013; 27: 3917–3927.
14. Verhaaren BF, Vernooij MW, de Boer R, Hofman A, Niessen WJ, van der Lugt A, Ikram MA: High blood pressure and cerebral white matter lesion progression in the general population. Hypertension, 2013; 61: 1354–1359.
15. Jonas BS, Lando JF: Negative affect as a prospective risk factor for hypertension. Psychosom Med., 2000; 62: 188–196.
16. Markovitz JH, Jonas BS, Davidson K: Psychological factors as precursors to hypertension. Curr Hypertens Rep., 2001; 3: 25–32.
17. Yan LL, Liu K, Matthews KA, Daviglus ML, Ferguson TF, Kiefe CI: Psychosocial factors and risk of hypertension: the coronary artery risk development in young adults (CARDIA) study. JAMA, 2003; 290: 2138–2148.
18. Grewen KM, Girdler SS, Hinderliter A, Light KC: Depressive symptoms are related to higher ambulatory blood pressure in people with a family history of hypertension. Psychosom Med., 2004; 66: 9–16.
19. Obialo CI, Hewan-Lowe K: Rapid progression to end-stage renal disease in young hypertensive African Americans with proteinuria. J Natl Med Assoc, 1998; 90: 649–655.

20. Markovitz JH, Jonas BS, Davidson K: Psychological factors as precursors to hypertension. Curr Hypertens Rep., 2001; 3: 25–32.
21. Iadecola C: Hypertension and dementia. Hypertension, 2014; 64: 3–5.
22. Calvey TN, Williams NE. Principles and Practice of Pharmacology for Anaesthetists. Fifth Edition ed. Blackwell Publishing, 2008.
23. Kim WY, Lee YS, Ok SJ, Chang MS, Kim JH, Park YC, et al. Lidocaine does not prevent bispectral index increases in response to endotracheal intubation. Anesth Analg, 2006; 102(1): 156-9.
24. Shin HY, Kim JW, Kim AR, Jang YH, Kim JM, Bae JI. The Effects of Lidocaine, Fentanyl, Nicardipine, and Esmolol on Hemodynamic and Bispectral Index Responses during Induction with Thiopental Sodium. Korean J Anesthesiol, 2007; 53(3): S7-S13.