ECRONICON OPEN ACCESS

EC ANAESTHESIA
Review Article

Adjuvant Drugs to Decrease the Adrenergic Response in Conventional Laryngoscopy

José Luis Álvarez-Juárez*

Medical Anesthesiologist of the Health Institute of the State of Mexico General Hospital "Dr. Gustavo Baz Prada", Nezahualcoyotl, Mexico

***Corresponding Author:** José Luis Álvarez-Juárez, Medical Anesthesiologist of the Health Institute of the State of Mexico General Hospital Dr. Gustavo Baz Prada", Nezahualcoyotl, Mexico.

Received: March 05, 2018; **Published:** June 13, 2018

Abstract

The procedure of making a laryngoscopy provides a great challenge for all physicians who are within the areas (operating rooms, emergency, critical care unit, internal medicine, etc.) thus being the period periintubación the algic time for the patient what It leads to awakening a cascade of autonomic responses as is hypertension and tachycardia leading to increased oxygen consumption, which can trigger heart attacks or cerebrovascular events ischemic or hemorrhagic, so it is vitally important proper management analgesia and patient hemodynamics to perform scheduled or emergency laryngoscopy. Finding a range of drugs to support the analgesic and hemodynamic monitoring.

Keywords: *Laryngoscopy; Adrenergic Response; Analgesia; Sedation; Alpha2-Agonist; Dexmedetomidine; Magnesium Sulfate; Lidocaine*

Introduction

The period of intubation is one of the moments of greatest stress during general anesthesia [1]. Tracheal intubation (IT) induces neurovegetative clinical responses, which are reflected in an increase in the adrenergic and algic response, being reflected in the hemodynamic changes.

Laryngoscopy and intubation of the trachea can be accompanied by hypertension, tachycardia, increased intracranial and intraocular pressure and may be associated with myocardial ischemia in susceptible individuals. Laryngoscopy, endotracheal intubation and other manipulations of the respiratory tract are highly harmful. They can induce profound changes in cardiovascular physiology, mainly through reflex responses. Although these responses may be of short duration and of little importance in healthy individuals, not so in subjects with various diseases such as underlying coronary artery disease or intracranial diseases.

This response may be exaggerated in patients with or without treatment of essential hypertension; some patients have a higher incidence of cerebrovascular diseases and coronary artery diseases. Pathologies that increase cardiovascular morbidity during anesthetic induction and laryngoscopy.

Keeping the patient in optimal conditions during the anesthetic state is the responsibility of our profession, so it is necessary to use different drugs, in order to provide analgesia, hypnosis, amnesia, neurovegetative protection and an adequate neuromuscular block, which are components essentials of adequate anesthesia [2]. More than 11% of patients develop a certain degree of myocardial ischemia during intubation. The key is to provide adequate depth of anesthesia with intravenous or inhalation agents prior to airway instrumentation. However there are several pharmacological strategies that have been proposed for the control of neurovegetative responses to intu-

bation, different medications such as lidocaine, magnesium sulfate, ὰ agonists such as dexmedetomidine and opioids, have been used to decrease adrenergic discharge and provide analgesia to the nociceptive stimulus.

Alpha 2 adrenergic agonists

A-2 adrenergic receptors (or adrenoreceptors) are transmembrane receptors that are composed of excitable G-proteins that cross the cell membrane and selectively connect to extracellular ligands, which can be endogenous mediators or exogenous molecules, such as drugs; these act by reducing the entry of calcium into the nerve terminals.

The α-2 adrenergic receptor consists of three isoreceptors: α-2a, α-2b and α-2c, which are linked to α-2 agonists and antagonists with similar affinities and share a homology of amino acid composition of approximately 70 to 75% [3]. Alpha-2 adrenergic activation is an essential part of the intrinsic network of pain control in the central nervous system. This is densely distributed in the gelatinous substance of the dorsal horn of humans and is believed to be the main site of action in which analgesic effects occur. The adrenergic receptors involved in analgesia are the ὰ-2a and ὰ-2c types, both located in the primary afferent nerve terminals of the C fibers and in some areas of the spinal cord, such as the superficial dorsal horn.

The spinal cord contains insignificant levels of ὰ-2b adrenergic receptors [4], these appear to be located at presynaptic, postsynaptic and extrasynaptic levels; They have been found in platelets, liver, pancreas, kidneys and eyes. Agonism at the α-2a receptor appears to promote sedation, hypnosis, analgesia, sympatholysis, neuroprotection and inhibition of insulin secretion. Agonism at the α-2b receptor abolishes tremor, generates analgesia in the spinal cord and induces vasoconstriction in the peripheral arteries. The α-2c receptor is associated with the modulation of sensory cognition processing [3].

Analgesic effect: analgesia for pain control is a key factor, since in the critical tables they increase the risk of morbidity and mortality [5]. Pain has psychic and physical effects, such as fear, anxiety and sleep disorders [6]. The analgesic response to the administration of dexmedetomidine appears to occur at the level of the dorsal root neuron, where the ὰ-2 agonists block the release of substance P in the nociceptive pathway. It is also mediated by the activation of descending inhibitory pathways, thanks to the blockade of aspartate and glutamate receptors. In this way, spinal hyperexcitability can be attenuated, which exerts a true preventive effect on pain [5,6]. In other words, its analgesic action is due to the inhibition of the release of excitatory neurotransmitters in the spinal cord, where there is a large number of ὰ-2 adrenergic excitators [7]. One of the pharmacological properties of α-2 agonists is to decrease the requirements of other drugs used in induction and anesthetic maintenance [8]. This could be explained by the inhibitory effect on the central transmission of noradrenergic type, characteristic of the α-2 agonists. It has been shown that the application Dexmedetomidine (DXM) with an intravenous infusion of 1 μg/kg in 10 minutes, followed or not by continuous infusion of 0.5 to 1 μg/kg/h, causes a significant reduction of opioid and non-opioid analgesics , trans and postoperative as well as in the care units of the patient in a critical state in adults and children [9].

Dexmedetomidine hydrochloride (DXM), an agonist of the ὰ-2 receptors in the cerulean locus, has shown significant efficacy for sedation [7]. It is a pharmacologically active agent of medetomidine, highly lipophilic, with great affinity for adrenoreceptors ὰ, which, when stimulated, decrease the release of noradrenaline, inhibit sympathetic activity, lower blood pressure (BP) and heart rate (HR) and produce Anxiolysis, sedation and analgesia [10,11], also decreases anesthetic requirements, attenuates the neuroendocrine response, produces sedation with preservation of psychomotor function, without affecting respiratory function [12].

Traditionally, intubation in awake patients is performed under the effects of sedation, using multiple medications, among which are fentanyl, remifentanil, midazolam, droperidol, thiopental and propofol among others, with the consequent well-known side effect of respiratory depression and sometimes Little collaboration of the patient, being necessary in all cases the application of large quantities of local anesthetics in the upper airway.

DXM is a ag-2 selective agonist, they are of multiple applications in the anesthesiology clinic, they have demonstrated that with its application can be significantly decreased the concomitant dose of opioids, benzodiazepines, propofol, inhaled anesthetic agents and many other sedative drugs. In long and short sedation is a safe and effective medication, as for example in the management of normal or complicated airway. Where its main action is to decrease the sympathetic tone produced by the intubation maneuvers. Its adequate sedative power without respiratory depression and an adjuvant effect in analgesia and anxiolysis is paramount. The use of dexmedetomidine for tracheal intubation with awake paciente induces a conscious sedation with a calm patient, collaborator and with spontaneous breathing without the risk of bronchoaspiration and without abrupt secretions.

Sedation with DXM should be considered in cases of difficult intubation awake and with difficult airway, as it provides excellent sedation, collaboration and analgesia in the airway with no respiratory depressant effect. Another advantage is that the application of local anesthetics and antisialogogues with this drug is eliminated [13].

Magnesium sulphate

The role of magnesium in the organism and its pharmacological properties continue to be studied and new situations appear in which this ion acquires a relevant role. The knowledge of its pharmacological, clinical and physiological characteristics has become essential for the doctor who is in the critical units. Magnesium is also used as a drug with different indications: in resuscitation, obstetrics, cardiology, cardiac surgery, pain treatment, anesthesia, pneumology, etc.

Magnesium acts at several levels: it inhibits the entry of calcium by competitive antagonism with calcium channels both in the cell membrane and in specific intracellular receptors (e.g. mitochondrial membrane). It also acts on the Na^+/K^+ ATPase to which it inhibits at high plasma concentrations. Finally, it is an antagonist of the N-Methyl-D-Aspartate (NMDA) receptor [14]. It is an antagonist of the NMDA receptor of glutamate, the main excitatory neurotransmitter, which explains its sedative effects. In the marrow blocks the pain pathways dependent on this transmitter.

He is also a cerebral vasodilator. Its relationship with the autonomic nervous system is due to its ability to inhibit the release of catecholamines in the adrenal gland [15].

Magnesium sulfate at a dose of 40 mg kg prior to orotracheal intubation (IOT) has been shown to be as effective as alfentanil at 10 μg/k and more than lidocaine at a dose of 1.5 mg/k in achieving not to modify the TA up to five minutes after the IOT in this type of patients. The disadvantage of these doses of both magnesium and opioid are side effects (mainly respiratory depression and muscle weakness in the newborn). In a subsequent study the same group found the same benefits without significant side effects in the association of 30 mg/k of magnesium sulphate with 7.5 μg/k of alfentanil [16]. The mechanism proposed by James et al. to explain this effect is that magnesium decreases the release of catecholamines in the adrenal gland [15,17]. Perioperative magnesium systemic administration reduces postoperative pain and opioid use. The administration of magnesium should be considered as a strategy to mitigate the pain of the IOT and the postoperative period in surgical patients.

There are numerous situations in which the risk of post-induction hypertension and anesthetic intubation can seriously compromise the patient's health such as aneurysmal aortic surgery, cerebral vessels, pheochromocytoma, and pregnant hypertension. The latter is the one that has studied the use of magnesium as an adjuvant in induction, probably due to the impossibility of using other strategies such as high doses of opiates.

IOT in patients at risk of hypertension or with a hemodynamic compromise due to an exaggerated rise in systemic blood pressure, pulmonary capillary pressure and in the pulmonary artery such as pregnant patients. The administration of magnesium sulfate at doses with a safety margin of between 30 to 50 mg/k/i.v for 10 to 15 minutes before performing laryngoscopy.

Intravenous or local lidocaine

Several methods of applying lidocaine have been used to reduce the cardiovascular response to orotracheal intubation, avoiding the hemodynamic changes that this entails. These methods include the administration of lidocaine in measured aerosol doses directly over the posterior pharynx, direct injection of lidocaine through the channel of a bronchoscope, or administration of intravenous lidocaine.

Local anesthetics (AL) prevent or relieve pain by interrupting nerve conduction. These bind to a specific receptor within the sodium (Na^+) channels in the nerves and block the movement of ions through it. The chemical and pharmacological properties of each drug determine its clinical use. LAs can be administered in a variety of ways, including; topical, infiltration, nerve or field block, intravenous, spinal or epidural, or as dictated by clinical circumstances.

The mechanism of action of LAs prevents the generation and conduction of the nervous impulse. Its main site of action is in the cell membrane, decreasing the increase in the permeability of membranes excitable to Na^+. In addition to Na^+ channels, ALs can bind to other membrane proteins. In particular, these can also block the potassium (K^+) channels [18]. Lidocaine is metabolized in the liver to monoethylglycinexylidide and glycinexylidide; it is excreted in the urine and its toxic effects are observed with doses higher than 7 mg/k/i.v, producing cardiovascular depression and seizures due to central nervous system toxicity [19-21]. Its effect on the repair of tissue damage through the synthesis of collagen mucopolysaccharides has also been demonstrated [22]. And by the decrease in damage induced by lipopolysaccharides through the inactivation of mitochondrial potassium channels [23]. Antithrombotic effects [24,25] and on platelet aggregation [26]. Decreased postoperative tinnitus [27]. As well as its effects on the inflammatory cascade [28]. Dose: Attenuation of the vasopressor response in orotracheal intubation: 1 - 2 mg/k i.v. (1% - 2%) 2 - 4 minutes. Before laryngoscopy. Topical anesthesia: 0.6 - 3 mg/k. Transtracheal: 80 - 120 mg. Blockade of superior laryngeal nerve: 40 - 60 mg [14,16]. Intravenous or endotracheal lidocaine decreases the vasopressor response to laryngoscopy. Its administration i.v, owes its effect in part, by its systemic analgesic action and also by the local analgesic effect to spread throughout the tracheobronchial vasculature. The decrease (dose-dependent) of intracranial pressure is secondary to the increase in cerebral vascular resistance and the decrease in cerebral blood flow. Therapeutic doses do not decrease systemic vascular resistance, myocardial contractility and cardiac output. Repeated doses cause an increase in serum levels due to its slow accumulation. Lidocaine spray 10%: It is indicated to provide topical anesthesia in accessible mucous membranes before a laryngoscopy or manipulation with instruments or other explorations of: mouth, larynx, nasal cavity, pharynx and trachea; It is also indicated to suppress nauseous reflexes and/or other laryngeal or esophageal reflexes to facilitate intubation.

In a prospective study, Skalar., *et al.* showed that inhalation of lidocaine in a dose dependent from 40 to 120 mg (2 mg/k) before anesthetic induction is an effective, safe and convenient method to decrease the cardiovascular response [20].

Miller and his group demonstrated that administration of lidocaine intravenously, at a dose of 1.5 mg/k five minutes before laryngoscopy and tracheal intubation, decreases the pressor response and no plasma concentrations are observed that can be toxic to patients [29,30].

Lidocaine administered in any of the three forms: dose measured in aerosol, intravenous and by nerve block (regional) is effective and safe to reduce tachycardia and hypertension that is triggered during endotracheal intubation.

Beta-blockers

The main pharmacological activity of beta-blockers (BB) is exercised at cardiovascular level, highlighting the antihypertensive activity of its effects, due to its chronotropic, dromotropic and negative inotropic effect.

Esmolol is a cardioselective beta-blocker with ultra-short action, considered the ideal drug to attenuate the hemodynamic repercussion associated with laryngoscopy and intubation [31,32].

Beta-adrenergic receptors activate the enzyme adenyl cyclase, stimulating the formation of cAMP, which in turn activates catalytic reactions by stimulating the addition or binding of phosphate groups or key substrates. According to their location, the observed effects are subdivided into: B-1, postsynaptic, are located mainly at cardiac level. Its stimulation causes increased heart rate, increased contractility and conduction velocity in atria and ventricles, increased automatism in the AV node, His bundle and Purkinje system. B-2, postsynaptic, are located in bronchial smooth muscle, in arterioles, in veins, stomach, intestine, uterus, ciliary muscle, β cells of the islets of Langerhans, in hepatocytes, and in juxtaglomedular apparatus. As the β-1 receptors induce the formation of cAMP, causing bronchodilation, vasodilation, increased insulin release, stimulation of glycogenolysis and gluconeogenesis and relaxation of the uterine smooth muscle. B-3, located mainly in adipocytes, increase lipolysis by activation of a specific lipase and increase lipemia.

Esmolol (methyl-3 [4- (2-hydroxy-3 [isopropylamino] propyx) phenyl] is a specific, water-soluble cardioselective β-1 blocker, with no intrinsic sympathetic activity or membrane stabilization at therapeutic doses. has an onset of action of approximately one minute and an elimination half-life of nine minutes after stopping the infusion, this makes its titration easy according to the response obtained, and due to its metabolism by plasma esterases can be used in patients with both renal and hepatic failure, without the need to adjust the dose, administering an initial bolus of esmolol of 0.500 - 1 mg/k in one minute, and with a maintenance dose of 25 - 50 μg/k/minute which can be increase every 10 - 20 minutes at 25 μg/k/minute according to the response without going over a maximum dose of 300 μg/k/minute.

In a meta-analysis and previous studies it was shown that the administration of esmolol helps to prevent tachycardia and hypertension during laryngoscopy and intubation [33,34]. Helping to maintain hemodynamic stability. It is important to mention that esmolol lacks analgesic properties, so it is convenient to add some drug with analgesic properties. In a large multicentre placebo controlled trial, esmolol at a dose of 100 or 200 mg suppressed the hemodynamic response to endotracheal intubation, particularly when combined with a moderate dose opioid. However, esmolol doses of 200 mg were associated with a doubling of arterial hypotension [35].

Recently, the combination of lidocaine (1.5 mg/kg) and esmolol at a dose of 1 mg/kg effectively attenuated the pressor response to intubation, but was not as effective as 1 μg/kg remifentanil [36].

Inhaled

Inhaled anesthetics have a series of direct effects on VA, for example all are bronchodilators. The irritation of the VA is accompanied by an increase in the salivary, laryngeal and bronchial secretions; its capacity to produce these changes varies among the different inhaled agents, with sevoflurane and halothane being the least irritating inhalants. The stimulation of the respiratory receptors seems to be the element responsible for the tachycardia and hypertension observed. The concomitant use of opioids and benzodiazepines decreases the irritant effect of inhaled volatile agents on VA. The cardiovascular response to the harmful manipulation of the respiratory tract are initiated by proprioceptors that respond to tissue irritation in the supraglottic region and in the trachea, located near the mucosa of the respiratory tract, these same receptors are constituted by mechanoreceptors with fibers of small diameter. The location of these receptors and their nerves explains why topical anesthesia of the airway is an effective means of attenuating cardiovascular responses to respiratory interventions. Frequently caused bradycardia in infants and young children during laryngoscopy or intubation is the autonomous equivalent of the response of laryngospasm. This reflex results from an increase in vagal tone in the sinoatrial node and is virtually a monosynaptic response, a noxious stimulus in the airway. In adults, the most common response to manipulation of the respiratory tract is arterial hypertension, a response that includes the generalized release of norepinephrine from the adrenergic nerve endings and the secretion of epinephrine from the adrenal medulla. In addition to autonomic nervous system activation, laryngoscopy and endotracheal intubation result in stimulation of the central nervous system, as evidenced by increases in electroencephalographic activity (EEG), brain metabolic rate and cerebral blood flow (FSC), compromised increased intracranial pressure (ICP), which, in turn, can lead to herniation of brain contents and severe neurological deterioration.

The effects of endotracheal intubation on the pulmonary vasculature are less known than the responses obtained in the systemic circulation. They are often associated with changes in airway reactivity associated with intubation. Acute bronchospasm or main bronchial intubation causes a marked maldistribution of poorly ventilated pulmonary perfusion, causing desaturation of the pulmonary venous blood and the subsequent reduction of arterial systemic blood pressure (O_2). The impact of these changes can be profound in patients with severely compromised myocardial function or intravascular volume depletion. For inhalational anesthetics, endotracheal intubation using inhalation, it should not be surprising that a MAC is insufficient to block the cardiovascular response, it is known that at least 1.5 to 1.6 MAC is required to completely block the adrenergic and cardiovascular response to a simple surgical incision of the skin. The dose of inhaled anesthetic required to prevent cough during endotracheal intubation with sevoflurane may exceed MAC, by a factor of 2.86 in adults, although this factor appears to be close to 1.3 in young children. Consequently, it seems that the dose of volatile anesthetic required to block the cardiovascular response to endotracheal intubation must be excessively high, resulting in a profound cardiovascular depression before endotracheal intubation. However, from the cerebrovascular point of view, this approach is totally impractical, since inhaled anesthetics cause cerebral vasodilation and marked increases in intracranial pressure (ICP) in patients with compromised intracranial involvement. In addition, from the cardiovascular point of view, hypotension and reduction of cerebral perfusion pressure before intubation would be totally unacceptable for patients with cerebrovascular disease or brain injury [37].

Conclusions

In the period of orotracheal peri-intubation, it has been demonstrated that there is a great adrenergic and analgic discharge for the patients who are subjected to it, being this of vital importance for the doctors who perform laryngoscopies, since the ignorance of this can lead to that patients suffer serious complications such as: acute myocardial infarction and/or cerebral vascular event, increasing these in susceptible patients.

It is known that the cornerstone for mitigating adrenergic responses and providing adequate analgesia are opioid analgesics (fentanyl, sufentanil, morphine, remifentanil, etc.), however, they are not always available, so the use of other drugs is necessary. either as adjuvants or as a single use and do not perform conventional laryngoscopy with "midazolam and vecuronium" as it is not providing analgesia or hemodynamic protection.

Bibliography

1. Troy AM., *et al*. "Tracheal intubating conditions using propofol and remifentanyl target-controlled infusions". *Anaesthesia* 57.12 (2002): 1195-1212.

2. Howie MB., *et al*. "Comparison of three remifentanyl dosefinding regimens for coronary artery surgery". *Journal of Cardiothoracic and Vascular Anesthesia* 17.1 (2003): 51-59.

3. Haselman MA. "Dexmedetomidine: a useful adjunct to consider in some high-risk situation". *AANA Journal* 76 (2008): 335-339.

4. Nacif-Cohelo C., *et al*. "Perturbation of ion channel conductance alters the hypnotic response to the alfa 2-adrenergic agonist dexmedetomidine in the locus ceruleus of the rat". *Anesthesiology* 81.6 (1994): 1527-1534.

5. Panzer O., *et al*. "Pharmacology of sedative-analgesic agents: dexmedetomidine, remifentanil, ketamine, volatile anesthetics, and the role of peripheral mu antagonists". *Critical Care Clinics* 25.3 (2009): 451-469.

6. Unlugenc H., *et al*. "The effect of pre-anaesthetic administration of intravenous dexmedetomidine on postoperative pain in patients receiving patient controlled morphine". *European Journal of Anaesthesiology* 22.5 (2005): 386-391.

7. Guo TZ., *et al*. "Dexmedetomidine injection into the locus ceruleus produces antinociception". *Anesthesiology* 84.4 (1996): 873-881.

8. Sturaitis MK., *et al*. "Effects of intraoperative dexmedetomidine infusion on hemodynamic stability during brain tumor resection". *Anesthesiology* 97.2 (2002): A310.

9. Mi WD., *et al*. "Haemodynamic and electroencephalograph responses to intubation during induction with propofol or propofol/fentanyl". *Canadian Journal of Anesthesia* 45.1 (1998): 19-22.

10. Sheinin B. "Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and preoperative fentanyl". *British Journal of Anaesthesia* 68.2 (1992): 126-131.

11. Aantaa R., *et al*. "DXM a novel alpha 2 adrenergic agonist. A review of its pharmacodynamics characteristics drugs of the future" 18.1 (1993): 49-56.

12. Ven RM., *et al*. "Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care". *Critical Care* 4.5 (2000): 302-308.

13. Grant SA., *et al*. "Dexmedetomidina infusión for sedation during fiberoptic intubation. A report of three cases". *Journal of Clinical Anesthesia* 16.2 (2004): 124-126.

14. Hughes R., *et al*. "Use of isotonic nebulised magnesium sulphate as an adjuvant to salbutamol in treatment of severe asthma in adults: randomised placebocontrolled trial". *Lancet* 361.9375 (2003): 2114-2117.

15. James MF. "Use of magnesium sulphate in the anaesthetic management of pheochromocytoma: a review of 17 anaesthetics". *British Journal of Anaesthesia* 62.6 (1989): 616-623.

16. Ashton WB., *et al*. "Attenuation of the pressor response to traqueal intubation by magnesium sulfate with and without alfentanil in hypertensive proteinuric patients undergoing caesarian section". *British Journal of Anaesthesia* 67.6 (1991): 741-747.

17. James MF and Cronje L. "Pheochromocytoma crisis: the use of magnesium sulfate". *Anesthesia and Analgesia* 99.3 (2004): 680-686.

18. De Carlos JM and Viamonte MA. "Farmacología de los anestésicos locales". Anales (1999): 22.

19. Levitt MD and Dresden GM. "The efficacy of esmolol versus lidocaine to attenuate the hemodynamic response to intubation in isolated head trauma patients". *Academic Emergency Medicine* 8.1 (2001): 19-24.

20. Skalar BZ., *et al*. "Nebulized lidocaine response to tracheal intubation". *Journal of Clinical Anesthesia* 4.5 (1992): 382-385.

21. Groeben H., *et al*. "Airway anesthesia alone does not explain attenuation of histamine induced bronchospasm by local anesthetics: A comparison of lidocaine, ropivacaine and dyclonine". *Anesthesiology* 94.3 (2001): 519-526.

22. Butterworth JF and Hammon JW. "Lidocaine for neuroprotection: More Evidence of efficacy". *Anesthesia and Analgesia* 95.5 (2002): 1131-1133.

23. Druker M., *et al*. "Experimental studies on the effect of lidocaine on wound healing". *World Journal of Surgery* 22.4 (1998): 394-397.

24. Manuela JM., *et al*. "Local anesthetic induced protection against lipopolisaccharide-induced injury in endothelial cells: The role of mitocondrial adenosine triophosphate-sensitive potassium channels". *Anesthesia and Analgesia* 102.4 (2006): 1108-1113.

25. Cooke ED., *et al*. "Intravenous lidocaine in prevention of deep venous thrombosis after elective hip surgery". *Lancet* 2.8042 (1997): 797-799.

26. Luostarinen V., *et al*. "Antithrombotic effects of lidocaine and related compounds on laser induced microvascular injury". *Acta Anaesthesiologica Scandinavica* 25.1 (1981): 9-11.

27. Feinstein MG., *et al*. "An analysis of the mechanism of local anesthetic inhibition of platelet aggregation and secretion". *Journal of Pharmacology and Experimental Therapeutics* 197.1 (1976): 215-228.

28. Baguley DM., *et al*. "The inhibitory effect of intravenous lidocaine infusion on tinnitus after translabyrinthine removal of vestibular Schwanoma: a double blind, placebo controlled, crossover study". *Otology and Neurotology* 26.2 (2005): 169-176.

29. Pastor L. "Anestesia cardiovascular. 2nd edition". México: McGraw-Hill Interamericana (1997): 362-363.

30. Hamaya Y and Dohi S. "Differences in cardiovascular response to airway stimulation at different sites and blockade of the responses by lidocaine". *Anesthesiology* 93.1 (2000): 95-103.

31. Kindler CH., *et al*. "Effects of intravenous lidocaine and/or esmolol on hemodynamic responses to laryngoscopy and intubation: A doubleblind, controlled clinical trial". *Journal of Clinical Anesthesia* 8.6 (1996): 491-496.

32. Atlee JL., *et al*. "The use of esmolol, nicardipine, or their combination of blunt hemodynamic changes alter laryngoscopy and tracheal intubation". *Anesthesia and Analgesia* 90.2 (2000): 280-285.

33. Figueredo E and Garcia-Fuentes EM. "Assessment of the efficacy of esmolol on the haemodynamic changes induced by laryngoscopy and tracheal intubation: a meta-analysis". *Acta Anaesthesiologica Scandinavica* 45.8 (2001): 1011-1022.

34. Zalunardo MP., *et al*. "Cardiovascular stress protection following anesthesia induction. Comparison of clonidine and esmolol". *Anaesthesist* 50.1 (2001): 21-25.

35. Miller DR., *et al*. "Bolus administration of esmolol for controlling the haemodynamic response to tracheal intubation: The Canadian Multicentre Trial". *Canadian Journal of Anesthesia* 38.7 (1991): 849-858.

36. Min JH., *et al*. "Attenuation of hemodynamic responses to laryngoscopy and tracheal intubation during rapid sequence induction: Remifentanil vs. lidocaine with esmolol". *Minerva Anestesiologica* 76.3 (2010): 188-192.

37. Hassan HG., *et al*. "Hemodynamic and catecholamine responses to laryngoscopy with vs. without endotracheal intubation". *Acta Anaesthesiologica Scandinavica* 35.5 (1991): 442-447.

Volume 4 Issue 7 July 2018