International Journal of Research in Medical Sciences
Chandrashekarappa K et al. Int J Res Med Sci. 2015 Jun;3(6):1457-1461
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: 10.18203/2320-6012.ijrms20150167

Research Article

Intravenous low dose clonidine premedication for attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation

Chandrashekarappa Kavi[1,*], Ravindra CG[2], Kiran Mallappa[3], Kumara AB[4]

[1]Associate Professor, Department of Anaesthesiology, Subbiah Institute of Medical Sciences, Purule, Shimoga, India
[2]Associate Professor, [3]Assistant Professor, [4]Senior Resident, Department of Anaesthesiology, Shimoga Institute of Medical Sciences, Shimoga, India

Received: 20 April 2015
Accepted: 06 May 2015

***Correspondence:**
Dr. Chandrashekarappa Kavi,
E-mail: dr.chandrukavi@gmail.com

ABSTRACT

Background: Laryngoscopy and endotracheal intubation are almost always associated with an increased sympathetic activity. To attenuate the presser response, various drugs have been tried. This study aims at finding out if the low dose of clonidine (1.5µg/kg) is best suited for this purpose.
Methods: This was a prospective study which involved two groups of patients. Each group had 30 patients who presented for elective, non-cardiovascular surgeries. The patients in group-C received Clonidine (1.5 µg/kg) and the patients in group-N received Normal saline. Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Mean blood pressure (MBP) were recorded before and after intubation and at 1, 5, and 10 mins. The obtained clinical data were analyzed statistically with analysis of variance.
Results: In our study, HR, SBP, and DBP and MBP all increased during intubation and thereafter in the control groups. Pretreatment with clonidine (1.5 µg/kg) significantly attenuated the cardiovascular and catecholamine responses to tracheal intubation
Conclusion: Preoperative administration of a single dose of clonidine blunted the hemodynamic responses more than the placebo during Laryngoscopy and Intubation with reduced anesthetic requirements.

Keywords: Clonidine, Pressor response, Anesthetic requirement

INTRODUCTION

Laryngoscopy and endotracheal intubation is one of the most frequent techniques of a secure airway. But both the process is noxious and is associated with hemodynamic variations. Increase in the blood pressure and heart rate due to the reflex sympathetic discharge caused by an epipharyngeal and laryngopharyngeal stimulation is invariably seen. This increased sympatho-adrenal activity may result in hypertension, tachycardia and arrhythmias.[1]

These changes are well tolerated in healthy fit individuals but can be fatal in patients with arterial hypertension, coronary artery disease or intracranial hypertension. Intravenous or topical Lignocaine,[2] vasodialtors[3] like NTG, adrenergic blockers[4], narcotics[5] like fentanyl and inhaled anaesthetics[6] for deeper plane of Anesthesia, administration of alpha & beta blockers, calcium channel blockers, have been tried to attenuate these presser response. The non - pharmacological methods like smooth and gentle intubation with a shorter duration of laryngoscopy (< 15 sec), insertion of LMA in place of endotracheal intubation & blocking Glossopharyngeal and Superior laryngeal nerves have been used to attenuate the cardiovascular response to laryngoscopy and endotracheal intubation.

Recently, clonidine, an alpha-2 adrenergic agonist, is being used[7] as premedication to blunt the stress response to the surgical stimuli and decrease the need of narcotic and anaesthetic. This prospective, randomized, double-blinded study was planned to evaluate the efficacy of clonidine for the attenuation of presser response at lower dose during laryngoscopy and intubation, effect on anesthetic requirements.

METHODS

After institutional approval, a randomized double blind study was designed. 60 patients aged between 20-60 years, of ASA grade 1 and 2 posted for surgeries like tonsillectomy, thyroidectomy, cholecystectomy and breast surgeries under general anaesthesia were enrolled after getting written informed consent from patients. The patients were randomly divided into 2 groups of 30 each, viz: Group-C (Study group): were given Injection clonidine, 1.5µg/kg in 100ml of normal saline as premedication intravenously, 15 min prior to induction of anesthesia. Group-N: (Control group): received 100 ml of normal saline infusion. For both the groups same type of anesthesia and analgesia was followed.

Patients with ASA grade 3 and 4, patients with difficult airway, patients less than 20 years and more than 60 years of age, patients with bronchial asthma, uncontrolled hypertension, and diabetes mellitus were excluded from the study. The patients were monitored throughout the procedure by pulse oximeter, NIBP and ECG. Patients were premedicated with Inj. pentazocine lactate 0.5mg/kg.

Group-C patients received Inj. Clonidine 1.5 µg/kg, in 100ml normal saline, intravenously, 15 min prior to induction of anesthesia. Group-N patients received 100ml of normal saline intravenously 15min prior to induction. All patients were preoxygenated with 100% oxgyen for 3mins. Inj. Thiopentone sodium (2.5%) dose being 5mg/kg with abolition of eye lash reflex as end point was used for induction followed by succinylcholine 1.5mg kg^{-1} and ventilated with Magills circuit for 1 minute. After adequate relaxation, laryngoscopy was performed with a Macintosh Laryngoscope and intubation was performed with a cuffed oral endotracheal tube of appropriate size, with a strict and vigil monitoring of hemodynamic parameters like Heart Rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Mean blood pressure (MBP) at regular intervals: pre-induction, just prior to induction and at 0 min (laryngoscopy and intubation), 1 min, 5min and 10 minutes post intubation. Surgical stimulus was avoided during the study period. Anesthesia was maintained with oxygen, nitrous oxide, halothane and vecuronium bromide (0.08mg/kg) incremental dose of which was given every 20 minutes. At the end of surgery, neuromuscular blockade was reversed with inj. neostigmine 0.05 mg/kg and inj. glycopyrrolate 0.01mg/ kg. Extubation done and patients were shifted to recovery room for further observation.

RESULTS

Observation and results were obtained from the two groups by statistical analysis with paired and unpaired T tests and the 'p' value was calculated.

$p > 0.05$ was considered as not significant.

$p < 0.05$ was considered as significant

$p < 0.01$ was considered as highly significant.

Table 1: Demographic Data of the Patients- in Study and Control Groups.

	Group-C	Group-N	' P' value
Age (Y)	38.04±12.07	39.06±12.50	p>0.05 NS
Sex (M/F)	14/16	16/14	p>0.05 NS
Weight (Kg.)	53.68±7.48	52.08±6.44	P>0.05 NS

The Patients in the two groups were comparable with respect to age, weight and sex (Table I). The mean age in study group was 38.04±12.07 years and mean weight was 53.68±7.48 kg. There were 14 males and 16 females in the study group. The mean age in control group was 39.06±12.50 years and mean weight was 52.08±6.44 kg. There were 16 males and 14 females in the study group.

Statistical analysis with paired t test was done. There was no significant percentage change in heart rate from the baseline (p>0.05) throughout the procedure in the study group.

In the control group, the percentage increase in the heart rate from the baseline was maximum after intubation (19.7%) and it was highly significant (p<0.01). The percentage change in the heart rate remained elevated from the baseline throughout the procedure and was highly significant (p<0.01)

Statistical analysis with unpaired 't' test was done. Results showed that in the preoperative and preinduction periods there was no statistically significant (p>0.05) difference in systolic blood pressures in the two groups. After intubation, at 1 min, 5 min, 10 min of intubation, the statistical difference in two groups was highly significant (p<0.01) with a significant increase in the mean systolic blood pressures in the control group.

Statistical analysis with unpaired t test was done. Results showed that in the preoperative and preinduction periods, there was no statistically significant difference (p>0.05) in the diastolic blood pressure in the two groups. After intubation, at 1 min, 5 min, 10 min of intubation, , the statistical difference in the two groups was highly significant (p<0.01) with a significant increase in the mean diastolic blood pressure in the control group.

Statistical analysis with unpaired t-test was done. Results showed that in preoperative and preinduction periods,

there was no statistically significant (p>0.05) difference in the mean blood pressures in the two groups. After intubation, 1 min, 5 min, 10 min of intubation, the statistical difference in the two groups was highly significant (p<0.01), with a significant increase in the mean blood pressure in the control group.

Table 2: Comparison of heart rate in Patients of Study and Control Groups.

Heart	Rate (bpm)	Study drug (n=30)		Control drug (n=30)		
	Mean ±SD	% change from Baseline	p' value	Mean ±SD	% change from Baseline	'p' Value
Pre-Op	88.2±14.6	0.0	-	87.8±7.2	0.0	-
Before induction	89.0±14.5	0.9	0.539	81.9±7.4	5.0	< 0.001
After intubation	91.4±10.7	3.5	0.158	96.9±6.7	19.7	< 0.01
1 min after intubation	88.2±14.2	0.0	0.988	90.3±8.4	13.9	< 0.01
5 min after intubation	88.7±10.5	0.5	0.819	89.9±8.0	13.4	< 0.01
10 min after intubation	87.9±11.2	-0.3	0.912	88.1±8.4	11.7	< 0.01

Table 3: Comparison of Systolic Blood Pressure in Patients of Study and Control Groups.

Systolic Blood Pressure(mmHg)	Study Group (n=30)	Control Group(n=30)	'p' value	Significance
	Mean±SD	Mean±SD		
Pre-Op	124.1 ± 11.7	119.5 ± 9.1	0.097	NS
Preinduction	120.5 ± 14.5	118.2 ± 7.6	0.438	NS
After intubation	122.5 ±16.2	135.0 ± 12.1	0.001	HS
1 min after intubation	117.2 ± 14.5	132.5 ± 9.2	0.001	HS
5 min after intubation	113.6 ± 11.9	136.5 ± 10.1	0.001	HS
10 min after intubation	112.5 ± 10.3	130.7 ± 6.5	0.001	HS

NS-Not significant, HS-Highly significant

Table 4: Comparison of Diastolic Blood Pressure in Patients of Study and Control Groups.

Diastolic Blood Pressure	Study Group (n=30)	Control Group (n=30)	'P' value	Significance
	Mean±SD	Mean±SD		
Pre-Op	82.7 ± 8.8	80.4 ± 6.2	0.2407	NS
Preinduction	79.3 ± 11.1	82.3 ± 7.6	0.2321	NS
After intubation	82.1 ± 10.9	88.9 ± 9.3	0.0111	HS
1 min after intubation	80.9 ± 11.4	89.3 ± 7.4	0.0013	HS
5 min after intubation	77.5 ± 8.8	87.9 ± 4.5	0.0001	HS
10 min after intubation	77.6 ± 6.5	89.5 ± 3.5	0.0001	HS

NS- Not significant, HS- Highly significant

Table 5: Comparison of Mean Blood Pressures in Patients of Study and Control Groups.

Mean Blood Pressure	Study Group (n=30)	Control Group (n=30)	'P' value	Significance
	Mean ± SD	Mean ± SD		NS
Pre-Op	96.8 ±9.8	94.1 ± 6.1	0.2034	NS
Preinduction	94.4 ± 11.5	93.6 ± 6.6	0.7324	HS
After intubation	96.0 ± 13.1	104.1 ± 8.2	0.0059	HS
1 min after intubation	93.1 ±13.4	103.5 ± 7.5	0.0005	HS
5 min after intubation	89.7 ± 9.5	103.7 ± 4.7	0.0001	HS
10 min after intubation	89.7 ± 7.4	102.7 ± 3.8	0.0001	

NS- Not Significant, HS- Highly Significant

DISCUSSION

The anaesthesia and surgery is associated with a rise in plasma catecholamine concentration and subsequent increase in the blood pressure, HR and the cardiac dysrhythmias. These above mentioned effects may have serious repercussions on the high-risk patients like those with cardiovascular disease, high blood pressure, increased intracranial pressure, or anomalies of the cerebral vessels. Attenuation of such responses is of great importance in the prevention of the perioperative morbidity and mortality.[8]

In 1941, Burstein et al,[9] found that the pressor response to laryngoscopy and endotracheal intubation was due to an augmented sympathetic activity which was provoked by the stimulation of the epipharynx and the laryngopharynx, which was further confirmed by Prys-Robert. This was in contraindication to the finding of Reid[10] et al., in 1940 who proposed that the stimulation of the upper respiratory tract provoked an increase in the vagal activity. The findings of Burstein et al., was further confirmed by Prys-Roberts.

During laryngoscopy there is mechanical stimulation of upper respiratory tract which includes tongue, nasopharynx, oropharynx and most importantly the epiglottis. Afferents are carried by the glossopharyngeal nerve and vagus nerve. These afferents are carried to the cardioaccelerator or vasomotor centre. Sympathetic efferent from this centre results in transient rise in heart rate and blood pressure. It has been shown by Kaplan that stress due to sympathetic activation causes myocardial oxygen demand to exceed beyond its coronary supply resulting in parts of myocardium being rendered ischemic.Clonidine[11] is a centrally acting selective partial α2 adrenergic agonist which also has a sympatholytic effect. More-over it attenuates stress induced sympathoadrenal response to painful stimuli, improves the intra-operative hemodynamic stability, reduces the incidence of peri-operative Myocardial Infarction episodes in patients with suspected or documented coronary artery disease & decreases anaesthetic requirements during surgery; So clonidine seems be well suited as premedication for attenuating hemodynamic response following laryngoscopy & intubation.[12] It is also beneficial in preventing postoperative nausea and vomiting (PONV) and shivering [13] in the postoperative period.

The mean age in study group was 38.04±12.07 years and mean weight was 53.68±7.48 kg. There were 14 males and 16 females in the study group. The mean age in study group was 39.06±12.50 years and mean weight was 52.08±6.44 kg. There were 16 males and 14 females in the study group. There was no significant percentage change in heart rate from the baseline throughout the procedure in the study group. In the control group, the heart rate remained elevated from the baseline throughout the procedure, but the percentage increase in the heart rate from the baseline was maximum after intubation (19.7%) and it was highly significant. There was no statistically significant ($p>0.05$) difference in systolic blood pressures in the two groups during the preoperative and preinduction periods. After intubation, at 1 min, 5 min, 10 min of intubation, the statistical difference in two groups was highly significant with a significant increase in the mean systolic blood pressures in the control group

There was no statistically significant difference in the diastolic blood pressure in the two groups in the preoperative and preinduction periods. After intubation, at 1 min, 5 min, 10 min of intubation, the statistical difference in the two groups was highly significant with a significant increase in the mean diastolic blood pressure in the control group. In preoperative and preinduction periods, there was no statistically significant difference in the mean blood pressures in the two groups. After intubation, at 1 min, 5 min, 10 min of intubation, the statistical difference in the two groups was highly significant, with a significant increase in the mean blood pressure in the control group.

These findings were similar to the findings found in the study done by Nameirakpam Charan et al[14] who found that Intravenous Clonidine was found to be more effective than intravenous Fentanyl in attenuating pressure response to laryngoscopy and intubation with the minimum equipotent dose. Anish Sharma N.G [15] and Shankaranarayana P P conclude that both clonidine and dexmedetomidine attenuates the pressor response during laryngoscopy and Intubation but Dexmedetomidine is better in attenuating the tachycardia response. The study conducted by Shirsendu Mondal[16] et al had similar finding where both clonidine and dexmedetomidine attenuates the pressor response during laryngoscopy and Intubation. Sakshi Arora[17] et al concluded in their study that a single intravenous low dose clonidine when combined with low dose is a practical, pharmacological and safe method with minimal side effects to attenuate the hyperdynamic response to laryngoscopy and intubation. R Anand Subramaniam[18] and Shalini G Anand in their study concluded that clonidine and dexmedetomidine are equally effective in reducing the stress response to Laryngoscopy and intubation. Sunita Goel, Manju Sinha[19] concluded that the sedation, analgesic sparing and anxiolytic effects of clonidine offer a distinct advantage. Javaherfroosh F, M. Raza Pipelzadeh, Namazi M[20] in their study showed that clonidine reduces postoperative nausea and vomiting following laparoscopic gynecological surgery.

Clonidine doses up to 4-5 µg kg-1 have been investigated frequently, though primarily for their anesthetic-sparing effects in the intraoperative period and for their opioid-sparing effects in the postoperative period.[21] We conclude that minimal dose of IV clonidine 1.5 µg/ kg cause

maximum attenuation of pressor response with minimal side effects like hypotension and sedation, and also reduced anesthetic requirements.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Prys-Roberts, Greene LT, Meloche R, Foex P. Studies of anaesthesia in relation to hypertension-II. Haemodynamic consequences of induction and endotracheal intubation. British Journal of Anaesthesia. 1971;43:541-47.
2. Denlinger JK, Ellison N, Ominsky AJ.Effects of intratracheallidocaine on circulatory responses to tracheal intubation. Anesthesiololgy 1974; 41: 409-12.
3. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with sodium nitroptusside. Anesth Analg 1979; 58: 116-9.
4. Safwat AM, Reitan JA, Misle GR, Hurley EJ. Use of propanolol to control rate-pressure product during cardiac anaesthesia. Anesth Analg 1981;60:732-5.
5. Martin DE, Rosenberg H, Aukburg SJ et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. Anesth Analg 1982; 61: 680-4.
6. Bedford RF, Marshall WK. Hemodynamic response to endotracheal intubation: four anaesthetics. Anesthesiology 1981;55:A270.
7. Singh S, Arora K. Effect of oral clonidine premedication on perioperative haemodynamic response and post-operative analgesic requirement for patients undergoing laparoscopic cholecystectomy. Indian J Anaesth. 2011 Jan-Feb; 55(1): 26–30.
8. Chraemmer-Jørgensen B, Hertel S, Strøm J, Høilund-Carlsen PF, Bjerre-Jepsen K. Catecholamine response to laryngoscopy and intubation. The influence of three different drug combinations commonly used for induction of anaesthesia. Anaesthesia. 1992;47(9):750-6.
9. Burstein CL, Lopinto FJ, Newman W. Electrocardiographic studies during endotracheal intubation. I. Effects during usual routine techniques. Anesthesiology. 1995;11(2):224-37.
10. Reid LC, Brace DE. Irritation of the respiratory tract and its reflex effect upon heart. Surg Gynaec and Obst. 1940;70:157-62.
11. Tanaka and T. Nisikawa. Effect of clonidine premedication on the pressor response to α-adrenergic agonists. BJA 1995;75:593-597.
12. Textbook of pharmacology & physiology in anesthetic practice- Robert K Stoelting-4th edition: 340-45.
13. Sia S. I.V. Clonidine prevents post-extradural shivering. British Journal of Anaesthesia, 1998; 81:145-146.
14. Nameirakpam Charan, Bijaya Hijam, Sanjot Ninave, S. Thoibahenba Singh, Upendra Keisham, Ibemhal Heisnam. A Double Blind Comparative Study of I.V. Clonidine and Fentanyl to see the Haemodynamic Response during Laryngoscopy and Intubation. Journal of Evolution of Medical and Dental Sciences 2014;3:10015-25.
15. Anish Sharma N.G. and Shankaranarayana P P, Premedication with I.V. dexmedetomidine Vs I.V. clonidine in attenuating the pressor response during laryngoscopy & endotracheal intubation, International Journal of Biomedical Research (2014) 05 (07).
16. Mondal S, et al. Comparison of dexmedetomidine and clonidine for attenuation of sympathoadrenal responses and anesthetic requirements to laryngoscopy and endotracheal intubation. Int J Basic Clin Pharmacol 2014;3(3):501-6.
17. Arora S, Kulkarni A, Bhargava AK. Attenuation of hemodynamic response to laryngoscopy and orotracheal intubation using intravenous clonidine. J Anaesthesiol Clin Pharmacol 2015;31:110-4.
18. R Anand Subramaniam, Shalini G Anand, Study of intravenous clonidine Vs intravenous dexmedetomidine to attenuate the response to laryngoscopy and intubation International Journal of Recent Trends in Science and Technology, March 2015; 14(2): 271-278.
19. Sunita Goel, Manju Sinha. Effect of oral clonidine premedication in patients undergoing laparoscopic surgery. Bombay Hospital Journal, 2006; 48(04): 587-591.
20. Javeherfroosh F, M Raza Pipelzadeh, Namazi M. Clonidine reduces postoperative nausea and vomiting in laparoscopic surgery. Pakistan J Med Sci, 2009;25(5):782-5.
21. Brest AN. Hemodynamic and cardiac effects of clonidine. J Cardiovasc Pharmacol 1980;2:S39-46.

DOI: 10.18203/2320-6012.ijrms20150167
Cite this article as: Chandrashekarappa K, Ravindra CG, Mallappa K, Kumara AB. Intravenous low dose clonidine premedication for attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation. Int J Res Med Sci 2015;3:1457-61.