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`Original Research Article

A Hospital-Based Assessment of the Efficacy of Intravenous Clonidine 1 µg/ Kg in Attenuation of Hemodynamic Response to Orotracheal Intubation and Laryngoscopy

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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to assess the efficacy of intravenous Clonidine 1 µg/kg in attenuation of hemodynamic response to orotracheal intubation and laryngoscopy and observe.

Methods: The retrospective study was conducted at Shree Narayan Medical Institute and Hospital, Saharsa, Bihar, India for 12 months. Written informed valid consent was obtained from all patients participating in the study. 100 patients of either sex, between 20-60 years of age of ASA Grade I and II scheduled for surgery under General Anesthesia were studied.

Results: Thus there was a statistically significant increase in HR (P=0.000) compared to baseline value. There was statistically significant increase in SBP at 0 minute, 1 minute, 3 minutes and 5 minutes whereas negligible decrease after 10 minutes compared to baseline value. After intubation there was statistically significant increase in DBP (P<0.01) compared to baseline value.

Conclusion: Clonidine at a dose of 1 µg/kg body weight diluted in 10 ml Normal saline given 10 minutes before induction significantly attenuates the hemodynamic responses to laryngoscopy and orotracheal intubation with minimal side effects like bradycardia. However, the study has to be done on a larger population and in high risk patients for further evaluation.

Keywords: Clonidine, Hemodynamic Response, Laryngoscopy, Orotracheal Intubation.

Introduction

Laryngoscopy and orotracheal intubation are potent stressful stimuli that provoke hemodynamic response like tachycardia and hypertension that can lead to myocardial ischemia, ventricular arrhythmia, left ventricular failure, and cerebral hemorrhage. The mechanisms of the responses to laryngoscopy and orotracheal intubation are proposed to be by somatic visceral reflexes. [1] Stimulation of proprioceptors at the base of the tongue during laryngoscopy induces impulse dependent increases of systemic blood pressure, heart rate (HR), and plasma catecholamine concentrations. Subsequent orotracheal intubation recruits additional receptors that elicit augmented hemodynamic and epinephrine responses as well as some vagal inhibition of the heart. [2] These events are especially detrimental in individuals who have limited myocardial reserve due to coronary artery disease, cardiac dysrhythmia, cardiomyopathy, congestive heart failure, hypertension, and geriatric population. [3]

Various drug regimens and techniques have been used from time to time for attenuating the stress response to laryngoscopy and intubation, including opioids, barbiturates, benzodiazepines, beta blockers, calcium channel blockers, vasodilators, etc. [4-8] Alpha-2 agonists like clonidine [9] and dexmedetomidine [10] have been used recently for attenuation of sympathoadrenal stimulation caused by tracheal intubation and surgery. Clonidine stimulates α2 adrenergic inhibitory neurons in the medullary vasomotor center. As a result there is a decrease in sympathetic nervous system outflow from central nervous system to peripheral tissues. [11]

Intravenous anesthetic induction agents do not adequately or predictably suppress the circulatory responses evolved by endotracheal intubation. So

prior to laryngoscopy, additional pharmacological measures like use of volatile anesthetics, topical and intravenous lidocaine, opioids, vasodilators– SNP, NTG, Calcium channel blockers and β-blockers have been tried but none was found ideal. [12,13] Clonidine, a central α–2 agonist has sedative, analgesic and antihypertensive actions. [14] Hence, there is a need to study the effects of intravenous clonidine for attenuation of hemodynamic stress response to laryngoscopy and intubation.

The aim of the present study was to assess the efficacy of intravenous Clonidine 1 μg/kg in attenuation of hemodynamic response to orotracheal intubation and laryngoscopy and observe side effects of Inj. Clonidine.

Materials and Methods

The retrospective study was conducted at Shree Narayan Medical Institute and Hospital, Saharsa, Bihar, India for 12 months. Written informed valid consent was obtained from all patients participating in the study. 100 patients of either sex, between 20-60 years of age of ASA Grade I and II scheduled for surgery under General Anaesthesia were studied.

Group A (50) in which patients received Inj. Clonidine 1 μ/kg IV diluted in 10 ml normal saline 10 minutes prior to induction.

Group B (50) in which patients received 10 ml normal saline IV 10 minutes prior to induction.

Inclusion Criteria: ASA Grade I and II , Age 20-60 years of both sex, Weight between 40 -60 kg, patients posted for elective surgical procedure requiring general anesthesia, patients with written, valid and informed consent Grade I and II

Exclusion Criteria: Patient refusal to participate in the study, ASA Grade III and IV, pregnant patients, Patients on beta blocker drugs, patients with cardiovascular disorders, Patient suffering from renal disease, patients of COPD and with recent history of URTI, drug or alcohol abuse, patients with anticipated difficult intubation (MPC Grade III and IV), patient in whom time required for intubation exceeded 15 seconds and more than one attempt of intubation Patients scheduled for elective surgeries under general anesthesia were thoroughly evaluated and assessed preoperatively for inclusion in the study. Preanesthetic evaluation comprising of history of previous medical and surgical illnesses, previous anesthesia exposures, drug allergies along with general, physical examination , airway assessment was done by Mallampati grading to anticipate the possibility of difficult intubation. Basic blood investigations of Hemoglobin, Complete blood counts, Liver function test, PT(INR), Bleeding time, Clotting time, Urine analysis, Renal function test,

Electrolytes, radiograph of Chest, Electrocardiogram were performed. Other investigations if indicated were carried out. On the day of surgery patients NBM status was confirmed. Patient was taken inside the operation theatre, an intravenous (IV) line was secured with Angio catheter number 18 gauge on nondominant hand. Monitoring was continued using pulse-oximeter, noninvasive blood pressure monitor, ECG lead V was recorded. After intubation carbon dioxide monitoring along with agent analyzer were attached. Preinduction heart rate and blood pressure recording were taken. Preloading was done with Ringer Lactate 10 ml/kg. All patients were premedicated with tab. Diazepam 5 mg and tab. Ranitidine 150 mg night before surgery. All patients were premedicated with inj. Midazolam 0.03 mg/kg IV and inj. Ondansetron 0.08 mg/kg IV before induction. Patients of group A received inj. Clonidine 1 μg/kg diluted in 10ml normal saline 10 minutes before induction and Patients of group B received intravenous 10 ml normal saline 10 minutes before induction. Then they were preoxygenated for 5 min with 100% oxygen. General anesthesia was induced in patients with injection Thiopentone Sodium 6mg/ kg IV until loss of eye lash reflex. Intubation facilitated with inj. Vecuronium 0.1 mg/kg. All patients were ventilated with 100% oxygen at the rate of 10-12 L/min until intubation after administration of injection Vecuronium IV for 3 minutes. Direct laryngoscopy was done and patient was intubated by expert anesthesiologist within 15 seconds with proper size of endotracheal tube. Anesthesia was maintained with oxygen 50% , nitrous oxide 50%, and isoflurane . Muscle relaxation was maintained using injection Vecuronium IV. Patients were monitored throughout the surgical procedure with pulse-oximeter, noninvasive blood pressure monitor and ECG lead V. Hemodynamic responses were compared in both groups by measuring HR, SBP, DBP, MAP, SpO2, ECG (lead V5). Basal reading when the patient was shifted to OT (T0), 5 minutes after IV Clonidine (T1), at induction (T2), at intubation (T3), 1 minute after intubation (T4), 3 minutes after intubation (T5), 5 minutes after intubation (T6), 10 minutes after intubation(T7). Isoflurane concentration was adjusted to maintain systolic B.P. within 20% of preoperative values. Heart rate <60 beats/minutes was managed by inj. Atropine 0.6 mg IV. Mean Arterial Pressure< 60 mm Hg was managed with fluid challenges and Inj. Mephentermine 6 mg bolus IV and incremental doses if required. Upon completion of surgery, neuromuscular block was reversed with inj. Neostigmine and inj. Glycopyrrolate IV and patient was extubated.

Statistical Method Employed:

All quantitative data was presented as mean ±SD (standard deviation). Quantitative data was analyzed by Student's t test. p<0.01- Statistically highly significant (HS) p<0.05- Statistically significant (S). p>0.05- Statistically not significant (NS). The statistical software SPSS version was 23.0, used for the analysis of the data and Microsoft Word and

Excel was used to generate graphs, tables etc.

Results

Table 1: Comparison between the groups according to Heart Rate (bpm)

Heart Rate bpm	Group A	Group B
Baseline	86.34 ±15.865	92.14±8.846
0 minute	83.58± 9.7658	124.62±9.354
1 minute	81.32±9.200	116.74±7.556
3 minutes	78.96±8.942	113.76±7.257
5 minutes	81±9.480	109.23±6.725
10 minutes	75.30±8.879	96.63±8.160

In group A (Clonidine), the baseline mean HR was 86.34 ±15.865 bpm. Mean HR after intubation at 0 minute, 1 minute, 3 minutes, 5 minutes and 10 minutes were 83.58± 9.7658, 81.32±9.200, 78.96±8.942, 76. 81±9.480, 75.30±8.879 bpm respectively. Thus there was significant fall in mean HR after intubation compared to baseline value and this was statistically highly significant.

(P=0.0001) In group B the baseline mean HR was 92.14±8.846 bpm. Mean HR after intubation at 0 minute, 1 minute, 3 minutes, 5 minutes, and 10 minutes were 124.62±9.354,116.74±7.556,113.76±7.257,109.23 ±6.725, 96.63±8.160 bpm respectively. Thus there was a statistically significant increase in HR (P=0.000) compared to baseline value.

Table 2: Comparison between the groups according to Systolic BP (mmHg)

SBP	Group A	Group B
Baseline	128.42 ±12.758	130.00±6.464
0 minute	115.32±9.334	159.04±4.372,
1 minute	112.11±9.006	152.36±4.464
3 minutes	105.35±18.112	143.57±5.645
5 minutes	105.25±10.895	138.12±7.820
10 minutes	102.90±8.816	127.80±6.261

In group A (Clonidine), the baseline SBP was 128.42 ±12.758 mmHg. The mean SBP after intubation at 0 minute,1 minute, 3 minutes, 5 minutes and 10 minutes were 115.32±9.334, 112.11±9.006, 105.35±18.112, 105.25±10.895, 102.90±8.816 mmHg respectively. It showed significant fall in SBP after intubation compared to baseline value and this was statistically highly significant. In group B the baseline SBP was

130.00±6.464 mmHg. SBP after intubation at 0 minute, 1 minute, 3 minutes, 5 minutes and 10 minutes, were 159 .04±4.372, 152.36±4.464, 143.57±5.645, 138.12 ±7.820, 127.80±6.261 mmHg respectively. There was statistically significant increase in SBP at 0 minute, 1 minute, 3 minutes and 5 minutes whereas negligible decrease after 10 minutes compared to baseline value.

Table 3: Comparison between the groups according to Diastolic BP (mmHg)

DBP	Group A	Group B
Baseline	75.45±4.496	79.41±6.254
0 minute	81.12±9.842	98.42±4.432
1 minute	78.16±8.662	97.33±4.936
3 minutes	74.76±7.293	93.06±5.284
5 minutes	68.96±7.690	87.48±7.263
10 minutes	72.64±8.036	78.06±6.832

In group A (clonidine), the baseline DBP was 75.45±4.496 mmHg. The DBP after intubation at 0 minute, 1 minute, 3 minutes, 5 minutes and 10 minutes were 81.12±9.842, 78.16±8.662, 74.76±7. 293, 68.96±7.690, 72.64±8.036 mmHg respectively. There was significant fall in DBP

after intubation compared to baseline value and this was statistically highly significant. In group B the baseline DBP was 79.41±6.254 mmHg. DBP after intubation at 0 minute, 1 minute, 3 minutes, 5 minutes and 10 minutes were 98.42±4.432, 97.33±4.936,93.06±5.284,87.48±7.263,78.06±6.8

32 mmHg respectively. After intubation there was statistically significant increase in DBP (P<0.01) compared to baseline value.

Discussion

Laryngoscopy and tracheal intubation are commonly accompanied by increase in arterial blood pressure and heart rate. [15] The principle mechanism in this hypertension and tachycardia is the sympathetic response [16], which may be the result of increase in catecholamine activity3. Transitory hypertension and tachycardia are probably of no consequence in healthy individuals. But either or both may be hazardous to those with hypertension, myocardial insufficiency and cerebrovascular diseases. [17] This laryngoscopy reaction in such individuals may predispose to development of pulmonary edema, dysrhythmias, myocardial insufficiency and cerebrovascular accident. [18]

Thus there was a statistically significant increase in HR (P=0.000) compared to baseline value. U.A Carabine et al [19] used 1.25 µg/kg and 0.625 µg/kg IV Clonidine and noted that the degree of tachycardia was significantly lower at induction (p<0.01) and intubation (p<0.05) with 1.25 µg/kg, but one patient developed bradycardia of 45 beats/minute. While with 0.625 µg/kg the significantly lower rate was noted from intubation for 3 minutes period (p<0.05).Deepshikha C Tripathi et al. (2011) [20] used 1 µg/kg and 2 µg/kg IV Clonidine in 100 ml normal saline 30 min before induction found that heart rate decrease at intubation but not more than 20% of baseline with 1 µg/kg (p<0.05).

Altan A et al [21] studied clonidine at a dose at 3 µg/kg noted that, following laryngoscopy and intubation, HR rose by 10 /min in the control group, whereas in the clonidine group, HR decreased by 10 /min, which is statistically highly significant (p<0.01). Ray M et al [22] Evaluated clonidine at a dose of 3 µg/kg noted that following laryngoscopy and intubation, HR at 1 min rose by 19 bpm in control group and only 1 bpm in clonidine group, the difference being statistically significant. Tripathi et al [23] in has studied that Clonidine, 2 µg/ kg intravenously, 30 min before induction is safe and effective in preventing the hemodynamic stress response during laparoscopic cholecystectomy. Sameena kousar et al [24] compared effect of Fentanyl and Clonidine for attenuation of the hemodynamic response to laryngoscopy and endotracheal intubation and found that Clonidine showed better attenuation of the sympathetic response While with 2 µg/kg IV Clonidine heart rate decrease was more than 20% from baseline. There was statistically significant increase in SBP at 0 minute, 1 minute, 3 minutes and 5 minutes whereas negligible decrease after 10

minutes compared to baseline value. After intubation there was statistically significant increase in DBP (P<0.01) compared to baseline value. Similarly, Tripathi D (2011) [23], Arora S et al [25] found that with 1ug/kg SBP, DBP and MAP decreased from baseline after intubation. Though, various studies found intravenous clonidine effective in attenuating the hemodynamic changes during laryngoscopy and intubation, there is wide difference in the dose of clonidine used.

Conclusion

Clonidine at a dose of 1 µg/kg body weight diluted in 10 ml Normal saline given 10 minutes before induction significantly attenuates the hemodynamic responses to laryngoscopy and orotracheal intubation with minimal side effects like bradycardia. However, the study has to be done on a larger population and in high risk patients for further evaluation.

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