Efficacy of Intravenous Clonidine to Attenuate Cardiovascular Stress Response to Laryngoscopy and Tracheal Intubation – A Prospective Randomized Double Blind Study

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ABSTRACT

Introduction: Hemodynamic stress response to laryngoscopy and intubation although transient, can lead to life threatening complications in susceptible patients. The objective of the present study was to evaluate efficacy of 3mcg/kg intravenous clonidine infusion to attenuate hemodynamic stress response to laryngoscopy and tracheal intubation and its effect on the requirement of thiopentone sodium for induction of anaesthesia.

Material and methods: 60 ASA Physical Status 1 patients undergoing elective surgery under general anaesthesia with endotracheal tube were randomised into 2 groups to receive either a premedication infusion of 3 mcg/kg intravenous clonidine (Group A) or normal saline (NS) (Group B). Sedation score, dose of thiopentone sodium required for anaesthetic induction, Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), and Rate pressure product (RPP) were recorded at specific time intervals before, during and after tracheal intubation.

Results: Patients in Group A were significantly more sedated at the end of infusion ($p<0.05$). The dose of Thiopentone sodium required for induction of anaesthesia was significantly low in Group A ($p<0.05$). The increase in HR, SBP, DBP, MAP and RPP from their baseline values after laryngoscopy and tracheal intubation was significantly lower ($p<0.05$) and short lived in Group A.

Conclusion: Intravenous clonidine (3 micrograms/kg) given as an infusion over 10 minutes prior to induction of anaesthesia provided adequate sedation and blunted the stress response to laryngoscopy and tracheal intubation. It also reduced the dose of thiopentone sodium required for induction of anaesthesia.

Keywords: Intravenous clonidine, Sedation, Laryngoscopy, Tracheal intubation, Hemodynamic stress response.

INTRODUCTION

Laryngoscopy and tracheal intubation can produce major changes in hemodynamics of a patient.[1] Hemodynamic stress response to laryngoscopy and tracheal intubation occurs due to reflex sympathetic discharge caused by mechanical stimulation of pharynx and larynx resulting in tachycardia, hypertension and arrhythmias.[2-4] This short-lived hyper adrenergic state is of little consequence in healthy individuals, but it may lead to detrimental effects in patients with primary or secondary hypertension, ischaemic heart disease, poor cardiovascular reserve[2-4] and cerebrovascular diseases.[5] Various anaesthetic techniques and drugs are used to blunt this hemodynamic response to laryngoscopy and tracheal intubation. The technique or drug of choice depends on the urgency and duration of surgery, choice of anesthetic technique, medical condition of the patient, individual preference and availability of equipments. Alpha-2 adrenoceptor agonists are frequently used as an adjunct to anesthesia as these drugs reduce anesthetic requirements, attenuate adrenergic, hormonal, and hemodynamic stress responses to surgery, reduce anxiety, and lead to sedation.[3,5-7] clonidine, an imidazoline derivative is centrally acting α2 adrenoceptor agonist.[6-8] It decreases the central sympathetic outflow by increasing the reuptake of nor-adrenaline by stimulation of pre-synaptic α2 adrenoceptors.[7,8] Thus, it results in less nor-adrenaline to act on post synaptic membrane, in Nucleus Tractus Soliterious (NTS) and vasomotor centre of brain stem.[6,7] The current study was undertaken to evaluate the efficacy of intravenous Clonidine 3mcg/kg as a premedication for attenuation of hemodynamic stress response to laryngoscopy and intubation and on Thiopentone sodium requirement for induction of anaesthesia.

MATERIAL AND METHODS

This prospective, randomized placebo controlled study was carried out in 60 ASA I patients of either sex between the age group of 18 to 60 years, posted for elective surgery lasting for 4-5 hours under general anaesthesia requiring endotracheal intubation after obtaining approval from Institutional Ethics Committee. Patients diagnosed with hypertension, A-V blocks, cardiac arrhythmias, congestive cardiac failure, coronary artery disease, cerebrovascular disease, COPD, acute or chronic hepatic or renal failure, BMI > 30 Kg/m^2 and anticipated difficult intubation were excluded from the study. Any patient requiring a second attempt of laryngoscopy and intubation and with duration of laryngoscopy more than 30 seconds were also excluded from the study. A thorough preanaesthetic evaluation was carried out as per institutional protocol. Selected patients were randomised into 2 groups using computer generated randomised chart. Written informed consent was obtained from all patients. Group A

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How to cite this article: Swati Chhatrapati, Abhijeet B Shitole. Efficacy of intravenous clonidine to attenuate cardiovascular stress response to laryngoscopy and tracheal intubation – a prospective randomized double blind study. International Journal of Contemporary Medical Research 2016;3(5):1462-1467.

patients received Clonidine 3mcg/kg intravenously in 100ml of NS and Group B patients received only 100ml of NS. On the day of surgery, after confirming adequate starvation, IV access was secured and Ringer lactate was started at 2ml/kg/hr. In the operating room, baseline parameters like Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (SpO2) and respiratory rate (RR) were recorded and mean arterial pressure (MAP) and rate pressure product (RPP) were calculated from the above parameters.

Then, patients in Group A received Clonidine 3mcg/kg intravenously diluted in 100 ml of NS over 10 minutes with the help of infusion pump. Patients in Group B received only NS 100 ml over a period of 10 minutes with the help of infusion pump. HR, SBP, DBP, SpO2, RR, MAP, RPP and sedation score were recorded before starting infusion (BEFa), and then at 5 minutes (@5a) and 10 minutes (@10a) after infusion. The degree of sedation was graded as follows:

Sedation Score 0: Patient awake and talkative.

Sedation score 1: Patient sedated but easily arousable.

Sedation score 2: Patient asleep but immediately responding to verbal commands.

Sedation score 3: Patient asleep reacting to verbal commands with delay.

Sedation score 4: Patient asleep, not reacting to verbal commands.

Any other complaints like nausea, vomiting, headache, restlessness, pruritus bradycardia (pulse rate < 60 per minute), hypotension (decrease in SBP by>20% baseline), and allergic reaction were noted.

All patients received Injection Glycopyrrolate 0.004 mg/kg, Injection Ondansetrone 0.08 mg/kg, Injection Midazolam 0.02 mg/kg and Injection Ranitidine 1 mg/kg at the end of drug infusion. Patient was then induced with injection Thiopentone sodium in graded doses till loss of eye lash reflex. The dose of Thiopentone sodium required for induction was noted. After confirming the ability to ventilate, injection Vecuronium 0.1 mg/kg was given and patient was ventilated with 40% O_2 and 60% N_2O for 2 minutes 30 seconds and with 100% O_2 for 30 seconds. Patient's trachea was then intubated with appropriate-sized endotracheal tube by a senior anaesthesiologist having at least 1 year experience in endotracheal intubation. The entire procedure of intubation was completed in 30 seconds and in single attempt. Study parameters were recorded at different time intervals as follows: after induction with thiopentone sodium(AT), 3 minutes after giving injection Vecuronium (@MV), at the time of performing laryngoscopy (AL) and tracheal intubation(ATI) followed by 1 minute (@1b), 2 minutes (@2b), 3 minutes (@3b), 4 minutes (@4b), 5 minutes (@5b), 7 minutes (@7b) and 10 minutes (@10b) after tracheal intubation. Any surgical interventions like catheterization, nasogastric tube insertion and incision were allowed 10 minutes after intubation to avoid disturbances in data recording. Anaesthesia was maintained with O_2 40% and N_2O 60% and intermittent boluses of injection Vecuronium with addition of Propofol infusion started 10 minutes after intubation, on controlled ventilation with circle absorber system. Injection Fentanyl 2mcg/kg was given 10 minutes after endotracheal intubation only in Group B. Any evidence of tachycardia i.e. > 20 % increase in HR from baseline or hypertension i.e. > 20 % increase in SBP from baseline was treated by deepening the plane of anaesthesia, by increasing Propofol infusion rate and by supplementing injection Diclofenac sodium 1.5 mg/kg IV as a rescue analgesic. Patients in Group B received injection Fentanyl 1 mcg/kg/hour in repeated doses till 1 hour prior to end of surgery. After completion of surgery, neuromuscular blockade was antagonized with Injection Neostigmine 0.06 mg/kg and Injection Glycopyrrolate 0.008 mg/kg. Patients were extubated and shifted to Post anaesthesia care unit for observation and shifted to the ward when they fulfilled the shifting criteria.

STATISTICAL ANALYSIS

Data analysis was done by using SPSS version 16.0. Qualitative data was represented in the form of frequency and percentage and was compared by using Pearson Chi-Square test. Quantitative data was represented in the form of Mean±SD. Paired and unpaired t-tests were used for within and between group comparisons respectively. P value <0.05 was considered statistically significant. P value < 0.001 was considered statistically highly significant.

RESULTS

Both groups were comparable with respect to demographic characteristics (p>0.05) and duration of surgery (Table-1). The mean sedation score at the end of infusion in Group A was 1.87 ± 0.587 as compared to 0 in Group-B (p<0.001). At the end of infusion, 23.33% of patients had sedation score 1, 66.66% of patients had sedation score 2 and 10% of patients had sedation score 3 in Group A. None of the patients in Group A had respiratory depression. There was no statistically significant difference between the two groups with respect to RR (12.93± 0.9 per minute in Group A vs. 12.93±0.9 per minute in Group B) and SpO_2 at the end of infusion (P>0.05). The mean induction dose of thiopentone sodium in Group A was 3.8830 ± 0.3395 mg/kg compared to 5.8000 ± 0.5816 mg/kg in Group B (P< 0.05). The baseline HR, SBP, DBP, MAP and RPP were comparable in both the groups (p>0.05). There was statistically significant decrease in HR, SBP, DBP, MAP and RPP as compared to baseline in Group A at the end of infusion (p<0.001). Both groups showed significant reduction in arterial pressure after anaesthetic induction (p<0.05) (Tables 2 and 3).

Heart Rate (HR): The maximum increase in HR in Group A was 11.30 % (96.47±8.53) from baseline (86.67±4.96) at 1 minute after intubation as compared to 46.53% (124.80± 3.77) from baseline (85.17±4.11) in Group B (p<0.001). HR

		Group A	Group B	P Value
Age		28.77 ± 9.402	27.07 ± 9.727	>0.05
Weight		57.10 ± 3.595	56.67 ± 2.426	>0.05
Sex	Male	19 (63.3%)	22 (73.3%)	>0.05
	Female	11 (36.7%)	8 (26.7%)	>0.05
Duration of surgery (hrs)		5.7 ± 0.907	5.87 ± 0.819	>0.05

Table-1: Demographic Data and Duration of surgery

Volume 3 | Issue 5 | May 2016 | ICV: 50.43 |
International Journal of Contemporary Medical Research
ISSN (Online): 2393-915X; (Print): 2454-7379

Time	Heart rate HR			Systolic blood pressure SBP			Diastolic blood pressure DBP		
	Group A	Group B	P value	Group A	Group B	P value	Group A	Group B	P value
baseline	86.67 ± 4.96	85.17 ± 4.11	>0.05	123.67 ± 4.85	121.73 ± 2.56	>0.05	83.46 ± 2.62	83.40 ± 1.67	>0.05
5 minutes after infusion	79.20** ± 4.32	84.30 ± 3.42	<0.05	118.00** ± 4.58	121.07 ± 2.91	<0.05	79.13** ± 4.32	84.30 ± 2.91	<0.05
10 minutes after infusion	75.13** ± 4.10	84.67 ± 3.83	<0.05	113.87** ± 5.06	119.60* ± 4.25	<0.05	76.33** ± 4.00	79.87 ± 2.28	<0.05
At the time of induction with thiopentone sodium	85.13 ± 5.67	94.53** ± 5.67	<0.05	98.27** ± 6.68	113.00** ± 4.69	<0.05	69.80** ± 3.98	75.80** ± 2.94	<0.05
3 minutes after giving Vecuronium	81.93** ± 4.99	100.47** ± 5.03	<0.05	104.33** ± 7.54	115.80** ± 3.94	<0.05	72.87** ± 3.88	76.80** ± 2.44	<0.05
At the time of laryngoscopy	88.27 ± 5.89	110.53** ± 3.93	<0.05	114.87** ± 7.42	135.20** ± 3.51	<0.05	78.87** ± 4.94	88.53** ± 2.87	<0.05
at the time of tracheal intubation	95.93** ± 7.05	124.53** ± 3.59	<0.05	125.87 ± 6.66	147.67** ± 2.41	<0.05	84.73 ± 4.12	94.40** ± 2.54	<0.05
1 minute after tracheal intubation	96.47** ± 8.53	124.80** ± 3.77	<0.05	129.60** ± 7.34	146.27** ± 2.01	<0.05	86.87* ± 5.79	94.40** ± 2.54	<0.05
2 minutes after tracheal intubation	92.67** ± 7.69	124.80** ± 3.77	<0.05	126.73* ± 5.74	143.13** ± 2.01	<0.05	84.67 ± 4.31	91.40** ± 2.68	<0.05
3 minutes after tracheal intubation	87.93 ± 7.08	122.00** ± 3.64	<0.05	121.27* ± 4.85	139.47** ± 2.40	<0.05	80.73** ± 3.50	87.73** ± 2.33	<0.05
4 minutes after tracheal intubation	83.90* ± 5.91	117.73** ± 3.39	<0.05	118.33** ± 5.20	134.73** ± 2.60	<0.05	80.00** ± 3.10	83.73 ± 2.33	<0.05
5 minutes after tracheal intubation	79.63** ± 4.76	112.87** ± 2.76	<0.05	115.13** ± 4.16	131.07** ± 2.61	<0.05	76.60** ± 3.78	81.47** ± 1.65	<0.05
7 minutes after tracheal intubation	77.00** ± 4.57	108.27** ± 2.13	<0.05	112.20** ± 4.18	123.87* ± 3.10	<0.05	74.40** ± 3.54	81.27** ± 2.13	<0.05
10 minutes after tracheal intubation	74.07** ± 3.99	99.67** ± 4.64	<0.05	110.73** ± 3.26	119.47* ± 3.01	<0.05	73.07** ± 3.70	79.00** ± 1.55	<0.05

Table-2: Hemodynamic Parameters at various time intervals (HR, SBP, DBP)

Time	Mean arterial pressure MAP			Rate pressure product RPP		
	Group A	Group B	P value	Group A	Group B	P value
baseline	96.86 ± 3.17	96.18 ± 1.76	>0.05	10719.87 ± 779.01	10369.87 ± 591.16	>0.05
5 minutes after infusion	92.10* ± 4.24	92.62* ± 1.94	>0.05	9355.60** ± 742.24	10207.60 ± 516.00	<0.05
10 minutes after infusion	88.84** ± 4.05	93.11* ± 2.73	<0.05	8567.20** ± 749.68	10129.53* ± 642.76	<0.05
At the time of induction with thiopentone sodium	79.29** ± 4.12	88.20** ± 3.13	<0.05	8375.46** ± 894.32	10686.80* ± 784.82	<0.05
3 minutes after giving Vecuronium	83.35** ± 4.76	89.80** ± 2.71	<0.05	8560.93** ± 930.70	11638.80** ± 779.33	<0.05
At the time of laryngoscopy	90.86** ± 5.39	104.10 ± 2.13	<0.05	10156.00** ± 1109.02	14942.93** ± 626.35	<0.05
at the time of tracheal intubation	98.44 ± 4.76	112.15** ± 1.87	<0.05	12098.93** ± 1354.98	18388.13** ± 567.94	<0.05
1 minute after tracheal intubation	101.11** ± 6.17	111.69** ± 2.08	<0.05	12544.67** ± 1685.06	18256.00** ± 663.32	<0.05
2 minute after tracheal intubation	98.69* ± 4.61	108.64** ± 1.93	<0.05	11770.8** ± 1365.90	17865.47** ± 664.66	<0.05
3 minute after tracheal intubation	94.24** ± 3.73	104.98** ± 2.10	<0.05	10674.93 ± 1076.52	17016.27** ± 622.30	<0.05
4 minute after tracheal intubation	92.77** ± 3.62	100.73** ± 1.92	<0.05	9937.20** ± 925.28	15862.40** ± 544.88	<0.05
5 minute after tracheal intubation	89.44** ± 3.70	98.00** ± 1.51	<0.05	9166.93** ± 623.69	14792.27** ± 440.11	<0.05
7 minute after tracheal intubation	87.00** ± 3.56	95.47 ± 2.28	<0.05	8639.06** ± 597.77	13410.53** ± 463.13	<0.05
10 minute after tracheal intubation	85.62** ± 3.38	92.50** ± 1.90	<0.05	8205.73** ± 568.20	11902.53** ± 541.61	<0.05
** P< 0.001, * P< 0.05, Compared to baseline , For Tables 2 and 3						

Table-3: Hemodynamic Parameters at various time intervals (MAP, RPP)

reached near baseline values 3 minutes after intubation in Group A after which it remained significantly lower than baseline ($p<0.05$) throughout the assessment period. The lowest HR in Group A was 74.07±3.99 per minute ($p<0.001$). HR in Group B remained significantly higher than baseline after tracheal intubation ($p<0.05$) and did not return to baseline throughout the observation period (Tables 2 and 3, Figure 1).

Systolic Blood Pressure (SBP): The maximum increase in SBP in Group A was 4.80% (129.60±7.34 mmHg) from baseline (123.67±4.85 mmHg) at 1 minute after intubation as compared to 21.35% (147.73±2.41mmHg) from baseline (121.73±2.56 mmHg) in Group B which occurred at the time of intubation ($p<0.05$). SBP reached near baseline values 3 minutes after intubation in Group A after which it remained significantly lower than baseline throughout the observation period ($p<0.05$). In Group B, SBP remained significantly high till 7 minutes after intubation ($p<0.05$) and reached near baseline values towards the end of observation period. The maximum fall in systolic BP in Group A was 98.27 ± 6.68 mmHg i.e. 20.54%, which occurred after thiopentone sodium induction. ($p<0.001$) (Tables 2 and 3, Figure 2).

Diastolic Blood Pressure (DBP): The maximum increase in DBP in Group A was 4.08% (86.87±5.79 mmHg) from baseline (83.46±2.62 mmHg) at 1 minute after intubation as compared to 13.18% (94.40±2.54 mmHg) from baseline (83.40±1.67 mmHg) in Group B which occurred at the time of intubation($p<0.05$). In Group A, DBP reached near baseline values within 2 minutes after intubation whereas in Group B it took 4 minutes to reach near baseline value. Following this, DBP was significantly low as compared to baseline in both the groups ($p<0.05$). (Tables 2 and 3, Figure 3).

Mean arterial pressure *(MAP)*: The peak rise in MAP was 4.39% (101.11±6.17mmHg) from baseline (96.86±3.17mmHg) at 1 minute after intubation in Group A as compared to 16.60% (112.15±1.87 mmHg) from baseline (96.18±1.76 mmHg) in Group B which was seen at the time of intubation ($p<0.05$). MAP reached near baseline values within 3 minutes after intubation in Group A as opposed to 7 minutes in Group B. Following this, MAP was significantly low as compared to baseline in both the groups ($p<0.05$) (Tables 2 and 3, Figure 4).

Rate-pressure-product (RPP): Maximum rise in RPP was 17.02% (12544.67± 1685.06) from baseline (10719.87± 779.01) at 1 minute after intubation in Group A as compared to 77.32% (18388.13±567.94) from baseline (10369.87±591.16) in Group B which occurred at the time of intubation ($p<0.05$). RPP reached baseline values within 3 minutes of intubation in Group A after which it remained significantly low compared to baseline throughout the observation period ($p<0.05$). In Group B, RPP remained significantly higher compared to baseline throughout the observation period ($p<0.05$) (Tables-2 and 3, Figure-5).

DISCUSSION

In 1951, King BD et al described the hemodynamic changes associated with laryngoscopy and tracheal intubation in the form of tachycardia, and hypertension, with or without arrhythmias. It was interpreted to be due to reflex sympathoadrenal response. These nerves activate the supra segmental and hypothalamic sympathetic centers releasing catecholamines causing rise in arterial blood pressure and tachycardia.[9] These changes are short-lived. But even this transient change in hemodynamics may lead to myocardial ischemia and subsequent myocardial infarction in susceptible individuals.[10,11] This stress response can also lead to rise in intracranial and intraocular pressure, which can be hazardous in patients with open eye injuries, intracranial lesions and cerebro-vascular disease.[10] Clonidine is an alpha-2 adrenoreceptor agonist, which reduces the release of nor-epinephrine from nerve endings both centrally and peripherally and thus causes reduction in arterial pressure,[7,8]

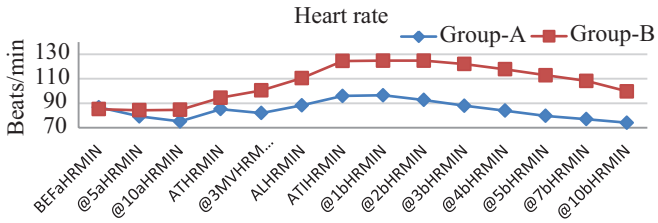

Figure-1: Comparison of Heart Rate (HR)

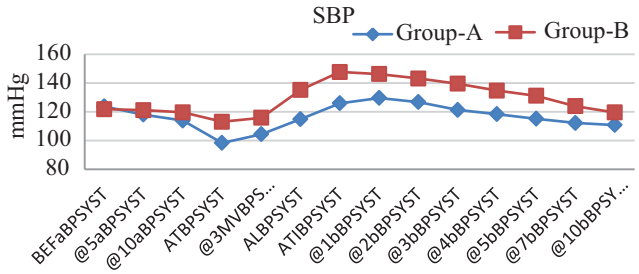

Figure-2: Comparison of Systolic Blood Pressure (SBP)

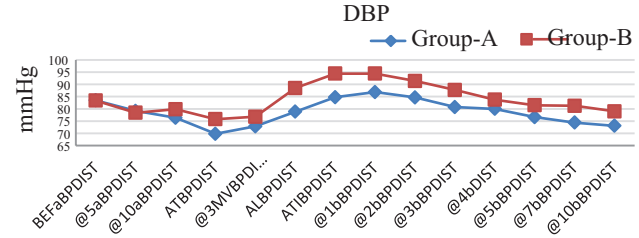

Figure-3: Comparison of Diastolic Blood Pressure (DBP)

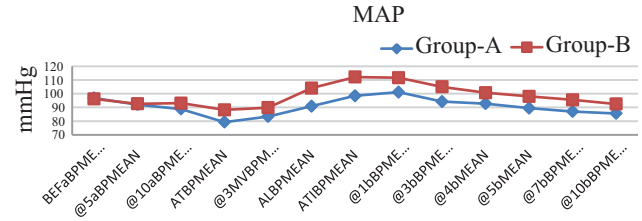

Figure-4: Comparison of Mean Arterial Pressure (MAP)

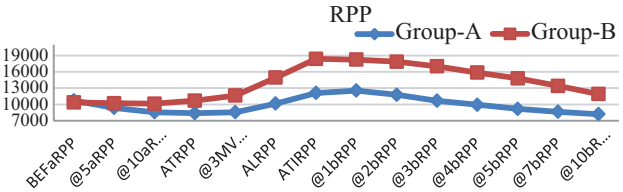

Figure-5: Comparison of Rate Pressure Product (RPP)

intraocular pressure,[12] and intracranial pressure[5] and protects myocardium from cardiovascular stress response.[13]

In the present study, we chose intravenous route of administration to relate pharmacodynamic effects more precisely to a certain dose. After intravenous route, the onset of action is immediate, distribution $t_{1/2}$ is 9 to 11 minutes and elimination $t_{1/2}$ is 9 hours. Analgesia, sedation and antihypertensive effects last for 8-9 hours.[13,14] The infusion was preferred in place of bolus dose to avoid reflex hypertension and tachycardia due to peripheral α-2 adrenoreceptor stimulation.[13] Kulka Peter J et al demonstrated that attenuation of pressor response to laryngoscopy and intubation by intravenous clonidine was dose-related till 4mcg/kg and, increasing the dose further was not found to be beneficial.[11] In most human studies, 4mcg/kg clonidine was applied without relevant signs of peripheral α-2 stimulation,[11] hence we chose 3mcg/kg dose of clonidine. We selected the optimal age range of 18 to 60 years. This is because, the variability of the heart rate change decreases with increasing age and younger patients show more extreme changes.[15]

In the present study, the mean sedation score at the end of infusion in Group A was 1.87 as compared to 0 in Group B ($p<0.001$). None of the patients in Group A had respiratory depression and SpO_2 was maintained in all the patients. The hypnotic or sedative effect of α2 adrenoreceptor activation has been attributed to locus coeruleus, which is the predominant noradrenergic nucleus in the brain with higher density of α2 adrenoreceptors and is an important modulator of vigilance.[11,16] Our finding is in accordance with studies done by Kulka Peter J et al,[11] Marinangeli F et al[17] and Kate Leslie et al[18] who demonstrated that clonidine-treated patients were significantly more sedated compared to placebo-treated patients. Aantaa R et al,[19] and Ooi R et al[20] showed that intravenous clonidine in doses of 3 mcg/kg and 3.5 mcg/kg respectively was not associated with respiratory depression. The induction dose of Injection Thiopentone Sodium was significantly lower in Group A compared to the Group B (3.8830 ± 0.3395 vs. 5.8000 ± 0.5816 mg/kg) ($P< 0.05$). The sedative and analgesic properties of clonidine could explain the induction agent's sparing effect. Kate Leslie et al[18] and Marinangeli F et al[17] also found significant reduction in the induction dose of thiopentone sodium after using intravenous clonidine in doses of 2.5 mcg/kg and 3 mcg/kg respectively.

Hemodynamic variables: The baseline HR, SBP, DBP, MAP and RPP were comparable in both groups ($p>0.05$). There was statistically significant decrease in HR, SBP, DBP, MAP and RPP in Group A compared to baseline at the end of infusion ($p<0.001$). This fall can be attributed to the centrally mediated sympatholytic effect of this drug.[11] Similar findings were also seen in the study by Sakshi Arora et al,[1] Kulka Peter J et al[11] and Anish Sharma N G et al.[21] Both groups showed significant reduction in arterial pressure after anaesthetic induction, indicating anaesthetised state and no surgical stimulation. This did not warrant any treatment. The cause of hypotension can be attributed to hypovolemia unmasked by the reduction of sympathetic tone by thiopentone induction.[22] In the study by Youhua Zhang et al, some patients in the clonidine group had SBP below 100 mmHg after induction with Thiopentone sodium. This hypotension was transient and only 3 out of 30 patients required administration of 100 ml bolus of NS.[23] The maximum fall in systolic BP in Group A in our study occurred after thiopentone induction ($p<0.001$). Though the fall was by 20% from the baseline SBP, it was short lived and did not warrant any inotropic support. HR, SBP, DBP, MAP and RPP were significantly decreased in Group A as compared to Group B from the end of infusion till 10 minutes after intubation ($p<0.05$).

The maximum increase in HR, SBP, DBP, MAP and RPP in Group A occurred at 1 minute after tracheal intubation and that in Group B at the time of intubation after which there was gradual decrease in all the parameters in both groups. However, the decline was more rapid in Group A. This finding was in accordance with other studies,[24,25] which concluded that plasma catecholamine concentration increased to the maximum at 1 minute after the laryngoscopy and came down by 3 minutes to 5 minutes after the laryngoscopy.

The maximum increase in heart rate in Group A was 11.30% while it was 46.53% in Group B ($P<0.001$). HR reached near baseline values 3 minutes after intubation in Group A and at the end of 10 minutes in Group B. This finding was in agreement with studies done by Kulka Peter J et al[11] and Zalunardo MP, Zollinger A et al[26,27] who concluded that during laryngoscopy and intubation, mean HR in clonidine pre-treated groups was significantly lower compared to placebo, and hemodynamic response to laryngoscopy and intubation was significantly attenuated by clonidine. Similar results were reported by Anish Sharma N G et al.[21] The maximum rise in SBP, DBP, MAP and RPP (4.80%, 4.08%, 4.39%, 17.02%) in Group A was significantly lower as compared to Group B (21.35%, 13.38%, 16.60%, 77.32%) ($P<0.05$%). The rise in SBP, DBP, MAP and RPP was sustained for 3 minutes, 2 minutes, 3 minutes, and 3 minutes respectively in Group A as opposed to 10 minutes, 4 minutes, 7 minutes and 10 minutes respectively in Group B. Similar attenuation of hemodynamic response was also seen by Manjula Sarkar et al[28] and Manjushree Ray et al.[29]

For healthy volunteers and patients with Ischemic heart disease, the critical limit of RPP was found to be 22,000 and 12,000 respectively.[30] In our study, clonidine did not allow the RPP to rise above 12544.67±1685.06, providing protection against angina or unwanted cardiac event in perioperative period. Similar findings were also seen in the study by Youhua Zhang et al.[23]

Limitations of our study

1. Our study was carried out in normotensive patients.
2. We did not measure the plasma catecholamine levels which is an objective means of measuring hemodynamic stress response.
3. We conducted the study only for initial 10 minutes after intubation. The intra operative requirement of anaesthetic agents, extubation response and postoperative sedation were not monitored.

CONCLUSION

Intravenous clonidine (3 mcg/kg) given as an infusion over 10 minutes prior to induction of anaesthesia provided adequate sedation without respiratory depression and

blunted the stress response to laryngoscopy and tracheal intubation without causing clinically significant bradycardia or hypotension. It also reduced the dose of Thiopentone sodium required for induction of anaesthesia.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 22-03-2016; **Published online**: 22-04-2016