www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 71.58
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v6i1.166

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Attenuation of Hemodynamic Response during Laryngoscopy and Endotracheal Intubation: Effect of Clonidine and Dexmedetomidine

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Abstract
Background: *Laryngoscopy and endotracheal intubation violate the patient's protective airway reflexes and invariably cause hemodynamic changes associated with increased heart rate, increased blood pressure and occasional disturbance in cardiac rhythm.*
Aim: *The aim of the study was to find the efficacy of α2-adrenoceptors agonist in attenuating pressor response while securing airway during surgery.*
Methods: *Ninety patients of ASA physical status I and II, in the age group between 25and 50 years, of either sex, undergoing various elective abdominal surgeries under general anaesthesia were randomly allocated into three groups. Both clonidine and dexmedetomidine administered intravenously just before laryngoscopy and endotracheal intubation effectively attenuated the hemodynamic response by limiting the extent of rises in heart rate and blood pressure.*
Result: *Dexmedetomidine has been found to provide better hemodynamic stability than clonidine.*
Keywords: *Laryngoscopy, .Dexmedetomidine, clonidine.*

Introduction

Laryngoscopy and endotracheal intubation is the traditional method of securing the airway for administration of anaesthesia. It causes haemodynamic changes associated with increased heart rate, increased blood pressure and occasional disturbance in cardiac rhythm.[1,2] In normotensive subjects these hemodynamic changes are short lived [3] and probably of little significance. However, these hemodynamic alterations are hazardous to the patients with hypertension, myocardial insufficiency or cerebrovascular disease.[4] may lead to left ventricular failure, pulmonary oedema and congestive cardiac failure. In patients with intracranial aneurysm or dissecting aneurysm of the aorta the increase in systemic blood pressure may cause rupture of vessels with life threatening consequences.

Various pharmacologic and non pharmacologic methods have been tried to limit the pressor response following the insertion of endotracheal tube.[5] Drugs like opioids, β-blockers, lidocaine, nitrates, calcium channel blockers or magnesium have already been used orally or parenterally to obtund this sympathoadrenal response. Recently, there is considerable interest in the use of α2-adrenergic agonists to provide haemodynamic stability during laryngoscopy and endotracheal intubation.

Clonidine and dexmedetomedine are both imidazoline subclass of α2-adrenoreceptor agonists, which reduce blood pressure and heart rate in a dosedependent fashion.[6] Dexmedetomidine is eight times more selective than clonidine for the α2-adrenergic receptors. The ratio of α2:α1 activity of dexmedetomidine is 1620:1 as compared with 220:1 for clonidine.[7,8,9]

Materials and Method

Ninety patients in the age group between 25 and 50 years, of either sex, belonging to ASA physical status I and II, undergoing various elective abdominal surgeries under general anaesthesia were selected for this study.

Patients with history of cardiovascular, respiratory, hepatic, renal diseases and those on antihypertensive drugs benzodiazepines and tricyclic antidepressants, history of drug abuse and having serious adverse reaction or allergy to trial drug, anticipated difficult intubation and pregnancy, were excluded from the study.

The 90 patients were randomly allocated into three equal groups (n=30): Group-C (clonidine), Group-D (dexmedetomidine), and Group-N (normal saline or control) 10 minutes prior to intubation. Randomization was achieved by closed envelopes chosen by patients prior to the procedure.

Group-C: Received clonidine (3 µg kg-1) in 50 ml normal saline

Group-D: Received dexmedetomidine (1 µg kg-1) in 50 ml normal saline.

Group-N: Received 50 ml normal saline.

The infusions were given approximately 10 minutes before induction and infused over 15 minutes through syringe pumps. All patients were premedicated with inj-pentazocine 0.5 mg/kg i.v. , inj. midazolam 0.05 mg/kg i.v and inj. Glycopyrolate 5 mcg/kg i.v. on operating room arrival. Induction of anaesthesia was done by 2.5% thiopental sodium 4-5 mg kg-1 slow intravenously till the eyelash reflex disappeared. Neuromuscular blockade was achieved by Vecuronium 0.1 mg kg-1 intravenously. Patients were then ventilated with 100% oxygen for about 3 minutes after injection of Vecuronium. Subsequently tracheal intubation with an appropriate size endotracheal tube was performed using a Macintosh laryngoscope in less than 15 seconds.

Hemodynamic parameters (HR, SBP, DBP and MAP) were recorded in the following specific time intervals:

•Before study drug infusion (baseline value)• 5 minutes after study drug infusion• After induction of anaesthesia• 1 minutes after intubation

•3 minutes after intubation• 5 minutes after intubation

Observation

Table 1 Comparison of demographic variables between three study groups

Demographic Variables	**Group C** (n =30) (Mean ± SD)	**Group D** (n =30) (Mean ± SD)	**Group N** (n =30) (Mean ± SD)	***p* value**
Sex (M : F)	12 : 18	10 : 20	10 : 20	0.8237
Age (years)	38.03 ± 8.16	39.07 ± 8.39	39.13 ± 8.37	0.8487
Body weight (kg)	56.07 ± 9.68	56.90 ± 9.94	55.83 ± 8.91	0.9029
Height (cm)	161.63 ± 9.39	160.03 ± 10.39	159.63 ± 9.57	0.7043
ASA grade (I : II)	24 : 6	24 : 6	23 : 7	0.9355

SD : standard deviation

Heart Rate

Table 2 Comparison of heart rates between and within the study groups at different points of time

Time interval	HEART RATES (beats per minute)			*p* value
	Group C (n =30) (Mean ± SD)	**Group D** (n =30) (Mean ± SD)	**Group N** (n =30) (Mean ± SD)	
Before study drug infusion (baseline) (T1)	83.13 ± 9.24	84.03 ± 9.14	83.27 ± 9.49	0.9213
5 minutes After study drug infusion (T2)	80.60 ± 8.52	79.17 ± 8.66 *	83.93 ± 8.79	0.0953
After induction of anaesthesia (T3)	78.03 ± 8.51 *	76.10 ± 8.18 **	81.80 ± 8.57	0.0320
1 minute after intubation (T4)	93.63 ± 7.06 **	87.63 ± 7.55	107.67 ± 6.38 **	< 0.0001
3 minutes after intubation (T5)	84.50 ± 7.29	81.83 ± 6.72	94.70 ± 8.41 **	< 0.0001
5 minutes after intubation (T6)	80.27 ± 6.48	78.00 ± 6.95 **	86.63 ± 6.63	< 0.0001

SD : standard deviation
*Statistically significant ($p< 0.05$) [when compared with baseline value within group]
**Statistically highly significant ($p< 0.01$) [when compared with baseline value within group]

Systolic Blood Pressure

Table 3 Comparison of systolic blood pressures between and within the study groups at different points of time

Time interval	SYSTOLIC BLOOD PRESSURE (mm of Hg)			*p* value
	Group C (n =30) (Mean ± SD)	**Group D** (n =30) (Mean ± SD)	**Group N** (n =30) (Mean ± SD)	
Before study drug infusion (baseline) (T1)	121.60 ± 11.76	122.47 ± 12.22	120.63 ± 12.37	0.8433
5 minutes After study drug infusion (T2)	115.77 ± 10.93	109.70 ± 11.97 **	118.57 ± 11.12	0.0104
After induction of anaesthesia (T3)	106.87 ± 10.76 **	101.33 ± 10.96 **	112.83 ± 11.37 *	< 0.0001
1 minute after intubation (T4)	130.77 ± 8.11 **	123.50 ± 9.10	148.00 ± 7.60 **	< 0.0001
3 minutes after intubation (T5)	117.67 ± 9.66	113.73 ± 8.51 **	130.23 ± 7.97 **	< 0.0001
5 minutes after intubation (T6)	110.53 ± 9.84 **	110.30 ± 8.66 **	119.97 ± 7.87	< 0.0001

SD : standard deviation
*Statistically significant ($p< 0.05$) [when compared with baseline value within group]
**Statistically highly significant ($p< 0.01$) [when compared with baseline value within group]

Diastolic Blood Pressure

Table 4 Comparison of diastolic blood pressures between and within the study groups at different points of time

Time interval	DIASTOLIC BLOOD PRESSURE (mm of Hg)			*p* value
	Group C (n =30) (Mean ± SD)	**Group D** (n =30) (Mean ± SD)	**Group N** (n =30) (Mean ± SD)	
Before study drug infusion (baseline) (T1)	80.83 ± 9.44	79.73 ± 9.47	79.27 ± 9.67	0.8082
5 minutes After study drug infusion (T2)	75.67 ± 9.09 *	72.10 ± 8.25 **	78.00 ± 9.17	0.0374
After induction of anaesthesia (T3)	69.97 ± 8.36 **	67.67 ± 7.69 **	73.53 ± 9.46 *	0.0307
1 minute after intubation (T4)	86.37 ± 9.21 *	81.83 ± 7.55	95.87 ± 7.21 **	< 0.0001
3 minutes after intubation (T5)	78.67 ± 9.30	75.93 ± 7.58	83.47 ± 7.21	0.0019
5 minutes after intubation (T6)	74.17 ± 9.24 **	73.13 ± 7.41 **	78.83 ± 6.52	0.0129

SD : standard deviation
*Statistically significant ($p< 0.05$) [when compared with baseline value within group]
**Statistically highly significant ($p< 0.01$) [when compared with baseline value within group]

Mean Arterial Pressure

Table 5 Comparison of mean arterial pressures between and within the study groups at different points of time

Time interval	MEAN ARTERIAL PRESSURE (mm of Hg)			*p* value
	Group C (n =30) (Mean ± SD)	**Group D** (n =30) (Mean ± SD)	**Group N** (n =30) (Mean ± SD)	
Before study drug infusion (baseline) (T1)	94.33 ± 10.19	93.90 ± 10.33	93.07 ± 10.57	0.8923
5 minutes After study drug infusion (T2)	89.07 ± 9.59 *	84.70 ± 9.41 **	91.43 ± 9.66	0.0246
After induction of anaesthesia (T3)	82.03 ± 9.14 **	78.90 ± 8.68 **	86.67 ± 10.09 *	0.0069
1 minute after intubation (T4)	101.13 ± 8.51 **	95.80 ± 7.91	113.20 ± 7.18 **	< 0.0001
3 minutes after intubation (T5)	91.73 ± 9.25	88.57 ± 7.61 *	99.00 ± 7.33 *	< 0.0001
5 minutes after intubation (T6)	86.30 ± 9.21 **	85.50 ± 7.51 **	92.50 ± 6.80	0.0014

SD : standard deviation
*Statistically significant ($p< 0.05$) [when compared with baseline value within group]
**Statistically highly significant ($p< 0.01$) [when compared with baseline value within group]

Table 6 Comparison of postoperative complications between three study groups

Postoperative complications	Group C (n = 30)	Group D (n = 30)	Group N (n = 30)	Statistical analysis
Bradycardia	3	2	0	
Hypotension	3	2	2	Chi-Square χ^2
Hypoxaemia	2	2	2	value 5.8070
Shivering	2	2	6	*p* value 0.6688
PONV	2	2	2	

PONV : postoperative nausea and vomiting

Discussion

Laryngoscopy and endotracheal intubation are associated with rise in heart rate, blood pressure and occasional disturbance in cardiac rhythm.[1,2] Although in normotensive subjects these responses of blood pressure and heart rate are transient and short lived,[3] they may prove to be detrimental in high risk patients especially in those with cardiovascular disease, increased intracranial pressure and anomalies of the cerebral blood vessels.[4] So, effective attenuation of haemodynamic response to laryngoscopy and tracheal intubation is of great importance in prevention of perioperative morbidity and mortality.

This randomized, double-blind, placebo-controlled study was undertaken to compare the usefulness of two most popular α_2-adrenergic agonists clonidine and dexmedetomidine in attenuation of the haemodynamic response following laryngoscopy and endotracheal intubation.

Ideally, dexmedetomidine should be used as continuous infusion after a loading dose to achieve a sustained clinical effect as it has a short distribution half life ($t_{1/2}$ α) of 6 minutes. This multiple dosing is not recommended for clonidine. Here we used only loading dose of dexmedetomodine to blind our study easily. This is a short clinical study and main focus was on the first few minutes following laryngoscopy and intubation.

After study drug infusion a significant fall in HR (*p* value < 0.05) and highly significant fall in NIBP (SBP, DBP and MAP) (*p* value < 0.01) were noted in Group D. Though a decreasing trend in hemodynamic parameters was observed in Group C after study drug infusion, but only DBP and MAP became significant (*p* value < 0.05). This is most probably due to the difference between the onsets of action of two study drugs. Dexmedetomidine has rapid onset of action (15 minutes) after its administration while clonidine exhibits its clinical effects 30 minutes after the initial dose.

In all groups peak haemodynamic surges were observed at 1 minute after intubation. HR increased from the baseline value by 12.6% and 4% in Group C and Group D respectively. In control group a rise of 29.3% in HR was noted and this was statistically highly significant (*p* value < 0.01). Similarly, BP increased by 7 to 7.5% in Group C, 1 to 2.5% in Group D and 21 to 23% in Group N (*p* value < 0.01). This one-minute post intubation peak corroborate with the result of the study by Derbyshire DR *et al* (1983) [10] and Shribman AJ *et al* (1987) [11] who concluded that plasma catecholamine concentration increased to their maximum at 1 minute after laryngoscopy.

These altered pressor responses were normalized after 3 minutes in Group C and 5 minutes in Group N. This finding is again in agreement with the study by Shribman AJ *et al* (1987),[11] which

shows that plasma catecholamine concentration comes down by 3 to 5 minutes after laryngoscopy. Haemodynamic parameters in Group D remained around the baseline value in first 2 to 3 minutes after intubation followed by a gradual fall in the next few minutes. Thereafter, no alteration in HR and BP was seen in Group D. Similar findings were documented by Kaya C *et al* (2006)[12] in their study with intramuscular dexmedetomidine.

A few patients in all groups showed certain dysrhythmias during laryngoscopy and intubation on continuous ECG monitoring .These included mostly sinus tachycardia and ventricular premature contractions. However, none of these dysrhythmias reached alarming levels during the study to require treatment and converted to normal sinus rhythms spontaneously. It has been shown by various authors like Bedford RF (1988) [13] and Shribman AJ *et al*(1987) [11] that reflex autonomic responses provoked by laryngoscopy and endotracheal intubation could cause various types of dysrhythmias.

Regarding other complications, three patients in Group C and two patients in Group D had bradycardia in the early postoperative period. Intravenous atropine 0.5 mg was prescribed them to normalize the HR. Postoperative hypotension was seen in three patients in Group C, two patients in Group D and two patients in Group N. They were treated with intravenous colloid infusion. Hypoxemia was seen in six patients (two in each group) in the early postoperative period, which was corrected by the administration of oxygen by face mask alone. None of them had to be intubated or required artificial ventilation postoperatively. Two patients in each group complained of shivering in the recovery room, which was resolved with warm blanket covering and oxygen supplementation. Postoperative nausea was complained by two patients in Group C, two patients in Group D and six patients in Group N. These patients were treated with intravenous ondansetron.

Conclusion

From these observations and analysis of the present study, it can be inferred that both clonidine and dexmedetomidine administered intravenously just before laryngoscopy and endotracheal intubation effectively attenuate the haemodynamic response by limiting the extent of rises in heart rate and blood pressure. Dexmedetomidine has been found to provide better haemodynamic stability than clonidine. Both the α_2-agonists are devoid of any serious adverse effect and found safe in this study.

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