Original Article

DOI: 10.17354/ijss/2015/575

Lignocaine and Dexmedetomidine in Attenuation of Pressor Response to Laryngoscopy and Intubation: A Prospective Study

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Abstract

Background: Dexmedetomidine is a α2 agonist with sedative, sympatholytic, and analgesic properties and hence, it can be a very useful adjuvant in anesthesia as stress response buster, sedative, and analgesic. We aimed primarily to evaluate the effects of dexmedetomidine on hemodynamic response to critical incidences such as laryngoscopy and endotracheal intubation.

Materials and Methods: In this randomized, comparative, prospective study total 60 patients of either sex, of American Society of Anesthesiologists (ASA) Grades I or Grade II, aged between 20 and 60 years undergoing elective surgical procedures with written and informed consent were selected for the study. 60 patients randomly assigned to one of the two groups of 30 each. Group L received intravenous lignocaine while Group D received intravenous dexmedetomidine. 60 patients of ASA physical Grades I and II undergoing laryngoscopy and endotracheal intubation were randomly allocated into two groups of 30 patients each. Group D patients received intravenous dexmedetomidine (1 mcg/kg) before laryngoscopy and intubation (infusion over 10 min with 50 ml syringe and infusion pump diluted in normal saline), and Group L received intravenous lignocaine (1.5 mg/kg) 3 min before laryngoscopy and intubation. Parameters noted were heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP). Statistical Package for Social Sciences 19.0 version software was used for statistical analysis.

Results: In Group L, significant hemodynamic stress response was seen following laryngoscopy and tracheal intubation. In dexmedetomidine group, the hemodynamic response was significantly attenuated. The results, however, were statistically better after 5 min of laryngoscopy and tracheal intubation than at 1 min. No significant side effects were noted other than bradycardia in a single patient of Group D.

Conclusion: Efficacy of dexmedetomidine (1 mcg/kg) in attenuation of the pressor response to laryngoscopy and intubation compared to lignocaine (1.5 mg/kg) is significantly higher in ASA-I and II patients with respect to HR, SBP, DBP, and MAP.

Key words: Dexmedetomidine, Endotracheal intubation, Hemodynamic stress response, Laryngoscopy

INTRODUCTION

Laryngoscopy and endotracheal intubation are part of the induction of general anesthesia. The occurrence of hemodynamic responses during laryngoscopy and endotracheal intubation is a well-known hazard.[1]

Access this article online

www.ijss-sn.com

Month of Submission : 10-2015
Month of Peer Review : 11-2015
Month of Acceptance : 12-2015
Month of Publishing : 12-2015

Laryngoscopy results in stimulation of larynx, pharynx, epipharynx, and trachea, which are extensively innervated by the autonomic nervous system, activation of which leading to various cardiovascular changes such as increase heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), dysrhythmias, cardiac asystole, and even sudden death.[2-6] These changes may prove to be detrimental especially in patients with ischemic heart disease, cerebrovascular disease, hypertension, old age, and diabetes mellitus. Several techniques have been studied to attenuate this stress response, but none of them are completely satisfactory. Hence, there is a constant search to attenuate the hemodynamic response to laryngoscopy and

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endotracheal intubation. Modern anesthesia practices, therefore, plan to prevent sympathetic discharge and provide hemodynamic stability perioperatively. Various agents in the form of opioid analgesics, benzodiazepines, beta blockers, calcium channel blockers, and vasodilators have been used to achieve this objective with variable success. In last few years, a great enthusiasm has been shown toward the use of α2 agonists in anesthesia practice because of their anxiolytic, sedative, sympatholytic, and analgesic-sparing properties.[7]

Dexmedetomidine, introduced in 1999 for human use, is a selective α2 agonist with 8 times more affinity for α2 adrenergic receptors compared to clonidine and possesses all the properties of α2 agonist without respiratory depression.[8,9] Intravenous use of dexmedetomidine in the perioperative period had been found to decrease serum catecholamine levels by 90%,[10] to blunt the hemodynamic response to laryngoscopy, tracheal intubation, pneumoperitoneum, and extubation,[11] to provide sedation without respiratory depression and to decrease post-operative analgesic requirements.[12]

The primary aim of this study was, therefore, to evaluate the effects of dexmedetomidine on hemodynamic response to critical incidences such ass laryngoscopy, endotracheal intubation, and compare with lignocaine.

MATERIALS AND METHODS

The present study was carried out from June 2010 to June 2011, after taking the permission and approval from the Departmental Ethical Committee and the written informed consent from the patients. It was a prospective, randomized, comparative, clinical study. 60 American Society of Anesthesiologists (ASA) physical status Grades I and II patients between 20 and 60 years, of either sex and posted for surgeries under general anesthesia with laryngoscopy and intubation, were included in the study. Patients with decreased autonomic control such as the elderly, diabetic patients, patients with chronic hypertension, or severe cardiac disease; patients on drugs such as β blockers or calcium channel blockers, pregnant, or lactating women; patients with a history of allergy to egg proteins and drugs particularly α2 agonists were not considered for the study. The patients were randomly allocated by envelope method into two groups of 30 patients each, Group D received intravenous dexmedetomidine (1mcg/kg) before laryngoscopy and intubation (infusion over 10 min with 50 ml syringe and infusion pump diluted in normal saline) and Group L received intravenous lignocaine (1.5 mg/kg) 3 min before laryngoscopy and intubation for attenuation of stress response. Infusion was prepared according to the Group D on the basis of the weight of the patient; the pump was set so as to deliver the targeted infusion rate. After taking the patient on the operation table, a multipara monitor was attached, and the baseline HR, SBP, DBP, and MAP were noted down. A wide bore intravenous cannula was inserted for giving the intravenous fluids, and another line was taken up for the infusion pump. Premedication was administered to all with 2 mcg/kg fentanyl, 0.03 mg/kg midazolam, and 5 mcg/kg glycopyrrolate 15 min before induction of general anesthesia by an intravenous route. At the time of induction, all the patients received injection ranitidine 50 mg and injection ondansetron 4 mg by the intravenous route. All patient were received either intravenous lignocaine (1.5 mg/kg) 3 min before laryngoscopy and intubation and Group D were received intravenous dexmedetomidine (1 mcg/kg) before laryngoscopy and intubation (infusion over 10 min with 50 ml syringe and infusion pump diluted in normal saline). Patients were pre-oxygenated with 100% oxygen for 3 min. Anesthesia was induced with 6 mg/kg thiopentone sodium and 0.1 mg/kg vecuronium. Laryngoscopy using Macintosh blade size 3 and intubation using the intratracheal tube (size 7.5-8 mm/cuffed) were carried out by a senior anesthesiologist or by a 2-year trained resident in anesthesiology. HR, SBP, DBP, and MAP were recorded before injection of study drug (baseline), after induction of anesthesia (before laryngoscopy) and 1, 3, and 5 min after intubation. Anesthesia maintained with O_2:N_2O (40:60), isoflurane mixture, and vecuronium. Manipulations, such as painting and draping the area, were not allowed till 5 min after intubation. At the end of the surgery, reversal was done with neostigmine 0.05 mg/kg and glycopyrrolate 10 mcg/kg. Extubation was done after adequate reversal of the non-depolarizing muscle relaxant. An observation made related to adverse effects of drugs and anesthesia-related problems and attended appropriately. Findings noted as per tables for further statistical analysis. The data obtained from the study were organized and analyzed by applying appropriate statistical tests. To test the statistical significance of the difference of categorical variables across two study groups (Group D vs. Group L), we used Statistical Package for Social Sciences 19.0. The statistically significant difference of average clinical parameters (such as HR, SBP, DBP, and MAP) between two study groups has been tested using independent sample *t*-test after confirming the underlying normality and equal variance assumptions. The $P < 0.05$ was considered statistically significant. All the hypotheses were formulated using two-tailed alternatives against each null hypothesis.

RESULTS

Both the groups under study were comparable to each other with respect to gender, ASA grading, age, weight, height, duration of surgery, and anesthesia (Tables 1-5).

Table 1: Gender wise distribution of patients in Group D and Group L

Gender	Group		*P* value
	Group D	Group L	
Male	18	18	0.99
Female	12	12	
Total	30	30	

Table 2: Distribution of patients with respect to ASA grade in Group D and Group L

ASA grade	Group		*P* value
	Group D	Group L	
I	22	22	0.99
II	8	8	
Total	30	30	

ASA: American Society of Anesthesiologists

Table 3: Comparison of age (years) in Group D and Group L

Group	Number of patients	Age (years) (mean±SD)	*P* value
Group D	30	39.50±11.56	0.857
Group L	30	40.03±11.22	

SD: Standard deviation

Table 4: Comparison of weight (kg) in Group D and Group L

Group	Number of patients	Weight (mean±SD)	*P* value
Group D	30	61.33±12.25	0.687
Group L	30	60.03±16.64	

SD: Standard deviation

Table 5: Comparison of height (cm) in Group D and Group L

Group	Number of patients	Height (mean±SD)	*P* value
Group D	30	159.67±12.32	0.198
Group L	30	155.07±14.91	

SD: Standard deviation

Table 6: Comparison of distribution of hemodynamic changes in terms of relative percentages in clinical parameters studied between Group L and Group D

% Change	B	BL	1 min	3 min	5 min
HR (%)					
Group L	0.0	3.63	9.36	11.23	5.93
Group D	0.0	−9.46	−8.13	−6.6	−11.46
SBP (%)					
Group L	0.0	−1.2	5	4.56	0.3
Group D	0.0	−21.28	−12.8	−18.47	−25.17
DBP (%)					
Group L	0.0	1.6	7.06	6.76	0.5
Group D	0.0	−10.5	−9.73	−11.5	−20.73
Mean BP (%)					
Group L	0.0	0.67	6.4	6.1	0.47
Group D	0.0	−13.4	−10.5	−13.53	−22.2

Values are Mean (SD). % Change is calculated with respect to baseline values. DBP: Diastolic blood pressure, BP: Blood pressure, SBP: Systolic blood pressure, HR: Heart rate

Comparison between Group L and Group D

Group L (lignocaine group)

In Group L after thiopentone sodium induction, there was increase in HR by 3.63%, fall in SBP by 1.2% and increase in MAP by 0.67% of baseline value (Table 6). 1 min after laryngoscopy and intubation, the HR was further increased by 9.36% of baseline value. At the end of 3 min, the HR remained 11.23% above baseline. At the end of 5 min, HR was 5.93% which was still higher than baseline value (Table 7). 1 min after laryngoscopy and intubation the SBP was increased by 5% of baseline value. At the end of 3 min, the SBP was 4.56% above baseline. At the end of 5 min, SBP was 0.3% which was comparable to the baseline value (Table 8). 1 min after laryngoscopy and intubation the MAP was increased by 6.4% of baseline value. At the end of 3 min, the MAP was 6.1% above baseline. At the end of 5 min, MAP was 0.47% which was comparable to the baseline value (Table 9).

Group D (dexmedetomidine group)

In Group D after thiopentone sodium induction, there was decrease in HR by 9.46% (compared to increase by 3.63% in Group L), fall in SBP by 21.28% (compared to decrease by 1.14% in Group L), and decrease in MAP by 13.4% of baseline value (compared to increase by 0.67% in Group L) ($P < 0.001$) (Table 6). 1 min after laryngoscopy and intubation the HR was lower than baseline by 8.13% (compared to increase by 9.86% in Group L). At the end of 3 min, the HR remained lower by 6.6% over baseline value (compared to increase by 11.23% in Group L). At the end of 5 min, HR was still on lower side by 11.46% (compared to increase by 5.93% in Group L) of baseline value ($P < 0.001$) (Table 6). 1 min after laryngoscopy and intubation, the SBP was lower by 12.8% of baseline value (compared to increase by 5.93% in Group L). At the end of 3 min, the SBP remained low by 18.8% of baseline (compared to increase by 4.56% in Group L). At the end of 5 min, SBP was still lower by 25.47% of baseline value (compared to increase by 0.3% in Group L) ($P < 0.001$) (Table 6). 1 min after laryngoscopy and intubation, the MAP was lower 10.5% of baseline value (compared to increase by 6.4% in Group L). At the end of 3 min, the MAP remained low by 13.53% of baseline (compared to increase by 6.1% in Group L). At the end of 5 min, MAP was 22.2% of baseline value (compared to increase by 0.47% in Group L) ($P < 0.001$) (Table 6).

Using two independent sample proportion test $P > 0.05$, therefore, there is no significant difference between the proportion of gender in Group D and Group L (Table 1).

Table 7: Comparison of pulse rate at baseline, before laryngoscopy, 1st min after laryngoscopy, 3rd min after laryngoscopy, and 5th min after laryngoscopy in Group D and Group L

Pulse rate	Number of patients	Group		*P* value
		Group D	Group L	
Baseline	30	78.13±13.73	76.97±10.89	0.717
Before laryngoscopy	30	68.67±11.70	80.60±6.58	<0.001
1st min after laryngoscopy	30	70.00±11.77	86.83±6.13	<0.001
3rd min after laryngoscopy	30	71.53±11.22	88.20±4.51	<0.001
5th min after laryngoscopy	30	66.67±8.54	82.90±4.64	<0.001

Table 8: Comparison of SBP at baseline, before laryngoscopy, 1st min after laryngoscopy, 3rd min after laryngoscopy, and 5th min after laryngoscopy in Group D and Group L

SBP	Number of patients	Group		*P* value
		Group D	Group L	
Baseline	30	121.80±10.55	122.47±8.01	0.784
Before laryngoscopy	30	100.52±7.94	121.27±7.73	<0.001
1st min after laryngoscopy	30	109.00±8.98	127.47±8.69	<0.001
3rd min after laryngoscopy	30	103.33±8.21	127.03±7.30	<0.001
5th min after laryngoscopy	30	96.63±8.84	122.77±6.13	<0.001

SBP: Systolic blood pressure

Table 9: Comparison of MAP at baseline, before laryngoscopy, 1st min after laryngoscopy, 3rd min after laryngoscopy, and 5th min after laryngoscopy in Group D and Group L

MBP	Number of patients	Group		*P* value
		Group D	Group L	
Baseline	30	91.00±7.80	90.23±6.44	0.680
Before laryngoscopy	30	77.60±6.87	90.90±5.73	<0.001
1st min after laryngoscopy	30	80.50±7.09	96.63±6.66	<0.001
3rd min after laryngoscopy	30	77.47±7.49	96.33±6.89	<0.001
5th min after laryngoscopy	30	68.80±8.19	90.70±5.33	<0.001

MAP: Mean arterial pressure, BP: Blood pressure

Using independent sample proportion test $P > 0.05$, therefore, there is no significant difference between proportions of ASA grade in Group D and Group L (Table 2).

Using two independent sample *t*-test $P > 0.05$, therefore, there is no significant difference between mean age (years) Group D and Group L (Table 3).

Using two independent sample *t*-test $P > 0.05$, therefore, there is no significant difference between mean weights (kg) Group D and Group L (Table 4).

Using two independent sample *t*-test $P > 0.05$, therefore, there is no significant difference between mean heights (kg) Group D and Group L (Table 5).

Using two independent sample *t*-test $P > 0.05$, therefore, there is no significant difference between mean pulse rates at baseline. $P < 0.05$, therefore, there is a significant difference between mean pulse rates at before laryngoscopy, 1st, 3rd, and 5th min after laryngoscopy in Group D and Group L (Table 7).

Using two independent sample *t*-test $P > 0.05$, therefore, there is no significant difference between mean SBP at baseline. $P < 0.05$, therefore, there is a significant difference between mean SBP at before laryngoscopy, 1st, 3rd, and 5th min after laryngoscopy in Group D and Group L (Table 8).

Using two independent sample *t*-test $P > 0.05$, therefore, there is no significant difference between mean DBP at baseline. $P < 0.05$, therefore, there is a significant difference between mean DBP at before laryngoscopy, 1st, 3rd, and 5th min after laryngoscopy in Group D and Group L (Table 10).

Using two independent sample *t*-test $P > 0.05$, therefore, there is no significant difference between mean MAP at baseline. $P < 0.05$, therefore, there is a significant difference between mean MAP at before laryngoscopy, 1st, 3rd, and 5th min after laryngoscopy in Group D and Group L (Table 9).

Table 10: Comparison of DBP at baseline, before laryngoscopy, 1st min after laryngoscopy, 3rd min after laryngoscopy, and 5th min after laryngoscopy in Group D and Group L

DBP	Number of patients	Group		*P* value
		Group D	Group-L	
Baseline	30	76.20±7.13	74.67±6.42	0.385
Before laryngoscopy	30	65.70±6.68	76.27±5.25	<0.001
1st min after laryngoscopy	30	66.47±6.80	81.73±6.20	<0.001
3rd min after laryngoscopy	30	64.70±7.36	81.43±6.65	<0.001
5th min after laryngoscopy	30	55.47±8.88	75.17±5.36	<0.001

DBP: Diastolic blood pressure

DISCUSSION

Dexmedetomidine is a highly selective α2 adrenergic agonist. It acts through three types of α2 receptors-α2 A, α2 B, and α2 C situated in the brain and spinal cord. The resultant action is sedation, anxiolysis, analgesia, and sympatholysis, the latter leading to hypotension and bradycardia. Activation of α2 A receptors in the brain stem vasomotor center results in suppression of norepinephrine release, hypotension, and bradycardia.

Stimulation of α2 A and α2 C in locus ceruleus causes sedation. In the spinal cord, activation of both α2 A and α2 C receptors directly reduce pain transmission by reducing the release of substance P. Looking at these pharmacological properties, it has been evaluated in the past to assess its effect on hemodynamic responses in patients undergoing laparoscopic surgeries. The molecule has been used in infusion form with or without bolus dose. Infusion rates varying from 0.1 to 10 mcg/kg/h[13-15] have been studied. However, with higher dose infusion of dexmedetomidine, high incidence of adverse cardiac effects have been observed.[15] A biphasic response to blood pressure occurs with a bolus dose.[10] Initially, there occurs hypertension followed by fall in blood pressure. This response is seen often more in young and healthy patients.[16] Stimulation of α2 B receptors in vascular smooth muscles is said to be responsible for this. Low-dose infusion of 0.25-0.5 mcg/kg/h results in an amonophasic response of 10-15% fall in mean arterial blood pressure and pulse rate.[10] Furthermore, in low dose, dexmedetomidine exhibits linear kinetics, meaning that a constant amount of drug is eliminated per hour rather than a constant fraction of the drug. Our study confirms the fact that critical incidences such as laryngoscopy and intubation do significantly increase the HR, SBP, DBP, and MAP in patients and dexmedetomidine attenuates this sympathoadrenal response and provides hemodynamic stability.[17,18] The effective attenuation dose with minimum side effects noted in our study was 1 mcg/kg infusion over 10 min. Apart from providing stress response attenuation, the added effects of dexmedetomidine are sedation and analgesia. Sedation produced by α2 agonists is unique in the sense that the patients can be easily aroused to co-operate during procedures and also respond to the verbal commands and then can return to sleep like state when not stimulated.[16] Keniya *et al.*,[18] who also shown that 1 mcg/kg dexmedetomidine effectively attenuated pressor response to laryngoscopy and subsequent intubation, where dexmedetomidine group was compared to the control group. After tracheal intubation, the maximal average increase was 8% in SBP and 11% DBP in dexmedetomidine group as compared to 40% and 25%, respectively, in the control group. Similarly, the average increase in HR was 7% and 21% in the dexmedetomidine and control groups, respectively. In our study, 1 min after laryngoscopy and subsequent intubation SBP and DBP was 12.8% and 9.7% below baseline values. Similarly, HR remained 8.13% below baseline in dexmedetomidine group ($P < 0.001$). So, in our study, attenuation of the pressor response is better than reference study may be due to a higher dose of intravenous fentanyl 2 mcg/kg versus 1 mcg/kg used in induction. Similarly, we used intravenous midazolam 0.03 mg/kg versus fixed dose of 1 mg in reference study for induction of anesthesia.

CONCLUSION

Dexmedetomidine (1 mcg/kg) serves as a very useful anesthesia adjuvant to control hemodynamic stress response to laryngoscopy and intubation, without any significant adverse effects. Efficacy of dexmedetomidine in attenuation of the pressor response compared to intravenous lignocaine (1.5 mg/kg) is significantly higher in ASA-I and II patients with respect to HR, SBP, DBP, and MAP.

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How to cite this article: Sale HK, Shendage VJ. Lignocaine and Dexmedetomidine in Attenuation of Pressor Response to Laryngoscopy and Intubation: A Prospective Study. Int J Sci Stud 2015;3(9):155-160.

Source of Support: Nil, **Conflict of Interest:** None declared.