Original Research Article

A comparative study of dexmedetomidine and labetalol for attenuation of hemodynamic stress response to laryngoscopy and intubation

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Abstract

Introduction: Control of the airway is one of the defining moments of Anesthesia. Now we use rigid direct laryngoscopes to view the larynx and adjacent structures under direct vision for endotracheal intubation. This causes direct trauma to the oropharynx and larynx and apart from this it also causes stimulation resulting in a rise in heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure. Tachycardia, hypertension, and dysrhythmias all occur during laryngoscopy and intubations.

Aim of the study: This study was done with the following intentions: To compare the efficacy of dexmedetomidine 1µg/kg; and labetalol 0.5 mg/kg in attenuating the cardiovascular responses to Laryngoscopy and Intubation, to observe any adverse effects of these two in the specified dosage.

Materials and methods: This prospective randomized comparative placebo-controlled double-blinded study was conducted in government Karur medical in the year 2019. After obtaining ethical committee approval, the study population was chosen. All the patients were assessed preoperatively with history, clinical examination, and required investigations informed written consent was obtained from the patient. The patients were randomly allocated into three groups. Group D (30 no) received Dexmedetomidine 1 µg/kg in 10ml normal saline i.v. over 10 min, 5min before induction of anesthesia. Group L (n: 30) received Labetalol 0.5 mg/kg 10ml normal saline i.v. over 10min, 5 min before induction of anesthesia. Group P (n: 30) received10ml normal saline i.v. over 10min, 5 min before induction of anesthesia. All patients were premedicated with Inj. Midazolam 2mg and Inj.

Glycopyrrolate 0.2 mg i.m. 45 min before surgery Heart rate, systolic and diastolic blood pressure, and oxygen saturation were recorded as the baseline value.

Results: There was a reduction in the heart rate and mean arterial pressure response to intubation in both Dexmedetomidine and Labetalol groups compared with placebo ($P<0.05$), but when both the groups were compared there was a statistically significant reduction of heart rate and arterial pressure response to intubation in Dexmeditomidine group ($P < 0.05$). There was no significant hypotension or bradycardia in any of the groups.

Conclusion: We conclude that Dexmeditomidine 1μ/Kg given slowly over 10 minutes intravenously 5 minutes before induction, attenuates the cardiovascular responses to laryngoscopy and intubation in a better manner than Labetalol 0.5mg/Kg.

Key words

Dexmedetomidine, Labetalol, Attenuation, Hemodynamic Stress Response, Laryngoscopy, Intubation.

Introduction

Control of the airway is one of the defining moments of Anesthesia. Before the twentieth century, intubation of the trachea had been described and performed rather crudely, Now we use rigid direct laryngoscopes to view the larynx and adjacent structures under direct vision for endotracheal intubation [1, 2]. This causes direct trauma to the oropharynx and larynx and apart from this it also causes stimulation resulting in a rise in heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure. Tachycardia, hypertension, and dysrhythmias all occur during laryngoscopy and intubations. The consequent rise in rate/pressure product may result in a myocardial oxygen demand which exceeds the oxygen supply resulting in myocardial ischemia [3]. This response is sympathetically mediated and can be attenuated by various drugs that block sympathetic activity and other drugs like calcium channel blocking drugs, lignocaine, and magnesium. Studies have documented myocardial ischemic changes due to reflex sympathoadrenal response immediately following laryngoscopy and intubation with a mean increase in systemic pressure of 40mmHg even in normotensive patients [4]. An increase in heart rate is more likely to produce signs of myocardial ischemia than hypertension on the ECG. Indeed, in an anesthetized patient, the incidence of myocardial ischemia on the ECG sharply increases in patients who experience a heart rate greater than 110bpm (ischemic threshold) [5]. A frequent recommendation is to maintain heart rate and blood pressure within 20% of the normal awake value for that patient. Many attempts have been made to attenuate the pressor response to laryngoscopy and intubation [6].

Materials and methods

This prospective randomized comparative placebo-controlled double-blinded study was conducted in government Karur medical in the year 2019. After obtaining ethical committee approval, the study population was chosen. All the patients were assessed preoperatively with history, clinical examination, and required investigations informed written consent was obtained from the patient. The patients were randomly allocated into three groups. Group D (30 no) received Dexmedetomidine 1 μg/kg in 10 ml normal saline i.v. over 10 min, 5min before induction of anesthesia. Group L (n: 30) received Labetalol 0.5 mg/kg 10ml normal saline i.v. over 10min, 5min before induction of anesthesia. Group P (n: 30) received10ml normal saline i.v. over 10min, 5min before induction of anesthesia. All patients were premedicated with Inj. Midazolam 2mg and Inj. Glycopyrrolate 0.2 mg i.m. 45 min before surgery Heart rate, systolic and diastolic blood pressure, and oxygen saturation were recorded as the baseline value.

Exclusion criteria: Difficult airway, Hypertension, Diabetes mellitus, Ischemic heart disease, Renal disease, Cerebrovascular disease, Patients on beta-blockers, alpha-blockers, Bronchial asthma, Allergy to study drug.

SBP, DBP, MAP, HR, and SpO_2 were monitored 1 minute after infusion of study drug, 1 minute after induction, and 1, 3, 5, 10 and 15 minutes after intubation. During intubation, laryngoscopy duration and Cormack Lehane score were noted. Any incidence of hypotension or bradycardia was recorded. Hypotension is defined as a decrease in MAP 30% or more from baseline and treated with inj. ephedrine 6 mg. Bradycardia is defined as HR<50/min and treated with inj. atropine 0.6 mg.

Statistical analysis

We used the Chi-Square test, ANOVA, and Post-Hoc test as appropriate. p<0, 05 was considered statistically significant. The results were presented as means and SD.

Results

The study was done in 90 patients belonging to ASA class I and II undergoing elective surgeries under general anesthesia. The patients were categorized into 3 groups. Group D - Dexmeditomidine, Group L - Labetalol, Group P – Placebo.

The groups were matched for demographic data, and there was no statistically significant difference found between the groups in age, sex, and weight (**Table – 1**).

Baseline parameters were compared between groups as per **Table - 2**. There was no statistically significant difference between the groups (SD- Standard deviation, 'P' Value >0.05).

After administration of the study drug blood pressure, heart rate, and saturation were recorded 1 minute following the injection of the drug, 1 min after induction,1 min,3 min, 5 min, 10 min, and 15 min after laryngoscopy and intubation.

Table – 1: Demographic characteristics between groups.

	Male	**Female**
Group D	**19**	**11**
Group L	**16**	**14**
Group P	**11**	**19**

Table – 2: Baseline parameters.

	Group D	**Group L**	**Group P**	**P-Value**
SBP ±SD	119.3±8.8	121.5± 11	121.7 ±8.9	0.564
DBP ±SD	78.8 ±6.65	81.2 ±6.7	80.4 ±5.4	0.339
MAP ±SD	92.17 ±6.3	94.5 ±7.3	93.9 ±6.6	0.380
HR±SD	85.13± 8.96	88.±10	81.8± 11	0.064

Table - 3: Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure after drug injection.

After drug injection	**Group D**	**Group L**	**Group p**	**' P'**	**Significance**
Heart rate	65.87±5.3	76.7±8.9	79.8±8.62	0.001	Significant
Systolic B.P	118.07±9.5	113±8.3	119.8±8	0.709	Not significant
Diastolic B.P	76.7±7.7	76.7±6	79.3±4.7	0.196	Not significant
MAP	90.4±7.4	88.53±6.7	92.5±5.3	0.063	Not significant
SPO_2	98.7±0.7	99±0.5	99±0.5	0.101	Not significant

Table – 4: Deviation of heart rate from baseline.

Heart Rate	Group D	Group L	Group P	'P'
After drug	65.9 ±5.3	76.7± 9	80± 8.6	0.001
After induction	73.3 ±4.13	83.5± 7.25	86.7 ±8.2	0.001
After intubation 1min	76.4±5.6	95.2±10.6	114±12.97	0.001
3 min	74.4±5.6	91±10.64	108±11	0.001
5 min	72.5±5.77	86.57±8.9	100.7±9.69	0.001
10 min	71.1±4.84	83.0±7.3	91.9±9.2	0.001
15 min	70.83±4.1	81.3±7.2	87.47±7.7	0.001

Table – 5: Comparison between group D and group L.

Heart Rate (Mean ± SD)	Group D	Group L	'P'
After drug	**65.9 ±5.3**	**76.7± 9**	**0.001**
After induction	**73.3 ±4.13**	**83.5± 7.25**	**0.001**
After intubation 1min	**76.4±5.6**	**95.2±10.6**	**0.001**
3 min	**74.4±5.6**	**91±10.64**	**0.001**
5 min	**72.5±5.77**	**86.57±8.9**	**0.001**
10 min	**71.1±4.84**	**83.0±7.3**	**0.001**
15 min	**70.83±4.1**	**81.3±7.2**	**0.001**

Table – 6: Comparison of systolic arterial pressure response.

Blood Pressure mean ± SD	Group D	Group L	Group P	'P'
Baseline	119.3± 8.8	121.5 ±11	121.7± 8.9	0.564
After Drug	118±9.5	113±8.3	119±8	0.090
After Induction	112.4±8.5	108.9±8.3	111.3±9	0.288
After Intubation 1min	118.9±7.4	131.1±9.2	152.67±9.6	0.001
3 Min	116.9±7.7	127.67±8.5	146±8.6	0.001
5 Min	114.5± 7.8	124.9 ±8.1	139.7± 6.8	0.001
10 Min	111.9 ±7.7	121.9 ±7.5	133.2± 6.7	0.001
15 Min	111.8 ±6.8	120.23 ±7.3	127 ±6.1	0.001

Table – 7: Comparison of diastolic arterial pressure response.

Blood pressure (Mean ± SD)	Group D	Group L	Group P	'P'
Baseline	78.8±6.6	81.2 ±6.7	80.37±5.4	0.339
After drug	76.73±7.7	76.7±6.3	79.33±4.9	0.196
After induction	73.2±6.9	73.67±6.4	73.77±5.2	0.932
After intubation 1min	79.8±5.5	88±5.8	106.97±8.4	0.001
3 min	76.73±4.7	86.57±6.2	101.73±6.8	0.001
5 min	74.9 ±4.2	84.2± 5.9	96.3± 6.7	0.001
10 min	73.73 ±3.4	80.8± 4.5	90.43± 6.4	0.001
15 min	73.27± 3.4	79.8 ±4.8	83.87± 5.8	0.001

Table - 3 showed the mean heart rate, mean systolic and mean diastolic blood pressure after injection. There was a statistically significant difference in the mean heart rate of patients across 3 groups ($p< 0.01$). The mean heart rate of group D was lower than that of both groups L and P. There was no statistical difference in the mean systolic diastolic blood pressure and SPO_2 among the 3 groups.

Heart rate decreased after injection of the drug in dexmedetomidine group and labetalol group compared to placebo (**Table – 4**). The fall in heart rate was more in group D than in group L. Heart rate increase after intubation is more in Placebo group than Group D or Group L (SD standard deviation, 'P'<0.05-Significant).

Table – 8: Comparison of mean arterial pressure response.

Blood pressure (Mean ± SD)	Group D	Group L	Group P	'P'
Baseline	92.17± 6.3	94.4 ±7.3	94± 6.3	0.380
After drug	90.43±7.4	88.5±6.7	92.57±5.3	0.063
After induction	86.47±6.7	85.1±6.6	73.77±5.2	0.701
After intubation 1min	92.87 ±5.5	102.7± 6.6	122.5 ±7.7	0.001
3 min	90 ±4.8	100 ±6.6	116.37± 7.2	0.001
5 min	88.1± 4.6	97.6± 6.3	110.3 ±6.5	0.001
10 min	86.73 ±3.9	94.4 ±5.2	104.8 6.4	0.001
15 min	86.13 ±3.8	93.2± 5.5	97.9 5.2	0.001

Table – 9: Comparison map group D and group L.

Heart rate (Mean ± SD)	GROUP D	GROUP L	'P' Value
Baseline	92.17± 6.3	94.4 ±7.3	0.379
After drug	90.43±7.4	88.5±6.7	0.501
After induction	86.47±6.7	85.1±6.6	0.686
After intubation 1min	92.87 ±5.5	102.7± 6.6	0.001
3 min	90 ±4.8	100 ±6.6	0.001
5 min	88.1± 4.6	97.6± 6.3	0.001
10 min	86.73 ±3.9	94.4 ±5.2	0.001
15 min	86.13 ±3.8	93.2± 5.5	0.001

Heart rate response to laryngoscopy and intubation was effectively suppressed in the dexmed group (GroupD) compared to the labetalol group (Group L) as per **Table - 5**. (SD-Standard deviation, 'P'<0.05-Significant)

SAP, DAP, and MAP after injection of the drug and after induction were comparable between the groups (**Table – 6, 7, 8**). There was no statistically significant difference ('p'>0.05). After laryngoscopy and intubation SAP, DAP and MAP increased at 1 min, 3 min, 5 min, 10 min and 15 min in group P compared to group D and group L ('P'<0.05). In group D the pressures after intubation at 1 min, 3 min, 5 min, 10 min, and 15 min intervals were less than group L (**Table – 9**). Airway scoring; MMS and CLG were comparable between the groups.

Discussion

Laryngoscopy and endotracheal intubation frequently induce a cardiovascular stress response characterized by hypertension and tachycardia. This sympathoadrenal stress response to laryngoscopy increases myocardial O_2 demand leading to ischemia and acute heart failure in susceptible individuals. Given the frequent occurrence of hypertension and tachycardia during laryngoscopy even in normotensive individuals, it is perhaps rather surprising that complications have not been met very often [8]. One reason for this may be the transient nature of hypertension which usually lasts less than 10 minutes. It is possible however that some of the complications that occur during intubation or even later in the course of anesthesia may be precipitated by an episode of hypertension and tachycardia, following endotracheal intubation. ELLIOF (1980) observed left ventricular wall dysfunction following endotracheal intubation [9]. This reflex sympathetic response may be diminished or modified locally, centrally, and peripherally and attempts have been made to accomplish this using all these approaches with varying success [10]. In an attempt to blunt these potentially adverse hemodynamic responses, different techniques and agents were used by many with varying success. Sympathetic system activation plays the main role in the occurrence of transient but significant tachycardia and hypertension during intubation [11]. Use of Vasodilators like Sodium nitroprusside results in reflex tachycardia, lability in blood pressure, cerebral

vasodilation with an elevation of intracranial pressure, and pulmonary venous admixture. Opioid analgesics will attenuate the hemodynamics at the expense of respiratory depression [12]. The $\alpha_2\alpha$receptors are involved in regulating the autonomic and cardiovascular systems. α_2 receptors are located on blood vessels, where they mediate vasoconstriction, and on sympathetic terminals where they inhibit norepinephrine release.α_2 receptors are also located within the central nervous system and their activation leads to sedation, a reduction of tonic levels of sympathetic outflow, and an augmentation of cardiac-vagal activity. This can result in a decrease in heart rate and αcardiac output [13]. The use of α_2 agonists in the perioperative period has been associated with reduced anesthetic requirements and attenuated heart rate and blood pressure responses to stressfulαevents. Also,α_2 receptors within the spinal cord modulate pain pathways, thereby providing some degree of analgesia [14]. Dexmedetomidine compared to Clonidine is a much more selective alpha2-adrenoceptor agonist, which might permit its application in relatively high doses for sedation and analgesia without the unwanted vascular effects from activation of alpha1-receptors. Also, Dexmedetomidine is a shorter-acting drug than clonidine and has a reversal drug for its sedative effect, Atipamezole [15]. In our study, we used Dexmedetomidine 1μ/kg and labetalol 0.5mg/kg and compared with placebo. Both the drugs produce peak effect after 5 minutes. We had induced all the patients 5 minutes after preinjection [16]. In some patients dexmedetomidine resulted in a minimal increase in arterial pressure. This transient hypertension is due to $\alpha_1$mediated vasoconstriction. This transient hypertension is less than that seen with clonidine since dexmedetomidine has more selectivity over α_2 receptors. Giving the loading dose over 20 minutes also minimizes transient hypertension. Bradycardia after dexmedetomidine was reported in some studies with the bolus injection [17]. In our study dexmedetomidine over 10 min with continuous monitoring of heart rate, none of the patients developed bradycardia that required atropine. Dexmedetomidine over 10 min with continuous monitoring of arterial oxygen saturation with pulse oximeter showed no desaturation (SpO2-<95%) in any patient. Labetalol in a dose of 0.5 mg/kg had reduced the heart rate. But the reduction was modest compared to dexmedetomidine the reduction in arterial pressure after labetalol was mild (**Table - 9**) that was statistically insignificant. Heart rate increase and arterial pressure reduction after induction were minimal in all 3 groups and there was no statistically significant difference between the groups. There was no significant hypotension on induction with dexmedetomidine or labetalol compared to placebo [18]. After intubation, the blood pressure and heart rate were increased significantly in the placebo group, while labetalol preinjection reduced the response significantly though there was a little rise in MAP and HR. Dexmedetomidine preinjection effectively attenuated the hemodynamic response to intubation compared to labetalol. Sympathetic response to intubation lasted for 15 minutes arterial pressure and heart rate returned to baseline values in 15 minutes in the placebo group [19]. In our study all the patients remained in supine position postoperatively.no postural hypotension-related side effects were reported. Side effect was seen with labetalol when the patient was allowed to sit within 3 hours after injection. Dexmedetomidine reduced the requirement of inhalational agents and opioids intraoperatively compared to placebo [20]. With Labetalol the hemodynamics and anesthetic requirements after30 to 45 minutes were similar to the placebo group. Extubation and recovery were comparable in all 3 groups. A bolus dose of both Dexmedetomidine and Labetalol was effective in attenuating the hemodynamic response to intubation .but the effect was complete and better with Dexmedetomidine [21].

Conclusion

We concluded that Dexmeditomidine 1 μg/Kg given slowly over 10 minutes intravenously 5

minutes before induction, Attenuates the cardiovascular responses to laryngoscopy and intubation in a better manner than Labetalol 0.5 mg/Kg.

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