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Comparison of Dexmedetomidine, Fentanyl and Lignocaine in Attenuation of Haemodynamic Response to Direct Laryngoscopy and Intubation

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ABSTRACT
Background & Aims*: Laryngoscopy and endotracheal intubation are noxious stimulus causing intense cardiovascular reflex due to sympathoadrenal discharge. The aim of this study was to compare effect of dexmedetomidine, fentanyl and lignocaine in attenuation of haemodynamic response to laryngoscopy and intubation.*
Methods: *This hospital based, randomized, double blinded, comparative study was conducted after obtaining approval from the Institutional Ethics Committee and written informed consent from all patients. Ninety patients of ASA physical status I/II scheduled for elective surgical procedure under general anaesthesia were included in this study. These patients were randomized into three groups by chit in box method, patients in Group D received dexmedetomidine 0.6 mcg/kg diluted up to 10 ml in normal saline; in Group F received fentanyl 2 mcg/kg diluted up to 10 ml in normal saline and in Group L received 2% lignocaine 1.5 mg/kg diluted up to 10 ml in normal saline. Primary outcome variable haemodynamic response was measured at 1,3,5,7 &10 minutes after intubation. Secondary outcome variable was any adverse effects.*
Results:*All groups were comparable with regards to demographic profile and baseline haemodynamic parameters. A statistically significant reduction (p <0.05) in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was observed in group D when compared to group F & group L.*
Conclusion: *Intravenous dexmedetomidine (0.6µg/kg) showed better attenuation of haemodynamic response to laryngoscopy and intubation as compared to i.v. fentanyl (2µg/kg) and i.v. lignocaine (1.5 mg/kg 2%) when given 5 minutes prior to intubation without causing any adverse effect.*
Key words: *Attenuation, dexmedetomidine, fentanyl, intubation, laryngoscopy, lignocaine, haemodynamic response*

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I. Introduction

Laryngoscopy and intubation are mandatory procedure for most of the patients posted for surgery under general anaesthesia. Laryngoscopy and intubation cause significant rise in catecholamine level, it leads to an intense reflex increase in heart rate (HR), blood pressure, intraocular pressure, intracranial pressure and predisposes for cardiac arrhythmias.[1] These changes are due to reflex sympathetic discharge provoked by stimulation of epipharynx and laryngopharynx.[2] It may lead to catastrophic events like myocardial infarction, acute heart failure and cerebrovascular accidents in susceptible individuals.[3] Therefore it has become imperative to develop a novel technique or use drugs to prevent this potentially hazardous response. Various means are being used like limiting the duration of laryngoscopy to 15 s, use of drugs like beta blockers, calcium channel blockers, alpha-2 adrenergic agonists, lignocaine, opioids and magnesium sulphate.

Lignocaine an aminoethylamide, when used intravenously minimizes blood pressure fluctuations after endotracheal intubation by direct myocardial depression, peripheral vasodilatation and by affecting synaptic transmission. [4]

Dexmedetomidine, a selective alpha-2 adrenergic agonist, increases the hemodynamic stability by altering the stress induced sympathoadrenal responses to intubation [5], [6] without affecting intraoperative cardiovascular stability. It also has opioid and anesthetic agent sparing properties.

Fentanyl, an opioid attenuates haemodynamic response by increasing the depth of anaesthesia and by suppressing noxious stimulation caused by intubation. [7]

Present study was designed to compare the effectiveness of dexmedetomidine, fentanyl and lignocaine in attenuating the haemodynamic response to laryngoscopy and endotracheal intubation as primary outcome variable and to observe adverse effects caused by them as secondary outcome variable.

II.Material & Methods

This hospital based, randomized, double blinded, comparative study was conducted at a tertiary care centre after obtaining approval from the Institutional Ethics Committee and Research review board along with written informed consent from all patients.

Ninety patients of American Society of Anaesthesiology (ASA) physical status I or II, aged 20 to 60 yrs, weighing 40 to 70 kg scheduled for elective surgical procedure under general anaesthesia were included in this study. Patients with anticipated difficult intubation, cardiac diseases, hypertension, reactive airway diseases, major organ dysfunction and un-willing to participate in the study were excluded.

All patients were examined thoroughly in pre anaesthetic clinic, including history, general physical examination and necessary blood investigations one day prior to surgery. Patients were explained about the anaesthetic technique and perioperative course and written informed consent was taken.

All the ninety patients were randomly divided into three groups of thirty patients using chit in box method. These allocated groups were kept in closed envelopes. The three groups were

Group D (n=30) - Patients received dexmedetomidine 0.6 mcg/kg diluted up to 10 ml in normal saline

Group F (n=30) - Patients received fentanyl 2 mcg/kg diluted up to 10 ml in normal saline

Group L (n=30) - Patients received 2% lignocaine 1.5 mg/kg diluted up to 10 ml in normal saline

On arrival in operation theatre, fasting status, consent and PAC was checked. Intravenous access was obtained with 20G cannula and 5 mL/kg/hour Ringer's lactate infusion was started. Multipara monitoring of heart rate (HR), electrocardiogram (ECG), non invasive blood pressure (NIBP) and SpO2 was established. Baseline vital parameters were recorded (t_0).

All the patients were premedicated with inj. glycopyrrolate 0.2 mg, inj. midazolam 1 mg and preoxygenated with 100 % oxygen for 3 minutes. Study drug was administered 5 minutes before intubation according to the group allocated. The patients were blinded to the study drug they received. The anaesthesiologists who prepared and administered the study drug were also different.

Then patients were induced with 5 mg/kg thiopental and inj. succinylcholine 2 mg/kg intravenously. Three minutes later direct laryngoscopy was done and patients were intubated with appropriate size endotracheal tube. The patients in whom endotracheal intubation could not be achieved within 45 s were excluded from the study. All patients received 40 % O_2 (2 L/min), 60% N_2O (2 L/min) and 0.4 % V/V isoflurane during maintenance of anesthesia. Inj. atracurium 0.5 mg/kg followed by 0.1 mg/kg was given for muscle relaxation.

Parameters of HR, SBP, DBP, MAP and oxygen saturation were recorded 2 minutes after premedication (t_1), 5 minutes after study drug administration (t_2) then at 1(t_3), 3 (t_4),5 (t_5),7 (t_6) and 10 (t_7) minutes after intubation in all patients. These parameters were compared with baseline levels. Surgical incision was given following completion of the data collection process. The patients were ventilated in order to maintain end tidal CO_2 levels between 30 and 35 mm Hg. During surgery HR, SBP, MAP, DBP and SpO_2 levels were recorded at 5 min intervals. At the completion of surgery, reversal was done with IV glycopyrrolate 0.01 mg/kg and IV neostigmine 0.05 mg/kg. After adequate recovery, patients were shifted to post anaesthesia care unit.

Statistical analysis

SPSS (Statistical Package for Social Sciences) for Windows version 18.0.0 was used for statistical analysis. All the quantitative data were summarized in the form of mean ±SD. The difference between mean values of the three groups was analyzed using ANOVA one way test and within groups using paired t-test. All the quantitative data were summarized in form of proportions. The differences between proportions were analyzed using Chi square test. The comparisons were considered as not significant ($p > 0.05$), significant ($p < 0.05$) or highly significant ($p < 0.001$) in a confidence interval of 95%.

A sample size of 29 was calculated at alpha error 0.05 and power of study 80% assuming minimum detectable difference of heart rate (beats/min) after endotracheal intubation among the groups was 8.54 ± 11.25 (as per seed article)

III.Observations &Tables

All the three groups were comparable in terms of age, weight, gender and ASA physical status. ($p > 0.05$) [Table 1]

Table 1: Demographic variables in the groups

Variables	Group D (Mean±SD)	Group F (Mean±SD)	Group L(Mean±SD)	P value	LS
Age (yrs)	40.0±12.1	40.3±11.3	44.0±9.7	>0.05	NS
Weight(kg)	55.2±6.3	55.6±6.8	56.6±5.1	>0.05	NS
Sex(m/f)	16/14	15/15	18/12	>0.05	NS
ASA(I/II)	25/5	23/7	26/4	>0.05	NS

Baseline HR was comparable among all groups (p>0.05). Mean HR in Group D increased at all time intervals except at t_2 but this change was not statistically significant with comparison to baseline HR (p>0.05), while at t_2, it decreased significantly ($p < 0.001$); increased at t_1, t_3 and t_4 in Group F ($p < 0.05$, $p < 0.001$, and $p < 0.05$ respectively) and increased at t_1, t_2, t_3, t_4 , t_5 and t_6 in Group L. When the three groups were compared with each other, mean HR was lower in Group D than other two groups at t_2, t_3, t_4, t_5 and t_6 ($p < 0.05$ for all).[Table 2]

Table 2: Comparison of Heart Rate at various time intervals between the groups

Time interval	Group D (Mean±SD)	Group F (Mean±SD)	Group L (Mean±SD)	P value b/w three groups	LS
t_0	95.2±15.3	96.3±15.4	94.5±13.3	p>0.05	NS
t_1	97.4±16.5	101.3±14.1*	100.2±12.4**	p>0.05	NS
t_2	87.1±13.5**	93.5±10.5	98.2±12.3*	p<0.05	S
t_3	98.7±11.8	105.2±13.3**	109.3±11.3**	p<0.05	S
t_4	97.2±11.8	104.0±9.5*	105.8±10.6**	p<0.05	S
t_5	96.7±12.2	99.5±10.4	104.1±8.6**	p<0.05	S
t_6	95.2±9.2	96.1±8.6	101.1±7.1**	p<0.05	S
t_7	92.7±10.4	93.3±9.5	94.3±6.1	p>0.05	NS

*p value <0.05, ** p value <0.001(comparison with baseline level within group)

Baseline SBP was comparable among all groups (p>0.05). Mean SBP decreased at t_1, t_2, t_5, and t_6 in Group D ($p < 0.001$ at t_1, t_2 and <0.05 at t_5, t_6) ; decreased at t_1, t_2 and t_3 in Group F ($p < 0.001$ t_2 and p<0.05 for t_1, t_3) and decreased at at t_1, t_2, and t_7 ($p < 0.001$ for all) and increased at t_3, t_4, and t_5.(p <0.001 , p <0.001 ,p<0.05 respectively) in Group L .When the groups were compared with each other, mean SBP was lower in Group D than other groups at t_3, t_4, t_5 and t_6 ($p < 0.05$ for all),while at other time intervals, this decrease in SBP was not significant statistically.[Table 3]

Table 3: Comparison of SBP at various time intervals between the groups

Time interval	Group D (Mean±SD)	Group F (Mean±SD)	Group L (Mean±SD)	P value b/w three groups	LS
t_0	126.6±6.1	126.5±8.8	128.4±5.5	p>0.05	NS
t_1	119.2±10.7**	122.7±12.8*	123.8±5.5**	p>0.05	NS
t_2	108.7±10.6**	113.3±10.7**	115.7±6.1**	p>0.05	NS
t_3	125.0±9.4	132.7±13.6*	150.0±5.1**	p<0.05	S
t_4	125.4±8.7	128.2±12.9	140.2±4.9**	p<0.05	S
t_5	122.3±11.1*	121.5±24.0	131.4±4.9*	p<0.05	S
t_6	121.3±12.9*	125.4±±14.6	128.8±4.7	p<0.05	S
t_7	124.0±10.4	124.9±11.7	121.1±5.3**	p>0.05	NS

*p value <0.05, ** p value <0.001(comparison with baseline level within group)

Baseline DBP was comparable among all groups (p>0.05). Mean DBP decreased at t_1 and t_2 ($p < 0.05$ and $p < 0.001$ respectively) and increased at t_3 and t_4 in Group D ($p < 0.05$ and $p < 0.001$ respectively);

decreased at t_1 and t_2 ($p < 0.001$ for both) and increased at t_3 and t_4 in Group F ($p < 0.001$ and $p < 0.05$ respectively) ; decreased at t_1 and t_2 ($p < 0.001$ for both) and increased at t_3, t_4, t_5 and t_6 in Group L ($p < 0.001$for all). When the groups were compared with each other, mean DBP was significantly lower in Group D than other groups at t_2, t_3, t_4, t_5 and t_6 ($p < 0.05$ for all) [Table 4]

Table 4: Comparison of DBP at various time intervals between the groups

Time interval	Group D (Mean±SD)	Group F (Mean±SD)	Group L (Mean±SD)	P value b/w three groups	LS
t_0	82.4±6.0	82.7±5.9	82.7±4.5	p>0.05	NS
t_1	79.3±6.2*	80.2±6.7**	81.3±5.3**	p>0.05	NS
t_2	70.0±8.9**	75.1±8.3**	76.3±5.3**	p<0.05	S
t_3	88.6±4.48*	95.1±8.6**	100.5±4.4**	p<0.05	S
t_4	87.6±5.8**	88.6±9.5*	94.8±4.1**	p<0.05	S
t_5	84.9±8.2	85.3±11.0	91.0±3.5**	p<0.05	S
t_6	83.6±9.6	84.9±9.9	88.8±3.8**	p<0.05	S
t_7	85.4±9.5	82.8±11.1	81.7±5.0	p>0.05	NS

*p value <0.05, ** p value <0.001(comparison with baseline level within group)

Baseline MAP was comparable among all groups (p>0.05). Mean arterial pressure was decreased at t_1 and t_2 ($p < 0.001$ for both) and increased at t_3 in Group D ($p < 0.05$); decreased at t_1 and t_2 ($p < 0.001$ for both) and increased at t_3 and t_4 in Group F ($p < 0.001$ and $p < 0.05$ respectively); decreased at t_1 and t_2 ($p < 0.001$ for both) and increased at t_3, t_4, t_5 and t_6 in Group L ($p < 0.001$for all). When the groups were compared with each other, MAP was significantly lower in Group D than other groups at t_3, t_4, t_5 and t_6 ($p < 0.05$ for all) [Table 5]

Table 5: Comparison of MAP at various time intervals between the groups

Time interval	Group D (Mean±SD)	Group F (Mean±SD)	Group L (Mean±SD)	P value b/w three groups	LS
t_0	97.1±5.0	97.3±6.2	98.0 ±4.1	p>0.05	NS
t_1	92.6±7.1**	94.4±7.9**	95.5 ±4.3**	p>0.05	NS
t_2	85.7±8.7**	87.9±8.3**	89.4 ±4.3**	p>0.05	NS
t_3	99.7±5.8*	107.6±8.9**	117.0 ±3.8**	p<0.05	S
t_4	100.1±6.1	101.8±10.1*	109.9 ±3.3**	p<0.05	S
t_5	97.3±8.6	97.4±12.4	104.5±2.8**	p<0.05	S
t_6	96.2±10.1	98.4±10.7	102.2 ±3.1**	p<0.05	S
t_7	98.3±9.5	96.8±10.4	94.9 ±4.2**	p>0.05	NS

*p value <0.05, ** p value <0.001(comparison with baseline level within group)

Regarding side effects, hypotension and bradycardia was noted in 6.66% of patients in group D which might be due to bolus dose of dexmedetomidine.No incidence of *hypotension* and bradycardia was seen in group F and group L.Hypertension was seen in 10% of patients in group D and 20 % of patients in group F and 33.3% of patients in group L. Tachycardia was seen in 20%, 23% and 40% of patients in group D, group F and group L respectively. No incidence of ST/T changes or abnormal cardiac rhythm was noted all three groups.

IV. Discussion

Laryngoscopy and endotracheal intubation provokes transient but marked reflex sympathoadrenal discharge manifesting as hypertension, tachycardia and arrhythmias. The enhanced cardiovascular reflexes may prove to be detrimental for patients with cardiovascular and cerebrovascular diseases. Shribman *et al*. found that laryngoscopy alone or followed by tracheal intubation increases arterial pressure and catecholamine levels while intubation significantly increases HR. [8] These changes were reported to be greatest 60 s after intubation of the trachea that lasts for 5-10 min. If no specific measures are taken to prevent this hemodynamic response, the HR can increase from 26% to 66% depending on the method of induction and the SBP can increase from 36% to 45%.[8], [9] Therefore preventing the increase in sympathoadrenergic activity due to endotracheal intubation becomes an important concern while providing general anaesthesia. Several drugs and novel techniques have been tried by anaesthesiologists to attenuate the stress response to laryngoscopy and endotracheal intubation.

Dexmedetomidine, a selective α_2 adrenergic agonist, fentanyl, an opioid and lignocaine are being used regularly for this purpose. When we compared these medications with each other, we observed that dexmedetomidine controlled heart rate and blood pressure better.

Among all three groups, increase in heart rate was lowest in the dexmedetomidine group while it was highest in the lignocaine group, this difference was significant statistically. Bradycardia was observed in 6.66% of patients in group D; it might be due to bolus dose of dexmedetomidine. [10] Our observations are in accordance with Gandhi et al [11] and Gurulingappa et al [12].

We observed that increase in systolic blood pressure after the intubation was lowest in the dexmedetomidine group while it was highest in the lignocaine group. This fall in SBP in group D was significant at t_3, t_4, t_5 and t_6 time interval; this can be attributed to sedation, sympatholysis, analgesia,cardiovascular stabilization caused by dexmedetomidine. Similar trends were observed in studies. [11], [12], [13] They also concluded better attenuation of the sympathetic response with dexmedetomidine; it remained till the end of 7 minutes.

In all three groups mean diastolic blood pressure showed significant decrease at 2 minutes after PAM, which may be due to anxiolytic effect of midazolam which decreases DBP to some extent.[14] Five minutes after the study drug was given, DBP was decreased significantly in all groups.This fall could be attributed to sympatholytic and sedative action of dexmedetomidine and fentanyl and due to direct myocardial depression and peripheral vasodilatation caused by lignocaine, along with blood pressure lowering effect of thiopentone.

We observed that increase in diastolic blood pressure after intubation was lowest in dexmedetomidine group while it was highest in lignocaine group and the difference was statistically significant from five minutes after the study drug injection to 7 minutes after intubation, similar to other studies. [11], [12], [15] Similar trends were observed for mean arterial pressure.

V. Conclusion

Hence we conclude that i.v.dexmedetomidine (0.6µg/kg) showed better attenuation of haemodynamic response to laryngoscopy and intubation as compared to i.v. fentanyl (2µg/kg) and i.v. lignocaine (1.5 mg/kg 2%) when given 5 minutes prior to intubation without causing any adverse effect.

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References

[1]. Derbyshire, D. R., Chmielewski, A., Fell, D., Vater, M Achola, K. &Smith,G. Plasma catecholamine responses to tracheal intubation. British Journal of Anaesthesia 1983, 55, 855-859.
[2]. Fox EJ, Sklar GS, Hill OH, Vilaneur R and King BD: Complications related to the pressor response to endotracheal intubation. Anaesthesiology 1977; 47:524-525.
[3]. PyrsRoberts, Foex P, Biro GP and Roberts JG: Studies of anaesthesia in relation to hypertension V: Adrenergic Beta receptor blockade. Br. J. Anaesth. 1973; 45: 671.
[4]. AbouMadi, M. N., Keszler, H. &Yacoub, M. Cardiovascular reactions to laryngoscopy and tracheal intubation following small and large intravenous doses of lidocaine. Canadian Anesthetist Society Journal1977, 24(1):129.
[5]. Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Ind J Anaes 2011; 55(4):352–357. doi: 10.4103/0019-5049.84846. [PubMed] [Free full text]
[6]. Scheinin B, Lindgren L, Randell T, Scheinin H, Schenin M. Dexmedetomidine attenuates sympatoadrenal response to tracheal intubation and reduces the need for thiopentone and postoperative fentanyl. Br J Anaesth 1992; 68:126-131. [PubMed]
[7]. Feng CK, Chan KH, Liu KN, Or CH, Lee TY. A comparison of lidocaine, fentanyl, and esmolol for attenuation of cardiovascular response to laryngoscopy and tracheal intubation. ActaAnaesthesiol Sin 1996; 34:617.
[8]. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. Br J Anaesth. 1987;59:295–9. [PubMed]
[9]. Helfman SM, Gold MI, DeLisser EA, Herrington CA. Which drug prevents tachycardia and hypertension associated with tracheal intubation: Lidocaine, fentanyl, or esmolol? AnesthAnalg. 1991;72:482–6. [PubMed]
[10]. Lawrence CJ, lange SD.-Effects of a single pre-operative Dexmedetomidine dose on Isoflurane requirements and peri-operativehaemodynamic stability. Anaesthesia1997; 52: 736-744.
[11]. Gandhi S, Goyal V, Radhkrishnan K, Balakrishnan M. Comparison of Dexmedetomidine with fentanyl in attenuation of pressor response during laryngoscopy and intubation. IOSR J Pharm 2014; 4:28–38.

[12]. Gurulingappa, MdAsifAleem, M.N. Awati, Adarsh S. Attenuation of Cardiovascular Responses to Direct Laryngoscopy and Intubation. A Comparative Study Between i.v. Bolus Fentanyl, Lignocaine and Placebo (NS) Jcdr 2012; Vol-6(10): 1749-1752.
[13]. Yildiz, Munise, Tavlan, Aybars, Sema, Reisli, Ruhiye, Yosunkaya, Alper, Otelcioglu, Seref. Effect of Dexmedetomidine on haemodynamic responses to laryngoscopy and intubation: Perioperative haemodynamic and anaesthetic requirements. Drugs in R and D 2006;7: 43-52
[14]. Ronald D**.** Miller, Lars I**.** Eriksson, Lee A**.** Fleisher, Jeanine P**.** Wiener-Kronish**:** Millers anaesthesia, Edition 8;2010**:**719-814,859-902,1600**.**
[15]. Splinter WM, Cervenko F. Haemodynamic responses to laryngoscopyand tracheal intubation in geriatric patients: Effects of fentanyl,lidocaine and thiopentone. Can J Anaesth 1989;36:370-6.

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