



A Double Blind Comparative Study of Efficacy of Intravenous Dexmedetomidine With Lignocaine and Intravenous Clonidine With Lignocaine in Attenuating Hemodynamic Response to Laryngoscopy And Tracheal Intubation During General Anaesthesia

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ABSTRACT

Aims and objectives : To compare the efficacy of adding iv Dexmedetomidine 0.5µg/kg or intravenous clonidine 3µg/kg to iv lignocaine 1.5mg/kg for attenuating increase in HR, SBP, DBP and MAP and during laryngoscopy and intubation under general anaesthesia and to study their side effects.

Material & Methods : 60 normotensive patients scheduled for elective surgical procedures were randomly divided into three groups of 20 each. All patients were premedicated with glycopyrrolate 0.2mg i.v., tramadol 3mg/kg along with study drug either clonidine 3µg/kg (CL) or dexmedetomidine 0.5µg/kg (DL) or normal saline (NL) according to the inclusion and exclusion criteria of study. All patients were induced with thiopentone 5 mg/kg i.v preservative free lignocaine 1.5mg i.v and succinylcholine 1.5mg/kg i.v and laryngoscopy and intubation was done with appropriate sized endotracheal tube. HR, systolic, diastolic blood pressure were recorded before induction, postintubation, 1, 3, 5, and 10 minutes after laryngoscopy.

Conclusions : Dexmedetomidine + lignocaine combination produced better attenuation of tachycardia response to laryngoscopy and intubation at first minute.

KEYWORDS : Attenuation, hemodynamic response, laryngoscopy, intubation, lignocaine, clonidine, Dexmedetomidine.

INTRODUCTION

Hypertension and tachycardia during intubation under general anaesthesia have been reported since 1950^[1,2]. Increase in blood pressure and heart rate occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation, which in turn leads to increased plasma norepinephrine concentration^[3]. These changes may be associated with morbidity and mortality in patients with heart disease and hypertension, provoking complications like bleeding, increased intracranial and intraocular pressure. There are various techniques by which this intubation-related stress response can be attenuated, all of which depend on reduction in input stimuli or the blockade of adrenergic responses e.g. deep anaesthesia, topical anaesthesia, use of ganglionic blockers, beta blockers^[4], antihypertensive agents like phentolamine^[5], Sodium nitroprusside, nitroglycerine^[6] and calcium channel blockers^[7,8].

Intravenous preservative free lignocaine with its well established centrally depressant and anti-arrhythmic effect is a more popular method to minimize this pressor response^[9,10]. This drug is used routinely for general anaesthesia cases in our institution. Clonidine, an α_2 adrenoceptor agonist attenuates adrenergic haemodynamic stress response^[11]. It is effective in attenuating increase in heart rate and mean arterial pressure during endotracheal intubation^[12]. Clonidine, and has a shorter duration of action. Dexmedetomidine is considered full agonist at α_2 receptors as compared to Clonidine which is considered as a partial agonist. Similar to Clonidine, Dexmedetomidine, also attenuates the haemodynamic response to tracheal intubation, decreases plasma catecholamine concentration during anaesthesia and decreases perioperative requirements of inhaled anaesthetics.^[13] In spite of so many studies, so far not many studies have been published for comparing the efficacy of combination of drugs. Hence the present study was undertaken to compare advantages and efficacy of combining intravenous Dexmedetomidine with intravenous lignocaine, and

intravenous clonidine with intravenous lignocaine on blunting hemodynamic responses to endotracheal intubation during general anaesthesia in our institution.

AIMS & OBJECTIVES

The main objectives of the present study are:

1. To compare the efficacy of intravenous Dexmedetomidine 0.5µg/kg with intravenous lignocaine 1.5mg/kg, and intravenous clonidine 3µg/kg with intravenous lignocaine 1.5mg/kg on changes in the heart rate, Systolic blood pressure, Diastolic blood pressure and Mean arterial blood pressure during laryngoscopy and intubation under general anaesthesia.
2. To evaluate any side effects associated with the use of these drugs.

Materials and Methods

METHODS OF COLLECTION OF DATA –

Research Setting: Department of Anaesthesia, NIMS Medical College JAIPUR, a tertiary care teaching hospital in Northern India.

Study Population: Patients, scheduled for elective surgeries were included in the study.

Sampling Frame: Cases planned to undergo surgery

Sample size: 60 patient scheduled for elective surgeries were included in the study.

Inclusion Criteria:

- Adult patients aged between 15 to 50 years of both sex.
- Patients belonging to ASA class I and II posted for elective surgeries under general anaesthesia.

Exclusion Criteria:

- Patient refusal
- Patients belonging to ASA class III, IV and V.
- Patients with comorbid diseases like hypertension, diabetes mellitus and ischemic heart disease.
- Expected difficult intubation
- Patients posted for Emergency surgeries.
- If patient is allergic to any of these drugs

METHOD

60 patients are randomly allocated to three different groups of 20 each. A specially designed proforma was used to collect the data which includes patient's particulars, indication for surgery, the anaesthetic details, intra-operative monitoring, observation for side effects etc. as group DL, CL, and NL.

1.Group DL – received Dexmedetomidine 0.5µgm/kg iv 3 minutes before induction +lignocaine 1.5mg/kg IV after induction.

2.Group CL –received clonidine 3mcg/kg iv bolus 3 minutes before induction+lignocaine 1.5mg/kg IV after induction.

3.Group NL –received normal saline 4ml iv 3 minutes before induction. + lignocaine 1.5mg/kg IV after induction.

All the patients were visited the day before surgery and preanaesthetic counselling was done and after that informed written consent was taken from them. All patients received Alprax0.5mg orally at night on the day before surgery.

Anaesthetic procedure :

- On arrival in the operating room, patient's basal parameters- B.P, heart rate and ECG were recorded using NIBP and ECG monitor respectively.
- Intravenous access was established with 18G cannula and an IV infusion of Ringer lactate or normal saline was started
- All the patients were premedicated with inj. Glycopyrrolate 0.2 mg iv. and inj tramadol 3mg /kg iv
- Patients in each group received respective drugs as per timing and dose mentioned earlier. The study drug was prepared by anaesthesia co pg and the observer was unaware of drug.
- After preoxygenating the patient. All patients were induced by Thiopentonesodium 5mg/kg iv. then intravenous lignocaine 1.5mg/kg given. After this Succinyl choline 1.5mg/kg was given and laryngoscopy was performed and patient was intubated using appropriate size cuffed endotracheal tube.
- Maintenance with Oxygen 33% & Nitrous Oxide 66% combination and inhalational agent used was Isoflurane(0.5 to 1%) through Bain's circuit on controlled ventilation.
- Muscle relaxant used was Vecuronium Bromide.
- After the completion of surgery reversal was done with Glycopyrrolate(0.2mg/kg) and Neostigmine (0.05mg/kg) and patient were extubated and shifted to SICU.

Assesment:

HR, systolic, diastolic blood pressure were recorded before induction, postintubation, 1,3,5, and 10 minutes after laryngoscopy

Results

Table.1: Age Distribution

Age group	Group DL	Group CL	Group NL
< 25 yrs	05 (25%)	05 (25%)	02 (10%)
26 – 35 yrs	05(25%)	08(40%)	10 (50%)
36 – 45 yrs	05 (25%)	05 (25%)	05 (25%)
> 45 yrs	05 (25%)	02 (10%)	03 (15%)
Total	20 (100%)	20 (100%)	20 (100%)

The above table showed age wise distribution of the study subjects and it ranged from 15 to 50 years.

Table.2: Sex Distribution

Sex	Group DL	Group CL	Group NL
Male	11(55%)	09(45%)	12(60%)
Female	09(45%)	11(55%)	08(40%)
Total	20(100%)	20(100%)	20(100%)

DL Group had 55% of the patients male and 45% female and it was 45 % and 55 % respectively in CL group while in group NL 60% of the patients were male and 40% of the patients were females.

Table.3: Age in years and weight in kg in all the three groups

Variabls	Group DL	Group CL	Group NL	P Value
Age	38.00 +/- 12.95	33.50 +/- 8.80	35.85 +/- 9.39	0.40
Weight	54.80 +/- 4.56	53.25 +/- 4.29	53.60 +/- 5.80	0.58

There was no significant age and weight difference between the three groups (p>0.05).

ANALYSIS OF HEART RATE

Table.4: Heart rate (bpm) in all three groups

Heart rate	Group DL(A)	Group CL(B)	Group NL(C)	P Value
Baseline	89.85 +/- 13.9	97.80 +/- 21.73	91.95 +/- 10.83	0.28
Pre laryngoscopy	85.00 +/- 16.21	99.55 +/- 16.90	93.35 +/- 11.28	0.01
One min	98.25 +/- 12.34	109.50 +/- 14.54	115.15 +/- 11.33	0.00
Three min	98.00 +/- 11.37	104.10 +/- 15.17	109.75 +/- 12.34	0.02
Five min	96.25 +/- 11.18	100.95 +/- 15.71	103.20 +/- 14.56	0.28
Ten min	94.10 +/- 9.83	97.45 +/- 16.50	97.85 +/- 15.06	0.42

ANOVA test

All values are in mean +/- sd

ANALYSIS OF HEART RATE

The above table shows various changes in heart rate at basal, pre-laryngoscopy, post intubation different (1, 3, 5, 10,) time intervals from the onset of laryngoscopy and intubation in all the 3 study group is presented

Group DL(A)

The basal and pre-laryngoscopy mean heart rate and standard deviations in this group were 89.85 +/- 13.9 and 85.00 +/- 16.21 respectively. After 1min of intubation 8.4bpm (9.34%) increase in the mean value of heart rate was observed with values of 98.25 +/- 12.34 and remained higher with a mean heart rate of 98.00 +/- 11.37 at 3 minutes. Subsequently a decreasing trend in the heart rate was noted starting from 5 minutes to 10 minutes after laryngoscopy.

Group CL(B)

The basal and pre-laryngoscopy mean heart rate and standard deviations in this group were 97.80 +/- 21.73 and 99.55 +/- 16.90 respectively. After 1min of intubation 11.7bpm (11.93%) increase in mean heart rate was observed with mean heart rate and standard deviations of 109.50 +/- 14.54. Then there was a decreasing trend in the heart rate from 3 minutes to 10 minutes after laryngoscopy.

Group NL(C)

The basal and pre-laryngoscopy mean heart rate and standard devi-

ations in this group were 91.95 +/- 10.83 and 93.35 +/- 11.28 respectively. After 1min of intubation 23 bpm(25.01 %) increase in heart rate was observed with mean heart rate and standard deviations of 115.15 +/- 11.33. Subsequently a decreasing trend in the heart rate was noted starting from 3 minutes to 10 minutes after laryngoscopy. Mean heart rate at 3, 5 minutes and 10 min were , 109.75 +/- 12.34, 103.20 +/- 14.56 and 97.85 +/- 15.06.

There was significant attenuation of heart rate response at prelaryngeal and one minute and 3min recordings in DL group compared to NL group , But there were no significant difference at five and ten minutes of recording. there were no significant differences in attenuation of heart rate response between NL and CL groups during at different times after laryngoscopy and intubation.

Analysis of systolic blood pressure

Table.5: SBP (mmHg) in all three groups

SBP	Group DL(A)	Group CL(B)	Group NL(C)	P Value
Baseline	122.15 +/- 8.12	117.30 +/- 9.78	117.50 +/- 8.34	0.15
Pre laryngoscopy	114.50 +/- 7.30	114.15 +/- 15.26	113.75 +/- 15.07	0.98
One min	138.50 +/- 10.51	134.33 +/- 14.16	155.80 +/- 13.03	0.00
Three min	127.35 +/- 11.60	121.85 +/- 11.63	140.65 +/- 15.06	0.00
Five min	119.65 +/- 11.20	117.65 +/- 13.83	126.65 +/- 12.17	0.06
Ten min	116.20 +/- 9.71	119.95 +/- 12.28	119.80 +/- 9.57	0.06

ANOVA test

All values are in mean +/- sd

Analysis of systolic blood pressure

The various changes in systolic blood pressure at basal, prelaryngoscopy ,post intubation at different (1 ,3, 5, 10,) time intervals from the onset of laryngoscopy and intubation in all the 3 study group is presented.

Group DL (A)

The basal and pre laryngoscopy mean SBP and standard deviations in this group were 122.15 +/- 8.12 and 114.50 +/- 7.30 respectively . After 1min of intubation 16.35 mm Hg (13.38%) increase in mean SBP was observed with mean SBP and standard deviations of 138.50 +/- 10.51 . Subsequently a decreasing trend in the SBP was noted starting from 3 minutes to 10 minutes after laryngoscopy. Mean SBP at 3,5 minutes and 10 minutes were 127.35 +/- 11.60, 119.65 +/- 11.20 and 116.20 +/- 9.71 .At 10 minutes post laryngoscopy the SBP almost returned to base line with a mean value of 119.95 +/- 12.28.

Group CL(B)

In this group basal systolic blood pressure was 117.30 +/- 9.78 . After giving study drug prelaryngoscopy SBP decreased by 3mm of mm Hg to 114.15 +/- 15.26. Increase in systolic blood pressure of 17.03 mmHg (14.51%) with a mean of 134.33 +/- 14.16 was observed at 1 minute following laryngoscopy. After 3 min SBP fell by 12mmHg with a mean of 121.85 +/- 11.63 , from there on a gradual fall in SBP was observed at 5 minutes mean SBP was 117.65 +/- 13.83 . At 10 minutes post laryngoscopy the SBP almost returned to base line with a mean value of 119.95 +/- 12.28.

Group NL (C)

In this group basal systolic blood pressure was 117.50 +/- 8.34 . After giving study drug prelaryngoscopy SBP decreased by 4 mm Hg to 113.75 +/- 15.07. increase in systolic blood pressure of 38.3mm Hg(32.59%) with a mean of 155.80 +/- 13.03 was noted at 1 minute following laryngoscopy. After 3 min SBP fell by 23.15 mmHg(19.70%) with a mean of 140.65 +/- 15.06, from there on a gradual fall in SBP was noted . At 5 minutes it was 126.65 +/- 12.17. At 10 minutes post laryngoscopy the systolic blood pressure almost returned to base line with a mean value of 119.80 +/- 9.57.

No significant variations were noted in all groups in SBP at basal and after giving study drug. The increase of systolic blood pressure at one and three minutes after intubation was significantly less in CL group and DL group compared to NL group, But there was no significant reduction in increase of SBP at five and ten minutes of recording. There was no significant changes in attenuation of SBP response between CL group and DL group at any time of recording.

Analysis of diastolic blood pressure

Table 6: DBP (mmHg) in all three groups

DBP	Group DL(A)	Group CL(B)	Group NL(C)	P Value
Baseline	83.90 +/- 5.55	79.95 +/- 7.60	77.35 +/- 7.48	0.11
Pre laryngoscopy	77.15 +/- 9.04	77.50 +/- 13.87	75.30 +/- 18.72	0.39
One min	90.60 +/- 7.68	90.25 +/- 13.75	101.75 +/- 8.14	0.00
Three min	84.65 +/- 7.80	79.90 +/- 11.93	92.85 +/- 11.73	0.00
Five min	80.35 +/- 10.27	79.60 +/- 15.73	82.55 +/- 13.49	0.76
Ten min	76.10 +/- 7.65	72.40 +/- 13.78	77.15 +/- 9.80	0.34

ANOVA test

All values are in mean +/- sd

Analysis of diastolic blood pressure

Statistical analysis of changes in systolic blood pressure at basal, prelaryngoscopy, post intubation at different (1 ,3, 5, 10,) time intervals from the onset of laryngoscopy and intubation in all the 3 study group is presented .

Group DL (A)

In this group pre-induction diastolic blood pressure was 83.90 +/- 5.55 After giving study drug prelaryngoscopy DBP decreased by 11 mm Hg to mean of 77.15 +/- 9.04. Increase in diastolic blood pressure of 6.70mmHg (7.9%) with a mean of 90.60 +/- 7.68 was noted at 1 minute following laryngoscopy. After 3 min DBP fell by 6mmHg(6.8%) with a mean of 84.65 +/- 7.80 , from there on a gradual fall in DBP was noted . At 5 minutes it was 80.35 +/- 10.27. At 10 minutes post laryngoscopy the DBP decreased to less than base line with a mean value of 76.10 +/- 7.65.

Group CL (B)

In this group pre-induction diastolic blood pressure was 79.95 +/- 7.60 . After giving study drug prelaryngoscopy DBP decreased by 1 mm Hg to mean of 77.50 +/- 13.87. Increase in diastolic blood pressure of 10.30 mm Hg(12.8%) with a mean of 90.25 +/- 13.75 was noted at 1 minute following laryngoscopy. After 3 min DBP was 79.90 +/- 11.93, from there on a gradual fall in DBP was noted . At 5 minutes it was 79.60 +/- 15.73. At 10 minutes post laryngoscopy the DBP decreased to less than base line with a mean value of 72.40 +/- 13.78.

Group NL (C)

In this group pre-induction diastolic blood pressure was 77.35 +/- 7.48 . After giving study drug prelaryngoscopy DBP decreased to mean of 75 .30 +/- 18.72 . Increase in diastolic blood pressure of 24.40 mm Hg(31.54%) with a mean of 101.75 +/- 8.14 was noted at 1 minute following laryngoscopy. After 3 min DBP fell by 15.5 mmHg(20.0%) with a mean of 92.85 +/- 11.7 , from there on a gradual fall in DBP was noted. At 5 minutes it was 82.55 +/- 13.49 . At 10 minutes post laryngoscopy the DBP decreased to less than base line with a mean value of 77.15 +/- 9.80.

No significant variations were noted in all groups in diastolic blood pressure at basal and after giving study drug. There was significant attenuation of DBP response at one minute and three minutes after intubation in DL group and CL group compared to NL group however there was no significant difference in attenuation of DBP at five and ten minutes of recording. There was no significant difference in attenuation of DBP response between CL group and DL group at any time of recording.

Analysis of MAP

Table.7: MAP (mmHg) in all three groups

Heart rate	Group DL(A)	Group CL(B)	Group NL(C)	P Value
Baseline	96.55 +/- 7.01	91.45 +/- 8.58	94.55 +/- 20.07	0.43
Pre laryngoscopy	84.50 +/- 6.49	87.50 +/- 11.90	88.35 +/- 13.08	0.96
One min	107.30 +/- 13.01	103.35 +/- 13.22	116.80 +/- 10.66	0.00
Three min	97.25 +/- 8.61	95.35 +/- 11.16	107.75 +/- 14.36	0.00
Five min	93.25 +/- 10.31	84.70 +/- 11.64	97.25 +/- 12.25	0.36
Ten min	90.25 +/- 7.55	84.70 +/- 11.64	95.65 +/- 13.61	0.37

ANOVA test

All values are in mean +/- sd

Analysis of MAP

Statistical analysis of changes in MAP at basal, prelaryngoscopy ,post intubation at different (1 ,3, 5, 10,) time intervals from the onset of laryngoscopy and intubation in all the 3 study group is presented .

Group DL (A)

In this group basal MAP was 94.55 +/- 7.01 . After giving study drug prelaryngoscopy MAP decreased by 7.06 mm Hg to mean of 87.50 +/- 6.49 .Increase in MAP Of 10.30 mm Hg(11.13%) with a mean Of 107.30 +/- 13.01 was noted at 1 minute following laryngoscopy. After 3 minutes mean MAP was 97.25 +/- 8.61, from there on a gradual fall in MAP was noted . At 5 minutes it was 93.25 +/- 10.31. At 10 minutes post laryngoscopy the MAP almost returned to base line with a mean value of 90.25 +/- 7.55.

Group CL (B)

In this group pre-induction MAP was 91.45 +/- 8.58 . After giving study drug prelaryngoscopy MAP decreased by 4mm hg to mean of 87.50 +/- 11.90 . Increase in MAP Of 11.9(13.01%) mm hg with a mean Of 103.35 +/- 13.22 was noted at 1minute following laryngoscopy. After 3 min mean MAP was 95.35 +/- 11.16, from there on a gradual fall in MAP was noted as at 5 minutes it was 91.70 +/- 15.00 . At 10 minutes post laryngoscopy the DBP almost returned to base line with a mean value of 84.70 +/- 11.64.

Group NL (C)

In this group pre-induction MAP was 94.55 +/- 20.07 . After giving study drug prelaryngoscopy MAP decreased by 6 mm Hg to mean of 88.35 +/- 13.08 .Increase in MAP Of 22.25 mm Hg (24.35%) with a mean Of 116.80 +/- 10.66 was noted at 1 minute following laryngoscopy. After 3 min mean MAP was 107.75 +/- 14.36 , from there on a gradual fall in MAP was noted . At 5 minutes it was 97.70 +/- 12.25. At 10 minutes post laryngoscopy the systolic blood pressure almost returned to base line with a mean value of 95.65 +/- 13.61.

No significant variations were noted in all groups in mean arterial pressure at basal and after giving study drug. There was significant reduction of increase in MAP at one minute and three minutes after intubation in DL group and CL group compared to NL group, however there was no significant difference in attenuation of MAP between DL group and CL group at any time of recording.

Table 8: Side effects in all three groups

Complications	Group DL(A)	Group CL(B)	Group NL(C)
Hypotension	1	1	-
Bradycardia	2	-	-
Arrhythmias	-	-	-
Others	-	-	-

During study side effects like bradycardia was noted in 2 pts in DL group and hypotension was noted in 1 patient in CL group 1 in CL Group .these side effects were insignificant.

DISCUSSION

In my study for analysis of heart rate no significant variations were noted in all groups in heart rate at basal recording. There was increase of heart rate response that was observed after giving study drug in DL group. There heart rate increased at prelaryngeal and one minute recordings in DL group compared to CL groups, Heart rate responses after the first minute (till 10 minutes) however, were not significantly different between these groups, There was significant attenuation of heart rate response at prelaryngeal and one minute and 3min recordings in DL group compared to NL group , But there were not much difference at five and ten minutes of recording.

Analysis of systolic blood pressure in this study showed no significant variations were noted in all groups in SBP at basal and after giving study drug. The increase of systolic blood pressure at one and three minutes after intubation was significantly less in CL group and DL group as compared to NL group, But there was not much reduction in increase of SBP at five and ten minutes of recording.

The diastolic blood pressure in study showed no significant variations at basal and after giving study drug. There was increase of DBP response at one minute and three minutes after intubation in DL group and CL group as compared to NL group however there was no significant difference in decrease of DBP at five and ten minutes of recording. However significant difference in attenuation of DBP response between CL group and DL group at any time of recording was noted.

Analysis of mean arterial blood pressures showed no significant variations in all groups in mean arterial pressure at basal and after giving study drug. There was significant reduction of increase in MAP at one minute and three minutes after intubation in DL group and CL group compared to NL group, however there was no significant difference in attenuation of MAP between DL group and CL group at any time of recording.

CONCLUSIONS

Based on the present clinical comparative study the following conclusions can be made.

Rise in the HR, SBP, DBP, MAP were observed in all the three groups at one minute following laryngoscopy and intubation and these responses persisted for about 5 minutes after which they returned towards baseline values. However, patients of NL group showed maximum rise in heart rate, SBP, DBP and MAP, compared to other groups which were statistically and clinically highly significant. In group DL (Dexmedetomidine + lignocaine) there was statistically significant attenuation of heart rate responses at one minute as compared to CL group. HR responses after the first minute (till 10 minutes), however were not significantly different between these groups. With respect to attenuation of blood pressure responses, there were no significant differences between DL and CL groups during at different times after laryngoscopy and intubation.

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