

Original Research Article

STUDY OF EFFICACY OF DEXMEDETOMIDINE AND CLONIDINE IN ATTENUATING THE HAEMODYNAMIC RESPONSE DURING LARYNGOSCOPY AND INTUBATION

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Abstract

Introduction: Endotracheal intubation started in last quarter of 19th century, it is one of the most performed procedure in the field of anaesthesia. It is nothing but placement of endotracheal tubes of appropriate size orally or via nasal route. It involves direct laryngoscopy for visualisation of vocal cord. These processes of laryngoscopy and translaryngeal placement of endotracheal tube are noxious stimulus to the tracheal and laryngeal mucosa. Following these stimulus there is increase sympathetic and sympathoadrenal activity as evidenced by increase in plasma catecholamine concentration. It ultimately leads to tachycardia and hypertension and increased oxygen consumption leading to haemodynamic instability. The aim of the present study is to study the relative efficacy of single intravenous dose of dexmedetomidine and clonidine on attenuation of hemodynamic responses during and after laryngoscopy and endotracheal intubation.

Objectives: the objectives of the study

1. To find out role of dexmedetomidine and clonidine in attenuating the haemodynamic response during laryngoscopy and intubation.
2. To compare the efficacy of clonidine and dexmedetomidine preoperatively in attenuating pressor response during laryngoscopy and intubation.
3. To note for any adverse effect of these two drugs

Materials & Methods

Hemodynamic parameters (HR, SBP, DBP, MAP) are recorded and any adverse drug reactions (eg hypotension or hypertension, tachycardia or bradycardia or any arrhythmia) are noted in specific time intervals. Before study drug infusion, After study drug infusion, Just after laryngoscopy and intubation/LAI or 0 min, 1 minute, 2 minutes, 3 minutes, 5 and 10 minutes after intubation.

Statistical analysis: Recorded data was analyzed with standard applicable standard method and finding were discussed in detail to obtain any appropriate conclusion. For statistical analysis P value < 0.05 will be considered significant.

Conclusion: Laryngoscopy and endotracheal intubation are two most consistent procedures leading to significant increase in heart rate and blood pressure. This has been attributed to a sympathetic response as evidenced by an increase in the circulating catecholamines levels. These changes are found to be greatest 60 seconds after intubation and may even last for 5-10 min post intubation. It is for this purpose several studies has been undertaken to search for an effective and safe means both pharmacologically and non-pharmacologically to blunt this response. In this study we compared the role of dexmedetomidine(1mcg/kg) and clonidine(3 mcg/kg),two α_2 agonists in attenuating the pressor response during laryngoscopy and intubation.

Conclusion: This Single Blind Parallel Group Randomized controlled study concludes that dexmedetomidine in the dose of 1 mcg/kg is better than clonidine in the dose of 3mcg/kg in attenuating the haemodynamic response following laryngoscopy and endotracheal intubation.

Key-words: randomized controlled study, clonidine, dexmedetomidine, laryngoscopy and endotracheal intubation

Introduction:

Endotracheal intubation in last quarter of 19th century, it is one of the most performed procedure in the field of anaesthesia. It is nothing but placement of endotracheal tubes of appropriate size orally or via nasal route. It involves direct laryngoscopy for visualisation of vocal cord. These processes of laryngoscopy and translaryngeal placement of endotracheal tube are noxious stimulus to the tracheal and laryngeal mucosa. Following these stimulus there is increase sympathetic¹ and sympathoadrenal activity as evidenced by increase in plasma catecholamine concentration.² It ultimately leads to tachycardia and hypertension and increased oxygen consumption leading to haemodynamic instability.^{3,4} These haemodynamic responses are unpredictable, variable and transient. It is well tolerated by normotensive patients. But such responses are exaggerated and found to be somewhat detrimental in hypertensive patients secondary to adaptive cardiovascular changes and sympathetic activity.⁵ It may lead to myocardial infarction, cardiac dysrhythmia, cerebrovascular accident. Various non-pharmacologic and pharmacologic methods have been used to blunt this response.⁶ Non pharmacologic methods like smooth and gentle intubation with shorter duration of laryngoscopy even with the help of video laryngoscope,⁷ insertion of Laryngeal Mask Airway in place of endotracheal tube, blocking of glossopharyngeal and superior laryngeal nerves have been employed to attenuate this response.

Aim of the study:

To study the relative efficacy of single intravenous dose of dexmedetomidine and clonidine on attenuation of hemodynamic responses during and after laryngoscopy and endotracheal intubation.

Objectives: the objectives of the study

4. To find out role of dexmedetomidine and clonidine in attenuating the haemodynamic response during laryngoscopy and intubation.
5. To compare the efficacy of clonidine and dexmedetomidine preoperatively in attenuating pressor response during laryngoscopy and intubation.
6. To note for any adverse effect of these two drugs.

Materials and Methods:

The present study was conducted in Department of Anaesthesiology, Institute of Post Graduate Medical Education and Research, Kolkata for the period of one year. We included the Patients pertaining ASA-I and ASA-II from Department of Surgery and Department of Gynecology who are undergoing elective surgery during the study period and Patients treated preoperatively with clonidine or dexmedetomidine who were having lower chance of attenuation of pressor response during laryngoscopy and intubation.

Inclusion Criteria: Patient scheduled for elective surgery under General Anaesthesia, Patient with ASA physical status I and II in the age group 25-45 years.

Exclusion Criteria: Patient refusal, Patients undergoing emergency surgery, Allergy to trial drugs, History of drug and alcohol abuse, Patients on cardio active drugs like alfa2 agonist, methyldopa, beta blockers, calcium channel blocker, ACE inhibitors, Anticipated difficult intubation (Mallampati grade III or IV), Pregnancy and Patients with severe systematic disorders like diabetic, musculoskeletal and neurological disease.

Study design: Single Blind Parallel Group Randomized controlled study

Sample design: Patients were randomly allocated into two equal groups, group-C (Clonidine at 3µg/kg) and group-D (Dexmedetomidine at 1µg/kg).

Methods of data collection: Patient's pulse, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), SpO₂, Electrocardiogram are monitored. Respiratory rate and pattern are monitored

Laboratory parameters: Routine hematological investigations like Hb%, TLC, DLC, ESR, platelet count, Blood sugar (Fasting and Post Prandial), Serum urea and creatinine. Chest X-ray (PA view), ECG-all 12 leads as required.

Parameters and Procedures

Parameters studied: Hemodynamic parameters (HR, SBP, DBP, MAP) are recorded and any adverse drug reactions (eg hypotension or hypertension, tachycardia or bradycardia or any arrhythmia) are noted in specific time intervals. Before study drug infusion, After study drug infusion, Just after laryngoscopy and intubation/LAI or 0 min, 1 minute, 2 minutes, 3 minutes, 5 and 10 minutes after intubation.

Procedure: On the day before surgery: Patients' written informed consent (in Bengali or Hindi or English). 8 hour preoperative fasting guidelines Tab pantoprazole 40 mg and tab midazolam 7.5 mg at bedtime were given.

On the day of surgery: After getting institutional ethical committee approval, 70 patients of ASA physical status I or II, age between 25yrs to 45yrs undergoing elective surgery under general anaesthesia are divided into two equal groups randomly-Group C (Clonidine at 3µg/kg in 100 ml in

Normal Saline) and Group-D(Dexmedetomidine at 1µg/kg in 100 ml Normal Saline).These drugs are prepared in volumetric infusion set and infusions were given 20 minutes before induction and infused over 15 minutes through infusion pumps. Then the patients are transferred to operation theatre. Pre-anaesthetic evaluation was performed in each patient including detailed history taking, thorough clinical examination, assessment of spine, airway examination and usual hematological investigation .Chest X ray & ECG was done as required. After arrival of the patient in operation theatre, monitors (ECG leads, blood pressure cuff and pulse oximeter probe) will be attached. Anaesthesia machine, airway equipment, Suction apparatus drugs for resuscitation and general anaesthesia will be kept ready in hand before starting the procedure. The patients will be monitored by NIBP, continuous ECG, pulse oximetry and EtCO₂ throughout the surgery. In supine position after premedication with 5mcg/kg glycopyrolate and fentanyl 2 µg/kg iv patient is preoxygenated with 100% O₂ for 3 minutes, general anaesthesia was induced with IV propofol 2-3mg/kg followed by atracurium 0.5mg/kg iv to facilitate endotracheal intubation After pre-oxygenation for 3 minutes tracheal intubation was done with proper size Macintosh laryngoscope in less than 15 seconds and was confirmed by bilateral chest auscultation and EtCO₂ monitoring. Anaesthesia was maintained with nitrous oxide and oxygen with appropriate concentration of isoflurane. Muscle relaxation is maintained by intermittent dose of atracurium 0.1mg/kg IV. Heart rate, systolic blood pressure(SBP), diastolic blood pressure (DBP) mean arterial pressure(MAP), respiratory rate, Spo₂ values were recorded Controlled ventilation with Bain’s coaxial breathing system to maintain an EtCO₂ level between 35-40 mm of Hg. Any hypotension (mean arterial pressure lower than 20% of baseline) or bradycardia (heart rate < 50/min) incidents will be treated with phenylephrine 50-100 microgram or atropine 0.6 mg increments. A decrease in SpO₂ to < 90% was defined as hypoxia and will be treated accordingly. After completion of surgery, neuromuscular block will be reversed with appropriate dose of neostigmine and glycopyrolate. Patient was transferred to recovery room.

Methods Of Data Collection: Case record form: pre-operative check-up & intraoperative monitoring of SBP,DBP,MAP,HR.

Statistical analysis: Recorded data was analyzed with standard applicable standard method and finding were discussed in detail to obtain any appropriate conclusion. For statistical analysis P value<0.05 will be considered significant.

RESULTS

GROUP	MEAN	MIN.	MAX.	STD. DEV.	S.E. OF MEAN	p-value
D (age)	40.857	33	45	3.264	0.5518	0.6132
C (age)	40.514	33	47	3.364	0.5686	
D (weight)	67.314	52	79	7.843	1.326	0.8660
C (weight)	66.914	57	81	5.818	0.9834	
D	MALE	18	17	35		0.472
C	FEMALE	14	21	35		
	TOTAL	32	38	70		

Table 2: Shows the baseline HR, SBP, DBP & MAP in study subjects

	Groups	N	MEAN	Standard Deviation	S.E Of Mean	P Value
Baseline HR	D	35	77.886	5.362	0.9063	0.1059
	C	35	75.657	6	1.014	
Baseline SBP	D	35	120	7.922	1.339	0.0507
	C	35	124.49	10.733	1.814	
Baseline DBP	D	35	72.429	5.387	0.9105	0.1034
	C	35	74.657	5.896	0.9966	
Baseline MAP	D	35	88.257	5.387	0.9106	0.08
	C	35	90.486	5.101.	0.8623	

Table 3: Shows comparison of Heart Rate after infusing study drugs

	Group	N	Mean	Standard Deviation	S.E of Mean	P value
Baseline BL	D	35	77.886	5.362	0.9063	0.1059
	C	35	75.657	6	1.014	
Post Drug PD	D	35	73.829	4.878	0.8245	0.1216
	C	35	71.8	5.9	0.9973	
After laryngoscopy & Intubation 0 min LAI	D	35	83.886	5.764	0.9743	<0.0001
	C	35	91.086	6.099	1.031	
After 1 min	D	35	82.829	4.253	0.7189	<0.0001
	C	35	91.914	8.504	1.437	
After 2 min	D	35	80.6	4.38	0.7404	<0.0001
	C	35	90.371	7.712	1.304	
After 3 min	D	35	81	5.122	0.8658	0.0002
	C	35	86.971	7.306	1.235	
After 5 min	D	35	77.943	7.708	1.303	0.0180
	C	35	80.2	6.033	1.020	
After 10 min	D	35	79.629	5.568	0.9412	0.0180
	C	35	83.343	7.154	1.209	

Table 3: Shows comparison of SBP after infusion of study drugs

	Group	N	Mean	Standard Deviation	S.E of Mean	p value
Baseline BL	D	35	120	7.922	1.339	0.0507
	C	35	124.49	10.733	1.814	
Post Drug PD	D	35	118.46	8.205	1.387	0.3921
	C	35	120.37	10.276	1.737	
After laryngoscopy & Intubation 0 min LAI	D	35	122.34	7.689	1.3	<0.0001
	C	35	131.06	8.667	1.465	
After 1 min	D	35	122.86	7.682	1.298	<0.0001
	C	35	136.63	15.636	2.643	
After 2 min	D	35	124.34	7.65	1.293	0.0005
	C	35	135	15.454	2.612	
After 3 min	D	35	119.06	6.682	1.129	<0.0001
	C	35	132.57	13.908	2.351	
After 5 min	D	35	118.06	5.985	1.012	<0.0001
	C	35	130.8	12.35	2.087	
After 10 min	D	35	118.6	6.422	1.086	0.0003
	C	35	127.43	12.045	2.036	

Table 4: Shows comparison of DBP after infusion of study drugs

	Group	N	Mean	Standard Deviation	S.E of Mean	p value
Baseline BL	D	35	72.429	5.387	0.9105	0.1034
	C	35	74.657	5.896	0.9966	
Post Drug	D	35	70.886	5.229	0.8838	0.0697

PD	C	35	73.286	5.660	0.9567	
After laryngoscopy & Intubation 0 min LAI	D	35	74.771	5.151	0.8707	<0.0001
	C	35	84.771	5.336	0.9020	
After 1 min	D	35	75.257	3.744	0.6329	<0.0001
	C	35	83.971	8.753	1.48	
After 2 min	D	35	76.371	3.361	0.5682	<0.0001
	C	35	83.514	8.315	1.405	
After 3 min	D	35	74.886	3.504	0.5923	<0.0001
	C	35	81.143	7.554	1.277	
After 5 min	D	35	72.286	6.008	1.015	<0.0001
	C	35	79.086	6.887	1.164	
After 10 min	D	35	71.086	6.075	1.027	<0.0001
	C	35	77.571	5.387	0.9105	

	Group	N	Mean	Standard Deviation	S.E of Mean	p value
Baseline BL	D	35	88.257	5.387	0.9106	0.08
	C	35	90.486	5.101	0.8623	
Post Drug PD	D	35	86.8	5.379	0.9092	0.1039
	C	35	89.0	5.78	0.9770	
After laryngoscopy & Intubation 0 min LAI	D	35	90.629	5.001	0.8452	<0.0001
	C	35	100.23	5.275	0.8917	
After 1 min	D	35	90.971	3.884	0.6566	<0.0001
	C	35	101.6	10.43	1.763	
After 2 min	D	35	92	3.812	0.6433	<0.0001
	C	35	100.6	10.086	1.705	
After 3 min	D	35	89.571	3.76	0.6355	<0.0001
	C	35	98.371	8.822	1.491	
After 5 min	D	35	87.514	4.78	0.8079	<0.0001
	C	35	96.486	7.395	1.341	
After 10 min	D	35	86.886	5.274	0.8914	<0.0001
	C	35	94.2	6.672	1.128	

DISCUSSION

Laryngoscopy and endotracheal intubation are two most consistent procedures leading to significant increase in heart rate and blood pressure. This has been attributed to a sympathetic response as evidenced by an increase in the circulating catecholamines levels. These changes are found to be greatest 60 seconds after intubation and may even last for 5-10 min post intubation. It is for this purpose several studies has been undertaken to search for an effective and safe means both pharmacologically and non-pharmacologically to blunt this response. In this study we compared the role of dexmedetomidine(1mcg/kg) and clonidine(3 mcg/kg),two α_2 agonists in attenuating the pressor response during laryngoscopy and intubation.

Inter group comparison of mean values of Heart Rate was done by student unpaired t test and difference found to be statistically different at LAI/0 min, 1min,2 min, (**p value <0.0001**) 3 min(**p value 0.0002**) ,5 min,10 min (**p value 0.0180**) post laryngoscopy and intubation between the two groups it being less in Group D than Group C in the aforementioned point of time. Considering p

value <0.05 significant it is evident that following endotracheal intubation change in Heart Rate in Group C is significant compared to Group D. In the present study it is evident that following laryngoscopy and endotracheal intubation which is regarded as a noxious stimuli to the airway heart rate rises in both the groups of patients. But the patients receiving dexmedetomidine as premedication heart rate rise is not so much significant as compared with the patients receiving clonidine(Group C). Inter group comparison of mean values of MAP was done by student unpaired t test and difference found to be statistically different at LAI/0min, 1min,2 min,3 min ,5 min,10 min(**p value <0.0001**) post laryngoscopy and intubation between the two groups it being less in Group D than Group C in the aforementioned point of time. Considering p value <0.05 significant it is evident that following endotracheal intubation change in MAP in Group C is significant compared to Group D. So during laryngoscopy and intubation this study shows that premedication with dexmedetomidine at the dose of 1mcg/kg 10-15 minutes before is better in attenuating the sympathoadrenal response than clonidine at the dose of 3 mcg/kg. The findings of our study are similar to the study conducted in the past by other researches⁸⁻¹².

Limitations in this study

1. Plasma concentrations of the study drugs was not measured
2. Single dose of dexmedetomidine and clonidine is used. A dose response study may be useful in determining the appropriate dose of study drugs.
3. Small sample size

CONCLUSION:

This Single Blind Parallel Group Randomized controlled study concludes that dexmedetomidine in the dose of 1 mcg/kg is better than clonidine in the dose of 3mcg/kg in attenuating the haemodynamic response following laryngoscopy and endotracheal intubation.

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