Intramuscular clonidine versus intramuscular dexmedetomidine to attenuate haemodynamic response to laryngoscopy and intubation: open label randomized trial

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Abstract

Background: Patients undergoing laryngoscopy and intubation show fluctuations in their hemodynamic responses. This is due to effect of the procedure on the sympathetic response. High risk patients are more affected due to this. Hence many anesthetic agents were tried to attenuate these responses.

Aim: To compare effect of intramuscular dexmedetomidine and clonidine premedication in modifying the haemodynamic response following laryngoscopy and tracheal intubation.

Material and Methods: Hospital based comparative study was carried out among 50 patients(ASA grade I and II; 20-50 years) undergoing elective surgeries requiring laryngoscopy and intubation. 25 patients were randomly assigned into either group. Clonidine IM 4 μg/kg was given to group A and dexmedetomidine 2μg/kg IMwas given to group B 40min before induction. IV glycopyrrolate, midazolam was used as pre-medication. IV propofol and succinylcholine was used for induction. Hemodynamic parameters like systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and heart rate (HR) were recorded at baseline, after administration of drug, before induction, at laryngoscopy,1min, 3 min, 5min after intubation.

Results: The study showed that HR (105.8±7.43 vs. 88.76±5.94), SBP (149±11.06 vs. 133.8±10.41), DBP (87.4±4.1 vs. 82.4±4.7) and MAP (107.9±4.85 vs. 99.52±5.30)significantly differed between groups A & B at intubation. The hemodynamic values at laryngoscopy, 1, 3, 5 min, were significantly higher in clonidine group compared to dexmedetomidine group (HR=83.40±5.82 vs. 78.84±2.95; DBP=75.44±4.69 vs. 78.52±4.07). Values at other recorded intervals did not differ significantly.

Conclusion: Both clonidine and dexmedetomidine in the given doses were able to attenuate the hemodynamic response. But dexmedetomidine was found to be better compared to clonidine.

Keywords: Clonidine; dexmedetomidine; Haemodynamic Response; Intubation; Laryngoscopy; Premedication.

Introduction

The circulatory response to laryngoscopy and intubation occurs following upper airway stimulation via somatovisceral reflexes. The response is transient peaking at 1-2 minutes returning to baseline at 5 minutes. This transient pressor response is unpredictable and inconsistent. It has been observed that the mechanical stimulation of four areas of the upper respiratory tract, the nose, the epipharynx, the laryngopharynx and tracheo-bronchial tree, induce the reflex cardiovascular response, associated with enhanced neuronal activity in cervical sympathetic fibres. Attempts were made to differentiate between effect of laryngoscopy and those of tracheal intubation and their individual contribution to haemodynamic changes.[1] Prys-Roberts et al (1971) observed that a majority of patients developed reflex tachycardia and hypertension well before the act of intubation.[2]

So, it is laryngoscopy rather than endotracheal intubation which generates the stimulus. A correlation between pressor response and plasma catecholamine concentration is implicated in causation of this

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haemodynamic response.[3]

The healthy patients can easily tolerate these changes without much difficulty. But patients with co-morbidities are susceptible to these transient changes also. There can be serious side effects like arrhythmias, bleeding in the cerebrum, left ventricular failure, myocardial ischemia etc.[4]

Convulsions may be precipitate in eclamptic patients[5]. Almost all types of dysrhythmias have been reported in addition to sinus tachycardia and sinus bradycardia. The common abnormalities are nodal rhythm, atrial and ventricular extra- systoles and pulsus alternans, less commonly multifocal extra-systoles, pulsus bigeminy and atrial fibrillation have been reported. It has been shown by radionucleotide studies that there is sudden decrease in the function of the left ventricle as a response to intubation. This is more when compared to exercise stress seen in patients with coronary artery disease after exercise.[6]

In patients with increased intra cranial pressure, there is a risk of herniation of intra-cranial contents which can lead to cerebral ischemia. Various agents like fentanyl, morphine, lidocaine etc have been tried to minimize these damages that may occur in high risk patients after intubation.[7]

A number of anaesthetic agents are tried to attenuate this response. Alpha (α)-2-Adrenergic receptor agonists like clonidine and dexmedetomidine blunt the sympathoadrenal response.

Intramuscular premedication in the preoperative room has its own advantages over intravenous and other routes of premedication. Task of securing the cannula is not required which sometimes might be difficult.

Need for the study: Many studies used these agents to attenuate the intubation response by giving intravenously prior to laryngoscopy and intubation. Few studies used intramuscular clonidine and dexmedetomidine. In the present study we tried to compare the effect of intramuscular Clonidine and Dexmedetomidine premedication in modifying the haemodynamic response following laryngoscopy and tracheal intubation.

Materials and Methods

A clinical comparative study was carried out at Navodaya Medical College Hospital and Research Centre, Raichur for a period of two years. Ethical committee clearance was obtained and all the patients gave their written informed consent for participation in the study.

Fifty patients undergoing various elective ENT, General surgery and Gynaecological procedures like Laparoscopic Assisted Vaginal Hysterectomy, Total Abdominal Hysterectomy, Diagnostic Laparoscopy, Functional Endoscopic Sinus Surgery, Modified Radical Mastoidectomy, Hemithyroidectomy, Laparoscopic Appendectomy, Herniorrhaphy etc were selected for the study.

Patients with ASA grades I & II, aged 20-50 years of both sexes, Mallampati Classes I and II, undergoing elective surgeries were included in the present study. Age< 20 and >50 years, ASA grades III & IV, Mallampati class III & IV, Nasogastric tube insertion, using drugs that affect autonomic nervous system, undergoing procedures requiring head and neck manipulation, history of allergy to any study drugs and unwilling patients were excluded.

Patients were selected after thorough pre anaesthetic assessment and investigations. Investigations like haemoglobin, complete blood count, Random blood sugar, Blood urea and serum creatinine, ECG, X ray chest - AP View were carried out.

During the study period, it was possible to study 50 cases given the constraint resources. They were randomly allocated using table of random numbers in two groups. Blinding was not possible in the present study as the author was directly involved with all the patients. 25 Patients were randomly allocated to group A who received intramuscular clonidine 4 µg/kg, 40min before induction. 25 patients were randomly allocated to group B who received dexmedetomidine 2μ g/kg, 40 min before induction

All the patients were visited the day before surgery and preanesthetic counselling done. 18 G cannula was used to secure IV line on surgery day. Patients were given either IM clonidine 4 μg/kg or dexmedetomidine2μg/kg IM according to group allocation and monitored. Later patient was taken to the operation theatre. Patient was monitored for ECG, blood pressure and oxygen saturation. Hemodynamic parameters like blood pressure (mean arterial, systolic and diastolic) as well as heart rate were recorded at baseline, after administration of drug, before induction, at laryngoscopy, 1min, 3 min, 5 min after intubation. IV midazolam and glycopyrrolate was given in standard doses to all patients.

100% oxygen was given for 3 min prior to induction to all patients. IV propofol in sufficient dose was used for initiating anesthesia. For blockade of neuromuscular response, IV vecuronium in the dose of 0.1 mg/kg was used. 50% nitrous oxide was used to ventilate the lungs. Macintosh laryngoscope was used for laryngoscopy. Appropriate size cuffed endotracheal tube was used for intubation. Intubation was swiftly achieved within 20 seconds; otherwise such cases

were excluded. All initial recordings were noted before surgery was commenced.

Halothane and 66% nitrous oxide in oxygen were used for maintaining anesthesia during surgery. Inspiratory halothane concentration was tracked and adjusted based on any variation in the MAP and heart rate from baseline. Neostigmine in the dose of 0.05 mg/kg and IV glycopyrrolate in the dose of 0.008 mg/kg was used to antagonise the residual neuromuscular blockade.The parameters were recorded were Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), Peripheral oxygen saturation.

The recordings were noted at various intervals Preoperatively i.e. 40 mins before the estimated commencement of surgery(baseline values); After administration of study drug; Before induction; At laryngoscopy; 1 min after intubation; 3 mins after intubation; 5 mins after intubation. **Statistical Analysis:** Comparison between groups was doneusing students t-test. Results were considered statistically significant for pvalues <0.05 and p values <0.001 were considered highly significant.

Results

All 50 patients participated and completed the study.

Table1: Anthropometric measurements of the subjects (Mean±SD)

Groups	Age (years)	Weight (kg)	Male/ female
Group A (N=25)	28.28+9.52	48.76+6.379	13/12
Group B (N=25)	34.12+11.27	51.48+8.053	10/15
P value	0.0535	0.1918	0.6527

Patients in both groups were comparable to each other in terms of age, weight and number of males and females. The difference in these parameters in two groups was not found to be statistically significant (p > 0.05). (Table 1)

Table 2: Showing the intergroup comparison of baseline haemodynamic parameters (Mean ± SD)

Parameters	Group A (N=25)	Group B (N=25)	P value
Heart rate	81.2+7.12	78.4+6.02	0.1399
Systolic blood pressure	129.9+12.23	128.8+11.73	0.7514
Diastolic blood pressure	76.88+5.84	77.04+5.5	0.921
Mean arterial blood pressure	94.55+6.64	94.15+5.08	0.8233

The heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure at baseline were not significantly different in two group patients (p > 0.05). (Table 2)

Table 3: Showing the intergroup comparison of haemodynamic parameters after Administration of study drug (Mean ± SD)

Parameters	Group A (N=25)	Group B (N=25)	P value
Heart rate	83.60+6.78	83.32+5.48	0.8732
Systolic blood pressure	128.8+12.04	124.2+11.19	0.1611
Diastolic blood pressure	75.76+5.72	74.12+4.52	0.2666
Mean arterial blood pressure	93.46+6.41	90.66+5.15	0.096

The heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure after administration of study drug were not significantly different in two group patients (p > 0.05). (Table 3)

Table 4: Showing the intergroup comparison of haemodynamic parameters before induction (Mean±SD)

Parameters	Group A (N=25)	Group B (N=25)	P value
Heart rate	102.9+10.6	88.84+5.3	<0.0001
Systolic blood pressure	145.3+11.03	133.05+9.61	0.0002
Diastolic blood pressure	85.80+3.95	82.36+4.34	0.0052
Mean arterial blood pressure	105.6+4.86	99.38+4.65	<0.0001

The heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were significantly lower in dexmedetomidine group patients compared to clonidine group (p < 0.05) before induction. (Table4)

Table 5: Showing the intergroup comparison of haemodynamic parameters at laryngoscopy(Mean ± SD)

Parameters	Group A (N=25)	Group B (N=25)	P value
Heart rate	105.8+7.43	88.76+5.94	< 0.0001
Systolic blood pressure	149+11.06	133.8+10.41	< 0.0001
Diastolic blood pressure	87.4+4.1	82.4+4.7	0.0002
Mean arterial blood pressure	107.9+4.85	99.52+5.30	< 0.0001

The heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were significantly lower in dexmedetomidine group patients compared to clonidine group ($p < 0.05$) at intubation. (Table 5)

Table 6: Showing the intergroup comparison of haemodynamic parameters 1, 3 and 5 minutes after intubation (Mean ± SD)

Time (min) after intubation	Parameters	Group A (N=25)	Group B (N=25)	P value
1 minute	HR	92.40+7.2	86.24+4.39	0.0006
	SBP	136.5+10.81	131.8+9.13	0.106
	DBP	80.96+3.56	80.80+4.68	0.8924
	MAP	99.4+4.01	97.78+4.4	0.1803
3 minutes	HR	88+6.31	80.80+3.6	< 0.0001
	SBP	130.2+11.53	129.7+8.97	0.8702
	DBP	76.68+4.25	79.96+4.56	0.0115
	MAP	94.52+4.88	96.54+4.77	0.145
5 minutes	HR	83.40+5.82	78.84+2.95	0.0010
	SBP	127.6+11.98	128.8+9.02	0.6908
	DBP	75.44+4.69	78.52+4.07	0.0168
	MAP	92.81+5.76	95.25+4.69	0.1079

One minute after intubation heart rate was significantly lower in dexmedetomidine group compared to clonidine group ($p < 0.05$) but systolic blood pressure, diastolic blood pressure, and mean arterial pressure were not significantly different. Three minutes after intubation heart rate and diastolic blood pressure was significantly lower in dexmedetomidine group compared to clonidine group ($p < 0.05$) but systolic blood pressure, and mean arterial pressure were not significantly different. Five minutes after intubation heart rate and diastolic blood pressure was significantly lower in dexmedetomidine group compared to clonidine group ($p < 0.05$) but systolic blood pressure, and mean arterial pressure were not significantly different.(Table 6)

Discussion

We found that the hemodynamic parameters were significantly lower in dexmedetomidine group compared to the clonidine group. Menda F et al[8] noted that the hemodynamic responses were blunted effectively in the dexmedetomidine group patients compared to placebo group patients after laryngoscopy and intubation. They also pointed out that at all intervals the dexmedetomidine group patients exhibited the lower values of hemodynamic parameters compared to the baseline values. Similarly, Sulaiman S et al[9] in their study when they compared the dexmedetomidine with saline placebo found that dexmedetomidine group had mean heart rate of 69.10±10.7 beats per minute compared to 84.67±11.3 beats per minute in placebo group.

Taittonen MT et al[10] carried out a study in 60 patients with clonidine in the dose of 4 μg/kg and we also used same dose. They used dexmedetomidine in the dose of 2.5 μg/kg while we used in the dose of 2 μg/kg.Their patients underwent under general anesthesia for various plastic surgery procedures observed that it took three-minute time for hemodynamic values to reach to baseline values in the dexmedetomidine group but it took significantly more time for patients in clonidine group i.e. five minutes for hemodynamic values to reach to baseline values. We also found that most of the time the values were significantly lower in dexmedetomidine group compared to the clonidine group.

Hussain SY et al[11] divided 90 cases of ASA grade I and II into three groups viz. clonidine, dexmedetomidine, and normal saline and recorded hemodynamic parameters at regular intervals. They used clonidine in the dose of clonidine 2 μg/kg while we used 4 μg/kg; they used dexmedetomidine in the dose of 1 μg/kg while we used 2 μg/kg. They observed that compared to saline group patients, the hemodynamic values were significantly lower in clonidine and dexmedetomidine group patients. The values were significantly lower in dexmedetomidine group compared to the clonidine group similar to the findings of the present study. They concluded that dexmedetomidine is more effective compared to clonidine.

Sarkar A et al[12] studied 75 patients with ASA grade I and II in the age group of 18-55 years. They randomly divided them into three group of 25 each viz. placebo, dexmedetomidine (0.5 μg/kg) and clonidine (3 μg/kg) while we used 4 μg/kg; they used dexmedetomidine in the dose of 0.5 μg/kg while we used 2 μg/kg. They noted that the systolic blood pressure was significantly lesser in clonidine and dexmedetomidine group

compared to placebo group patients at all intervals of recordings. They also noted that mean arterial blood pressure which was higher in dexmedetomidine group at initiation reduced significantly after intubation in the dexmedetomidine group compared to placebo group. Similar was the case for heart rate. But in clonidine group, significant lower values were recorded compared to placebo group at all intervals except at induction and at infusion. Thus, the authors concluded that dexmedetomidine should be used as drug of choice in patients undergoing intubation and laryngoscopy to attenuate the hemodynamic response. The authors did not give direct comparison between dexmedetomidine and clonidine directly as they compared these drugs with placebo group while we directly compared these two drugs.

Kakkar A et al[13] carried out a randomized controlled trial and divided the patients into three groups. One group received clonidine 1 μg/kg, second group received dexmedetomidine 0.5 μg/kg and third group received dexmedetomidine 1 μg/kg. All patients were operated under general anesthesia and underwent laryngoscopy and intubation. They noted that response to intubation was not different in three groups. The patients who received dexmedetomidine 1 μg/kg had significantly more incidence of hypotension compared to other two group patients. Patients receiving dexmedetomidine in two groups with different doses have shown significantly increased incidence of bradycardia compared to the patients in the clonidine group. Thus, we conclude that the incidence of side effects was lesser with clonidine compared to dexmedetomidine even though both clonidine and dexmedetomidine are effective in attenuating the hemodynamic responses to intubation and laryngoscopy

Conclusion: Both the dexmedetomidine and clonidine were found to attenuate the hemodynamic responses to intubation and laryngoscopy. But the overall response to IM dexmedetomidine 2μg/kg was found to be better compared to IM 4μg/kg clonidine.

Limitations of the study: Due to limited time and resources, the sample size of 25 each in two groups was used which is very small. Blinding was not possible as the author was directly involved in the study. Hence results of this study should be interpreted cautiously. But overall the results are comparable to previous studies.

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