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A COMPARATIVE STUDY BETWEEN INTRAVENOUSLY ADMINISTERED CLONIDINE AND DEXMEDETOMIDINE FOR ATTENUATION OF SYMPATHOMIMETIC RESPONSE TO LARYNGOSCOPY AND INTUBATION

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ABSTRACT

Laryngoscopy and intubation leads to increased sympathomimetic response such as hypertension, tachycardia. Clonidine and Dexmedetomidine are alpha-2 agonist that decreases sympathetic outflow from the central nervous system. This is a prospective double blinded randomized study involving 60 patients coming for the surgery under general anesthesia. Patients were divided into two groups, group C (n=30) was given clonidine 1µg/kg in 10ml normal saline 10 minutes before induction while group D (n=30) was given dexmedetomidine 1µg/kg in 10ml normal saline over 10 minutes before induction. Hemodynamic variables were noted at 1,3,5,10,15,20,25,30 minutes after intubation. There was statistically significant difference between two groups in changes in pulse rate, systolic blood pressure and mean arterial pressure but not in diastolic blood pressure and oxygen saturation. Dexmedetomidine was more effective in attenuating pressure response to laryngoscopy and intubation as compared to clonidine..

Key words: Clonidine, Dexmedetomidine, Laryngoscopy, Intubation, General anesthesia.

INTRODUCTION

Endotracheal intubation and laryngoscopy are the mainstay for maintaining airway while providing general anesthesia. In 1940 Ried and Brace described pressure response to laryngoscopy and intubation [1]. Rise in catecholamines due to pressure response is short lived but detrimental in high risk patients especially those with cardiovascular diseases, increased intracranial pressure or cerebral vessel anomalies [2-4]. A number of agents like beta blockers, opioids, nitroglycerine spray, lignocaine spray 10% are used to attenuate pressure response to laryngoscopy [5-8]. Centrally acting alpha 2 agonist reduces noradrenaline release from the central nervous system leading to reduced central sympathetic outflow. Clonidine is commonly used alpha 2 agonist as premedicant [9, 10]. Dexmedetomidine is more specific alpha 2 agonist approved by FDA for sedation in mechanically ventilated patients in ICU [11-14]. In our study, efficacy of clonidine and dexmedetomidine in attenuating sympathetic response to laryngoscopy and tracheal intubation was compared and evaluated in normotensive patients undergoing routine elective surgical procedures under general anesthesia.

METHODS AND MATERIAL

The study was conducted after due permission from the ethical committee and review board of the institute. Written informed consent from the patients was taken. This prospective randomized double blinded study was carried out on 60 ASA grade 1 and 2 patients aged 20 years to 50 years scheduled for routine elective surgical

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procedures under general anesthesia. Patients were randomized into two groups, Group C- clonidine group (receiving 1 mcg/kg) and Group D- dexmedetomidine group (receiving 1 mcg/kg) using 60 folded chit paper, on half of which was written clonidine and on half of which was written dexmedetomidine.

Inclusion criteria:

- Patients scheduled for elective surgeries under general anesthesia
- Age between 20 to 50 years of both the sexes.
- Patients with ASA grade I or II.
- Mallampati airway assessment of grade I OR grade II
- Patients weighing between 30 to 70 kilograms

Exclusion criteria:

- Unwilling patients
- Emergency surgeries
- Anticipated difficult intubation
- Patients with cardiovascular disease
- Patients with major organ dysfunction
- Patients on drugs affecting autonomic nervous system
- Patients having known allergy to study drug
- Airway abnormalities
- Psychiatric patients

A detailed history, complete general examination and routine blood investigations were done. Patient was kept nil by mouth for 6 hours prior to surgery. In the operation theatre, Routine monitors like non-invasive blood pressure, pulse oximeter and E.C.G. applied and heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure recorded as a baseline value that was designated as A. After securing intravenous line, intravenous infusion started with 500 ml of inj. DNS. Premedication Inj. Glycopyrrolate (4mcg/kg), Inj. Midazolam (0.04mg/kg), Inj. Ondansetron (0.1mg/kg) given IV slowly to all patients. Patients of group C received IV clonidine 1µg/kg diluted in 10 ml normal saline 10 mins before induction while group D received IV dexmeditomidine 1µg/kg diluted in 10 ml normal saline over 10 minutes before induction. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure were recorded and designated as B-pre induction value after study drug. Induction was achieved with Inj. Propofol 2mg/kg IV slowly followed by Inj. succinylcholine at a dose of 1.5mg/kg IV stat. Oral Intubation was done with appropriate sized, disposable, high volume low pressure cuffed endotracheal tube. Laryngoscopy and intubation was done within 30 seconds. Anaesthesia was maintained with oxygen (50%), N2O (50%), sevoflurane, Inj. vecuronium and with controlled ventilation. Immediately after intubation at 1, 3, 5, 10, 15, 20, 25 and 30 minutes interval, heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and SpO2 were recorded and designated as follows:

I = immediately after intubation
I+1 = one minute after intubation
I+3 = three minutes after intubation
I+5 = five minutes after intubation
I+10 = ten minutes after intubation
I+15 = fifteen minutes after intubation
I+20 = twenty minutes after intubation
I+25 = twenty five minutes after intubation
I+30 = thirty minutes after intubation.

The anesthesiologist who was measuring the blood pressure and heart rate was unware of the study. At the end of the surgery, inhalational agents were discontinued, thorough oral and pharyngeal suction was done and effect of non-depolarising muscle relaxants was reversed with inj. glycopyrrolate 8µg/kg and inj. Neostigmine 0.05 mg/kg and patient extubated.

Data were entered in excel sheet. Statistical analysis was done by applying t- Test (two samples assuming equal variance). P value < 0.05 was considered as significant level.

RESULT

The groups were comparable with respect to age, sex and weight.

Comparison of two groups with regard to mean change in pulse rate ± SD from baseline is done in this table 5 at various time intervals. P<0.05 shows that there is significant difference in changes in the pulse rate from baseline between two groups at all point of study except pre-anesthetic and basal value when the groups were comparable.

Comparison of two groups with regard to mean change in systolic blood pressure ± SD from base line value is done in this table 6 at various time intervals. P<0.05 shows that there is significant difference among mean changes from baseline between two groups at all point of study except in pre anesthetic and basal value when the two groups were comparable.

Comparison of mean changes in diastolic blood pressure ± SD from baseline value between two groups is done in this table 7 at various time intervals. P value > 0.05 showed that there was no significant difference in mean changes in diastolic blood pressure between two groups at all points of study.

Comparison of two groups with regard to mean arterial pressure ± SD from baseline value at various time intervals is done in this table 8. P value < 0.05 showed that there was significant difference in mean changes in mean arterial pressure between two groups at all points of study except pre anesthetic and base line value when two groups were comparable and after study drug.

Table 9 shows comparison of two groups with regard to SpO2 ± SD from baseline value, in patients of two groups at various time intervals. P value > 0.05 showed no significant difference in spo2 between two groups at all points of study.

Table 1. ASA Grading

ASA grade	Group C	Group D
I	0	1
II	30	29
Total	30	30

*ASA- American society of Anesthesiology

Table 2. Comparison of Age distribution of patients in two groups

Age (years)	Group C (%)	Group D (%)	Total
20-30	20(66.66)	16(53.33)	36
31-40	5(16.66)	8(26.66)	13
41-50	5(16.66)	6(20)	11
Total	30	30	60
Mean ± SD	28.3 ± 10.6	32.2 ± 9.8	

Table 3. Comparison of Weight distribution of patient in two groups

Weight(kg)	Group C(%)	Group D(%)	Total
0-30	00(00)	00(00)	00
31-60	25(83.33)	18(60)	43
61-70	05(16.66)	12(40)	17
Total	30	30	60
Mean ± SD	54.41 ± 8.25	58.16 ± 9.81	

Table 4. Sex Distribution

Sex	Group C	Group D	Total
Female	16	16	28
Male	14	14	32
Total	30	30	60

Table 5. Comparison of change in pulse rate (mean ± SD) in two groups

HR	Group C		Group D		P value (comparison between group C and D)
	Mean	±SD	Mean	±SD	
Pre-anesthetic	95.43	9.12	94.93	8.08	0.82
A-Basal	100.73	9.46	97.33	9.45	0.16
B-after study drug	89	12.55	79.13	10.19	0.00
I-immediately after intubation	97.13	11.79	82.3	9.55	0.00
I+1 MIN	97.26	11.35	81.03	9.39	0.00
I+3 MINS	96.26	10.95	80.53	9.62	0.00
I+5 MINS	96.07	10.83	79.4	10.02	0.00
I+10 MINS	96.27	10.3	79	9.94	0.00
I+15 MINS	95.53	9.94	79.23	9.76	0.00
I+20 MINS	95.47	9.68	78.6	9.51	0.00
I+25 MINS	95.06	9.24	78.53	9.58	0.00
I+30 MINS	95.7	9.10	78.8	9.40	0.00

*HR-heart rate, SD-standard deviation, MINS-minutes

Table 6. Comparison of change in systolic blood pressure (mean ± SD) in two groups

SBP	Group C		Group D		P value (comparison between group C and D)
	Mean	±SD	Mean	±SD	
Pre-anesthetic	124	9.12	126.53	11.41	0.37
A-Basal	123.33	10.28	126.66	10.61	0.22
B-after study drug	119.4	7.44	113.06	8.28	0.001
I-immediately after intubation	124.4	6.63	114.06	9.60	0.00
I+1 MIN	122.46	6.48	112.33	9.35	0.00

I+3 MINS	121.4	6.19	109.66	8.42	0.00
I+5 MINS	119.93	5.97	109.33	8.09	0.00
I+10 MINS	121.4	6.62	108.33	9.62	0.00
I+15 MINS	120.93	7.82	107.26	9.16	0.00
I+20 MINS	121.71	7.57	109.06	8.72	0.00
I+25 MINS	122.26	8.19	109.2	8.29	0.00
I+30 MINS	123.53	7.29	111	9.22	0.00

*SBP- systolic blood pressure

Table 7. Comparison of change in Diastolic blood pressure (mean ± SD) in two groups

DBP	Group C		Group D		P value (comparison between group C and D)
	Mean	±SD	Mean	±SD	
Pre-anesthetic	75.66	6.78	78	6.10	0.16
A-Basal	77.33	7.39	80	6.43	0.14
B-after study drug	72.66	5.49	74.33	5.04	0.22
I-immediately after intubation	74.73	4.82	74	4.98	0.56
I+1 MIN	73	5.34	74	4.98	0.45
I+3 MINS	72.86	5.21	73	5.34	0.92
I+5 MINS	72.46	4.28	72	6.10	0.73
I+10 MINS	71.66	3.79	72	6.10	0.80
I+15 MINS	71.66	3.79	71.53	6.33	0.92
I+20 MINS	71.66	3.79	72.2	6.67	0.92
I+25 MINS	71.66	3.79	72.66	6.91	0.49
I+30 MINS	72	4.06	73	6.51	0.47

*DBP-diastolic blood pressure.

Table 8. Comparison of Mean arterial pressure (mean ± SD) in two groups

MAP	Group C		Group D		P value (comparison between group C and D)
	Mean	±SD	Mean	±SD	
Pre-anesthetic	91.8	7.42	94.17	6.91	0.20
A-Basal	92.66	8.04	95.55	7.02	0.14
B-after study drug	88.26	5.40	87.03	5.78	0.40
I-immediately after intubation	91.36	4.82	87.2	6.30	0.006
I+1 MIN	89.48	5.3	86.66	6.01	0.05
I+3 MINS	89.11	4.90	85.1	5.89	0.006
I+5 MINS	88.3	4.08	84.16	6.33	0.003
I+10 MINS	88.26	3.68	84.13	6.74	0.004
I+15 MINS	88.13	3.89	83.36	6.73	0.0015
I+20 MINS	88.36	4.01	84.4	6.76	0.007
I+25 MINS	88.56	4.29	84.73	6.88	0.013
I+30 MINS	89.23	4.40	85.6	6.83	0.019

*MAP-mean arterial pressure

Table 9. Comparison SpO2 (mean ± SD) in two groups

SPO2	Group C		Group D		P value (comparison between group C and D)
	Mean	±SD	Mean	±SD	
Pre-anesthetic	99.83	0.37	99.8	0.40	0.74
A-Basal	99.63	0.49	99.46	0.50	0.20
B-after study drug	99.8	0.40	99.8	0.40	1
I-immediately after intubation	99.26	0.44	99.13	0.34	0.20
I+1 MIN	99.5	0.50	99.33	0.47	0.10
I+3 MINS	99.36	0.49	99.33	0.47	0.79
I+5 MINS	99.46	0.50	99.43	0.50	0.79

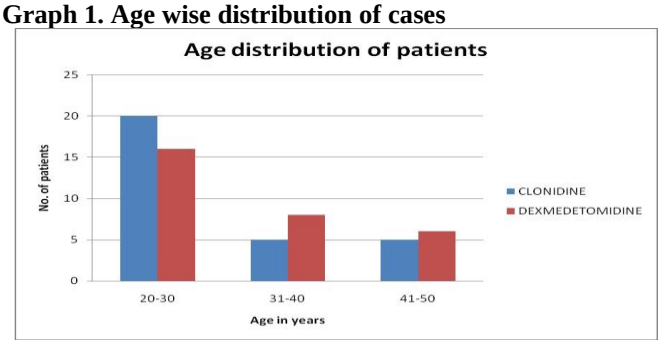
I+10 MINS	99.4	0.49	99.13	0.57	0.06
I+15 MINS	99.4	0.49	99.33	0.47	0.59
I+20 MINS	99.4	0.49	99.36	0.61	0.81
I+25 MINS	99.5	0.50	99.4	0.62	0.49
I+30 MINS	99.43	0.50	99.36	0.56	0.63

Table 10. Comparison of side-effects and complications between two groups

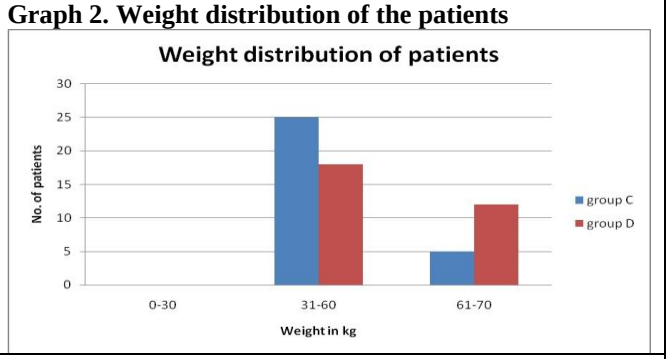
Side-effects	Group C	Group D
Nausea	Nil	Nil
Vomiting	Nil	Nil
Bradycardia	Nil	Nil
Tachycardia	Nil	Nil
Hypertension	Nil	Nil
Hypotension	Nil	Nil
Respiratory depression	Nil	Nil

No side effects or complications were noted in any patients in both the groups.

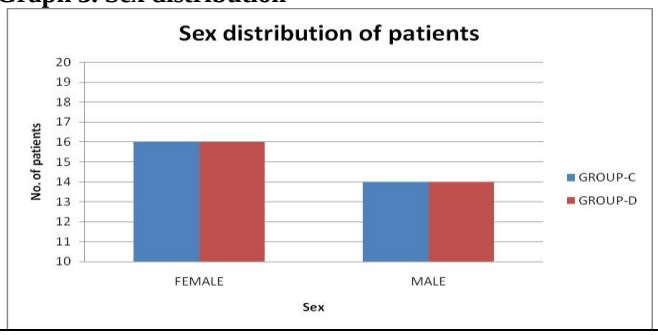
Graph 1. Age wise distribution of cases



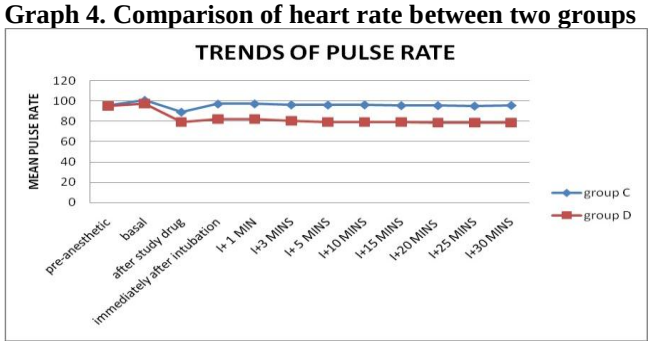
Graph 2. Weight distribution of the patients



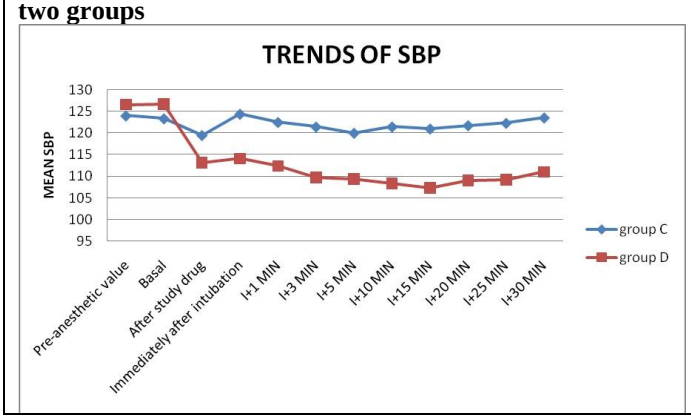
Graph 3. Sex distribution



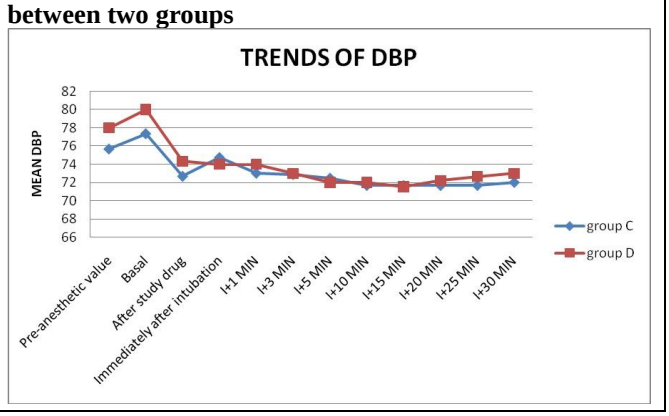
Graph 4. Comparison of heart rate between two groups



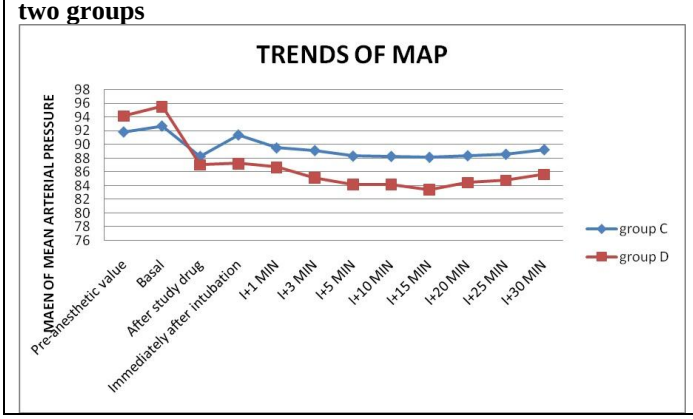
Graph 5. comparison of systolic blood pressure between two groups



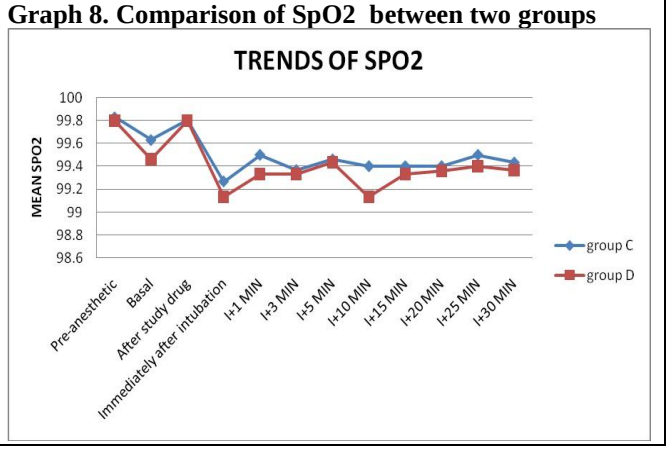
Graph 6. Comparison of diastolic blood pressure between two groups



Graph 7. Comparison of mean arterial pressure between two groups



Graph 8. Comparison of SpO2 between two groups



DISCUSSION

α2 receptor agonist acts on the imidazoline receptor in the locus ceruleus and reduce sympathetic outflow from the central nervous system [15]. Clonidine is a centrally acting partial α2 agonist (α2:α1=220:1). Use of clonidine before carbon dioxide pneumoperitoneum has been reported to reduce catecholamine release and attenuate hemodynamic changes during laparoscopy. Dexmedetomidine is a highly selective α2 agonist (α2:α1= 1620:1) [16]. Sunil Chiruvella used 1µg/kg of clonidine as intravenous infusion versus 1µg/kg dexmedetomidine as premedication for maintainance of hemodynamic stability in laparoscopic cholecysyectomy and found that dexmedetomidine was more effective in attenuating hemodynamic response to pneumoperitoneum. Anand Subramaniam used 1µg/kg dexmedetomidine versus 1µg/kg clonidine to attenuate the response to laryngoscopy and intubation and found that both are equally effective in reducing the stress response to laryngoscopy and intubation [17, 18].

The present study was designed to study the effectiveness of dexmedetomidine and clonidine in attenuating the hemodynamic responses to endotracheal intubation and to note any significant side effects caused by the drug. The demographic profile of the patients in terms of age, body weight, sex ratio was comparable in both the groups. The patients were of ASA grade I and II so most patients had no systemic disease significantly altering the drug metabolism in patients selected for study.

The mean baseline variables (pulse rate, systolic blood pressure, mean arterial pressure, diastolic blood pressure) were similar in both the groups so desired study population was achieved with appropriate randomization. After study drug, there was statistically significant difference between two groups in all the variables (pulse rate, systolic blood pressure, and mean arterial pressure) except diastolic blood pressure.1min, 3min, 5min, 10min, 15min, 20min, 25min, 30min after intubation, there was statistically significant difference between two groups in mean pulse rate, systolic blood pressure and mean arterial pressure but not in diastolic blood pressure and oxygen saturation. The mean oxygen saturation remained above 98% in both the groups at all points of the study. Between the two groups there was no significant difference in the incidence of side-effects.

CONCLUSION

Dexmedetomidine (1µg/kg) is more effective in comparison to Clonidine (1µg/kg) in blunting the hemodynamic response to laryngoscopy and endotracheal intubation in patients undergoing general anesthesia and can be used safely at induction of general anesthesia.

ACKNOWLEDGMENT

Nil

CONFLICT OF INTEREST

Nil

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