COMPARISON STUDY OF DEXMEDETOMIDINE WITH CLONIDINE FOR ATTENUATION OF THE HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

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ABSTRACT

BACKGROUND

Dexmedetomidine is an α2 adrenoreceptor agonist with sedative, analgesic and anxiolytic properties. It has been investigated recently for its potential safety in neuro, cardio and reno-protection.

The purpose of this study is to compare Dexmedetomidine (Dexomid) with Clonidine for the attenuation of the pressor response to laryngoscopy and intubation.

MATERIALS AND METHODS

This prospective study was done on 60 adult patients. The patients in Group D were given dexomid 1 μg/kg diluted in 10 mL of distilled water IV over 10 minutes beginning 15 mins before the laryngoscopy and in Group C were given IV clonidine 1 μg/kg 5 minutes before the laryngoscopy.

RESULTS

The results of the present study prove that the use of dexomid as a premedication is more useful for the patients who undergo laryngoscopy and intubation when compared to clonidine. Raise of vitals from baseline to 1 minute after intubation were less; heart rate 14.67%, systolic BP 7.23% in the dexomid group when compared to the clonidine groups heart rate and systolic BP 17.26%, 12.68% respectively.

CONCLUSION

Dexmedetomidine is a very useful drug for pre-medication before the laryngoscopy and intubation, which significantly reduced the sympathetic pressor response. Its effect was higher than that of clonidine. But care has to be taken while giving the drug.

KEYWORDS

Dexmedetomidine, Clonidine, Intubation, Sympathetic Stimulation, Pressor Response.

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BACKGROUND

Laryngoscopy and tracheal intubation are always associated with haemodynamic changes due to the reflex sympathetic stimulation may result in tachycardia, hypertension and arrhythmias.[1] To blunt pressor response, various pharmacological agents have been tried. Dexmedetomidine like clonidine is an agonist of α_2-adrenergic receptors agent with a sedative, analgesic, sympatholytic and anxiolytic effects that blunt many of the cardiovascular responses in the perioperative period.[2]

MATERIALS AND METHODS

Source of Data

This present study was a prospective study carried out from December 2014 to February 2016. A prospective study was done on 60 adult patients.

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The patients were posted for routine surgical procedures under GA. Approval of the Institutional Ethical Committee and written consent of all patients taken. The patients were randomly divided into two groups 30 each, Group D for the dexomid and Group C for the clonidine respectively. All the patients were ASA-1 or ASA-II adult patients between the age group of 20 - 60 years.

All the patients were pre-medicated with tablet diazepam 5 mg overnight of the surgery. The patients with ASA grades III and IV with cardiovascular disease and known hypersensitivity to these drugs were excluded from the study.

Procedure

Standard multiparameters monitor (ECG, pulse oximeter, non-invasive blood pressure) connected and monitored in all the patients and vitals recorded at required intervals. The patients in Group D were given dexomid 1 μg/kg diluted in 10 mL distilled water IV over 10 mins, 5 mins before the laryngoscopy. The patients in Group C were given clonidine 1 μg/kg IV 5 minutes before the laryngoscopy. All the patients were pre-medicated with Inj. Midazolam 1 mg, ondansetron 4 mg and Inj. Glycopyrrolate 0.2 mg IV.

All the patients were pre-oxygenated with 100% oxygen for 5 minutes. The patients induced with Inj. Thiopentone sodium 5 mg/kg IV and Succinylcholine dose of 2 mg/kg IV. The patients were allowed to breathe 100% oxygen via a face

mask. When they stopped breathing, manually ventilated till laryngoscopy and the intubation was done which within 15 to 20 seconds in a single attempt. The patients' heart rate, Systolic Blood Pressure (SBP), Mean Arterial Pressure (MAP) and Diastolic Blood Pressure (DBP) were recorded at base level, after study drug, after induction, immediately after the laryngoscopy and intubation (1 min), (4 mins), (7 mins) and (10 mins). The data at each of the measurement points was collected, compared and analysed by using the Analysis of Variance (ANOVA) and the Student's t-test.

RESULTS

All the groups were comparable in the age and gender distribution. There was no significant intergroup difference from the baseline [Table 1 and 2].

Heart Rate [HR]

The changes in the heart rate and their statistical comparisons have been presented in the [Table 3/Graph 1].

The increase in the heart rate was maximum in the clonidine group 17.26% (94 ± 31.29 to 110.23 ± 11.22) and the minimum increase was in dexomid group 14.67% (94.35 ± 4.74 to 108.14 ± 10.54), which occurred after giving the study drug and the laryngoscopy and intubation (1 min). The results of the heart rate between the two groups remained statistically significant at all times of the assessment (P < .001), i.e. at 1, 4, 7 and 10 minutes.

Systolic Blood Pressure [SBP]

The changes in the systolic blood pressure and their statistical comparisons have been presented in the [Table 4/Graph 2].

No significant variation was found at the baseline in all the groups and statistically insignificant difference was observed among the dexomid and the other group at the subsequent assessments (P < .001). The attenuation of the rise in the systolic blood pressure was highly significant in the dexomid group than the other groups.

A rise in SBP only 7.23% was observed in dexmedetomidine group from baseline (118.3 ± 9.24) to (126.85 ± 10.34) 1 minute after intubation, whereas in clonidine group it was higher 12.68% from baseline (117.9 ± 9.02) to (132.85 ± 3.51) 1 minute after intubation.

This attenuation of the systolic blood pressure was insignificant in both the groups when compared at 1, 4, 7 and 10 minutes (P < 0.001). A rise was seen in the 1st minute followed by fall nearer to the baseline in two groups more so in dexomid group followed by clonidine (P < 0.001).

Mean Arterial Pressure (MAP)

The changes of results in the mean arterial pressure are shown in Table 5.

A less significant difference was seen in all the groups at 1, 4, 7 and 10 minutes intervals (P < 0.001). A significant difference was observed from the dexomid and clonidine group at all the levels. The rise was raise of MAP in clonidine group 10.33% (88.50 ± 8.13 to 97.65 ± 3.57); in the dexomid group it was only 8.11% (88.75 ± 8.83 to 95.95 ± 5.31), which occurred from base level to immediately after the induction and the laryngoscopy (1 minute). Among the study groups, clonidine was less effective in attenuating the pressure response than Dexomid group.

Diastolic Blood Pressure (DBP)

The changes in the diastolic blood pressure and their comparative statistics are shown in [Table 6].

A significant difference was observed in all the groups (P < .001) at all levels. The rise was 8.34% (82.10 ± 8.75 to 88.95 ± 9.06) clonidine group and in dexomid group 7.48% (81.55 ± 8.36 to 87.65 ± 7.85 with baseline to after 1 min of intubation. The suppression of the rise in the diastolic blood pressure 1 minute after intubation were statistically significant in all groups at 1, 4, 7 and 10 minutes (P < .001).

The attenuation of the pressor response by clonidine and the dexomid at all the levels, i.e. at 1, 4, 7 and 10 mins as compared and the difference was observed.

Master Chart showing Results in Percentage

Comparison Parameters in Percentage		Clonidine	Dexomid
Heart rate: Baseline to after giving study drug	⇩	17.29%	17.98%
Baseline to after 1minute of intubation	⇧	17.26%	14.67%
1 minute after intubation to after 10 minutes of intubation	⇩	23.38%	23.76%
Systolic blood pressures: Baseline to after giving study drug	⇩	1.91%	4.35%
Baseline to after 1minute of intubation	⇧	12.68%	7.23%
1 minute after intubation to after 10 minutes of intubation	⇩	10.17%	10.77%
Mean blood pressures: Baseline to after giving study drug	⇩	1.98%	5.47%
Baseline to after 1minute of intubation	⇧	10.33%	8.11%
1 minute after intubation to after 10 minutes of intubation	⇩	8.71%	10.27%
Diastolic blood pressures: Baseline to after giving study drug	⇩	5.24%	9.5%
Baseline to after 1minute of intubation	⇧	8.34%	10.18%
1 minute after intubation to after 10 minutes of intubation	⇩	11.19%	12.16%

Demographic Data

Age in Years	Group C	Group D
20 - 30	8 (26.67%)	7 (23.33%)
31 - 40	10 (33.33%)	9 (30%)
41 - 50	6 (20%)	8 (26.67%)
51 - 60	6 (20%)	6 (20%)
Total	**30 (100%)**	**30 (100%)**

Table 1. Age Distribution of the Patients between Groups and the Respective Percentages

*Not much variation in age distribution.

Sex Distribution	Group C	Group D
Male	18 (60%)	17 (56.67%)
Female	12 (40%)	13 (44.33%)
Total	**30 (100%)**	**30 (100%)**

Table 2. Sex Distribution, Male and Female and their Percentage between Groups

*Not much variation in Sex distribution.

Time in Minutes	Group C (n = 30)	Group D (n = 30)	P value
Baseline	94 ± 3.29	94.3 ± 4.74	0.069
After study drug	77.75 ± 8.67	77.35 ± 9.47	0.046
After induction	74.1 ± 7.83	71.6 ± 9.47	0.001
1 min after intubation	110.23 ± 11.2	108.14 ± 10.54	0.001
4 mins after intubation	98.44 ± 11.52	96.76 ± 12.37	0..001
7 mins after intubation	94.54 ± 10.89	90.35 ± 11.35	0.001
10 mins. after intubation	84.46 ± 10.32	82.45 ± 10.58	0.001

Table 3. Comparison of Heart Rate in beats per minutes (bpm) between Three Groups of Patients

*Heart results are statistically very significant.

Time in Minutes	Group C (n=30)	Group D (n=30)	P value
Baseline	117.9 ± 9.02	118.3 ± 9.24	0.887
After study drug	115.65 ± 5.20	113.15 ± 4.15	0.0317
After induction	113.85 ± 4.31	111.5 ± 3.32	0.0196
1 min after intubation-	132.85 ± 3.51	126.85 ± 3.87	0.0006
4 mins after intubation-	119.75 ± 3.13	115.45 ± 3.63	0.0026
7 mins after intubation-	120.35 ± 3.05	116.75 ± 2.84	0.0051
10 mins after intubation	119.35 ± 3.07	113.2 ± 3.91	0.0001

Table 4. Comparison of SBP (mmHg) between Groups

*BP results are statistically very significant.

Time in Minutes	Group C Clonidine	Group D Dexomid	P value
Baseline	88.50 ± 8.13	88.75 ± 8.83	0.213
After study drug	86.75 ± 2.71	83.90 ± 3.34	0.0311
After induction	79.05 ± 9.35	75.70 ± 7.43	0.049
1 min after intubation	97.65 ± 3.57	95.95 ± 5.31	0.0037
4 mins after intubation	88.45 ± 4.72	85.35 ± 1.76	0.0186
7 mins after intubation	86.70 ± 2.23	85.4 ± 2.60	0.256
10 mins after intubation	89.15 ± 3.60	86 ± 2.14	0.009

Table 5. Comparison of Mean Arterial Pressure (MAP) between Three Groups

*Very significant 1 minute after intubation.

Time in Minutes	Group C (n = 30)	Group D (n = 30)	P value
Baseline	82.10 ± 8.75	81.55 ± 8.36	0.434
After study drug	77.80 ± 7.84	72. ± 7.05	0.0026
After induction	73.75 ± 7.33	70 ± 6.23	0.0012
1 min after intubation	88.95 ± 9.06	87.65 ± 7.85	0.0204
4 mins after intubation	84.2 ± 9.55	79.2 ± 9.35	0.0014
7 mins after intubation	82.2 ± 9.09	79.7 ± 9.29	0.188
10 mins after intubation	79 ± 8.16	77 ± 6.4	0.0144

Table 6. Comparison of DBP (mm g) between Groups

*Very significant 1 and 4 minutes after intubation.

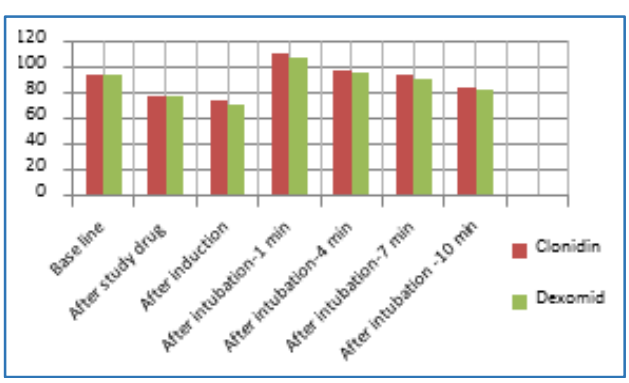

Chart 1. Heart Rate comparison between Groups at Different Times

#There is variation in heart rate 1 minute after induction.

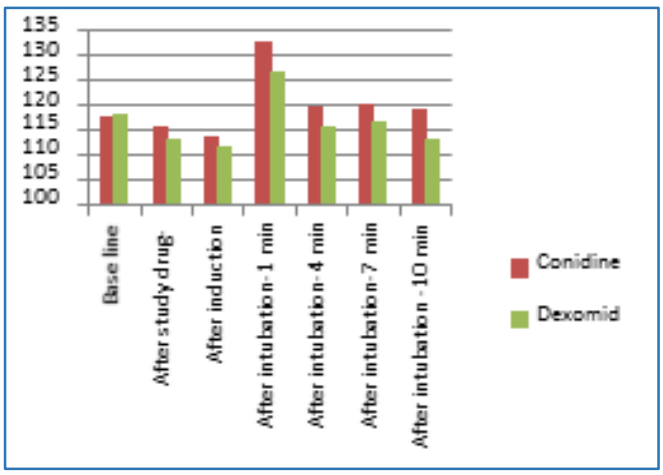

Chart 2. Comparison of SBP (mmHg) between Groups at Different Times

#There is variation in SBP 1 minute after induction.

DISCUSSION

The tracheal intubation and laryngoscopy are always associated with a rise in the heart rate and blood pressure. These effects may have serious repercussions on the high-risk patients. Attenuation of such responses is of great importance in the prevention of the perioperative morbidity and the mortality.[3]

The haemodynamic response to laryngoscopy and endotracheal intubation has been a topic of discussion since 1940; Burstein et al found that the pressor response was due to an increased sympathetic activity which was provoked by the stimulation of the epipharynx and the laryngopharynx, which was further confirmed by others.[4]

The alpha-2 adrenoceptor agonists have been used as pre-medicants, because of their benefit in reducing the pressor response.[5] Dexmedetomidine is a novel agent with a wide safety margin and excellent sedative and moderate analgesic properties.[6]

Dexmedetomidine is a useful medication with many clinical applications. The medication has shown efficacy in decreasing the need for sedative medications.[7] It is highly selective with a wide safety margin, excellent sedative capacity and moderate analgesic properties. This drug seems to have promising future applications in vital organ protection.[8] Our study limited to vital recordings and comparing the results. We have not done any estimation of serum catecholamines.

The patients in all the groups did not show any statistically significant differences in their age or sex distributions. We selected the optimal age range of 20 to 60 years. This is because the variability of the heart rate changes decreases with increasing age and younger patients show more extreme changes. All the groups were similarly pre-medicated regarding anxiolysis. At various times values of HR, SBP, DBP and MAP showed statistically significant difference in two groups. At 1 minute after the laryngoscopy and intubation, the rise in the heart rate and the blood pressure was the maximum in the groups. The heart rate rise was 14.67%, 17.26% in the dexomid (D) and clonidine respectively. The rise was statistically highly significant within each group.

Jigyasa Shahani[9] in his study found that mean heart rate in clonidine group was 81.91 ± 6.84 and in the dexomid Group B 80.94 ± 7.09 (P value = 0.56 implies no statistical significance) after the study drug.

But Mondal S, et al[10] showed that dexmedetomidine significantly attenuated the sympathetic response to laryngoscopy and intubation. Clonidine also reduced the pressor response, but its effect was far lower than that of dexmedetomidine in attenuating the response.[11] Our study results is also similar to their results.

Sağıroğlu et al[12] conducted a study with different doses of dexmedetomidine and found that to control haemodynamic responses to tracheal intubation, dexmedetomidine 1 mcg/kg is more effective. Our result is also similar to above study.

However, the dexomid group showed better attenuation of the HR as compared to the other group, which was statistically significant ($P < 0.001$). We found that the heart rate in all groups returned to the basal value, 4 mins after the intubation and that it remained lower than the basal value up to stating of the surgery. These values were statistically highly significant. Tracheal intubation is associated with increases in arterial pressure, heart rate and plasma catecholamine concentrations.[13] In the present study pre-treatment with dexmedetomidine 1 μg/kg attenuated, but not totally obtunded, the cardiovascular response to tracheal intubation after induction of anaesthesia. In patients undergoing general or gynaecological surgery, numerous studies have shown that dexmedetomidine blunts cardiovascular response to intubation[14,15] and our findings are in accordance with them.

Baseline heart rate was 94 ± 3.29 in Group C and 94.3 ± 4.74 in Group D and decreased to 77.75 ± 8.67 in Group C and 77.35 ± 9.47 after giving the test drugs. MAP also showed decline trend in both groups 88.50 ± 8.13 to 86.75 ± 2.71 in Group C and from 88.75 ± 8.83 to 83.90 ± 3.34 in Group D, which was more reduced with statistically significant. Many other authors have used single dose dexmedetomidine prior to induction and have achieved suppression of haemodynamic responses during laryngoscopy and intubation and also have noticed the reduction of anaesthetic requirement.[15] Dexmedetomidine and clonidine attenuated the heart rate response, but the return to baseline value was quicker in dexmedetomidine.[16] Stress responses to extubation is equally suppressed by dexmedetomidine given prior to reversal.[16]

At 4 minutes, there was still a rise from the pre-induction values of the heart rate and the blood pressure in all the groups. But the values showed a decline from those at 7 minutes, the decline being more rapid in the dexomid group. This finding showed a statistically significant attenuation of the heart rate in the clonidine group ($P < 0.01$).

At 10 minutes, the haemodynamic response declined in all the groups. The decline in the heart rate was significant in all groups. In clonidine Group C and dexomid Group D, a fall of 23.38 and 23.76% respectively was recorded from 1 minute after intubation values.

Overall, the patients in our study showed a definite and a significant rise in the heart rate and the blood pressure in response to laryngoscopy and intubation. There was a statistically significant difference in the magnitude of the rise between the 2 groups. The heart rate was attenuated more

effectively in the Dexomid group 14.67% as compared to those in the Clonidine group 17.26%.

In all groups, the systolic blood pressure increased maximally after 1 minute of intubation and it gradually decreased over 10 minutes. With the administration of dexomid, the minimum increase 7.23% as compared to the pre-induction value was 12.68% in the clonidine group. This may be due to an active baroreflex response to the change in the pressures.[7] The maximum increase in the mean blood pressure was 8.11% in the dexomid group as compared to the baseline value in the clonidine group 10.33% ($P < .001$) at 1 minute after intubation was highly significant in contrast to the other groups ($P < .001$).

The attenuation of the mean arterial pressure in the dexomid group was highly significant as compared to that in the clonidine group ($P < .001$). Similarly, the diastolic blood pressure increased from the baseline value to one minute after intubation in the dexomid group 7.48 and it gradually decreased over 10 minutes and in clonidine 8.34 ($P < .001$).

Dexmedetomidine is a highly selective α2 receptor agonist having eight times high affinity and α2 selectivity compared to clonidine and has a shorter duration of action than clonidine.[17] With dexmedetomidine use, there is a significant reduction in circulating catecholamines with a decrease in blood pressure and a modest reduction in HR.[17] Our results are also in agreement with the above research.

These results of the present study should encourage the routine use of either dexomid or clonidine as a premedication for the patients who undergo laryngoscopy and intubation. By providing improved haemodynamics, dexomid is more beneficial as compared to the clonidine in any clinical setup.

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

CONCLUSION

Using drug like dexmedetomidine before the laryngoscopy and intubation significantly reduced the sympathetic pressor response; its effect was higher than that of clonidine. But care has to be taken while giving the drug.

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