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Comparison between Dexmedetomidine Hydrochloride and Clonidine Hydrochloride on Attenuation of Haemodynamic Response Following Laryngoscopy and Intubation

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Abstract: Direct laryngoscopy and tracheal intubation predictably lead to tachyarrhythmia and hypertension which are usually transient and variable, but these may be fatal in high risk patients. These haemodynamic responses can be attenuated by variable premedication. Dexmedetomidine and clonidine, alpha 2 adrenergic agonist, might do so. The present study was aim to compare these drug for attenuation of haemodynamic response after laryngoscopy and intubation. Hundred adult patients of ASA grade I and II were randomly allocated into two groups of 50 each. We used either dexmedetomidine (group D) 0.5 mcg/kg or clonidine (group C) 3 mcg/kg I.V in 100 ml NS, 10 min before induction. We observed haemodynamic changes during laryngoscopy and intubation, sedation score and any side effects of drugs. The sedation is very significant ($p<0.001$) in group D at 5 min and highly significant ($p=0.0001$) at 10 min. Both are effective in attenuating haemodynamic responses but dexmedetomidine is better than clonidine without significant side effects. We concluded that i.v dexmedetomidine is better to attenuate the sympathetic response to laryngoscopy and intubation without any major side effect than clonidine in healthy patients undergoing elective surgeries

Keywords: Dexmedetomidine HCL, Clonidine HCL, Laryngoscopy, Intubation, Haemodynamic response.

INTRODUCTION

Laryngoscopy and tracheal intubation are nearly always associated with an increase in the blood pressure and heart rate due to the reflex sympathetic discharge which is caused by epipharyngeal and laryngopharyngeal stimulation. This increased sympathoadrenal activity may result in hypertension, tachycardia and arrhythmias [1].

Various pharmacological & non pharmacological methods have been used to attenuate the haemodynamic response to laryngoscopy & endotracheal intubation [2]. Pharmacological methods like use of inhalational anaesthetic agents, pre-treatment with i.v. lidocaine, narcotics, topical anaesthesia, ß-blockers, calcium channel blockers, ace inhibitors, vasodilators etc. have been used. None of the above approaches or agents has proved to be ideal. Hence the search for an ideal agent to attenuate the hemodynamic responses is still continuing [3]. Alpha-2 agonists are used in modern anaesthesia practice due to their various beneficial effects like sedation, analgesia, attenuation of stress response and reduction in anaesthetic requirement [4]. Clonidine a centrally acting alpha-2 agonist has a beneficial effect on the hyperdynamic response to endotracheal intubation. More-over it attenuates stress induced sympathoadrenal response to painful stimuli, improves the intraoperative haemodynamic stability, reduces the incidence of peri-operative MI episodes in patients with suspected or documented coronary artery disease and decreases anaesthetic requirements during surgery. Dexmedetomidine is a highly selective, specific & potent alpha- 2 adrenergic agonist. Compared to clonidine it is said to be 7-10 times more alpha- 2 selective & has a shorter duration of action than clonidine. Pre-treatment with dexmedetomidine attenuates haemodynamic response to tracheal intubation [3].

Therefore, we conduct a study to compare the effect of two alpha- 2 agonists, dexmedetomidine hydrochloride and clonidine hydrochloride in attenuating haemodynamic response during laryngoscopy & endotracheal intubation.

MATERIALS AND METHODS

This is a prospective, randomized control study conducted in 100 patients of ASA physical status

I & II belonging to either sex between the age group of 18 to 60 years undergoing elective head and neck surgeries under general anaesthesia after obtaining approval of hospital ethical committee and informed consent of patient.

Patients allergic to protocol drugs , on antipsychotic drugs, suffering from hypertension, AV blocks, cardiac arrhythmias, congestive heart failure, coronary artery disease, COPD, cerebrovascular disease, asthma, acute hepatic and renal failure were excluded from the study. Also patients with anticipated difficult intubation requiring a second attempt of intubation, BMI with>30kg/m2 were excluded from the study.

Prior to surgery pre anaesthetic evaluation was done and detail history of cardiovascular system, respiratory system, central nervous system, drug therapy and drug allergy was taken. A thorough clinical examination of the patient was done including general, physical and systemic. Airway assessment was done by Mallampati grading to anticipate the possibility of difficult intubation.

Routine investigation like complete blood count, coagulation profile, blood urea, serum creatinine, LFT, serum electrolytes, random blood sugar, blood grouping, urine analysis, HIV, HBsAg, ECG & X-ray chest were done. We randomly divided 100 patients in two groups of 50 each.

Group D – Patients received Inj. Dexmedetomidine HCL 0.5 mcg/kg i.v in 100ml of NS over a period of 10 min at constant rate prior to induction.

Group C -Patients received Inj. Clonidine HCL 3 mcg/kg i.v in 100ml of NS over a period of 10 min at constant rate prior to induction.

All patients were given tablet lorazepam 1mg orally at bed time on the previous night and tablet diazepam 5mg orally morning at 6:00 AM with sip of water on the day of surgery. After taking into operation theatre, vital sign monitor was attached to the patient and baseline HR, SBP, DBP, MAP, SpO_2 and respiratory rate were measured. An intravenous line was secured. All patients received study drug prior to induction.

We recorded HR, SBP, DBP, MAP, SpO2, ECG and Ramsay sedation score at 5 & 10 minutes after infusion. Inj. glycopyrrolate 0.004 mg/kg was given. All patients were preoxygenated for 3 minutes and induced with inj. thiopentone sodium 5 mg/kg and inj. succinyl choline 2mg/kg. After ventilation nasal intubation with proper sized portex cuffed tube was done. Ryle's tube was inserted and oral packing was done.

HR, SBP, DBP, MAP, SpO2 and ECG were recorded during laryngoscopy & intubation at 1, 2, 3, 4, 5, 7 & 10 min after intubation.

Anesthesia was maintained by Inj. Vecuronium bromide + O_2 + N_2O and traces of sevoflurane. At the end of surgery neuromuscular blockade was reversed. Side effects like bradycardia, tachycardia, hypotension, hypertension, arrythmia, agitation, sedation, dryness of mouth, shivering etc. were recorded.

Bradycardia – defined as HR < 60 beats/min.
Tachycardia - defined as HR> 100 beats/min
Hypertension - defined as SBP > 30% of baseline value
Hypotension - defined as SBP < 30% of baseline value
Arrhythmias – Any rhythm other than sinus
Sedation was observed according to Ramsay Sedation Scale

- Patient is anxious and agitated or restless, or both
- Patient is co-operative, oriented, and tranquil
- Patient responds to commands only
- Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
- Patient is asleep, exhibits a sluggish response to light glabellar tap or loud auditory stimulus.
- Patient is asleep, exhibits no response

Results of parametric data were reported on mean & SD. Data calculation and p value calculation is done by unpaired t-test using online software from-http:\\www.graphpad.com\quickcalcs\ttest. The resultant data between two groups were analyzed using students test whereas Z test was used to analyze data within group. P value of <0.05 was consider as a significant.

OBSERVATION AND RESULTS

Group D received inj. dexmedetomidine HCL 0.5 mcg/kg i.v while group C received inj. clonidine HCI 3 mcg/kg. The characteristics of patients in two groups were comparable in terms of age, weight, gender (Tab-1).

Table-1: Patients characteristics

	Group D	Group C	P Value	Significance
Age	45 ± 10.06	43.16 ± 10.47	0.3724	NS
Weight	55.56 ± 7.92	56.42 ± 8.52	0.6023	NS
Gender (M/ F)	38/12	38/12		

Table-2: Comparison of sedation score

	Group D	Group C	P Value	Significance
Before Infusion	1 ± 0	1 ± 0.0049	1	NS
Start Of Infusion	1 ± 0	1 ± 0	1	NS
5min After Infusion	2.16 ± 0.3703	2 ± 0	0.0029	VS
10min After Infusion	3 ± 0	2.16 ± 0.3703	0.0001	HS

This table shows that sedation is very significant ($p<0.001$) in group D at 5 min and highly significant ($p=0.0001$) at 10 min after infusion as compared to group C

Table-3: Comparison of SpO_2

	Group D	Group C	P Value	Significance
Before medication	100 ±0	100 ± 0.0049	1	NS
Start of infusion	100 ± 0.0053	100± 0.0057	1	NS
5min after infusion	100 ± 0	100 ± 0	1	NS
10min after infusion	100 ± 0	100 ± 0	1	NS

Oxygen saturation was 100% in both the group at all time intervals.

Table -4: Comparison of heart rate

	Group D	Group C	P Value	Significance
Baseline	85.14 ± 14.27	87 ± 13.24	0.5008	Ns
At Start Of Infusion	80.62 ± 13.25	84.4 ± 12.09	0.1394	Ns
5 Min After Infusion	76.92 ± 14.17	80 ± 8.88	0.1561	Ns
10 Min After Infusion	74.6 ± 13.9	76.66 ± 9.8	0.3938	Ns
At Induction	73.46 ± 14.26	74.4 ± 11.26	0.7153	Ns
At Laryngoscopy	79.84 ± 14.04	86.62 ± 6.79	0.0027	Hs
At Intubation	80.76 ± 13.07	88.8 ± 7.12	0.0002	Hs
1 Min After Intubation	83 ± 12.75	88.2 ± 8.08	0.0167	S
2 Min After Intubation	81.76 ± 12.78	87.38 ± 8.54	0.0112	S
3 Min After Intubation	80.86 ± 12.18	86.04 ± 10.03	0.0223	S
4 Min After Intubation	81.74 ± 12.29	87.02 ± 9.83	0.0196	S
5 Min After Intubation	81.04 ± 13.36	85.46 ± 9.62	0.0371	S
7 Min After Intubation	81.4 ± 14.31	82.32 ± 11.71	0.7257	Ns
10 Min After Intubation	80.68 ± 13.52	81.46 ± 11.5	0.7567	Ns

This table shows that during laryngoscopy, intubation and at 1, 2, 3, 4 & 5min after intubation there is significant($p<0.01$) decrease in HR in group D compared to group C. Five min after infusion and 5 min after intubation HR is not significant in both the groups.

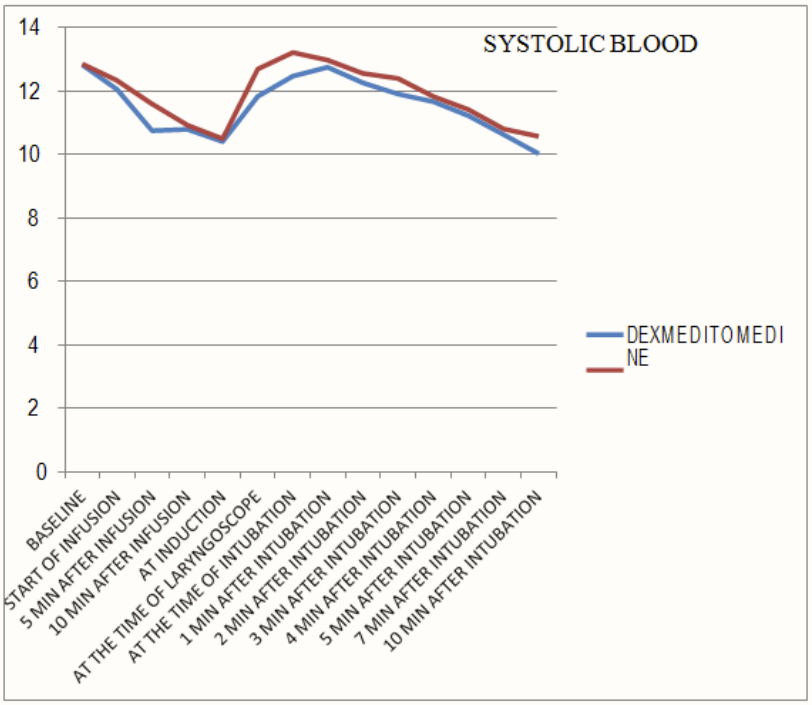

Fig-1

Fig-1 shows that in group D 5 min after infusion, during laryngoscopy and at 10 min after intubation there is highly significant decrease in SBP ($p < 0.0001$) compared to group C. During intubation there is significant decrease ($p=0.0155$) in group D. After intubation SBP increased in both the groups but, less in group D.

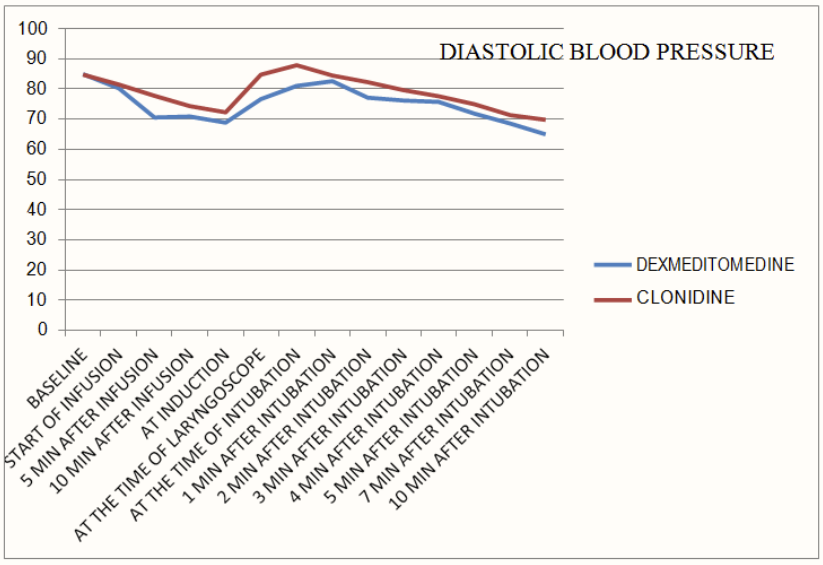

Fig-2

Fig-2 shows that in group D 5 min after infusion and 10 min after intubation highly significant decrease in DBP ($p < 0.0001$) compared to group C. During laryngoscopy, intubation and 2 min after intubation there is significant decrease ($p<0.01$) in group D. After intubation DBP increased in both the groups, but mean in group D is less compared to group C.

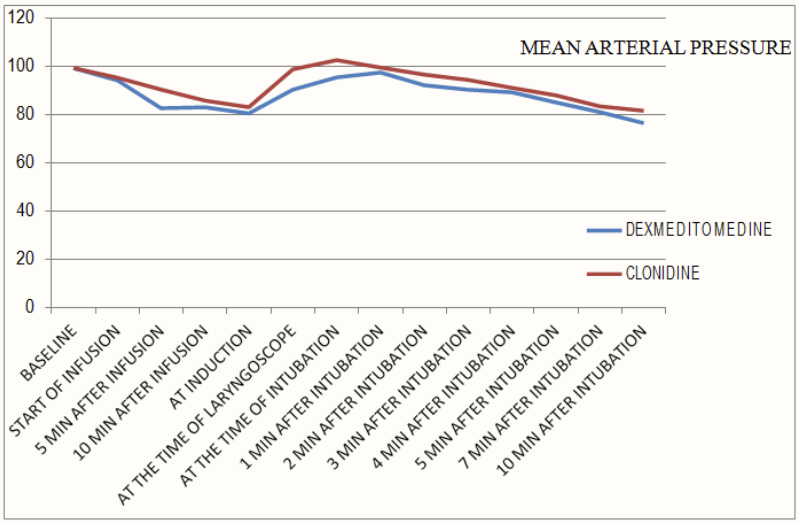

Fig-3: Shows that in group D 5 min after infusion of drug there is highly significant decrease (p=0.0001) in MAP

Compared to group C. During laryngoscopy, intubation and at 10 min after intubation there is significant decrease in MAP ($p < 0.01$) in group D. After intubation though there is increase in MAP in both the groups, but mean in group D is less than group C.

Table-5: Comparison of side effects

	GROUP D	GROUP C
Bradycardia	1	0
Hypotension	0	0
Arrhythmias	0	0
Dryness of mouth	0	0
Nausea & vomiting	0	0
Shivering	0	0

This table shows that only one patient in group D has bradycardia.

DISCUSSION

The endotracheal intubation and laryngoscopy were associated with a rise in plasma catecholamine concentration and subsequent increased in the blood pressure, HR and sometimes cardiac arrhythmias. These above mentioned 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 mortality [5].

A diversity of results exist about the protective measures against the haemodynamic and the catecholamine responses to laryngoscopy and intubation, but no single anaesthetic technique has become generally accepted as being effective in preventing or attenuating these response.

The α2-agonists, clonidine and dexmedetomidine decrease central sympathetic outflow by acting like a brake and modify intraoperative cardiovascular and endocrine responses favorably to surgical stimuli and laryngoscopy. Both clonidine and dexmedetomidine have been shown to reduce sympathetic nervous system activity and plasma catecholamine concentrations [6].

We studied the two most commonly used alpha 2 agonist to compare their efficacy in preventing stress response during intubation. In this study we used dexmedetomidine 0.5mcg/kg and clonidine 3 mcg/kg i.v over 10 minutes to attenuate stress response. Arindam Sarkar et al also used same drug and dose & which is followed by infusion [7]. Anish Sharma N.G & Shankaranarayana used clonidine 3mcg/kg and dexmedetomidine 1mcg/kg^2. Shirsendu Mondal et al used dexmedetomidine 1mcg/kg & clonidine 2mcg/kg to attenuate stress response after intubation [5].

Demographic data such as gender distribution, age and weight of the patient in both the groups were comparable. We compared the sedation score at 5 and 10 min after the infusion and observed that at 5 min in group D majority of the patient had sedation score of 2 (2.16 ± 0.37) and in group C sedation score was 2 (2 ± 0). At 10 min group D had sedation score of 3 (3 ± 0) and in group C it was 2 (2.16 ± 0.37). Sedation was highly significant ($p<0.0001$) in group D compared to group C, without any side effects like respiratory depression.

Study done by Shirsendu Mondal *et al.* [5], observed that dexmedetomidine group mean sedation

score was 2.5 ± 0.51 after 1 min and 2.55 ± 0.51 after 2 min. While in clonidine group it was 2.05 ± 0.39 after 1 min and 1.99 ± 0.51 after 2 min. S kumar et al studied clonidine and dexmedetomidine for laproscopy and concluded that dexmedetomidine provides more sedation and patients is more comfortable in postoperative period[4].

Baseline heart rate was comparable in both the groups. At 5 & 10 min after infusion heart rate decreased more in group D than group C. During laryngoscopy, intubation and after intubation HR in group D was significant decrease than group C but decrease in both group from baseline. Arindam Sarkar *et al*. [7] studied three groups and observed that dexmeditomidine group has significant lower heart rate than other group.

S Kumar *et al*. [4] observed that in both group heart rates was significantly lower than baseline value. Mean HR was lower in dexmedetomidine group than clonidine, but statistically insignificant. Systolic blood pressure was compared in both groups. After infusion of drug there was significant decrease in SBP. During laryngoscopy and intubation mean SBP were 118.2 ± 19.60 mm Hg in group D and 126.78 ± 11.63 mm Hg in group C, 124.54 ± 18 .56 mm Hg in group D and 131.94 ± 10.32 mm Hg in group C respectively.

We observed SBP up to 10 minutes and concluded that it remains low than baseline in both groups. Diastolic blood pressure in group D 5 min after infusion of drug, during laryngoscopy and intubation and at 10 min after intubation was significant decrease ($p < 0.01$) compared to clonidine group. After intubation there was increase in DBP in both the groups, but mean of Group D was less at all time intervals compared to group C but not above baseline.

Mean blood pressure at the start of infusion, 5 min after infusion of drug, during laryngoscopy and intubation were 87.22 ± 7.33 mmHg in group D vs 95.35 ± 7.41 mm Hg in group C, 82.81 ± 6.73 mm Hg in group D vs 90.35 ± 8.94 in group C, 90.44 ± 16.48 mmHg in group D vs 98.73 ± 9.34 mmHg in group C, 95.5 ± 15.11 mmHg in group D vs 102.55 ± 8.86 mmHg in group C respectively. We concluded that there was significant decrease in MAP ($p < 0.01$) in group D than group C. After intubation there was increase in MAP in both the groups, but not above baseline.

Anish Sharma *et al*. observed that after administration of the drug HR, SBP, DBP and MAP decreased in both dexmedetomidine and clonidine group. There was slight increase in BP at intubation in both the groups, but remained below the pre- induction value. At 3, 5 & 10 min after intubation BP displayed a downward trend and that was comparable in both the groups. HR, SBP, DBP, MAP returned to pre- induction values by 10 min of intubation. They concluded that during laryngoscopy and intubation HR, SBP, DBP, MAP increased in both the groups. Magnitude of increase in HR during laryngoscopy and intubation was higher in clonidine group compared to dexmedetomidine group and was statistically significant even at 3 min after intubation [2].

Arindam Sarkar *et al.* observed that mean SBP, DBP & MAP in dexmedetomidine group remained close to baseline where as steep rise in haemodynamic parameters in clonidine and placebo group [7]. Sunil chiruvella *et al*. in study observed that mean HR, SBP, DBP & MAP was lower in dexmedetomidine group than clonidine group. No significant episode of hypotension was found in any group [6]. S Kumar *et al*. observed that there was decrease in SBP in both group, but mean DBP were similar over the periods with slightly higher in clonidine than dexmedetomidine group. No difference in MAP in both groups and were equally efficious in preventing rise in MAP during the procedure [4].

Shirsendu Mondal *et al.* concluded that HR attenuation was better in dexmedetomidine group. The Maximum rise of SBP was 7.4% in dexmedetomidine group, 14.67 % in clonidine group and 25.56 % in control group from base line, while DBP was only 3.75 %, 19.23 % and 30.57 % respectively [5].

Arpita Laha *et al.* observed that after 1, 2, 3 & 5 min of intubation increase in HR was significantly less in dexmedetomidine group than control group. In both the groups SBP & DBP after intubation increased compared to baseline, but in dexmedetomidine group it came to baseline within 3 min of intubation [8]. We observed side effect like bradycardia, tachycardia, hypotension, hypertension, arrhythmias, dryness of mouth, shivering, nausea, vomiting etc. One patient in group D had bradycardia (HR–42 beats/min) was treated with inj. atropine sulphate 0.6 mg i.v. Sunil Chiruvella *et al*. [6] in their study observed that 4 patients had bradycardia while Varshali M. Keniya *et al*. [9] observed 2 patients and were treated with inj. atropine. S.Kumar *et al*. [4] showed that 5 pt has bradycardia in dexmedetomidine group and did not required any intervention. M. T. Taittanen *et al*. [10] observed bradycardia in one patient and nausea and vomiting in one patient in dexmedetomidine group. SukhminderJit Singh Bajwa *et al*. [11] observed that there was fall in SpO_2 up to 94-95% after completion of dexmedetomidine infusion, which returned to normal on waking up the patients. In our study no one patient has any other side effects as our dose was less (only 0.5mcg/kg).

During induction we did not used opioid in our study and it was seen that patients haemodynamic

response following intubation were attenuate more in dexmedetomidine group than clonidine group. Bijoy *et al*. [12] and Shirsendu Mondal *et al.* [5] concluded that intraoperatively dexmedetomidine showed significant cardiovascular stability compared to clonidine. Both clonidine and dexmedetomidine attenuates the pressor response but dexmedetomidine is better in attenuating the tachycardia response[2]. S. Kumar *et al*. [4] concluded that both drugs were equally effectivein attenuating hemodynamic response to pneumoperitonium but sedation and postoperative analgesia was more in dexmedetomidine group. Similar findings were observed by Sukhminder Jit Singh Bajwa *et al*. which showed that dexmedetomidine group attenuated pressor response more than Fentanyl group [11].

CONCLUSION

1. We concluded that intravenous dexmedetomidine HCl in a dose of 0.5mcg/kg and clonidine HCL in a dose of 3mcg/kg as a premedication effectively blunted the stress response to laryngoscopy and tracheal intubation. Dexmedetomidine HCL was superior to clonidine HCL in the attenuation of haemodynamic response; also it provides good sedation without any undesirable side effects.

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