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# A RANDOMISED CONTROLLED TRIAL TO COMPARE CLONIDINE AND DEXMEDETOMIDINE FOR ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION

Anesthesiology

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## ABSTRACT

**INTRODUCTION** - Laryngoscopy and intubation produce increase in heart rate and blood pressure due to sympathetic release which can be attenuated by various upcoming drugs. This study compared dexmedetomedine and clonidine to placebo for the effectiveness in attenuation of stress response and side effects caused by them. Objective was to compare Heart rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP) before and after laryngoscopy and intubation of patients who were given either clonidine or dexmedetomidine or Normal Saline as placebo.

**METHODS**–total 90ASA I and II patients were recruited with 30 in each group. Basal SBP, DBP, MAP, HR was recorded (T0). **Group A:** Received I.V. clonidine 1mcg/kg in 100ml Normal Saline over 10 minutes.**Group B:** Received I.V. dexmedetomidine 0.5mcg/kg in 100ml Normal saline over 10 minutes.**Group C:** Received 100 ml of normal saline over 10 minutes, constituting the control group.After 2 min (T1), 5 min (T2), 10 min (T3) SBP, DBP, MAP, and HR were recorded while the study drug was administered.SBP, DBP, MAP, HR was recorded at 2 min (T4), 5 min (T5), and 10 min (T6) after laryngoscopy and intubation.

**RESULTS-** In this study there was significant reduction in HR, SBP, DBP and MAP by dexmedetomidine and clonidine as compared to controls. Attenuation of response to intubation was better following premedication with dexmedetomidine than with clonidine.

## KEYWORDS

laryngoscopy, intubation, haemodynamics,clonidine,dexmedetomidine

## INTRODUCTION

Laryngoscopy and tracheal intubation evokes a transient but marked sympathetic response causing increase in heart rate (HR) and blood pressure (BP). These changes are maximum immediately after intubation and lasts for 5-10 minutes.

Conventional methods to prevent pressor response with minimum side effects include topical lignocaine sprays, deeper planes of anaesthesia by inhalational/intravenous (I.V.) agents or opioids, calcium channel blockers, vasodilators like sodium nitroprusside, nitroglycerine etc and researches are still in progress [1, 2]. Alpha 2- adrenoceptor agonists (α2 agonist) may provide an alternative method due to their anaesthetic sparing and hemodynamic stabilizing effects [3].

Premedication with clonidine (α agonist) blunts the stress response to the surgical stimuli and reduces the narcotic and anaesthetic requirements [4]. It increases the cardiac baroreceptor reflex sensitivity to an increase in the SBP, and stabilizes the blood pressure [5, 6]. Its mild selectivity to α2 adrenoceptors and long half-life has limited its use. Dexmedetomidine is a imidazole derivative and is highly selective α2 agonist [7]. Its specificity for α2 receptor is 8 times that of clonidine, and has an 2/1 binding affinity ratio of 1620:1. At low doses, slow infusions it acts on 2 receptors but at high doses or fast infusion of low doses selectivity is lost, acts on both 1and 2 receptors.

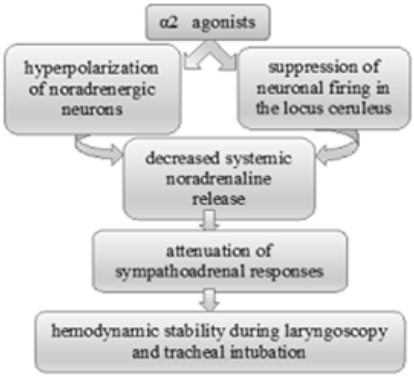


**Figure 1: Mechanism of action of α2 agonists**

## MATERIAL AND METHODS

After obtaining institutional ethical committee clearance and written informed consent from all patients study was conducted.

**Study Population -** Patients posted for elective surgery under general anaesthesia (GA).

**Study Design -** Prospective, single blind, randomized, placebo controlled study.

**Sample size -** 90ASA I and II patients (30 for each group).

**Sampling Technique -** Convenience type of non-probability sampling was used for the selection of study subjects based on randomization by closed envelope method

**INCLUSION CRITERIA -** Age 20-60 years of either sex, ASA grade I or II, elective surgical procedure, mallampatti classification 1 or 2.

**EXCLUSION CRITERIA -** No consent, anticipated difficult airway, Intubation time ≥20 sec, history of hypertension, diabetes mellitus and heart disease, ASA grade III & above or allergic to study drugs.

**METHODOLOGY** - After detailed clinical history, examination and investigations, patients were explained the procedure. Basal SBP, DBP, MAP and HR were recorded (T0). Patients were premedicated with Inj Glycopyrrolate 0.04mg/kg IV, Inj Ondansetron 0.16mg/kg IV and Inj Fentanyl 1mcg/kg I.V.

**Group A:** I.V. clonidine 1mcg/kg in 100ml Normal Saline (NS) over 10 minutes.

**Group B:** I.V. dexmedetomidine 0.5mcg/kg in 100ml NS over 10 minutes.

**Group C:** 100 ml NS over 10 minutes, constituting the control group.

After 2 min (T1), 5 min (T2), 10 min (T3) SBP, DBP, MAP, and HR were recorded while the study drug is administered.

Once the study drug was given all patients were pre-oxygenated and induced with 2-3mg/kg Inj. Propofol till loss of eyelash reflex. After

being able to successfully ventilate, Inj Succinylcholine 2mg/kg IV was given and intubation was done.

Atracuronium 0.5mg/kg IV given after intubation. SBP, DBP, MAP, HR was recorded at 2 min (T4), 5 min (T5), and 10 min (T6) after laryngoscopy and intubation. Surgery was commenced 10 min after laryngoscopy and intubation. No stimulus was applied during the study period.

Any fall in the MAP more than 20% from the baseline was treated with Inj mephentramine 3 mg I.V aliquots, and bradycardia (HR<40/min) was treated with Inj. Atropine 0.3 mg IV. These patients were excluded from the final analysis and extra patients were recruited to make 30 in each group.

**Statistical Analysis -** Collected data was transferred to SPSS version 17 software. Quantitative data was presented as mean and standard deviation and analysed using ANOVA test. Qualitative data was presented as frequency and percentage and analysed using chi-square test. P-value of < 0.05 was considered as significant.

**OBSERVATIONS -**

- Out of 90 subjects, 64.4% were females while 35.5% were males. Groups were comparable regarding gender distribution (p-0.712).
- ASA grade I: ASA grade II = 1:1. Groups were comparable based on ASA grade (p-0.87).
- Mean age and weight of subjects was 36.5 years and 63 Kg. Patients were evenly matched based on age and weight distribution.
- General examination findings i.e. HR, SBP, DBP and MAP were comparable in all patients. Any significant observations found during the study was due to the effect of study drugs.
- Heart Rate
- At T1, mean HR decreased by 5 beats/min in group B, group A and C showed no significant difference.
- At T2 and T3 HR decreased by 8 beats/min and 9 beats/min in group B and 2 beats/min and 3 beats/min in group A whereas control showed approximately no difference.
- T4 mean HR in group B was 8 beats / min less than the baseline and in group A it was 5 beats/ min more than baseline while in group C it was 13 beats /min more than the baseline.
- At T5, HR was 11 beats/ min less than the baseline in group B, almost same as baseline in group A and in group C it was 8 beats/ min more than baseline.
- At T6, HR was 15 beats/ min lower in group B and 6 beats/min lower in group A and similar to baseline in group C.

Thus, the HR decline was slightly more in dexmedetomidine group but the difference is not significant (p> 0.05). However the heart rate in control group was significantly high compared to both groups during all periods.

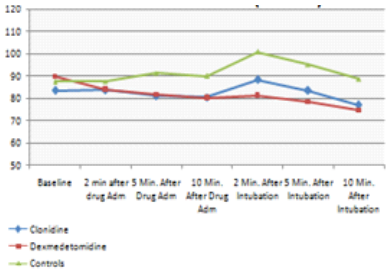


**Figure 2: Variation in heart rate (per minute)**

- **Blood Pressure**
- At T1SBP , DBP , MAP decreased by 7,3,3mm of Hg in group B, decreased by 5,3,2 mm Hg in group A compared to baseline and was similar to baseline in control group.
- At T2 , SBP , DBP , MAP decreased by 10,5,6 mm of Hg in group B, decreased by 4,8,8 mm Hg in group A and decreased by 1,4,3 mm of Hg in group C compared to baseline.
- At T3SBP , DBP , MAP decreased by 13,5,9mm of Hg in group B, decreased by 11, 10, 11 mm Hg in group A and decreased by 4, 4, 5 mm Hg in group C as compared to baseline.
- At T4 SBP , DBP, MAP decreased by 17,10,12mm of Hg in group B, decreased by 2,5,5 mm Hg in group A compared to baseline and increased by 11,9,10 mmHg compared to baseline in group C.
- At T5 SBP , DBP , MAP decreased by 30,13,17mm of Hg in group B, decreased by 14,10,10 mm Hg in group C compared to baseline and increased by 1,3,3 mmHg compared to baseline in group C.
- At T6 SBP , DBP , MAP decreased by 32,18,22 mm of Hg in group B, decreased by 24,15,19 mm Hg in group A compared to baseline and decreased by 5,1,3 mmHg compared to baseline in group C.
- Thus, there was an increase in BP at intubation in control group , on an average SBP,DBP and MAP increased by 15, 13 , 15 mmHg , clonidine group showed minimal response to intubation with on an average SBP,DBP and MAP increase by 9 , 5, 9 mmHg while in dexmedetomidine group there was no response to intubation and values of SBP , DBP , MAP decreased by 4,3,3 mm Hg than the values 10 min after drug administration(before intubation).
- Two patients had bradycardia after giving dexmedetomidine. They were treated with inj.Atropine 0.3 mg intravenously. These patients were excluded from the final analysis and two other patients were recruited to make the sample size thirty.
- Side effects like dryness of mouth and sedation which are found during the use of alpha 2 agonists were found in 5 patients (3 in group A and 2 in Group B) which did not require any intervention. No other serious adverse effects were noted in this study.

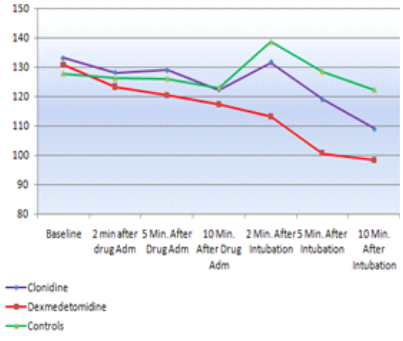


**Figure 3: Variation in SBP (mmHg)**

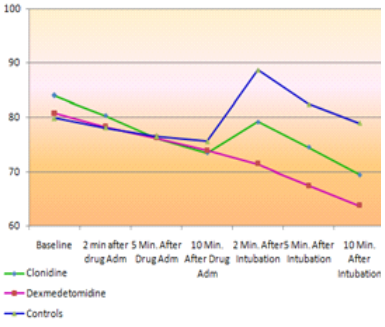


**Figure 4: Variation in DBP (mmHg)**

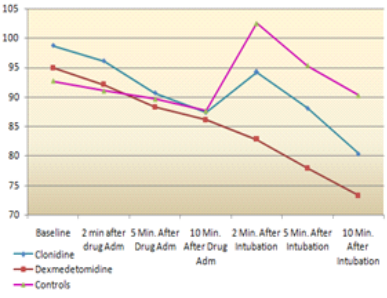


**Figure 5: Variation in MAP (mmHg)**

**RESULTS –**

- HR, SBP, DBP and MAP all were significantly lower in medication groups compared to control group after drug administration and after 2, 5 and 10 minutes of intubation. While SBP, DBP and MAP were significantly lower in group B compared to group C.
- In both groups A and B, all values remained below the pre-induction values while in group C significant increase in values after intubation was seen as compared to baseline values.
- Hypotension and bradycardia are considered the major side effects of alpha 2 agonists. In this study there was no significant incidence of hypotension and bradycardia.

**Table 1: Variation in HR, SBP, DBP, and MAP in group A, B, C at various points of time nd (no difference); ↓(decreased by);↑(increased by)**

| *Variables* | *After drug administration* | | | | | | | | | *After intubation* | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *2min* | | | *5min* | | | *10min* | | | *2min* | | | *5min* | | | *10min* | | |
| | *A* | *B* | *C* | *A* | *B* | *C* | *A* | *B* | *C* | *A* | *B* | *C* | *A* | *B* | *C* | *A* | *B* | *C* |
| *Heart rate (HR)* | ↓8 | ↓5 | nd | ↓2 | ↓8 | nd | ↓3 | ↓9 | nd | ↑5 | ↓8 | ↑ 13 | Nd | ↓11 | ↑8 | ↓6 | ↓ 15 | Nd |
| *Systolic blood pressure (SBP)* | ↓5 | ↓7 | nd | ↓4 | ↓10 | ↓1 | ↓11 | ↓ 13 | ↓4 | ↓ 11 | ↓ 17 | ↓2 | ↓14 | ↓30 | ↑1 | ↓ 24 | ↓ 32 | ↓5 |
| *Diastolic blood pressure (DBP)* | ↓3 | ↓3 | nd | ↓8 | ↓5 | ↓4 | ↓10 | ↓5 | ↓5 | ↓9 | ↓ 10 | ↓5 | ↓10 | ↓13 | ↑3 | ↓ 15 | ↓ 18 | ↓1 |
| *Mean arterial pressure (MAP)* | ↓2 | ↓3 | nd | ↓8 | ↓6 | ↓3 | ↓11 | ↓9 | ↓5 | ↓ 10 | ↓ 12 | ↓5 | ↓10 | ↓17 | ↑3 | ↓ 19 | ↓ 22 | ↓ 15 |

## DISCUSSION

Studies conducted by Shahni and colleagues [8], Kumar V and colleagues [9], Aggarwal and colleagues [10] used 1 µg/kg of clonidine for attenuating hemodynamic response to tracheal intubation. Sarkar and colleagues[11], Kakkar and colleagues[12] concluded that dexmedetomidine 0.5 µg/kg I.V. infusion given 10 to 15 mins prior to laryngoscopy attenuates the pressor response. Based on these studies, 1 µg/kg clonidine and 0.5 µg/kg dexmedetomidine was chosen in this study.

Kakkar and colleagues [12] compared 1 µg/kg clonidine, 0.5 and 1 µg/kg I.V. doses of dexmedetomidine. They found that the incidence of intubation response was similar in all three groups (P > .05). Both groups receiving dexmedetomidine had higher number of patients developing bradycardia and hypotension (more in 1 µg/kg group) as compared to patients receiving clonidine. It was concluded that dexmedetomidine 0.5 µg/kg, 1 µg/kg and clonidine 1 µg/kg attenuate the laryngoscopy and intubation response but but haemodynamic stability was more in 0.5 µg/kg I.V dexmedetomedine. Clonidine 1 µg/kg was associated with lesser side effects.

A study by Sharma and colleagues concluded that both clonidine and dexmedetomidine attenuates the pressor response during laryngoscopy and intubation but dexmedetomidine is better in attenuating the tachycardia response [13].

Aho M et al., conducted a double blind randomised controlled study to evaluate the effects of dexmedetomidine 0.6 µg/kg body weight and isoflurane requirements in patients undergoing abdominal hysterectomy. The authors observed that in all groups, blood pressure and heart rate increased after tracheal intubation but the response was significantly less in 0.6µg/kg body weight dexmedetomidine group ($p<0.05$) than in saline ($p<0.01$) group [3].

Many other studies have observed intramuscular and oral routes clonidine to attenuate the haemodynamic response to tracheal intubation

## CONCLUSION

In the present study there was significant reduction in HR, SBP, DBP, and MAP by dexmedetomidine and clonidine as compared to controls. Also attenuation of presser and tachycardia response to intubation was better following premedication with dexmedetomidine than with clonidine.

### Future implications

We suggest that a larger study should be carried out in future to compare the effects of different doses of dexmedetomedine and clonidine or other adjuvants in attenuating the response to laryngoscopy and intubation. The advantages and disadvantages of one regimen over another can be more clearly delineated along with less side effects and improved hemodynamic profile.

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