An Observational Study to Compare the Effect of Two Different Doses of Dexmedetomidine on Hemodynamic Response to Laryngoscopy and Endotracheal Intubation

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Abstract

Background: Laryngoscopy and intubation are associated with intensesympathoadrenal stimulation resulting in hypertension, tachycardia & arrhythmias consequent to the release of catecholamines. Various drug regimens and techniques have been used from time to time for attenuating the stress response to laryngoscopy and intubation, including opioids, barbiturates, benzodiazepines, beta blockers, calcium channel blockers, vasodilators etc. Dexmedetomidine is a highly selective alpha 2 receptor agonist having eight times higher affinity and alpha 2 selectivity compared to clonidine and has a shorter duration of action than clonidine.

Material and Method: 60 patients scheduled for elective surgical procedures under general anaesthesia belonging to ASA Grade I and II, in the age group of 18 to 60 years were divided into two study groups, D1 and D0.5 received dexmedetomidine 1 µg/kg and 0.5 µg/kg intravenously (iv) over 10 minutes before induction. Hemodynamic responses were compared in both groups by measuring Heart rate (HR),Systolic blood pressure (SBP),Diastolic blood pressure(DBP),Mean arterial pressure (MAP) and SpO_2 before giving the test drug (base line values),just before induction,during intubation and at 1 minute, 3 minutes, 5 minutes,10 minutes after intubation. Statistical data were analyzed by using student's unpaired t test.

Observation and Results: Group D1 had 4.70% rise in HR and Group D0.5 had 9.59% rise during intubation which was statistically significant($p<0.05$). Maximum rise in SBP and DBP in Group D0.5 was 14.53% and 12.84% respectively, whereas in Group D1 it was 5.55% and 8.90% respectively. In Group D0.5, rise in BP lasted longer after intubation compared to Group D1.

Conclusion: The present study demonstrated that ivdexmedetomidine 1µg/kg was better than dexmedetomidine 0.5µg/kg in attenuation of the pressor response of laryngoscopy and intubation without any significant side effects.

Keywords: *Dexmedetomidine, laryngoscopy, Intubation.*

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Introduction

Laryngoscopy and intubation are associated with intense sympathoadrenal stimulation resulting in hypertension, tachycardia & arrhythmias consequent to the release of catecholamine.(1) Patients with limited myocardial reserve, tachycardia and hypertension may result in myocardial ischemia, infarction (MI); arrhythmias or precipitate cardiac failure.(2) The hypertensive response may produce deleterious effects

in patients with raised intracranial pressures (ICP) or intraocular pressures (IOP), pheochromocytomas and vascular lesions such as intracranial arterio-venous malformations or those with aortic aneurysms and dissection.[2,3]

Various drug regimens and techniques have been used from time to time for attenuating the stress response to laryngoscopy and intubation, including opioids, barbiturates, benzodiazepines, beta blockers, calcium channel blockers, vasodilators etc.[4,5,6,7,8]

α2 adrenergic agonists namely clonidine and dexmedetomidine decrease sympathetic tone and preoperative use of clonidine has been shown to blunt the hemodynamic responses to noxious stimulation and to prevent overall hemodynamic variability.[9,10]

Dexmedetomidine is a highly selective α2 receptor agonist having eight times higher affinity and α2 selectivity and has a shorter duration of action than clonidine.[11,12]

Materials and Method

The study was conducted after obtaining permission from ethical committee in Dhiraj Hospital, S.B.K.S.M.I. & R.C. in department of anesthesiology. 60 patients of ASA I and II were allocated in 2 groups (n=30 in each group). They were included in the study only after obtaining a written informed consent. **Group D1**(n=30) received 1μg/kg and **Group D0.5**(n=30) received 0.5μg/kg body weight of dexmedetomidineiv over a period of 10 minutes.

Inclusion Criteria:

- Age between 18 years & 60 years
- ASA I and II.
- No known history of allergy, sensitivity to the study drugs
- Patient willing to sign informed consent.
- Mallampatti class I and II

Exclusion Criteria:

- Patient's refusal.
- ASA III and IV
- Known case of heart blocks, sinus bradycardia and hypotension, autonomic neuropathy
- Patients on beta blocker drugs
- Mallampatti class III, IV & V
- Allergy to trial drugs.
- Nasogastric tube insertion
- Patient undergoing procedures requiring head and neck manipulation

Patients were explained about the procedure of general anaesthesia and a written informed consent was obtained from them. Pre-operatively patient's history, systemic examinations and routine investigations were carried out.HR, SBP and DBP were recorded preoperatively.

Tab alprazolam 0.5 mg was given on the previous night of surgery and patients were kept nil by mouth overnight. In operation theatre multipara monitor was applied and baseline HR, SBP, DBP, SpO_2 and ECG were recorded. Intravenous line was secured and iv fluid was started.

All patients were premedicated with inj. ondansetrone 0.08mg/kg, inj. glycopyrrolate 0.004 mg/kg and inj. midazolam 0.05mg/kg iv.Group D1received dexmedetomidine 1μg/kg iv diluted in 50 ml normal saline using syringe infusion pump over 10 minutes. Group D0.5 patients were given intravenous dexmedetomidine 0.5 μg/kg iv diluted in 50 ml normal saline, using syringe infusion pump over 10 minutes.

After completion of dexmedetomidine infusion, patients were pre-oxygenated with 100% oxygen for 3 minutes. They were induced with 2.5% thiopentone sodium 5-7 mg/kgiv till the loss of eyelash reflex. Inj. succinylcholine 2mg/kg iv was given. Patients were intubated with appropriate sized cuffed endotracheal tubes. After checking the equal bilateral air entry endotracheal tube was fixed. Anaesthesia was maintained with oxygen and nitrous oxide (50%-50%), isoflurane and loading dose of inj. Atracuriumiv 0.5mg/kg and after that intermittent dose of 0.1mg/kg.

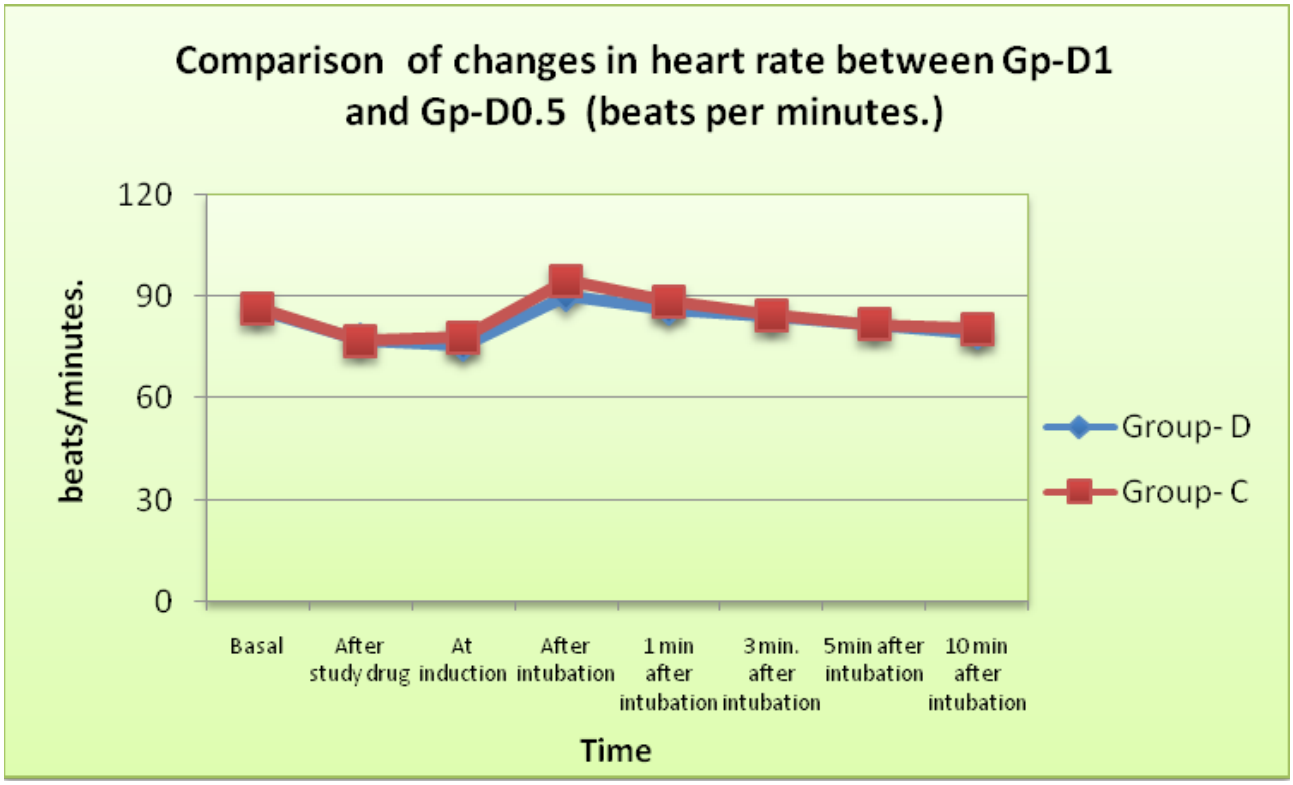
HR, SBP, DBP were recorded before giving the drug,just before induction of anaesthesia, during intubation and at 1 minutes, 3minutes, 5 minutes,10 minutes after intubation. After the surgical procedure was over, neuromuscular blockade was reversed with inj. neostigmine 0.05 mg/kg and inj. glycopyrrolate 0.008mg/kg iv. Once all recovery criteria were fulfilled trachea was extubated. Patients were monitored in the post-operative recovery room for 24 hours. They were observed for analgesia and side effects like nausea,

vomiting, sedation, respiratory depression, bradycardia and hypotension.

Observation and Results

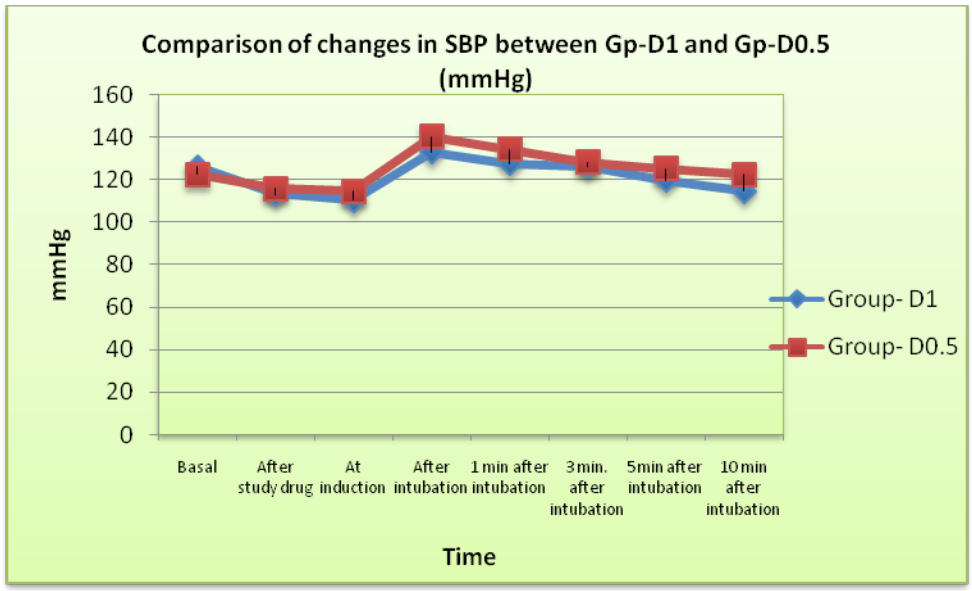
Statistical data were analyzed by using student's unpaired t test.

For age, weight, genderand ASA grade there was no statistically significant difference in patients of Group D1 and Group D0.5 (p >0.05)



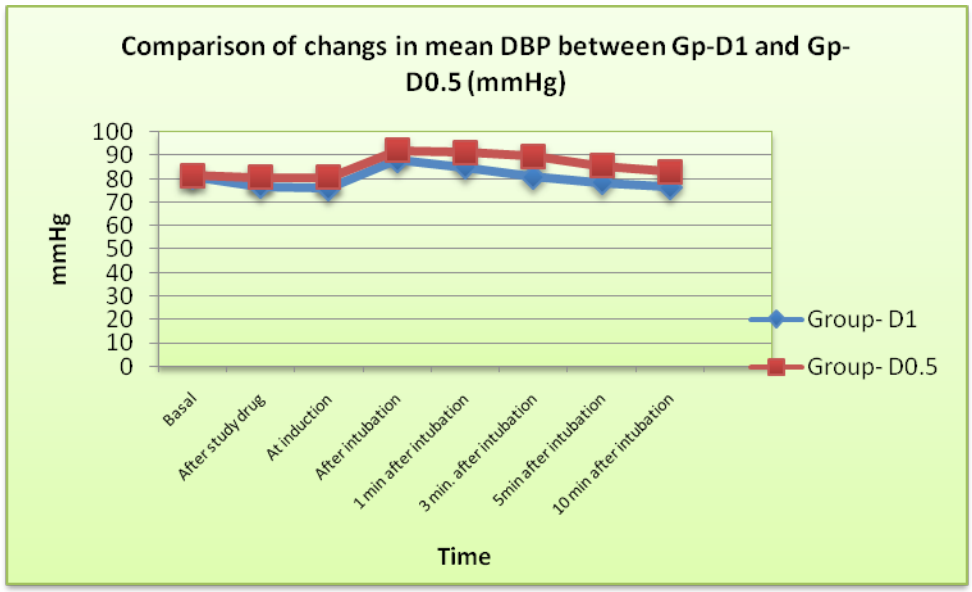
Graph 1: Showing Heart Rate at different time intervals in Group D1 and Group D0.5

Mean HR in Group D1 was 86.27±1.447 per minutes and in Group D0.5 it was 86.23±2.027 per minutes at baseline level, which was comparable (p>0.05). There was fall in HR in both Group D1 and Group D0.5. HR further decreased at induction in both groups. Group D1 had 12.36% fall whereas Group D0.5 had 9.74% fall from baseline value. In Group D1 at intubation mean HR was 90.33±1.431 per minutes showing 4.70% rise,whereas in Group D0.5 it was 94.50±0.5023 per minutes with 9.59% rise. The difference in mean HR between two groups was statistically significant (p < 0.05). Both groups showed maximum rise in HR during intubation but immediately after intubation it started decreasing. Rate of fall was almost equal in both groups till 5 minutes post intubation. At 10 minutes after intubation HR reached to 79.10±1.892 per minutes in Group D1 with 9.06% fall and in Group D0.5 80.40±1.650 per minutes with 6.76% fall. Difference in mean HR between two groups at any time interval was statistically insignificant (p> 0.05) except during intubation which was statistically significantly higher in group D1 than in group D0.5 (p < 0.05).



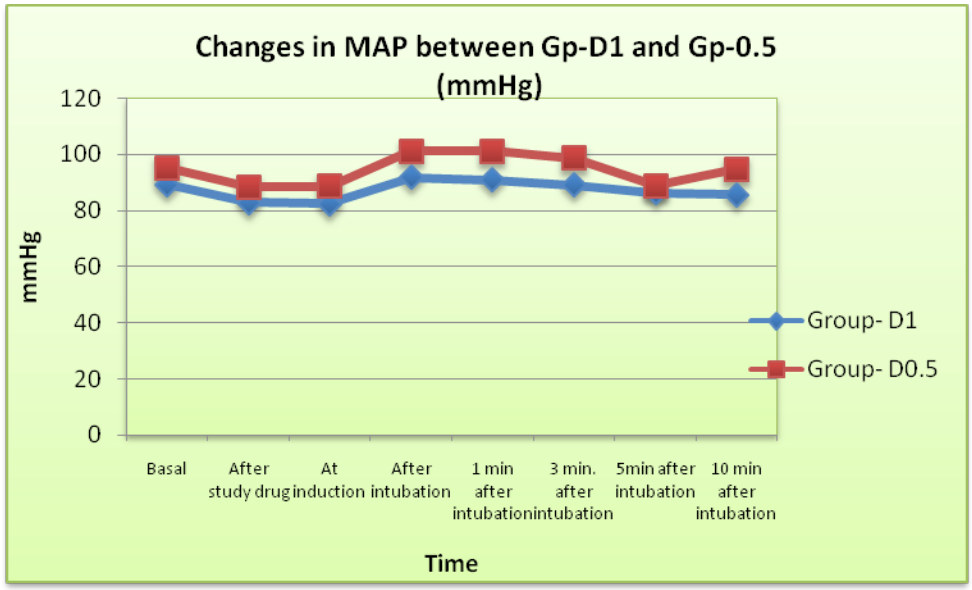
Graph 2: Mean SBP at different time interval in Group D1 and Group D0.5

At baseline mean SBP in Group D1 was 126.1± 1.281 mmHg and in Group D0.5 was 122.5±1.189 mmHg.There was fall in SBP from baseline value in both groups after study drug infusion and at induction but Group D1 had significant fall (12.7%) compared to Group D0.5 (6.19%) ($p<0.05$). During intubationin Group D1, it increased from 126.1± 1.281mmHg to 133.1± 0.913mmHg (5.55%) whereas in Group D0.5 it rose to 140.3±1.283mmHg from 122.5±1.189mmHg (14.53%). Difference in mean SBP between two groups was statistically highly significant ($p< 0.001$).SBP in both groups started falling immediately after intubation from its maximum level. In Group D1, at 5 minutes after intubation, SBP was below baseline value, whereas in Group D0.5 SBP remained higher than baseline value at 5 minutesand took 10 minutes to reach baseline value. Difference in SBP from 1 minute after intubation till 10 minutes post-intubation was statistically significant ($p< 0.05$).



Graph 3: Mean DBP at different time interval in Group D1 and Group D0.5

At baseline mean DBP in Group D1 was 80.87±1.679 mmHg and in Group D0.5 it was 81.53±1.049 mmHg. DBP in both groups decreased after study drug infusion and after induction. The difference was statistically significant ($p < 0.05$).There was maximum rise in DBP in both groups at intubation. In Group D1 it increased to 88.07±1.270 mmHg from its baseline value showing 8.9% rise whereas in Group D0.5 it went to 92.00±0.996 mmHg from basal DBP with 12.84% rise. This difference was statistically significant ($p < 0.05$). Immediately after intubation DBP in both groups started decreasing but the rate of fall in DBP in Group D1 was faster compared to Group D0.5 and at 3 minutes after intubation DBP in Group D1 was nearly same as baseline value. At 10 minutes post intubation DBP was 76.53±1.028 mmHg that was 5.36% lower than basal DBP, whereas in Group D0.5, DBP even at 10 minutes after intubation was higher than baseline DBP (83.13±1.137 mmHg).Difference in mean DBP between two groups at any time interval except at baseline was statistically significant ($p<0.05$).



Graph 4: Mean Arterial Pressure At Different Time Intervals Between Group D1 and Group D0.5

Mean arterial pressure at baseline in Group D1 was 95.94±0.848 mmHg and in Group D0.5 it was 95.52±0.925 mmHg which was comparable ($p>0.05$). There was fall in MAP in both groups after study drug infusion and after induction, which was statistically highly significant ($p<0.001$). In Group D1 MAP increased to 103.08±1.004 mmHg during intubation with rise of 7.00% from baseline value whereas in Group D0.5, the rise was 13.17%. The difference was statistically highly significant ($p < 0.0001$). In both groups after intubation MAP decreased from its maximum rise and in Group D1 at 3 minutespostintubation it reached to baseline level and at 10 minutes post intubation 7 % lower than baseline level but in Group D0.5, it remained above basal value even 10 minutes after intubation.Difference in MAP between two groups remained highly significant from time of intubation, till 10 minutes after intubation ($p< 0.0001$).Average dose of thiopentone used in Group D1 was 412.5±26.0 mg and in Group D0.5 it was 448.3±30.9 mg. The difference between two groups was statistically insignificant ($p>0.05$)

No side effects or complication were seen in any patients of either group.

Discussion

Laryngoscopy and endotracheal intubation are perceived as intense events during general anaesthesia. They give rise to a transient, but marked sympathoadrenal response. Therefore controlling this perioperative stress response is pivotal goal of anaesthesia practice [13]. Various pharmacological & non pharmacological method were evaluated either in premedication or during induction to attenuate these adverse stress responses but no single anaesthetic technique is effective in completely abolishing these responses. The drugs used were either partially effective or were with adverse effects.[14]

Dexmedetomidine offers a unique pharmacological profile with sedation, sympatholysis, analgesia, cardiovascular stability by altering the stress induced sympathoadrenal responses to intubation during surgery & during emergence from anaesthesia.Presynaptic activation of α2 adrenoceptor in the locus ceruleus in brain inhibits the release of nor epinephrine. In addition, the locus ceruleus is the site of origin for descending medullospinal noradrenergic pathway,known to be an important modulator of nociceptive neurotransmitter. Also, postsynaptic activation of α2 receptors in the CNS results in decrease in sympathetic activity leading to fall in heart rate.

We compared the efficacy of dexmedetomidine at a dose of 1μg/kg (Group D1) with 0.5μg/kg (Group D0.5) when administered over 10 minutes before induction of anesthesia in 30 patients of each group. The groups were comparable with respect to demographic factors like age, weight,gender. Baseline heart rate was comparable in both the groups. After 10 minutes of dexmedetomidine infusion, there was fall in heart rate in both the groups, Group D1>group D0.5. The fall continued even after induction in both the groups except during intubation. During intubation there was rise in heart rate in both the groups, Group D0.5 >Group D1. The difference being statistically significant ($p<0.05$).

Sagiroglu A et al[15] in 2009 and Sunil et al[16] in 2012 compared the effect of dexmedetomidine at two different doses i.e 0.5μg/kg vs 1μg/kg on attenuation of haemodynamic responses to laryngoscopy & intubation. They concluded that 1μg/kg is better in obtunding hemodynamic response to laryngoscopy. **Thus** comparable with our study.

Our study results were also in accordance with the results of **Yildizet al.[17] and Bijoy kumar panda et al**[18]. They too observed that dexmedetomidine when administered at a dose of 1μg/kg was able to suppress the heart rate response to laryngoscopy. SBP, DBP and MAP were better managed in the group receiving dexmedetomidine 1μg/kg.

Sagiroglu A**et al[15]** similarly observed that SBP, DBP and MAP values were lower post induction in both the groups of dexmedetomidine 1μg/kg and 0.5μg/kg, similar to the findings of our study.SBP and DBP were significantly lower at 60 seconds post intubation in dexmedetomidine 1μg/kg as compared to dexmedetomidine 0.5μg/kg.

Yildiz et al[17] also observed maximum increase in blood pressure immediately after intubation.During intubation increase in SBP in placebo group was 40% compared to 8% in the group of dexmedetomidine 1μg/kg. Also increase in DBP was 25% in placebo group as compared to 11% in the group of dexmedetomidine 1μg/kg.

The initial fall in blood pressure can be explained by peripheral α-2B adrenoceptors stimulation of vascular smooth muscles. The initial response is followed by further decrease in blood pressure. Both these effects are caused by inhibition of central sympathetic outflow overriding the direct stimulant effects.

Average requirement of thiopentone was noted during our study. The requirement was 8% less in the group receiving dexmedetomidine 1μg/kg when compared to dexmedetomidine 0.5μg/kg. The difference being not statistically significant($p>0.05$).Similar to our findings, **Bijoykumar panda et al**[18] has also observed statistically insignificant reduced requirement of thiopentone in dexmedetomidine group(1μg/kg) as compared to clonidine group (1μg/kg).

There was no side effect noted in our study.

Similarly, **Shirsedu et al**[19] have also not found any instability of vitals either with clonidine or dexmedetomidine . They compared clonidine at 2μg/kg with dexmedetomidine at 1μg/kg given over 10 minutes, in patients undergoing general surgery.

Bijoykumar panda et al[18] found bradycardia in only 2 patients out of 60 patients, using dexmedetomidine 1μg/kg when given over 10 minutes.

Belleville et al[20] found that dexmedetomidine which was given in 2 minutes at doses of 1-2μg/kg cause irregular ventilation and apnea episodes. Irregular breathing seen with high dose of 1-2 μg/kg probably related to deep sedation and anatomical features of the patient.

Such side effects were not seen in our study thus making dexmedetomidine at dose of 1μg/kg and 0.5μg/kg when given over 10 minutes to be free of side effects.

Conclusion

Dexmedetomidine at dose of 1μg/kg significantly attenuated the sympathetic response of laryngoscopy and intubation and also at dose of 0.5μg/kg reduced the

pressor response, but its effect was lesser than that of dexmedetomidine 1µg/kg. Thus this study showed that dexmedetomidine 1µg/kg is superior to dexmedetomidine 0.5µg/kg in the attenuation of hemodynamic response to laryngoscopy and endotracheal intubation with no side effects. Dexmedetomidine is helpful in decreasing the requirement of anaesthetic agent for induction.

Conflict of Interest: Nil

Source of Funding: Self

Ethical Clearance: Taken from Sumandeep Vidyapeeth Institutional Ethics Committee (SVIEC).

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