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COMPARATIVE STUDY OF IV DEXMEDITOMIDINE VS IV LABETALOL FOR ATTENUATION OF HAEMODYNAMIC STRESS RESPONSE TO LARYNGOSCOPY & ENDOTRACHEAL INTUBATION IN NEUROSURGERGICAL CASES

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Abstract

This study was done to compare the efficacy of bolus injection of Dexmedetomidine and Labetalol in attenuating the sympathoadrenal response accompanying laryngoscopy and endotracheal intubation in 60 patients divided into 2 groups.Group D - Dexmedetomidine 1µ/Kg Group L - Labetalol 0.5mg/Kg.60 patients of ASA I and II aged 18– 60 years undergoing neurosurgery under general anesthesia were chosen for the study. After obtaining ethical committee approval, the study population was chosen.Informed written consent obtained from the patient. Heart rate, systolic and diastolic blood pressure and

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oxygen saturation were recorded as base line value.All patients were monitored with ECG, pulse oximetry continuously and NIBP at 5 min intervals. Patients received study drug 5 min prior to induction according to the group. SBP, DBP, MAP, HR and SpO2 were monitored 1 minute after infusion of study drug, 1 minute after induction and 1,3,5,10 and 15 minutes after intubation.Results were tabulated and analysed. There was a reduction in the heart rate and mean arterial pressure response to intubation in both Dexmedetomidine and Labetalol groups , but when both the groups were compared there was statistically significant reduction of heart rate and arterial pressure response to intubation in Dexmedetomidine group. ($P < 0.05$).

Key words: Dexmedetomidine, Labetalol, endotracheal, intubation

Introduction

Tachycardia, hypertension and dysrhythmias all occur during laryngoscopy and intubations. The consequent rise in rate/pressure product may result in a myocardial oxygen demand which exceeds the oxygen supply resulting in myocardial ischaemia[1]. This response is sympathetically mediated and can be attenuated by various drugs that block sympathetic activity and other drugs like calcium channel blocking drugs, lignocaine and magnesium. Studies have documented myocardial ischaemic changes due to reflex sympatho adrenal response immediately following laryngoscopy and intubation with a mean increase in systemic pressure of 40mmHg even in normotensive patients. An increase in heart rate is more likely to produce signs of myocardial ischeamia than hypertension on the ECG. Indeed, in anaesthetized patient, the incidence of myocardial ischaemia on the ECG sharply increases in patients who experience a heart rate greater than 110bpm (ischaemic threshold).[2] A frequent recommendation is to maintain heart rate and blood pressure within 20% of normal awake value for that patient.

Many attempts have been made to attenuate the pressor response to laryngoscopy and intubation such as deep plane of anaesthesia, Topical anaesthesia, Use of ganglionic blockers , Use of intravenous local anaesthetics, Sodium nitroprusside infusion, Magnesium sulphate, Fentanyl, Use of sympathetic blockers(beta-blockers, alpha2

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agonists), Calcium channelblockers. It has become evident that, α_2 adrenoceptor agonists may also be a useful class of drugs in conjunction with anaesthesia[3]. They simultaneously potentiate the effects of general anaesthetic agents, reduce their dose requirements and attenuate sympathoadrenal responses to noxious stimuliencountered during anaesthesia and surgery, thus providing improved haemodynamic, metabolic and hormonal stability [4]. Dexmedetomidine is a highly selective and potent $\alpha_2$adrenoceptor agonist. It is a pureα_2 adrenoceptor agonist (α_1:α_2 ratio-1:1600) than clonidine which has only less selective agonist activity. (α_1:α_2 ratio-1:200)

Labetalol is combined $\alpha_1$andβ antagonist. In patients with no history of hypertension or significant cardiac disease, labetalol 0.3 or 0.6mg/kg i.v. is suited to blunting tachycardia and hypertension to laryngoscopy andintubation. In this study which was carried out in the Department of Anaesthesiology and Critical care at SCB medical college & hospital, we compared intravenous labetalol and dexmedetomidine in attenuating haemodynamic stress response (increase in heart rate and an increase in the mean arterial pressure) to laryngoscopy and intubation, and find out which drug is better.

MATERIAL & METHODS

The present study is a randomized prospective study conducted in the Department of Anaesthesia, SCB Medical College & Hospital after obtaining institutional ethical committee clearance and written informed consent from the patients.

Place of the study:

The study was conducted at SCB Medical College & Hospital, Cuttack.

Study setting:

Neurosurgery operation theatre and Postoperative Care Unit of SCB Medical College & Hospital.

Study Duration:

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The study was conducted for the period of two years, September 2020- August 2022.

Study Population:

Patients of ASA physical status I and II, scheduled for elective cases of neurosurgery in SCB Medical College & Hospital, Cuttack.

Sample size:

It was found that an approximate sample size of 30 would sufficient foreach of the 2 study groups getting probability of both type 1 error and type 2 error < 0.05 %.

Statistical analysis

The information collected were tabulated in Microsoft Excel version 16 and were analysed in SPSS version 23. All the quantitative variables were expressed in mean and standard deviation and all the categorical variables were expressed in proportion and percentages. For comparisons of two quantitative variables, unpaired t test was used and for comparison categorical variables, chi-square test was used. With 95% confidence interval, the p valueof <0.05 was considered statistically significant.

Inclusion Criteria

1. American Society of Anaesthesiologists (ASA) physical status I and IIpatients undergoing elective neuro surgery under general anaesthesia
2. Age group 18 to 60 years
3. Male & Female

Exclusion Criteria

1. Patient refusal
2. History of allergy to study drugs

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3. Patient on beta blockers, alpha blockers
4. Anticipated airway difficulty
5. Bronchial asthma
6. Ischemic heart disease, cerebrovascular disease, renal disease
7. ASA Grade III & IV
8. Diabetes mellitus, hypertension

Sample design:

Subjects were given computer generated random numbers and wereallocated into 2 groups (n = 30)

- **Group D (n=30):** They received dexmeditomidine 1mcg/kg slow ivover a period of 10 mins,5mins before induction of anaesthesia
- **Group L (n=30):** They received 0.5mg/kg labetalol 5mins beforeinduction of anaesthesia

Randomization:

Randomization is random allocation of the subjects to various arms (Intervention groups) of the trial. Randomization for this study will be done by random number distribution method. Here a serial number from 1 to 60will be distributed randomly by between two groups with the help of random number generator app. The patients selected for the study will be sequentially numbered and as per the previously assigned number to a particular group, thepatient will be given medication assigned to that group.

Blinding of the study

It was a double blinded study. The patients were unaware of the study groups. Study drugs were prepared in 10ml syringe by a single anaesthesiologist and were handed over to the anaesthesiologist performing the procedure. The anaesthesiologist performing procedure was blinded to the study drugs and groups and recorded the intraoperative and post-operative data.

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METHOD

A total number of 60 patients posted for elective laparoscopic cholecystectomy under general anaesthesia were divided into two groups of 30 each. For this study all the patients will be assessed preoperatively with history, clinical examination and required investigation. Informed written consent were obtained from patient. Patients satisfying inclusion criteria wererandomly allocated into two groups. Heart rate, systolic and diastolic blood pressure, mean arterial pressure and oxygen saturation were recorded as baseline value. After 1hr patients were taken to the operation theatre for surgical procedure. In operation theatre IV line were secured and iv infusion will be started. Routine standard monitors such as pulse oximetry, ECG, NIBP were monitored. All these patients were pre medicated with IV ondansetron 0.08mg/kg and Glycopyrolate 0.004mg/kg before induction of general anaesthesia. The study drugs were pre mixed to a volume of 10ml and to be presented as coded syringe by an anaesthesiologist who was not involved in the study.

The patients were randomly divided into 2 groups 30 each.

The patients in group D received Dexmedetomidine 1.0mcg/kg as slow iv infusion over a period of 10 minutes, 5min before induction of anaesthesia.

Group L received 0.5mg/kg labetalol , 5 min before induction of anaesthesia.

The patients were preoxygenated with 100% oxygen for 3 minutes afterstudy drug infusion. Then anaesthesia induction were done with iv propofol 2mg/kg followed by iv succinylcholine 2mg/kg. Ventilation of lung using 100% oxygen were done manually .Endotracheal intubation were done using direct laryngoscope with macintosh curved blade after 90 seconds of administration of succinylcholine and patient's airway were secured with appropriate size cuffed endotracheal tube within 15 seconds. Anaesthesia were maintained with 66% N2O in 33% O2 with intermittent isoflurane in 6L gas flow. Muscle relaxation during intra operative period were done by bolus iv dose of 0.08mg/kg followed by intermittent dose of 0.02mg/kg vecuronium

.After surgery anaesthesia were reversed with neostigmine 0.05 mg/kg and glycopyrolate 0.008mg/kg iv. After extubation patient will be monitored for complications like pain,

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hypotension, hypertension, respiratory depression, nausea, vomiting, bradycardia, tachycardia.

Results

Post intervention heart rate was measured between two intervention groups at various time interval and the comparison was illustrated. A significant difference was observed between two groups at after induction, at 1 min, 3 min, 5 min, 10 min and 15 minutes. ($p<0.05$)(fig 1)

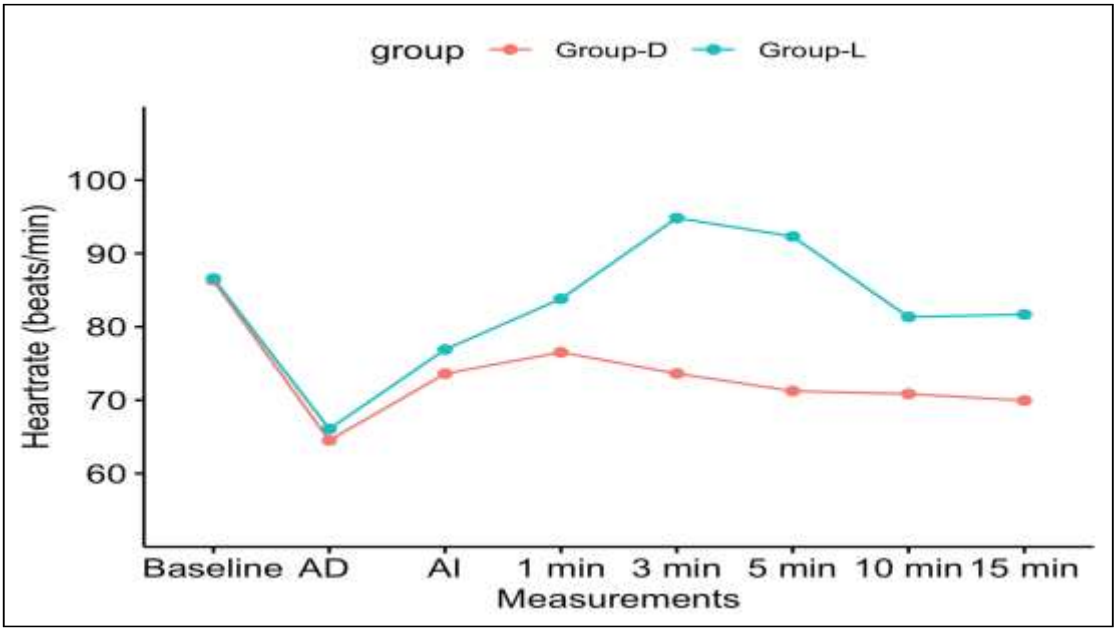

Figure 1: Comparison of heart rate at various time interval between twogroup

Post intervention systolic blood pressure (SBP) was measured between two intervention groups at various time interval and the comparison was illustrated . A significant difference was observed between twogroups at at 1 min, 3 min, 5 min, 10 min and 15 minutes. ($p<0.05$)(fig 2)

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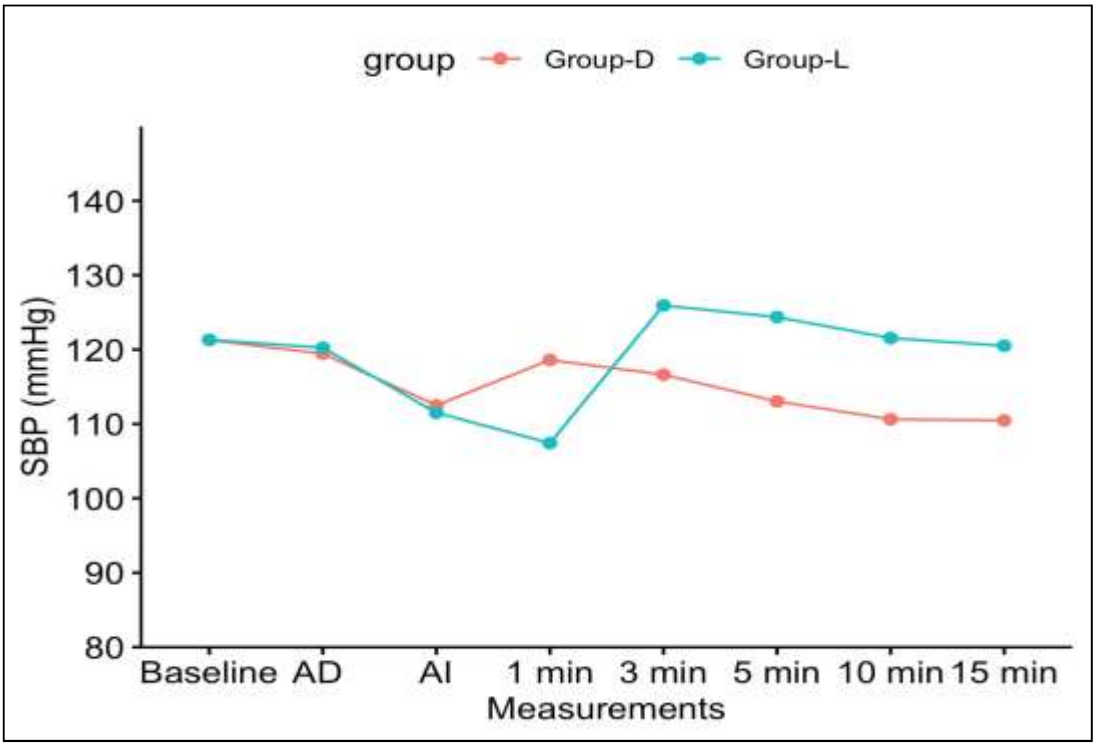
Figure 2: Comparison of mean systolic blood pressure (SBP)



Post intervention mean arterial pressure (spo2) was measured between two intervention groups at various time interval and the comparison was illustrated in table-11 . There was no significant difference in SPO2 levels at various time interval between two groups.($p>0.05$)(fig 3)

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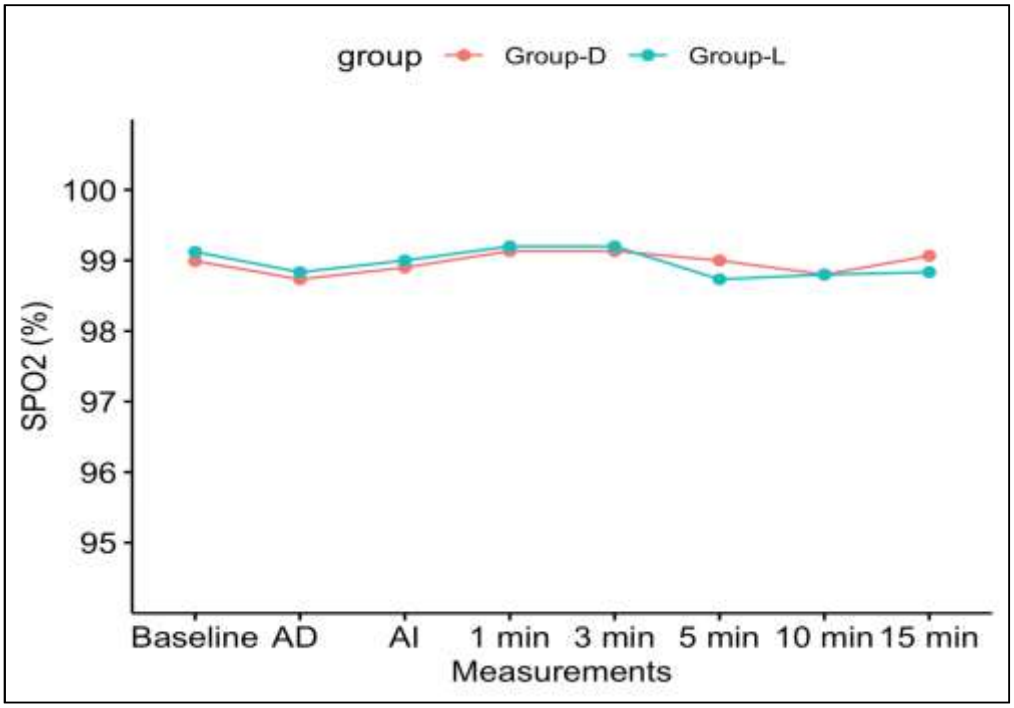
Figure 3: Comparison of SPO2 of the study participants at various time



Discussion

In view of the frequent occurrence of hypertension and tachycardia during laryngoscopy even in normotensive individuals, it is perhaps rather surprising that complications have not been met very often. One reason forthis may be the transient nature of hypertension which usually lasts less than 10 minutes. It is possible however that some of the complications that occur during intubation or even later in the course of anaesthesia may be precipitated by an episode of hypertension and tachycardia, following endotracheal intubation. ELLIOF (1980) observed left ventricular wall dysfunction following endotracheal intubation This reflex sympathetic response may be diminished or modified locally, centrally and peripherally and attempts have been made to accomplishthis using all these approaches with varying success.In an attempt to blunt these potentially adverse haemodynamic responses, different techniques and agents were used by many with varying success.Sympathetic system activation plays main role for the occurrence of transient but

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significant tachycardia and hypertension during intubation. Sinceany drug that antagonizes the Sympathetic system activation will attenuate these effects.STEINHAN and GASKIN (1963) used intravenous lignocaine, JAMESet al (1981) used lignocaine intratracheal spray, MASSON AND ECKANGOFF (1971) and DENLINGER J.K. (1974) and STOELTING(1978) used a combination of viscous lignocaine and topical intratracheal lignocaine and in 1979 LEAKO used a bolus ofSodiumnitroprusside.[5]A.J.COLE and C.JORDAN (1980) and RICHARD et al (1981) studied the effect of β blockers using metaprolol and propranolol respectively. LUNN (1979) BENNET and STANLEY (1980) and DONAL E.MARTIN (1982) [6-9]studied the effect of fentanyl in attenuating the intubation stress response.SARVESH P. SINGH, ABDUL QUADIR[10] compared the efficacy of esmolol and labetalol, in low doses, for attenuation of sympathomimeticresponse to laryngoscopy and intubationInhalation agents when used required deep levels and may delay recovery after short surgeries and can cause cardio vascular depressionUse of Vasodilators like Sodium nitroprusside results in reflex tachycardia, lability in blood pressure, cerebral vasodilation with elevation of intracranial pressure and pulmonary venous admixture Opioid analgesics will attenuate the hemodynamic at the expense of respiratory depression.The $\alpha 2$ receptors are involved in regulating the autonomic and cardiovascular systems. $\alpha 2$ receptors are located on blood vessels, where they mediate vasoconstriction, and on sympathetic terminals where they inhibit norepinephrine release. $\alpha 2$ receptors are also located within the central nervous system and their activation leads to sedation, a reduction of toniclevels of sympathetic outflow and an augmentation of cardiac-vagal activity. This can result in a decrease in heart rate and αcardiac output.The use of $\alpha 2$ agonists in the perioperative period has been associated with reduced anesthetic requirements and attenuated heart rate and blood pressure responses to stressful events. In addition,$\alpha 2$ receptors within the spinal cord modulate pain pathways, thereby providing some degree of analgesia.Dexmedetomidine compared to Clonidine is a much more selective alpha2-adrenoceptor agonist, which might permit its application in relatively high doses for sedation and analgesia without the unwanted vascular effects from activation of alpha1-receptors. In addition, Dexmedetomidine is shorter- acting drug than clonidine and has a reversal drug for its

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sedative effect, Atipamezole. These properties render Dexmedetomidine suitable for sedation and analgesia during the whole perioperative period: as premedication, as an anesthetic adjunct for general and regional anesthesia, and as postoperative sedative and analgesic.It was observed that dexmedetomidine used in premedication supresses the sympathetic activation which is due to the endotracheal intubation. Dexmeditomidine reduces the opioid requirement resulted in faster recovery.It was observed that dexmedetomidine used in premedication supresses the sympathetic activation which is due to the endotracheal intubation. Güler et al. found that the increase in blood pressure and heart rate during the extubation is decreased and the quality of extubation is increased by dexmedetomidine.Labetalol is an adrenergic receptor blocking agent with mild alpha1- and predominant beta-adrenergic receptor blocking actions (alpha:betablockade ratio of 1:7 for iv and 1:3 for PO administration). The onset of action of i.v. labetalol is 5 min.

Labetalol has the following advantages over other beta blockers

1. Decrease SVR leading to decrease in BP is by alpha -1 blockade
2. Vasodilation also produced by partial B2 agonist activity
3. Reflex tachycardia due to peripheral vasodilation is attenuated by B blockade
4. Cardiac output remains unchanged
5. Presynaptic alpha-2 receptors are spared- hence release of Norepinephrine is intact, which inhibits further release of catecholamine (Neg feedback mech)

In our study we used Dexmedetomidine 1μ/kg and labetalol 0.5mg/kg . Both the drugs produce peak effect after 5 minutes. We had induced all the patients 5 minutes after reinjection.In some patients dexmedetomidine resulted in minimal increase in arterial pressure. This transient hypertension is due to $\alpha_1$mediated vasoconstriction. This transient hypertension is less than that seen with clonidine since dexmedetomidine has more selectivity over α_2 receptors.Giving the loading dose over 20 minutes also minimizes the transient hypertension.[12] Bradycardia after dexmedetomidine was reported in some studies

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with the bolus injection. Scheinin et al reported that the use of α_2 agonist leads to bradycardia.[13]In our study dexmedetomidine over 10 min with continuous monitoring of heart rate, none of the patients developed bradycardia that required atropine.Dexmedetomidine over 10 min with continuous monitoring of arterial oxygen saturation with pulse oximeter showed no desaturation (spo2-<95%) in any patient.Ebert et al. didn't observe any apnoea, airway obstruction and hypoxemia with bolus doses of dexmedetomidine in their study and they reported that depression of respiration may be seen due to deep sedation.[14]In another study in which the infusion of opioid andα_2 adrenergic agonists were compared, it was concluded that dexmedetomidine doesn't cause significant respiratory depression and it decreases the risk of apnoea . Hofer et al reported that dexmedetomidine seems to be a good choice in the critical patients in whom ventilation can be depressed with narcotics.Labetalol in a dose of 0.5mg/kg had reduced the heart rate. But the reduction was modest compared to dexmeditomidine the reduction in arterial pressure after labetalol was mild that was statistically insignificant.Heart rate increase and arterial pressure reduction after induction was minimal in all 2 groups and there was no statistically significant difference between the groups. (P>0.05) Dexmedetomidine injection effectively attenuated the hemodynamic response to intubation compared to labetalol. In our study all the patients remained in supine position postoperatively. No postural hypotension related side effects were reported.(side effect seen with labetalol when the patient allowed to sit within 3 hours after injection.)Dexmedetomidine reduced the requirement of inhalational agents and opioids intraoperatively compared to labetalol.Extubation and recovery were comparable in 2 groups. Bolus dose of both Dexmedetomidine and Labetalol were effective in attenuating the hemodynamic response to intubation, but the effect was complete and better with Dexmedetomidine.

Conclusion

We conclude that, Dexmedetomidine 1µ/Kg given slowly over 10 minutes intravenously 5 minutes prior to induction, attenuates the cardiovascular responses to laryngoscopy and intubation in a better manner than Labetalol 0.5mg/Kg. There was no

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adverse effects of two drugs inspecified doses.

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