ORIGINAL RESEARCH

To compare the efficacy of intravenous butorphanol and clonidine as a premedicant for attenuation of hemodynamic pressor response to intubation

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ABSTRACT

Background and Objectives: Haemodynamic responses to direct laryngoscopy and tracheal intubation are noxious stimulus that should be attenuated by appropriate premedication, smooth induction, and rapid intubation. This study evaluates and compares the clinical efficacy of intravenous premedication with Butorphanol or Clonidine for attenuation of haemodynamic stress response to airway instrumentation, sedative, anxiolytic,analgesic effect and to assess the adverse events associated with these drugs.**Methods:** In thisdouble blind prospective randomized study, 60 patients of ASA I & II patients of either sex, aged 16-60 years, scheduled for various elective surgeries under general anaesthesia were included. They were randomly divided into 2 groups of 30 each, where group B received intravenous Butorphanol 40µg/kg and group C received intravenousClonidine of 3µg/kg 15minutes before surgery. After 3min of pre-oxygenation with 100% oxygen, patients were induced with Inj-Thiopentone 5-7mg/kg followed by Inj-suxamethonium 1.5mg/kg for intubation. After a min, intubation was done within 15 seconds and anaesthesia was maintained with 33%Oxygen+ 67%Nitrous Oxide + 0.8-1% Isoflurane. Further Inj. Vecuronium 0.05mg/kg was administered as and when required till the end of surgery. HR, SBP, DBPand MAPwere recorded at baseline,after premedication and 15 mins later to its administration, after induction & post intubation at 0, 3, 5, 10, 15min and for every 15min till the end of surgery. Sedation scoring, anxiety scoring and VAPS scoring were also compared. Statistical analysis was done using Student's t-test and Chi-Square test with p-value <0.05 was regarded as significant.**Results:** Attenuation of haemodynamic response to laryngoscopy and intubation was statistically significant in Clonidine group with P value of <0.05 compared to Butorphanol group. Sedation level was higher in Butorphanol group as compared to Clonidine group. Both the drugs were equally good in terms of anxiolytic and analgesic effect. None of the pre-medicated patients had any significant post-operative side-effects.**Conclusion:** Intravenous premedication with Clonidine 3µg/kg was superior to Butorphanol 40µg/kgin attenuation of haemodynamic stress response to laryngoscopy and intubation with good pre-operative sedation,anxiolysis and analgesia without any significant side-effects.

Key words: Clonidine, butorphanol, intubation, sedation, anxiolysis,analgesia

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INTRODUCTION

General anaesthesia is a medically induced state of unconsciousness with loss of protective reflexes, resulting from the administration of one or moregeneralanaestheticagents.Laryngoscopy and endotrachealintubationare the most essential skills for an anesthesiologist in maintaining the airway and also for safe conduct of general anaesthesia. Reidand Bruce in 1940, first described the haemodynamic responses to laryngoscopy and intubation[1].However, both laryngoscopy and intubation are noxious stimuli and are associated withhypertension, tachycardia and arrhythmias[1].

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The exact mechanism of haemodynamic changes to laryngoscopy and intubation has not been clarified till date. The principle mechanism in hypertension and tachycardia is the sympathetic response[2,3]which may be due to increase in catecholamine activity[4].

These haemodynamic changes are usually transitory, variable and unpredictable. In patients with hypertension, coronary artery disease or cerebrovascular diseases and intracranial aneurysms these type of haemodynamic changes may be hazardous[4-7].These transient changes can result in developmentof pulmonary edema[8], myocardial insufficiency[8],dysrrhythmias[9] and cerebrovascular accident[9].The magnitude of haemodynamic changes observed may be dependent on various factors such as the duration of laryngoscopy and intubation,premedicants used, the anaesthetic agent usedand depth of anaesthesia.

Since 1950 various attempts were made by investigators to reduce haemodynamic response to laryngoscopy and endotracheal intubation. They found that Intravenous anaesthetic induction agents did not adequately or predictably suppress the haemodynamicresponses producedby endotracheal intubation[10].So prior to initiating laryngoscopy, additional pharmacological measures like use of volatile anaesthetics[11]. topical and intravenous lidocaine[12], opioids[13], vasodilators-Sodium nitroprusside[14],Nitroglycerine[15], Calcium channel blockers[16]and β-blockers[17-19]have been tried by various authors. Many of these drugs are associated with various side effects and none of these drugs have been found to be effective to attenuate the sympathetic response to intubation.

Besides minimizing the cardiovascular response, inductionofpatients at risk must also satisfy the following requirements: It must be applicable regardless of patient group, prevent impairment of cerebral blood flow and avoid awareness of the patient; it should neither be time consuming nor affect the duration or modality of the anaesthetic technique and also should not have any effect on the recovery characteristics of the patient.

Aminoethanol phenanthrene compound like butorphanolhave been used for attenuating the sympathetic response [20] to intubation, other compounds like alpha-2 adrenergic agonists are also used among theseα-2 agonists clonidine is commonly used[21]. Potential advantages of using these drugs during anaesthesia are improved intraoperative haemodynamic stability, attenuated sympathoadrenal responses, reduced intraoperative requirements of anaesthetic agents and reduced postoperative pain[22-26].

There are no studies comparing Intravenous butorphanol and Intravenous clonidine, which have shown to reduce haemodynamic response to intubation and cause sedation. So here we are comparing 40µg/kg of IV butorphanoland3µg/kg of IV Clonidine as premedicants on attenuation ofhaemodynamic responses to laryngoscopy and endotracheal intubation.

So, in the present study an attempt has been made to study the clinical efficacy of Intravenousbutorphanol(40µg/kg) and Intravenous clonidine(3µg/kg) as premedicantsfor suppression of haemodynamic response to laryngoscopy and intubation with pre and postoperative sedation, anxiolysis,postoperative analgesia and adverse effects if any.

OBJECTIVES

To evaluate and compare the beneficial of intravenous Butorphanol and Clonidine as premedication in attenuating the hemodynamic responses associated with laryngoscopy and intubation in patients for general anaesthesia with respect to following features

- Anxiety.
- Sedation.
- Analgesia.
- Blood pressure (systolic,diastolic blood pressure and mean arterial pressure).
- Heart rate.
- Undesirable effects.

SOURCE OF DATA

The study will be conducted on patients aged between 18-60 years, ASA I and ASA II posted for various elective procedures under General Anaesthesia, Department of Anesthesiology, Sri Adichunchanagiri Hospital and Research Centre, B.G. Nagara.Tal-Nagamangala, Dist-Mandya.

STUDY DESIGN-PROSPECTIVE RANDOMIZED DOUBLE-BLIND STUDY

The study will be conducted on 60 patients of both sexes in the age group of 18-60 years of ASA I and ASA II undergoing various elective surgeries under general anaesthesia with the institutional ethical committee approval, written and informed consent will be taken from each patient. The patient will be allocated into 2 groups. Group B (butorphanol) and Group C (clonidine) (30 each). Group B will be premedicated with intravenous butorphanol 40µg/kg 15 mins prior to induction. Group C will be premedicated with intravenous clonidine 3µg/kg 15 mins prior to induction.

DURATION OF STUDY:18 months. (November 2015- April 2017).

INCLUSION CRITERIA

- Adult of age group 16 to 60 years of both sexes with ASA I and ASA II.
- Patients undergoing elective surgeries under general anaesthesia with minimum duration of 1-1.5 hours.

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EXCLUSION CRITERIA

- Patients aged below 16 years and above 60 years.
- Patients with known allergy to clonidine or butorphanol
- Patients who are reluctant to participate.
- Patients who had general anaesthesia with in 2 weeks.
- Patients withanticipated difficult intubation and obesity.
- Patient's having coexisting neurological, cardiovascular, renal, and alcoholic abuse or chronic pain syndrome.
- Patients who is on antihypertensive and antidepressant drugs.
- Patients with severe endocrinal diseases like uncontrolled hyperthyroidism, hypothyroidism anddiabetes mellitus.

PROCEDURE

Pre-anaesthetic evaluation was done. A routine pre-anaesthetic examination was conducted assessing;

- General condition of the patient.
- Airway assessment by Mallampatti grading and rule of 1-2-3.
- Measuring body weight of the patient.
- A detailed examination of the cardiovascular system, Respiratory system, Gastrointestinal System and Central Nervous System was done.

The following investigations were done in all the patients

- Complete blood count.
- HIV, HbsAg.
- Urine examination for albumin, sugar and microscopy (If indicated).
- Standard 12-lead electrocardiogram(If indicated).
- X-ray chest(If indicated).
- Blood sugar-Random Blood Sugar.
- Blood urea, Serum creatinine.

SAMPLE SIZE: The study was conducted on 60 patients. The population was divided into 2 groups of 30 patients in each group.

- Group B (n=30) patients were given 40µg/kg of Butorphanol intravenously 15 mins prior to induction.
- Group C (n=30), patients were given 3µg/kg of clonidine intravenously 15 mins prior to induction.
- Randomisation of the group was done using shuffled sealed opaque envelope method.
- The double-blind design of the study was assured by the fact that an anaesthesiologist who is not involved in the study, other person was opening the sealed envelopes and were administeringthe drugs to the patients 15 mins before the induction. The patient and the anaesthesiologist conducting the study, doing the observations were thus kept unaware of the content of the medications.
- All patients included in the study were premedicated with tablet ranitidine 150 mg and tablet alprazolam 0.5 mg orally at bed time the previous night before surgery. They were kept nil orally 10 pm onwards on the previous night.
- Before administration of intravenous premedication and after giving premedication's followed by 15 mins later, each patients anxiety score, baseline heart rate, Systolic and Diastolic blood pressure and SPO_2 were recorded. Sedation were analysed before and after giving premedication and later in the postoperative period using Ramsay sedation score and pain were analysed using visual analogue pain scale in the postoperative period.Patient were explained about VAPS scale day before surgery and how to express it depending upon the pain. A uniform anaesthetic technique was used in all groups.

RESULTS& ANALYSIS

A total of 60 patients, 30 in each group, were evaluated. Both the groups were comparable with respect to demographic and operational factors. Duration of time between intravenous premedication to anaesthetic induction (15 mins), duration of laryngoscopy(<15 seconds, only first attempt of intubation was considered) were also comparable.

Table 1: Distribution of patients according to type of surgery

Surgery	Group		Total
	1	2	
Appendicectomy	1	0	1
	3.3%	.0%	1.7%
Both bone fracture forearm for orif and nailing	2	3	5
	6.7%	10.0%	8.3%
Clavice fracture for ORIF & Plating	1	5	6
	3.3%	16.7%	10.0%
Epigastric hernia for Hernioplasty	1	0	1
	3.3%	.0%	1.7%
FESS	3	7	10
	10.0%	23.3%	16.7%
Fibroadenoma for excision	7	6	13
	23.3%	20.0%	21.7%
Near total thyroidectomy	0	1	1
	.0%	3.3%	1.7%

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Septoplasty	7	3	10
	23.3%	10.0%	16.7%
Thyroglossal cyst for excision	1	0	1
	3.3%	.0%	1.7%
Tonsillectomy	1	0	1
	3.3%	.0%	1.7%
Tympanoplasty	6	5	11
	20.0%	16.7%	18.3%
Total	30	30	60
	100.0%	100.0%	100.0%

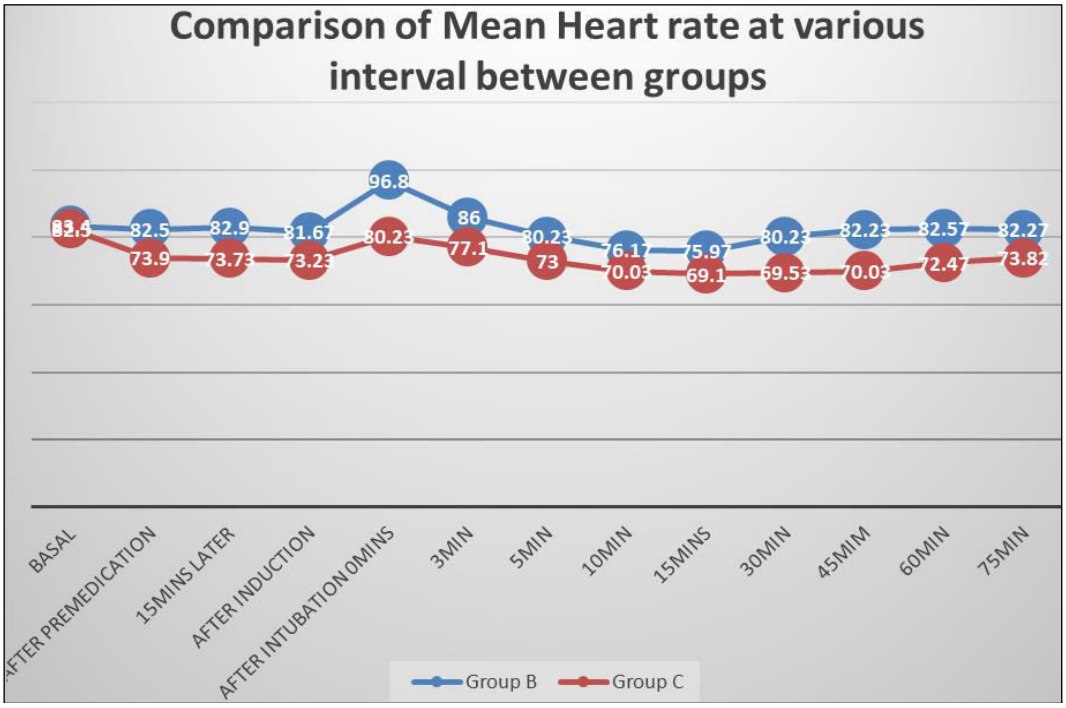

Fig 1: Graph showing comparison of Mean Heart rate at various interval between groups

There is no statistical significant difference among the two groups with regard to the basal mean heart rate. After premedication administration and 15mins later to its administration decrease in HR in group C(fall in HR around 8-10bpm from basal line)is significant compared to group B(fall in HR remained same or decreased by 1-2 bpm). There is increase in HR at zero minute after intubation in both the groups compared to the pre-intubation HR. The increase in HR in group B was about 15-16bpm and only about 8-9bpm in group C, which statistically highly significant with P value of <0.001. By 5^{th}-10^{th}mins after laryngoscopy and intubation, the HR in both the groups have reached the pre-intubation level. But in Group B HR was statistically on the higher side than Group C till end of surgery.

Table 2: Comparison of Mean MAP at various interval between groups

Map	Group	Mean	Standard deviation	P value
Basal	B	93.90	11.177	.460NS
	C	95.53	4.299	
After premedication	B	92.92	9.039	<0.001HS
	C	85.42	3.283	
15 mins later	B	89.78	8.602	0.001S
	C	83.51	3.737	
After induction	B	79.34	7.9	0.005S
	C	74.74	3.507	
After intubation 0min	B	95.70	8.323	<0.001HS
	C	82.63	3.131	
3 min	B	91.34	8.241	<0.001HS
	C	81.26	3.205	
5 min	B	89.16	7.556	<0.001HS

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	C	79.86	2.518	
10 min	B	87.18	6.233	<0.001HS
	C	79.36	2.756	
15 min	B	87.89	5.656	<0.001HS
	C	82.19	2.216	
30min	B	90.22	4.6	<0.001HS
	C	86.02	3.072	
45min	B	88.58	4.92	0.001S
	C	84.61	3.520	
60min	B	88.8	5.5	0.009S
	C	84.12	4.184	
75min	B	83.62	22.24	0.964NS
	C	83.45	2.968	

NS-Not Significant (p>0.05), (p<0.05)-Significant (S),(p<0.001)-Highly significant (HS)

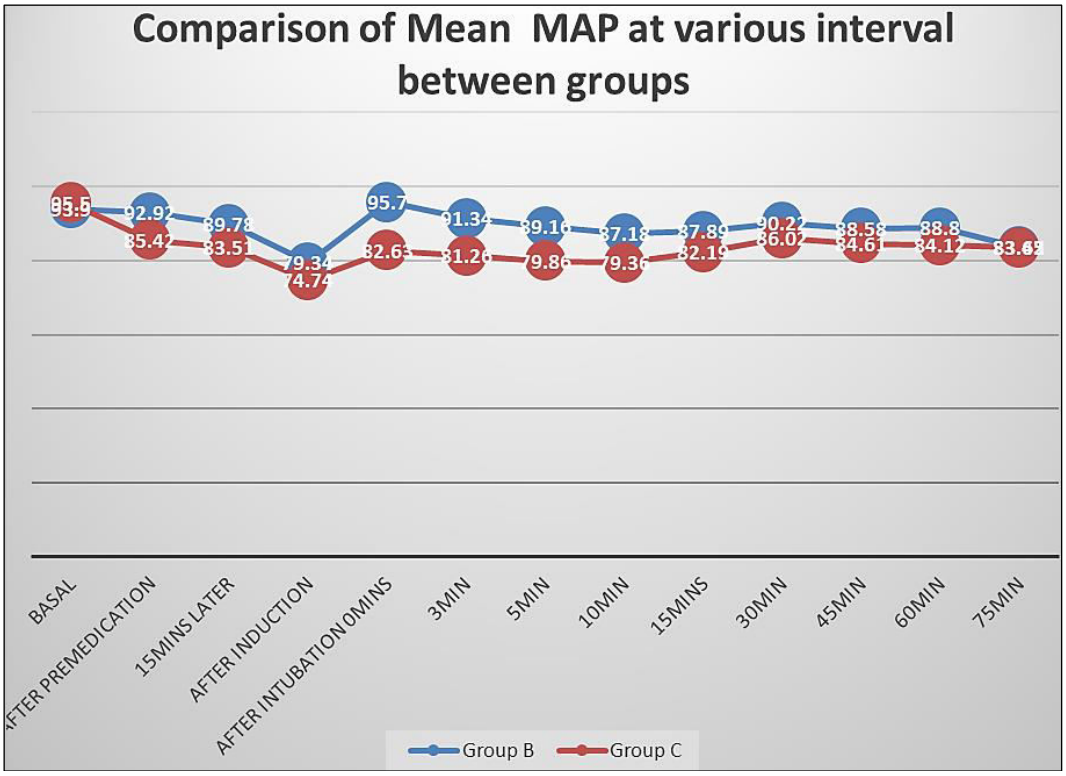

Fig 2: Graph showing comparison of Mean MAP at various interval between groups

There is no statistical significant difference among the two groups with regard to the basal mean arterial pressure. There is statistical significant difference among the two groups 15mins later to premedication administration,afterinduction and at 45th min and 60th min. The results are highly significant after premedication and after intubation till 30th min.The maximum increase in MAP in group C was by 7-8 mmHg as compared to group B which was 15-16 mmHg from pre-intubation values,observed at zero min of intubation. Also, the pre-intubation values of MAP was attained earlier in group C.

SUMMARY

A study entitled "to compare the efficacy of intravenous butorphanol and clonidine as premedicant for attenuation of hemodynamic pressor response to intubation" was undertaken in Department of anaesthesiology, Adichunchanagiri institute of medical sciences, B.G. Nagara, during the period November 2015 to April 2017.

Sixty patients aged between 16 years to 60 years of ASA Class 1 & 2, posted for elective procedures under general anaesthesia were included in study. The patients with severe hypertension, diabetes mellitus, endocrine disorders, difficult airway, obese and obstetric patients or with any other systemic diseases were excluded from this study. The study population was randomly divided into two groups, GroupB (n=30) who received Butorphanol 40µg/kg and Group C (n=30) who received Clonidine 3µg/kg slowly 15mins prior to induction intravenously.

Patients were induced with Inj-Thiopentone 5-7mg/kg followed by Inj-suxamethonium 1.5mg/kg for intubation.After a min, the laryngoscopy and intubation was done within 15 seconds and

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anaesthesia was maintained with 33%Oxygen+ 67%Nitrous Oxide + 0.8-1% Isoflurane. Further Inj. Vecuronium 0.05mg/kg was administered as and when required till the end of surgery. HR, SBP, DBP and MBP were recorded at baseline, after premedication administration and 15 mins later to its administration, after induction & post intubation at 0, 3, 5, 10, 15min and for every 15min till the end of surgery. Sedation scoring,anxiety scoring and VAPS scoring were also compared.

There was a significant increase in HR in the Butorphanol group as compared to Clonidine group at zero minute after laryngoscopy and intubation.

In the Clonidine Group there was a statistically significant fall in SBP, DBP & MAP as compared to Butorphanol group at various time intervals.

There was statistically significant difference in the sedation score between both the groups, in which Butorphanol group patients had better sedation.

Both the drugs had good anxiolysis and analgesics with minimum side effects, which was not statistically significant.

LIMITATIONS OF OUR STUDY

1. We did not study the amount of thiopentone and vecuronium required in each group.
2. We did not use neuromuscular monitoring to determine the peri-operative requirement of Vecuronium.
3. We did not measure the plasma catecholamine levels which is an objective means of measuring hemodynamic stress response.
4. We did not study the VAPS score beyond 120mins.
5. We did not study the awakening and recovery time in each group.

CONCLUSION

Both intravenous butorphanol40µg/kg and clonidine3µg/kg, administered 15 min prior to induction and laryngoscopy are effective premedicant drugs with safe and multimodal drug profile as they cause sedation, anxiolysis, analgesia with successful attenuation of haemodynamic response to laryngoscopy and intubation. Clonidine is better in attenuating pressor response, butorphanol has better sedation and both are good in terms of anxiolysis and analgesia.

In conclusion, the haemodynamic stability provided by clonidine3µg/kgwas more efficacious and superior than butorphanol40µg/kg with goodsedation,anxiolysis and analgesia without any significant side-effects.

REFERENCES

1. Reid L.C., andBrace D.E: Irritation of respiratory tract and its reflex effect on heart-Surgery Gynecology Obstetrics. 1940;70:157-162.
2. Morin AM, Gelbner G, Schwarz U, Kahl M, Adams HA, Hulf H, et al. Factors influencing pre-operative stress responses in coronary artery bypass graft patients. BMC Anaesthesiology 2004;4(7).
3. Kayhan Z, Aldemir D, Metler H, Ogus E. Which is responsible for the haemodynamic response due to the laryngoscopy and endotracheal intubation? Catecholamines, vasopressin or angiotensin? European Journal of Anaesthesiology 2005;22:780-5.
4. Kovac AL. Controlling the haemodynamic response to laryngoscopy and endotracheal intubation. Journal of Clinical Anaesthesia 1996;8:63-79.
5. Prys-Roberts C, Green LT, Meloche R, Foex P. Studies of anaesthesia in relation to hypertension II. Haemodynamic consequences of induction and endotracheal intubation. Br J Anaesth 1971;43:531-47.
6. Dalton B, Guiney T. Myocardial ischemia from tachycardia and hypertension in coronary heart disease – Patients undergoing anaesthesia. Boston: Ann Mtg American Society of Anaesthesiologists; 1972. pp. 201-2.
7. Cedric Preys Roberts. Anaesthesia and hypertension. Br J Anaesth 1984; 56:711-24.
8. Fox EJ, Sklar GS, Hill CH, Villanue Var, King BD. Complications related to the pressor response to endotracheal intubation. Anaesthesiology. 1977; 47:524-5.
9. Ronald D Miller. Miller's Anesthesia. 7th ed. Saunders:Churchill Livingstone;2010
10. Stoelting RK, Stephan F Dierdorf. Anaesthesia and co-existing disease. 4th ed. Philadelphia. Lippincott Williams & Wilkins; 2002.
11. King BD: Harris L, Greifenstein F, Elder J, Dripps RD. Reflex circulatory responses to direct laryngoscopy and intubation under general anaesthesia. Anaesthesiology. 1951;12:556-66.
12. Donlinger, JK Ellison N, Ominsky AJ. Effects of intrathecal lidocaine on circulatory responses to tracheal intubation. Anaesthesiology. 1974;41:409-12.
13. Dahlgreen N, Messeter K. Treatment of the stress response to laryngoscopy and intubation with Fentanyl. Anaesthesia. 1981;36:1022.
14. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with Sodium Nitroprusside. Anaesthesia Analgesia. 1979; 58:116-9.
15. Fossoulaki A, Kaniasis P. Intranasal administration of Nitroglycerine attenuates the pressor response to laryngoscopy and intubation of the trachea. Br J Anaesth. 1983;55:49-52.
16. Puri GD, Batra YK. Effect of Nifedepine on cardiovascular response to laryngoscopy and intubation. Br J Anaesth. 1988;60:579-81.
17. Prys-Roberts C, Foex P, Biro GP. Studies of anaesthesia in relation to hypertension versus adrenergic β receptor blockade. Br J Anaesth 1973; 45:671-80.

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18. McCammon RL, Hilgenberg JC, Stoelting RK. Effect of Propranolol on circulatory responses to induction of diazepam- nitrous oxide anesthesia and to endotracheal intubation. Anaesthesia Analgesia 1981;60(8):579-83.
19. Chung KS, Sinatra RS, Chung JH. The effect of an intermediate dose of Labetalol on heartrate and blood pressure responses to laryngoscopy and intubation. Journal of Clinical Anaesthesia 1992;4(1):11-15.
20. Laffery D A, KAY N H. Premedication with butorphanol. Br J Anaesth. 1984;56:363-7. http//dx.doi.org/10.1093/bja/56.4.363
21. Kulka PJ, Tryba M, Zenz M. Dose response effects of intravenous clonidine on stress response during induction of anaesthesia in coronary artery bypass graft patients. AnaesthAnalg 1995;80:263-8.

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