Original Article

Comparative evaluation of esmolol and dexmedetomidine for attenuation of sympathomimetic response to laryngoscopy and intubation in neurosurgical patients

Vinit Kumar Srivastava, Sanjay Agrawal[1], Sujeet Kumar Singh Gautam[2], Mukadder Ahmed[3], Sunil Sharma[4], Raj Kumar[4]

Department of Anaesthesiology, Apollo Hospitals, Bilaspur, Chhattisgarh, [1]Department of Anaesthesiology, Himalayan Institute of Medical Sciences, Dehradun, [2]Department of Anaesthesiology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, [3]Departments of Anaesthesiology, [4]Neurosurgery, Apollo Hospitals, Bilaspur, Chhattisgarh, India

Abstract

Background and Aims: The present study compared the efficacy of esmolol and dexmedetomidine for attenuation of the sympathomimetic response to laryngoscopy and intubation in elective neurosurgical patients.

Material and Methods: A total of 90 patients aged 20-60 years, American Society of Anesthesiologists physical status I or II, either sex, scheduled for elective neurosurgical procedures were included in this study. Patients were randomly allocated to three equal groups of 30 each comprising of Control group (group C) 20 ml 0.9% saline intravenous (IV), group dexmedetomidine (group D) 1 μg/kg diluted with 0.9% saline to 20 ml IV and group esmolol (group E) 1.5 mg/kg diluted with 0.9% saline to 20 ml IV. All the drugs were infused over a period of 10 min and after 2 min induction of anesthesia done.Heart rate (HR), systolic blood pressure, diastolic blood pressure, and mean arterial pressure were recorded baseline, after study drug administration, after induction and 1, 2, 3, 5, 10, and 15 min after orotracheal intubation.

Results: In group D, there was no statistically significant increase in HR and blood pressure after intubation at any time intervals, whereas in group E, there was a statistical significant increase in blood pressure after intubation at 1, 2, and 3 min only and HR up to 5 min.

Conclusion: Dexmedetomidine 1 μg/kg is more effective than esmolol for attenuating the hemodynamic response to laryngoscopy and intubation in elective neurosurgical patients.

Key words: Dexmedetomidine, endotracheal intubation, esmolol, hemodynamic response

Introduction

Laryngoscopy and tracheal intubation causes hypertension and tachycardia in anaesthetized patients, which is undesirable, especially in patients with cardiovascular or neurosurgical diseases undergoing anesthesia.[1] Topical or intravenous (IV) lidocaine, opioids, inhaled anesthetics, vasodilators, calcium channel blockers or adrenergic blockers[2-6] have been used successfully in decreasing the laryngoscopic response. Hypertension during intubation in neurosurgical patients may be associated with an increase in intracranial pressure (ICP), intracranial bleed, adverse hemodynamic effects which may increase the morbidity in such patients and prolonged hospital stay.[7] Thus, prevention and control of these hemodynamic responses are of utmost importance to preserve the cerebral homeostasis.

Esmolol is an ultra-short acting, β_1-cardioselective adrenergic receptor blocker with a distribution half-life of 2 min and an elimination half-life of 9 min. Esmolol appears quite suitable for use during a short-lived stress such as tracheal intubation. Dexmedetomidine is a highly selective α2-adrenoreceptor agonist. It produces dose-dependent sedation, anxiolysis, and analgesia due to its effect on central adrenergic outflow.

With the hypothesis that hemodynamic effects produced by esmolol or dexmedetomidine are similar in patients undergoing neurosurgical procedures, we planned this study to compare the efficacy of esmolol and dexmedetomidine for attenuation

Address for correspondence: Dr. Vinit K Srivastava, Department of Anaesthesiology, Apollo Hospitals, Bilaspur - 495 006, Chhattisgarh, India.
E-mail: drvinit75@gmail.com

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/0970-9185.155146

of the sympathomimetic response during laryngoscopy and intubation in patients undergoing elective neurosurgical procedures under general anesthesia.

Material and Methods

This prospective randomized, study was conducted after approval from institutional Ethics Committee and written informed consent from the patients.

A total of 90 patients aged 20-60 years, American Society of Anesthesiologists physical status I or II, either sex, scheduled for elective neurosurgical procedures [Table 1] were included in this study. Patients with predicted difficult intubation, laryngoscopy and intubation time >20 s, more than one attempt of intubation, on preoperative β-blocker therapy, systemic illness such as hypertension, diabetes, hepatic failure, and renal failure were excluded from the study. The patients were randomly allocated to three equal groups of 30 with the help of a computer generated table of random numbers to receive following drugs:

- Group dexmedetomidine (group D) received 1 μg/kg of dexmedetomidine diluted to a total volume of 20 ml with normal saline (0.9%) over a period of 10 min.
- Group esmolol (group E) 1.5 μg/kg diluted to a total volume of 20 ml with normal saline (0.9%) over a period of 10 min.
- Group control (group C) received 20 ml 0.9% saline over a period of 10 min.

All the drugs were given 12 min prior to induction of anesthesia and were prepared by an independent anesthesiologist not involved in the study, in identical syringes and infused with infusion pump (Perfusor Compact S, B Braun, Melsungan, Germany).

All the patients were premedicated with tablet lorazepam 2 mg and tablet ranitidine 150 mg night before and 2 h prior to surgery. In the operation room after establishing IV access, monitors such as noninvasive blood pressure, pulse oximetry, electrocardiography were applied. Invasive monitoring such as radial artery cannulation and right internal jugular vein cannulation was performed under local anesthesia. The test drugs were administered as per group allotted and followed by induction of anesthesia with injection midazolam 0.03 mg/kg, fentanyl 2 μg/kg, and thiopental sodium 5 mg/kg. Neuromuscular blockade was achieved by injection vecuronium bromide 0.15 mg/kg and intubation completed with appropriate sized cuffed endotracheal tube by a single operator in all the cases. Anesthesia was maintained with 66% nitrous oxide in oxygen (O_2:N_2O: 33:66), sevoflurane, intermittent boluses of injection vecuronium and fentanyl. Ventilation was adjusted to maintain an end-tidal carbon dioxide ($ETCO_2$) value between 30 and 35 mmHg. The $ETCO_2$ values were kept between 30 and 35 in cases with probability of increased ICP secondary to their pathology. Injection mannitol was administered wherever required in dose of 1-1.5 g/kg after 15 min of intubation. After completion of surgery, neuromuscular blockade was reversed with injection neostigmine 40 μg/kg and injection glycopyrolate 10 μg/kg and patients were extubated.

Table 1: Type of surgery

Type of surgery	Group C	Group D	Group E
Aneurysm surgery	1	2	3
AVM surgery	2	2	3
Brain tumor surgery	8	9	7
Pituitary surgery	2	2	3
MVD	1	2	2
AVM embolization procedure	2	1	0
CSF leak repair	1	0	1
Bone flap removal	2	0	1
Spine surgery	11	9	8
Arachnoid cyst decompression	0	1	1
ACM with syrinx	0	2	1

MVD = Micro-vascular decompression, CSF = Cerebrospinal fluid, AVM = Arteriovenous malformation, ACM = Arnold-Chiari malformation

Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded baseline, after study drug administration, after induction and 1, 2, 3, 5, 10, and 15 min after orotracheal intubation.

Any hypotension (SBP <20% baseline) was managed according to the status of central venous pressure (CVP). If CVP was low then a fluid bolus of normal saline 250-300 ml was administered. If hypotension did not respond to fluid administration, then injection mephentermine 3 mg IV was administered. If hypotension did not respond to two repeat doses of mephentermine then other means were sought as per the need. Any incidence of bradycardia (HR <50/min) was treated with injection atropine 300 μg IV.

Sample size was calculated based on the assumption that there would be a 30% reduction in the mean HR following therapy; this required 25 patients in each group for results to be significant (with $\alpha = 0.05$ and power of 80%). We enrolled 30 patients in each group to account for potential drop outs or protocol violations.

Statistical analysis was done using Excel Data Plugin (http://office.microsoft.com/en-in/excel-help/index-function-HP010090842.aspx). Data is represented as mean ± standard deviation. Demographic data were analyzed with Student's *t*-test. Intergroup comparison of HR, SBP, DBP,

and MAP was done with two-way analysis of variance and intra-group comparison of the above variables was done with paired *t*-test. $P < 0.05$ was considered significant.

Results

A total of 100 patients were assessed for eligibility, out of which 90 patients were included in the study after randomization and 85 patients (94.5%) completed the study. Ten patients were not included in this study on account of patient's refusal (six patients) and history of pregabalin consumption (four patients). Five patients were excluded from the study following initial randomization on account of intubation failure in the first attempt and bradycardia in group D (two patients) which require atropine; their data has been included for the comparison of demographic profile, however, they were not subjected to further statistical analysis. There was no significant difference amongst the groups with regard to demographic variables ($P > 0.05$) [Tables 1 and 2].

There was no difference in baseline hemodynamic parameters among the groups. After administration of the study drugs changes in HR were observed in groups D and E ($P < 0.001$) from the control group. Following induction, there was no difference in HR values between groups D and E ($P = 0.220$) but HR values were significantly decreased in group D and E ($P < 0.05$) compared with baseline value. Intubation caused an increase in the HR in all the groups, however, the increase in groups D and E were less than control group ($P < 0.001$) [Figure 1].

Systolic blood pressure and DBP values were statistically significantly lower in the group D after induction and all time observation of intubation, when compared with the groups C and E ($P < 0.001$). In group C, there was a statistically significant changes after intubation at 1-10 min period. In group D, there was no statistically significant increase after intubation at any time intervals, while in group E there was a statistical significant increase after intubation at 1, 2 and 3 min only [Figures 2 and 3].

Mean arterial pressure values were significantly lower statistically in the dexmedetomidine group comparative to group E and group C after all time observation of intubation ($P < 0.001$). There was no significant increase in MAP comparative to baseline at any time intervals of intubation in group D, while it was significant increase in group E at 1, 2, and 3 min after intubation only ($P < 0.05$) [Figure 4].

Bradycardia (HR <50/min) was observed in only two patients (6.66%) receiving dexmedetomidine, which responded to administration of IV atropine 300 µg IV. This fall in HR was not associated with decrease in blood pressure. No other side effect was observed in group C and group E.

Discussion

Our study demonstrated that the use of both esmolol and dexmedetomidine were effective in decreasing the hypertensive

Table 2: Demographic data

Variable	Group C	Group D	Group E
Mean age (years)	53.40±9.70	51.17±10.80	50.80±9.20
Weight (kg)	65.17±7.20	67.07±7.56	64.87±7.96
Male/female	23/7	24/6	20/10

Data are presented as either mean values ± SD or by absolute numbers, SD = Standard deviation

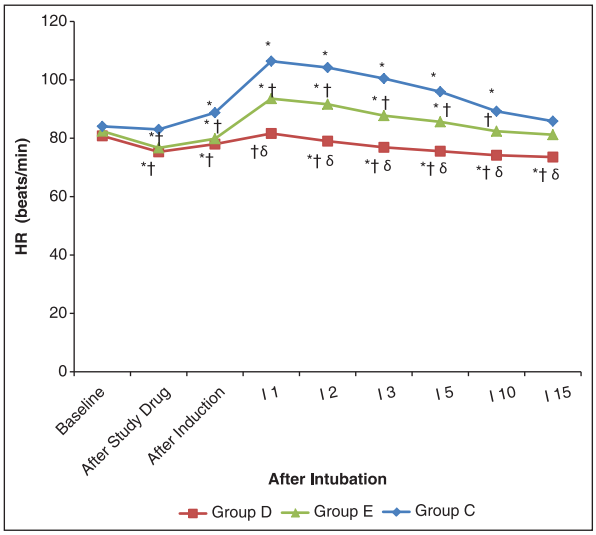

Figure 1: Changes in the heart rate observed in the three groups during the study period. *$P < 0.05$ within group (vs. baseline value), †$P < 0.001$ compared with group C, δ$P < 0.001$ group D versus group E. I_1-1 min, I_2-2 min, I_3-3 min, I_5-5 min, I_{10}-10 min, I_{15}-15 min after intubation

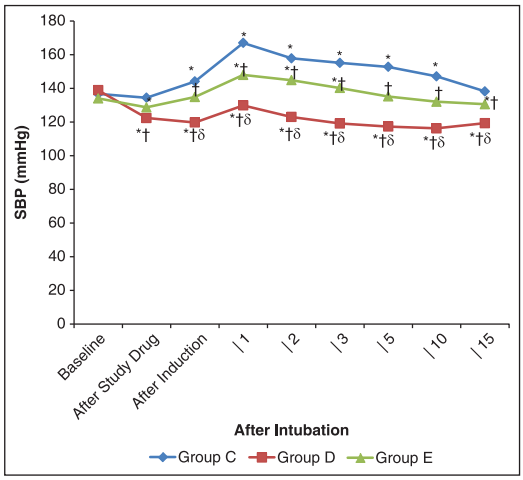

Figure 2: Changes in the systolic blood pressure observed in the three groups during the study period. *$P < 0.05$ within group (vs. baseline value), †$P < 0.001$ compared with group C, δ$P < 0.001$ group D versus group E. I_1-1 min, I_2-2 min, I_3-3 min, I_5-5 min, I_{10}-10 min, I_{15}-15 minute after intubation

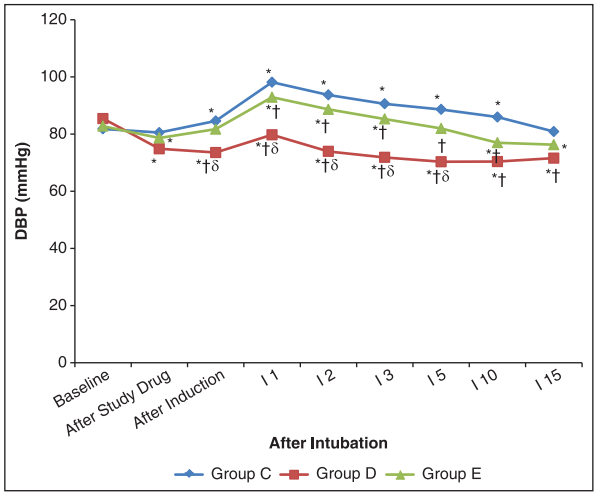

Figure 3: Changes in the diastolic blood pressure observed in the three groups during the study period. *$P < 0.05$ within group (vs. baseline value), †$P < 0.001$ compared with group C, δ$P < 0.001$ group D versus group E. I_1-1 min, I_2-2 min, I_3-3 min, I_5-5 min, I_{10}-10 min, I_{15}-15 min after intubation

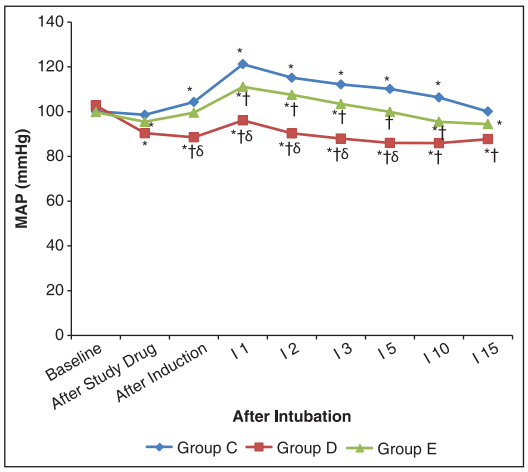

Figure 4: Changes in the mean arterial pressure observed in the three groups during the study period. *$P < 0.05$ within group (vs. baseline value), †$P < 0.001$ compared with group C, δ$P < 0.001$ group D versus group E. I_1-1 min, I_2-2 min, I_3-3 min, I_5-5 min, I_{10}-10 min, I_{15}-15 min after intubation

response to laryngoscopy and intubation though the use of dexmedetomidine was more effective for same.

Cardiovascular pressor response following laryngoscopy and tracheal intubation has been investigated extensively since King *et al*. were the first to report these changes.[8]

Blood pressure elevations during direct laryngoscopy for tracheal intubation becomes manifest after 15 s and reach peak if laryngoscopy is continued for 30-45 s. However, in situations when a rapid laryngoscopy is not assured or when a high risk patient is involved (coronary artery disease, intracranial hypertension, and intracranial aneurysm) it would seem prudent to attenuate pharmacologically blood pressure surges associated with laryngoscopy and intubation.

Different authors postulate that brief periods of hypertension during induction of anesthesia in neurosurgical patients may result in bleeding or increase in cerebral edema.[8] An ideal drug should have a rapid onset of action, be safe and easily administrable with a relatively short duration of action.

Esmolol is effective, in a dose-dependent manner, in the attenuation of the sympathomimetic response to laryngoscopy and intubation. Bensky *et al.*[9] suggested that small doses of esmolol (0.2 or 0.4 mg/kg) may block the sympathomimetic effects of laryngoscopy and intubation. Shrestha *et al.*[10] noted that higher doses of esmolol 1.5 mg/kg do not completely prevent the pressor and tachycardic response to laryngoscopy and intubation. Samaha *et al.*[11] has also found a similar effect in addition to ICP. In present study, pretreatment with esmolol 1.5 mg/kg attenuated, but did not totally obtund, the cardiovascular response to tracheal intubation after induction of anesthesia and these findings are similar with previous studies.[12] In addition, β-adrenoceptor blockade minimizes increase in HR and myocardial contractility (primary determinants of oxygen consumption) by attenuating the positive chronotropic and ionotropic effects of increased adrenergic activity.

Dexmedetomidine is α2-adrenergic agonist which produces its action by decreasing the catecholamine release from locus cereleus in the brain. It decreases the cerebral blood flow (CBF) while preserving the CBF-cerebral metabolic rate coupling, decrease ICP, attenuation of hypoxic injury to brain as well as decrease the vasodilation produced by use of inhalational agents.[13-15] Hence it is a potentially attractive adjunct for neuro-anesthesia to attenuate hemodynamic response. It has also been found to influence the catecholamine surge associated with endotracheal intubation.[16]

Various studies[17-19] have used dexmedetomidine in doses ranging from 0.5 to 10 μg/kg/h with not so much conclusive data but definitely associated with a significant incidence of bradycardia and hypotension in higher doses.[20] We used dexmedetomidine in a preoperative infusion dose of 1 μg/kg over 10 min and observed a consistent and reliable protection on HR and blood pressure with no severe side effects and the findings are very much similar to the observations of other studies. Our results are opposite to the study of Alagol *et al.*[21] where esmolol was found to control hemodynamics better than dexmedetomidine. However few studies have proven superiority of dexmedetomidine over esmolol.[22,23]

The hypotension and bradycardia caused by dexmedetomidine, theoretically, could limit its usage in bradycardic

patient due to increased ICP. In our study, bradycardia (HR <50/min) was observed in only two patients (6.66%) receiving dexmedetomidine, which responded to administration of IV 300 μg of atropine. This fall in HR was not associated with decrease in blood pressure.

Weaknesses of our study were the administration of a fixed dosage of study drug at a fixed interval before intubation; Moreover plasma catecholamines levels were not assessed by us to know the degree of suppression of neurohumoral pathway.

Conclusion

We emphasize the use of dexmedetomidine for attenuation of hypertensive response to laryngoscopy and intubation. It is more effective than esmolol in preventing such hemodynamic responses in neurosurgical patients.

References

1. Khan FA, Ullah H. Pharmacological agents for preventing morbidity associated with the haemodynamic response to tracheal intubation. Cochrane Database Syst Rev 2013;7:CD004087.
2. Gurulingappa, Aleem MA, Awati MN, Adarsh S. Attenuation of cardiovascular responses to direct laryngoscopy and intubation — A comparative study between iv bolus fentanyl, lignocaine and placebo (NS). J Clin Diagn Res 2012;6:1749-52.
3. Ko BJ, Oh JN, Lee JH, Choi SR, Lee SC, Chung CJ. Comparison of effects of fentanyl and remifentanil on hemodynamic response to endotracheal intubation and myoclonus in elderly patients with etomidate induction. Korean J Anesthesiol 2013;64:12-8.
4. Firoozbakhsh F, Mohammadi FH, Safari S, Khashayar P. The effect of intravenous nitroglycerine on blood pressure during intubation. Middle East J Anesthesiol 2008;19:859-67.
5. Moon YE, Lee SH, Lee J. The optimal dose of esmolol and nicardipine for maintaining cardiovascular stability during rapid-sequence induction. J Clin Anesth 2012;24:8-13.
6. Singh SP, Quadir A, Malhotra P. Comparison of esmolol and labetalol, in low doses, for attenuation of sympathomimetic response to laryngoscopy and intubation. Saudi J Anaesth 2010;4:163-8.
7. Basali A, Mascha EJ, Kalfas I, Schubert A. Relation between perioperative hypertension and intracranial hemorrhage after craniotomy. Anesthesiology 2000;93:48-54.
8. King BD, Harris LC Jr, Greifenstein FE, Elder JD Jr, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. Anesthesiology 1951;12:556-66.
9. Bensky KP, Donahue-Spencer L, Hertz GE, Anderson MT, James R. The dose-related effects of bolus esmolol on heart rate and blood pressure following laryngoscopy and intubation. AANA J 2000;68:437-42.
10. Shrestha GS, Marhatta MN, Amatya R. Use of gabapentin, esmolol or their combination to attenuate haemodynamic response to laryngoscopy and intubation. Kathmandu Univ Med J KUMJ 2011;9:238-43.
11. Samaha T, Ravussin P, Claquin C, Ecoffey C. Prevention of increase of blood pressure and intracranial pressure during endotracheal intubation in neurosurgery: Esmolol versus lidocaine. Ann Fr Anesth Reanim 1996;15:36-40.
12. Hussain AM, Sultan ST. Efficacy of fentanyl and esmolol in the prevention of haemodynamic response to laryngoscopy and endotracheal intubation. J Coll Physicians Surg Pak 2005;15:454-7.
13. Drummond JC, Dao AV, Roth DM, Cheng CR, Atwater BI, Minokadeh A, *et al.* Effect of dexmedetomidine on cerebral blood flow velocity, cerebral metabolic rate, and carbon dioxide response in normal humans. Anesthesiology 2008;108:225-32.
14. Ohata H, Iida H, Dohi S, Watanabe Y. Intravenous dexmedetomidine inhibits cerebrovascular dilation induced by isoflurane and sevoflurane in dogs. Anesth Analg 1999;89:370-7.
15. Jolkkonen J, Puurunen K, Koistinaho J, Kauppinen R, Haapalinna A, Nieminen L, *et al.* Neuroprotection by the alpha2-adrenoceptor agonist, dexmedetomidine, in rat focal cerebral ischemia. Eur J Pharmacol 1999;372:31-6.
16. Yildiz M, Tavlan A, Tuncer S, Reisli R, Yosunkaya A, Otelcioglu S. Effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation: Perioperative haemodynamics and anaesthetic requirements. Drugs R D 2006;7:43-52.
17. Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian J Anaesth 2011;55:352-7.
18. Menda F, Köner O, Sayin M, Türe H, Imer P, Aykaç B. Dexmedetomidine as an adjunct to anesthetic induction to attenuate hemodynamic response to endotracheal intubation in patients undergoing fast-track CABG. Ann Card Anaesth 2010;13:16-21.
19. Bajwa SJ, Kaur J, Singh A, Parmar S, Singh G, Kulshrestha A, *et al.* Attenuation of pressor response and dose sparing of opioids and anaesthetics with pre-operative dexmedetomidine. Indian J Anaesth 2012;56:123-8.
20. Ramsay MA, Saha D, Hebeler RF. Tracheal resection in the morbidly obese patient: The role of dexmedetomidine. J Clin Anesth 2006;18:452-4.
21. Alagol A, Arar C, Kaya G, Colak A, Turan N, Gunday I. Effects of dexmedetomidine and esmolol on hemodynamic response to tracheal intubation. Eur J Anaesthesiol 2005;22:134-5, A514.
22. Yavascaoglu B, Kaya FN, Baykara M, Bozkurt M, Korkmaz S. A comparison of esmolol and dexmedetomidine for attenuation of intraocular pressure and haemodynamic responses to laryngoscopy and tracheal intubation. Eur J Anaesthesiol 2008;25:517-9.
23. Uysal HY, Tezer E, Türkoglu M, Aslanargun P, Basar H. The effects of dexmedetomidine on hemodynamic responses to tracheal ntubation in hypertensive patients: A comparison with esmolol and sufentanyl. J Res Med Sci 2012;17:22-31.

How to cite this article: Srivastava VK, Agrawal S, Gautam SS, Ahmed M, Sharma S, Kumar R. Comparative evaluation of esmolol and dexmedetomidine for attenuation of sympathomimetic response to laryngoscopy and intubation in neurosurgical patients. J Anaesthesiol Clin Pharmacol 2015;31:186-90.
Source of Support: Nil, **Conflict of Interest:** None declared.