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Comparison of Esmolol and Dexamedetomidine Effects on Symphtomimmetic Response of Elective Surgical Patients After Laryngoscopy and Intubation.

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Abstract

Background: In anaesthetized patients laryngoscopy and tracheal intubation both are noxious stimuli's causes hypertension and tachycardia that are marked sympathetic response which are unwanted, particularly in patients with cardiovascular or neurosurgical diseases undergoing anesthesia. Dexmedetomidine has unique pharmacokinetics making it difficult to compare with other routinely used drugs such as esmolol and lignocaine. **Subjects and Methods:** Study population (n=90) of the current study was randomly divided into three groups. Group I (control), group II (dexmedetomidine) and group III (esmolol) respectively received 20 ml 0.9% saline, 1 g/kg of dexmedetomidine and 1.5 g/kg of esmolol. Base line, 5 minutes after the study drug administration, induction baseline and 1, 3, 5, 7, and 10 minutes after orotracheal intubation heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product were recorded. **Results:** There was no significant difference in mean heart rate ($p>0.05$) at baseline between all three groups. A significant increase in mean heart rate of group I (4.72 %) whereas a significant decrease mean heart rate of group II (20.71%) and group III (4.32%) were recorded. It is evident from figure 1 that there was a significant decrease in SBP, DBP and MAP group II and group III compare to group I after the infusion and just before intubation. Mean SBP values increased in all the three groups at 1 min after intubation. The values of SBP in Group II were significantly lower than that of Group I and Group III ($p < 0.01$). **Conclusion:** Findings of the current study suggest that both dexmedetomidine and esmolol were found effective in improving symphtomimmetic response to laryngoscopy and inintubation in normotensive patients. However, dexmedetomidine showed better attenuation of haemodynamic response compare to esmolol.

Keywords: Hemodynamic response, laryngoscopy, esmolol, dexamedetomidine.

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Introduction

In anaesthetized patients laryngoscopy and tracheal intubation both are noxious stimuli's causes hypertension and tachycardia that are marked sympathetic response which are unwanted, particularly in patients with cardiovascular or neurosurgical diseases undergoing anesthesia.[1] To attenuate the hemodynamic response to laryngoscopy and intubation topical or intravenous (IV) lidocaine, opioids, inhaled anesthetics, vasodilators, calcium channel blockers or adrenergic blockers have been used successfully.[2-6] The morbidity and prolonged hospital stay is increased in the patients with hypertension during intubation in neurosurgical patients may be associated with an increase in intracranial pressure, intracranial bleeding, adverse hemodynamic effects.[7,8] Thus to preserve the cerebral homeostasis; prevention and control of these hemodynamic responses are of utmost importance.[9] There have been published studies establishing the role of esmolol which is an ultra-short acting, β1-cardioselective adrenergic receptor blocker with a distribution half-life of 2 minutes and an elimination half-life of 9 minutes in attenuation of hemodynamic response to intubation.[10,11] However, the role of dexmedetomidine has still to be defined which is a highly selective α2-adrenoreceptor agonist.[12] It produces dose-dependent sedation, anxiolysis, and analgesia due to its effect on central adrenergic outflow.[7] Dexmedetomidine has unique pharmacokinetics making it difficult to compare with other routinely used drugs such as esmolol and lignocaine.[12-14] Therefore the present study was designed to evaluate the effects of dexmedetomidine and esmolol in attenuation the sympathomimetic response during laryngoscopy and intubation in normotensive patients undergoing elective surgery under general surgery.

Subjects and Methods

Study design

This study was a prospective, randomized, placebo-controlled, double-blinded trial. The protocol was approved by the Institutional Ethics Committee and written informed consent from the patients.

Sample

A total of 90 patients aged 20-60 years, either sex, scheduled for elective surgical procedures were included in this study.

Exclusion criteria

Patients with predicted difficult intubation, laryngoscopy and intubation time more than 20 seconds, more than one attempt of intubation, on preoperative -blocker therapy, systemic illness such as hypertension, diabetes, liver disorders and renal failure were excluded from the study.

Procedure

Study population of the current study was randomly divided into three groups of 30 patients with the help of a computer-generated table of random numbers. The patients were randomly allocated to three equal groups of 30 to receive the following drugs:

1. Group I (Control) received 20 ml 0.9% saline over a period of 10 min.
2. Group II (Dexmedetomidine) received 1 g/kg of dexmedetomidine diluted to a total volume of 20 ml with normal saline (0.9%) over a period of 10 min.
3. Group III (Esmolol) 1.5 g/kg of esmolol diluted to a total volume of 20 ml with normal saline (0.9%) over a period of 10 min.

All the drugs were given ten minutes before the induction of anesthesia and prepared by an independent anaesthesiologist not involved in the study, in identical syringes and infused with infusion pump patients were kept nil orally for 8 h prior to surgery. All patients were premedicated intravenously 10 minutes prior to induction with injection ondansetron 0.1 mg/kg, injection tramadol 2 mg/kg, and injection midazolam 0.05 mg/kg. In the operation room after establishing IV access, monitors were applied. Under local anaesthesia invasive monitoring such as radial artery cannulation and right internal jugular vein cannulation were performed as per group allocation. The test drugs were given and followed by induction of anesthesia with injection midazolam 0.03 mg/kg, fentanyl 2 g/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. Anaesthesia was maintained with 66% nitrous oxide in oxygen (O2:N2O: 33:66), sevoflurane, intermittent boluses of injection vecuronium and fentanyl.Ventilation was adjusted to maintain an end-tidal carbon dioxide value between 30 and 35 mmHg Injection mannitol was administered wherever required in the dose of 1-1.5 g/kg after 15 min of intubation. After completion of surgery, neuromuscular blockade was reversed with injection. neostigmine 40 g/kg and injection glycopyrrolate 10 g/kg than patients were extubated. Base line, 5 minutes after the study drug administration, induction baseline and 1, 3, 5, 7, and 10 minutes after orotracheal intubation heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product were recorded. Any hypotension was managed according to the status of central venous pressure. Any incidence of bradycardia was treated with injection atropine 300 g IV.

Statistical analysis

Study data were represented as a mean ±standard deviation. Demographic data were analyzed with ANOVA. While, Student t-test was used for intergroup comparison of HR, SBP, DBP. SPSS v 21 was used to for the entire statistical calculations. The p value <0.05 was considered as statistically significant.

Results

Results of the present study are expressed as mean ± sd. Demographic data of the present study showed there was an insignificant difference age (p>0.05), height (p>0.05), weight (p>0.05), BMI (p>0.05), sex ratio, ASA status and MPG class of the patients of all three groups. [Table 1]

Table 1: Distribution of patients according basic parameters.

Parameters	Group I (Control gr)	Group II (Dexmedetomidine gr)	Group III (Esmolol gr)	p value
Age (yrs)	36.8± 8.9	37.4± 7.6	36.3± 8.3	>0.05
Height (cm)	156.4± 7.5	155.8± 6.8	156.2± 6.4	>0.05
Weight (Kg)	56.6± 8.4	55.2± 9.1	55.8± 8.8	>0.05
BMI (Kg/m2)	23.1±4.6	22.7±3.8	22.9±3.5	>0.05
Sex Ratio	18:12	20:10	19:11	>0.05
ASA status	9:21	11:19	10:20	
MPG Class (I:II)	18:12	21:9	19:11	

There was no significant difference in mean heart rate (p>0.05) at baseline between all three groups. A significant increase in mean heart rate of group I (4.72 %) whereas a significant decrease mean heart rate of group II (20.71%) and group III (4.32%) were recorded. [Table 2]

Table 2: Comparison of heart rate in all three groups.

Parameters	Group I	Group II	Group III	p value
Baseline reading	90.62±11.4	89.98±10.8	91.14±12.6	>0.05
5 min after infusion	92.56±11.8	82.49±9.7	86.35±9.2	<0.05
Intubation baseline	91.9±10.8	74.36±8.9	84.6±8.4	<0.05
1 min intubation after	110.16±12.3	78.87±9.1	96.7±11.3	<0.01
3 min intubation after	112.62±11.4	80.46±8.2	94.2±10.7	<0.01
5 min intubation after	107.38±9.9	76.44±9.5	90.66±9.8	<0.01
7 min intubation after	103.6±10.5	73.42±8.8	88.12±8.5	<0.01
10 min intubation after	94.9±9.6	71.34±8.3	87.2±8.9	<0.01

[Table 3] showed that there was a significant decrease in heart rate of group II compares to group I after intubation. A significant increase in heart rate of group III in comparison of group II after intubation was recorded. Further, group III showed a significant decrease in heart

rate compare to group I patients after intubation. [Table 3]

Table 3 Comparison of heart rate with each other in all three groups.

Parameters	Group I vs Group II	Group II vs Group III	Group III vs Group I
Baseline reading	>0.05	>0.05	>0.05
5 min after infusion	<0.01	<0.05	>0.05
Intubation baseline	<0.01	<0.05	<0.05
1 min intubation after	<0.01	<0.01	<0.01
3 min intubation after	<0.01	<0.01	<0.01
5 min intubation after	<0.01	<0.01	<0.01
7 min intubation after	<0.01	<0.01	<0.01
10 min intubation after	<0.01	<0.01	<0.01

It is evident from [Figure 1] that there was a significant decrease in SBP group II and group III compare to group I after the infusion and just before intubation. Mean SBP values increased in all the three groups at 1 min after intubation. The values of SBP in Group II were significantly lower than that of Group I and Group III ($p < 0.01$).

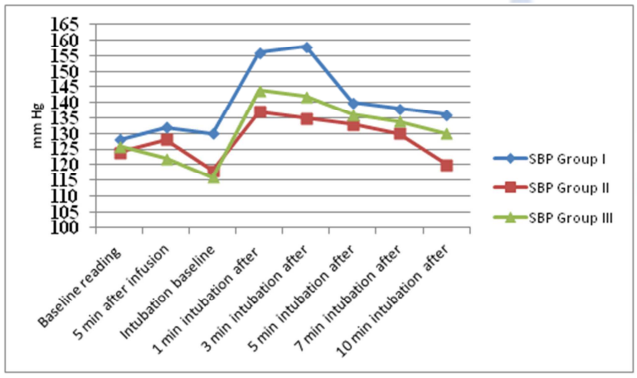

Figure 1: Comparison of mean systolic blood pressure in all three groups.

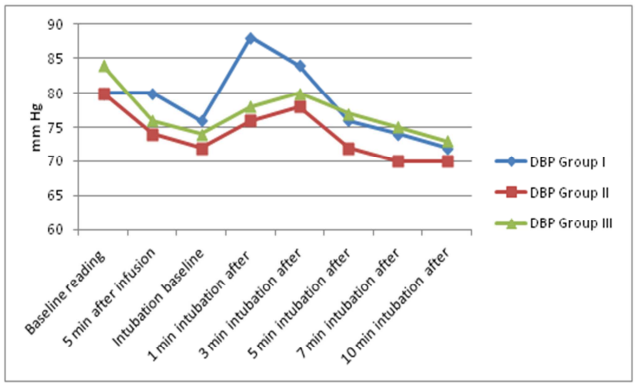

Figure 2: Comparison of mean diastolic blood pressure in all three groups.

[Figure 2] shows that there was a significant decrease in DBP group II and group III compare to group I after the infusion and just before intubation. Mean DBP values increased in all the three groups at 1 min after intubation. The values of DBP in Group II were significantly lower than that of Group I and Group III ($p < 0.01$).

It is evident from [Figure 3] that there was a significant decrease in MAP group II and group III compare to group I after the infusion and just before intubation. Mean MAP values increased in all the three groups at 1 min after intubation. The values of MAP in Group II were significantly lower than that of Group I and Group III ($p < 0.01$).

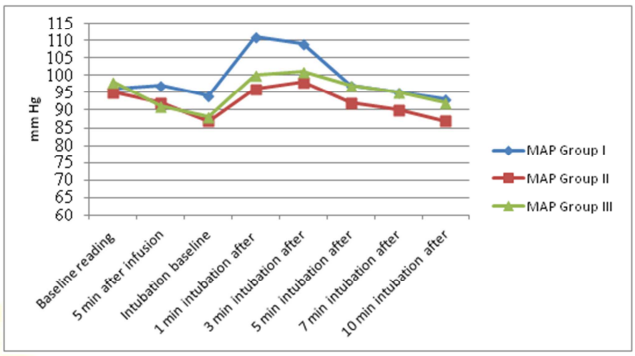

Figure 3: Comparison of mean arterial pressure in all three groups.

Further, [Figure 4] shows that there was an insignificant difference between rate pressure products of all three groups. ($p > 0.05$). Rate pressure products were significantly high in control group I and esmolol group III compare to dexmedetomidine group II.

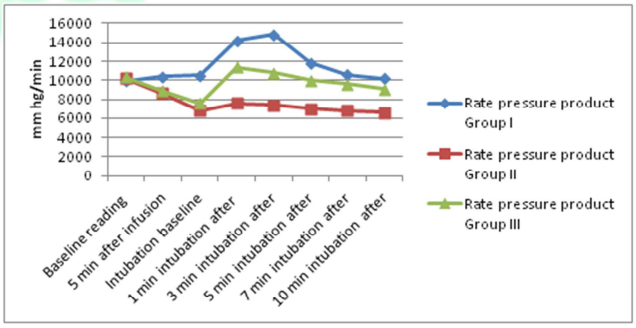

Figure 4: Comparison of rate pressure product in all three groups.

Discussion

Present study recorded that hemodynamic responses to laryngoscopy and tracheal intubation for 10 minutes as it has been suggested that haemodynmic changes disappear in 10 minutes.[16] Results showed that infusion of dexmedetomidine in group II patients before intubation was found more effective than group I esmolol infusion. Laryngoscopy and tracheal intubation are most critical part of inducing general anaesthesia.[1]

Increase of blood pressure and tachycardia is the results of sympathoadrenal response which is provoked by

laryngoscopy and intubation.[2,3] Numerous methods betal blockers, calcium chanel blockers, nitroprusside etc have been applied by clinicinas to attenuate the sympathetic response to laryngoscopy and intubation without any remarkable success.[15-18] Moreover, various adverse effects like hypertension, bradycardia etc of these drugs have been reported in the studies.[5-7]

In this way the hunt of ideal drug is still on. The present study recorded the effects of dexmedetomidine and esmolol in HR, SBP, DBP and MAP at various intervals up to 10 minutes. Time of laryngoscopy has been limited to <20 seconds as pressor response to laryngoscopy is evoked during first 50 seconds which lost or remain little if process is further prolonged.[16]

Various studies use beta blockers to improve the sympathomimetic responses to laryngoscopy and intubation. Though, improvement in HR is more pronounced via beta blockers instead of blood pressure.[17] Esmolol is a well known cardioselective beta blocker with instant action and quick elimination. That is why it is considered as a valuable drug to attenuate the haemodynamic response. 8 Esmolol (in doses from 0.5 to 2 mg/kg) being a beta blocker obstruct the beta‑adrenergic receptors resulting in diminish force of cardiac muscles and decrease of HR as well as blood pressure in response to intubation.[9,10,17] Sharma et al,[8] reported that esmolo was most effective in attenuating cardiovascular responses to laryngoscopy and intubation when it was used in the dose of 1–1.5 mg/kg. Kindler et al recorded esmolol was effective in controlling HR in 1 and 2 mg/kg dose before larngoscopy though it was not eddecive in controlling blood pressure in this dose.[9]

Dexmedetomidine has been reported better in attenuationg cardiac response after laryngoscopy and intubation in comparison of clonidine due to its higher selectivity compare to clonidine.[11] Studies suggest that dexmedetomidine controls the haemodynamic response to laryngoscopy and intubation via 2 ways. First it inhibits the release of epinephrine and non epinephrine via inhibiting androgenic receptors situated on presynaptic terminal sympathetic nerves. Second it acts on locu coeruleus leads to decrease sympathetic activity.[15-17] Scheinin et al suggested that dexmedetomidine in 0.6 g/kg dose is effective in controlling the cardiovascular response rather than suppressing to laryngoscopy and intubation.[6] Lee at al,[19] and Bajwa et al,[14] demonstrated that dexmedetomidine respectively in the doses of 1 mcg/kg and 1 gm/kg suppressed the haemodynamic response to laryngoscopy and intubation.

The present study incorporated higher dose of dexmedetomidine 1 gm/kg to decrease the adverse effects this drug was infused slowly over 10 minutes as rapid administration of dexmedetomidine has been found associated with high blood pressure and tachycardia.[8,9]

Findings of the current study showed that both dexmedetomidine and esmolol were significantly effective in controlling increase of HR followed by intubation. However, compare to control group. HR suppuration was more effective in dexmedetomidine group than esmolol group. In addition, increase of SBP, DBP and MAP were significantly attenuated after laryngoscopy and intubation in dexmedetomidine group compare to esmolol group and control group. There was an insignificant difference between esmolol and control groups. These findings are consistent with the earlier studies of Reddy et al, 20 Gupta et al and Selvaraj et al as they recorded significantly better attenuation of symphtomimmetic response with dexmedetomidine compare to esmolol.[21,22] Similarly, Srivastava et al,[23] reported that better cardiovascular response with dexmedetomidine in comparison of esmolol.

Results of the current study recorded that rate pressure product was significantly decreased in dexmedetomidine group compare to esmolol group and control group. These findings are in agreement with the findings of the previous studies of Gupta et al and Selvaraj et al as they recorded similar decrease of rate pressure product with dexmedetomidine compare to esmolol.[21,22] Rate pressure product is considered one of the important markers of oxygen demand of cardiac muscles.[24]

Conclusion

Findings of the current study suggest that both dexmedetomidine and esmolol were found effective in improving symphtomimmetic response to laryngoscopy and inintubation in normotensive patients. However, dexmedetomidine showed better attenuation of haemodynamic response compare to esmolol.

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