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DEXMEDETOMIDINE VERSUS ORAL PREGABALIN TO ATTENUATE HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND OROTRACHEAL INTUBATION: A COMPARATIVE STUDY

Anaesthesiology

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ABSTRACT

Hemodynamic pressor response to laryngoscopy and endotracheal intubation provokes tachycardia and hypertension that can lead to many adverse events in patients with cardiovascular disease. The main objective of the study is to compare the efficacy of intravenous DexmedetomIdine and oral Pregabalin premedication for attenuation of hemodynamic pressor response to laryngoscopy and intubation. **Methods-** A 100 patients of age group 18-60 years scheduled for elective surgeries under general anesthesia with ASA physical Status I and II divided into two groups each of 50. Group D received intravenous dexmedetomidine 1 mcg/kg over 10 minutes before induction, and Group P received oral pregabalin 150mg 1hr before intubation. Parameters observed were heart rate (HR), systolic, diastolic, and mean arterial blood pressure at baseline, after induction, immediately after intubation and then 1, 3, 5 and 10minutes thereafter. **Results-** Attenuation of HR in group dexmedetomidine is statistically significant($p<0.05$) compared to oral pregablin from time of induction till 10mins after intubation. SBP, DBP, MAP significantly($p<0.05$) decreased after intubation with intravenous dexmedetomidine as compared to oral pregabalin, till 10minutes after intubation. **Conclusion-** Intravenous Dexmedetomidine 1µg/kg is more effective than oral Pregabalin 150mg in attenuating hemodynamic response to laryngoscopy and orotracheal intubation.

KEYWORDS

Pregabalin, Dexmedetomidine, Attenuation, Pressor response, Laryngoscopy, intubation, Sedation, Anxiolysis, Premedication

INTRODUCTION

The airway instrumentation of direct laryngoscopy and tracheal intubation is powerful noxious stimuli which can lead to adverse hemodynamic pressor response especially in cardiovascular compromised patients, necessitating the need for attenuating the pressor responses by appropriate premedication, smooth induction, and rapid intubation.

Dexmedetomidine, an imidazole derivative and highly selective α2 adrenergic receptor agonist, is being used widely to attenuate hemodynamic responses[2-4]. Pregabalin has analgesic, anticonvulsant, and anxiolytic effects[5,6]. Several studies have demonstrated the efficacy of oral pregabalin on post-operative analgesia and reduction of parenteral analgesics[7-9]. Oral pregabalin attenuates pressor response to laryngoscopy and endotracheal intubation[10,11].

The aim of this study was to compare the efficacy of intravenous dexmedetomidine and oral pregabalin in attenuating the hemodynamic response to laryngoscopy and endotracheal intubation.

METHODS

The study was conducted after obtaining approval from Institutional Ethical Committee and informed patients consent during the period of August 2020 to july 2022. This prospective, randomized, double-blinded controlled study was conducted on 100 patients of age group 18-60 years scheduled for elective surgeries under general anaesthesia with American Society of Anesthesiologists (ASA) physical Status I and II.

Patients with a history of the cardiac, pulmonary or renal disease, obesity, anticipated difficult intubation, allergic to any anaesthetic medication, pregnant and lactating patients and those taking sedatives, hypnotics or anti hypertensives were excluded from the study. We also excluded cases where laryngoscopy exceeded 20 seconds or a second attempt was needed. Both patients and observer were totally blind about the groups and medications given.

All the patients were visited the day before surgery and pre anaesthetic examination was done and findings were recorded on predesigned and pretested proforma. All patients receives Tab. Ranitidine 150mg and Tab. Alprazolam 0.5 mg orally at night on the day before surgery.

In the pre-operative room, baseline heart rate (HR) along with systolic, diastolic, and mean arterial blood pressure was recorded. Patients were randomly divided into two groups each of 50 patients by computer-generated random table. Group D received intravenous dexmedetomidine 1 mcg/kg over 10 minutes before induction, and Group P received oral pregabalin 150 mg 1 hr before intubation.

Premedication - Injection glycopyrolate 0.2mg iv, injection ondansetron 0.1mg/kg iv, Injection Midazolam 0.05mg/kg will be given intravenously 2 minute before induction.

Anaesthesia technique: All the patients will be preoxygenated with 100% oxygen for 3 minutes before Induction. Patient is induced with Inj. Propofol 2mg/kg and administered slowly till loss of eyelash reflex. Injection Vecuronium was administered at a dose of 0.1 mg/kg body weight intravenously. Laryngoscopy is done using rigid laryngoscope with standard macintosh blade. Intubation is done with appropriate sized disposable high volume, low pressure cuffed endotracheal tube. The anaesthesia is maintained with oxygen (40%), nitrous oxide (60%), isoflurane (0.5%), Vecuronium 0.05mg/kg IV intermittent boluses and Intermittent positive pressure ventilation will be used to maintain end tidal carbon dioxide (EtCO2) between 35 and 40 mmHg. Intravenous fentanyl 2 µg/kg will be administered 15 minutes after intubation to avoid its effect on hemodynamic response. After completion of surgery, residual neuromuscular block is antagonized with appropriate intravenous doses of neostigmine (0.05 mg/kg) with glycopyrolate (0.01 mg/kg), and extubation is performed when respiration is spontaneous and adequate.

The following parameters will be recorded intraoperatively Heart rate, systolic blood pressure, diastolic blood pressure mean blood pressure were monitored

A. during induction,
B. immediately after intubation,
C. 1min,
D. 3min,
E. 5min and
F. 10min after tracheal intubation.

Positioning, epinephrine infiltration, throat packing were withheld till the completion of recording. Decrease in MAP by more than 20% from baseline or systolic arterial pressure <90 mm Hg will be treated by increasing the intravenous fluid infusion rate or incremental doses of ephedrine 6 mg IV bolus. Decrease in HR (<50 beats/minutes) was treated with atropine 0.6 mg IV.

Statistical analysis

The sample size was calculated by power analysis (power 80% and α error 0.05) from initial pilot studies. The calculated sample size for each group was 48 patients. Presuming the dropout rate to be 5%, it was decided to include 50 patients each group. Data were expressed as mean±standard deviation and analyzed by Student's t-test and Chi-square test. Probability (p) was considered to be significant if <0.05.

RESULTS

Out of the 100 patients, 50 patients in each group were evaluated and compared. Patients demographic profile were similar in both groups. The duration of laryngoscopy and intubation was similar in both

groups. No significant difference was found among them with respect to age, sex, weight.

Attenuation of HR in group dexmedetomidine (68.02±5.08/minutes) immediately after intubation was statistically significant than group pregabalin (73.46±8.95/minutes)

Table 1- comparision of heart rate between dexmedetomidine and pregabalin group.

HEART RATE						
Time Interval	Group-D		Group-P		Unpaired t test	
	Mean	Std. Deviation	Mean	Std. Deviation	P Value	Significance
Basal	78.94	5.01	80.26	5.57	0.216	NS
After induction	67.44	4.48	75.90	8.26	0.000	HS
Immediately after intubation	68.02	5.08	73.46	8.95	0.000	HS
1 Min	68.48	4.99	74.56	7.74	0.000	HS
3 Min	72.12	6.92	75.68	7.04	0.012	S
5 Min	72.12	6.92	76.48	6.23	0.001	HS
10 Min	72.52	6.62	82.94	6.42	0.000	HS
NS = NOT SIG, HS = HIGHLY SIG, S = SIG						

SBP, DBP, MAP significantly($p<0.05$) decreased after intubation with intravenous dexmedetomidine as compared to oral pregabalin, till 10 minutes after intubation.

Table 2- comparision of systolic blood pressure between dexmedetomidine and pregabalin group.

SBP						
Time Interval	Group-D		Group-P		Unpaired t test	
	Mean	Std. Deviation	Mean	Std. Deviation	P Value	Significance
Basal	130.74	14.40	129.62	15.34	0.707	NS
After induction	108.76	12.89	119.32	14.77	0.001	HS
Immediately after intubation	107.56	12.96	117.72	14.02	0.001	HS
1 Min	106.30	13.27	119.96	14.09	0.001	HS
3 Min	108.56	13.58	120.14	14.22	0.001	HS
5 Min	111.44	14.40	121.50	14.27	0.001	HS
10 Min	110.80	14.48	129.16	16.33	0.001	HS
NS = NOT SIG, HS = HIGHLY SIG						

Table 3- comparision of diastolic blood pressure between dexmedetomidine and pregabalin group.

DBP						
Time Interval	Group-D		Group-P		Unpaired t test	
	Mean	Std. Deviation	Mean	Std. Deviation	P Value	Significance
Basal	79.92	5.71	78.26	7.06	0.199	NS
After induction	71.08	6.06	74.34	7.16	0.016	S
Immediately after intubation	69.28	6.35	72.60	7.56	0.019	S
1 Min	67.84	7.05	73.22	7.39	0.000	HS
3 Min	70.48	6.45	72.14	7.45	0.236	NS
5 Min	69.86	6.38	72.68	7.46	0.045	S
10 Min	69.02	6.62	78.12	6.15	0.000	HS
NS = NOT SIG, HS = HIGHLY SIG, S = SIG						

Table 4 - comparision of mean blood pressure between dexmedetomidine and pregabalin group.

MAP						
Time Interval	Group-D		Group-P		Unpaired t test	
	Mean	Std. Deviation	Mean	Std. Deviation	P Value	Significance
Basal	96.96	8.10	95.52	9.35	0.413	NS
After induction	83.44	7.54	89.34	9.46	0.001	
Immediately after intubation	80.36	7.50	87.86	9.15	0.000	HS
1 Min	78.98	7.65	89.12	8.97	0.000	HS
3 Min	83.02	7.88	88.36	9.11	0.002	HS
5 Min	83.14	8.11	89.38	8.91	0.000	HS
10 Min	82.30	8.37	95.18	8.50	0.000	HS
NS = NOT SIG, HS = HIGHLY SIG,						

No post-operative respiratory depression, nausea, and vomiting were found, and no other post-operative complication was recorded in any group during our study.

DISCUSSION

Laryngoscopy and tracheal intubation are noxious stimuli which can cause reflex cardio vascular responses as described by Reid and Brace[22]. Orotracheal intubation using laryngoscope normally needs elevation of epiglottis exposing the glottic opening. This maneuver causes sympathetic stimulation leading to increase in heart rate and blood pressure. Even increase in pulse pressure of around 10 mmHg is associated with 20% or even higher risk of any adverse events occuring in renal, cardiovascular and central nervous systems in both hypertensive and normotensive individuals[21].

Attenuation of the sympathoadrenal stress response is important especially in high-risk patients [12]. Various methods such as α or β adrenergic blockers, opioids, topical or systemic lignocaine are being used to attenuate hemodynamic response [13-15]. Dexmedetomidine possess anxiolytic, sedative, analgesic, and sympatholytic properties. It may be used as premedicant, adjunct to balanced anaesthesia as it remarkably reduces the doses of the anaesthetic drugs [16].

Dexmedetomidine produces hyperpolarization of noradrenergic neurons and suppression of neuronal firing in the locus cerelous that leads to decrease in systemic noradrenalin release and attenuation of sympathoadrenal response during laryngoscopy and intubation [4].

Pregabalin, (S)-3-(aminomethyl)-5-methylhexonic acid is a new structural, and non-functional analog of gamma-aminobutyric acid acts at pre synaptic calcium channels to modulate neurotransmitter release in the central nervous system(CNS) and used as an adjuvant in the treatment of partial seizures, general anxiety disorders, neuropathic pain [1-2]. Pregabalin (pree-γ-lin) binds to the α2-δ site an auxiliary subunit of voltage-gated calcium channels in the CNS, inhibiting excitatory neurotransmitter release [17].

In our study, intravenous dexmedetomidine was found to be more effective than oral pregabalin in attenuating hemodynamic response to laryngoscopy and endotracheal intubation. There was statistically significant difference ($p<0.05$) in change of mean HR and SBP, DBP and MAP from induction till 10 minutes after intubation in dexmedetomidine group compared to oral pragablin.

Pregabalin as a premedicant for reducing the hemodynamic pressor response to airway instrumentation during general anaesthesia was studied by **Rastogi Bhawan et al.,**[23]. The results of this study, which used two different pregabalin doses of 75 mg and 150 mg, showed that the pressor response decreased in a dose-dependent manner and all patients maintained stable hemodynamics throughout the intraoperative period without experiencing any side effects or prolonged recovery times. Additionally, pregabalin pretreatment effectively sedated the patients prior to surgery. Based on the result of the previous study, the dose of pregabalin was chosen as 150 mg [10] .Chaudhary et al. have shown that oral pregabalin and clonidine have both effectively blunt hemodynamic pressure response to laryngoscopy without prolongation of recovery time and side effects [19] .

In **Menda *et al.*,**[20] a prospective, randomised, double-blind study, dexmedetomidine infusion (1 mcg/kg or saline placebo) before induction was used, along with low doses of fentanyl and etomidate, to lessen the haemodynamic stress change to intubation in 30 patients undergoing myocardial revascularization while receiving beta blocker therapy. When compared to the placebo group, the dexmedetomidine group experienced a greater drop in heart rate after induction. Heart rate significantly increased in the placebo group one minute after intubation, while it reduced in dexmedetomidine group. Incidence of hypertension which required treatment was significantly higher in the placebo group.

It is found that intravenous dexmedetomidine is more effective in attenuating the hemodynamic response to laryngoscopy and intubation than other agents [3].

When assessing techniques to lessen the hemodynamic pressor responses of airway instrumentation, the induction agents may influence the results. We have used propofol as an induction agent, which produces hypotension more than thiopental and bradycardia, which has helped to compensate in part the hemodynamic changes induced due to laryngoscopy and intubation in all patients [23]. The salivary and tracheobronchial mucus secretions necessitate prophylactic administration of intravenous glycopyrrolate.

The limitation of the study was that sedation score and recovery time was not compared.

CONCLUSION

Intravenous dexmedetomidine 1 µg/kg is more effective than oral pregabalin 150 mg in attenuating hemodynamic response to laryngoscopy and orotracheal intubation.

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