Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 01, 2024

Original Research Article

COMPARISON OF INJECTION LIGNOCAINE (PRESERVATIVE FREE) 1.5 MG/KG IV WITH ORAL PREGABALIN 150 MG FOR ATTENUATION OF HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION

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Received: 02-12-2023 / Revised: 07-12-2023 / Accepted: 05-01-2024

ABSTRACT

Background

Laryngoscopy and endotracheal intubation are associated with a transient hemodynamic stress response which needs attenuation**.** The anesthesiologists have tried various methods and drugs for this purpose. The aim of present study was to investigate the effects and comparison of intravenous lignocaine 1.5mg/kg and oral pregabalin 150mg on blunting haemodynamic stress response.

Method

Total 80 adult patients of ASA grade I and II were enrolled in this study and randomly allocated into two groups of 40 each. Group I (n=40): Patients received injection Lignocaine (preservative free) 1.5 mg/kg iv 3 minutes prior to laryngoscopy. Group II (n=40): Patients received oral pregabalin 150 mg 1 hour prior to laryngoscopy. HR, SBP, DBP and MAP were recorded before induction considered as 0 minute and 1, 3, 5 and 10 minutes after laryngoscopy and intubation.

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Results

Injection Lignocaine had better control on HR and SBP following laryngoscopy. Oral pregabalin had better control on SBP, DBP and MAP. On comparison between two drugs, there was significant difference in HR, DBP and MAP. It was found that lignocaine had better control on HR at 1minute following laryngoscopy as compared to pregabalin ($p<0.05$). Whereas, with comparison to lignocaine, pregabalin had better control of DBP at 1, 3 and 5minutes following laryngoscopy and intubation. MAP was also effectively controlled with pregabalin at 1- and 3-minutes following laryngoscopy and intubation. Both the drugs were effective in controlling SBP with no significant difference.

Conclusion

Thus, pregabalin and lignocaine both drugs are better for attenuating hemodynamic response, but lignocaine exerts better effect on HR and pregabalin has better effect on controlling DBP and MAP following laryngoscopy and intubation.

Keywords: Laryngoscopy; Endotracheal intubation; Hemodynamic stress response; Lignocaine; Pregabalin

INTRODUCTION

Endotracheal intubation is a safe technique for conduct of general anesthesia, in that it offers protection against aspiration and facilitates positive pressure ventilation. Manipulation of the respiratory tract such as during laryngoscopy and endotracheal intubation are associated with reflex sympathetic response, resulting in hemodynamic and cardiovascular changes consisting of increased circulating catecholamines [1], heart rate, blood pressure, myocardial oxygen demand, and arrhythmias [2]. This transient hypertension and tachycardia may be hazardous in elderly and those with hypertension, myocardial insufficiency and cerebrovascular diseases, myocardial infarction, and thyrotoxicosis [3]. So, it is necessary to blunt this response in such individual.

For attenuation of this hemodynamic response to laryngoscopy and tracheal intubation, various drugs and techniques have been studied which include deep general anesthesia, topical anesthesia, intravenous lignocaine, vasodilators, beta blockers, calcium channel blockers, ά2 agonists, magnesium sulphate, antiepileptics and opioids. However, no modality was devoid of drawbacks and limitations [4].

Lignocaine is an amide (-NHCO-) synthetic local anaesthetic which acts on sodium channels. Monoethylglycinexylidide is a metabolite of lignocaine, has approximately 80% of the activity of lignocaine for protection against cardiac dysarrythmias [4, 5].

Pregabalin, a gabapentinoid compound, relatively new drug, which was originally introduced as antiepileptic and also have analgesic, anticonvulsant, and anxiolytic effects. It acts by presynaptic binding to the α-2- subunit of voltage-gated calcium channels that are widely distributed in the brain and exert antinociceptive and antiseizure properties. By altering calcium currents, pregabalin reduces the release of several excitatory neurotransmitters, including glutamate, nor-epinephrine, and substance P, which are supposed to be responsible for its antinociceptive property [6-8]. This property of pregabalin might account for its attenuation of hemodynamic response to laryngoscopy. Hence, the present study was undertaken to see the effects of injection lignocaine 1.5mg/kg (preservative free)

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and pregabalin 150mg for attenuation of hemodynamic response to laryngoscopy and intubation and comparison between two drugs.

MATERIALS AND METHODS

After obtaining institutional ethical committee approval and written informed consent from all the patients, this a prospective, randomized, controlled study was conducted in the Department of Anaesthesiology, at Tertiary Care Hospital during a period of 2 years. A total of 80 patients of either sex, age between 18-65 years, ASA grade I and II, who undergoing any elective planned surgery under general anaesthesia were included in the study. Patients were randomly allocated into two groups of 40 each. Randomization of patients was done using computerized randomization chart. Patients of age <18 and >65 years, patients with known allergy, bradycardia, sick sinus syndrome, cardiac, renal, hepatic, respiratory disease, anticipated difficult airway, morbid obesity, coagulation abnormalities, patients taking antihypertensive drugs and pregnant women were excluded from the study.

Pre-op investigations were conducted including haemoglobin, bleeding time, clotting time, urine examination, blood sugar level, serum electrolytes, ECG, X-ray chest, airway assessment with mallampati score. Nil by mouth status was confirmed. Group II patients received tablet pregabalin 150 mg orally with sip of water 1 hour prior to induction. All patients received Inj. Glycopyrrolate 5ug/kg intramuscularaly 30 minutes prior to induction. After taking patient inside the OT, Inj. Ondansetron 0.08 mg/kg intravenous (iv) Inj. Midazolam 0.03 mg/kg iv and Inj. Pentazocin 0.3 mg/kg iv were given. In the operating room Ringer's Lactate solution was started. ECG, SpO2, NIBP monitors were attached.

Preoxygenation was done with 100% Oxygen (O2). Group I patients were given injection lignocaine (preservative free) 1.5 mg/kg intravenous, 3 minutes prior to laryngoscopy and intubation. The parameters were recorded prior to induction: HR, SBP, DBP, MAP, SpO2 and ECG and labelled as 0-minute parameters. All patients were induced with injection thiopentone sodium 2.5% solution, 5 -7 mg/kg i.v. till the loss of eyelash reflex followed by inj. succinylcholine 1.5 mg/kg i.v. as muscle relaxant. Patient was ventilated with 100% O2. After adequate relaxation smooth and gentle laryngoscopy was performed by the trained anesthetist who was unaware of study and drugs used for study.

After endotracheal intubation, heart rate, systolic and diastolic blood pressure, mean arterial pressure, ECG and SPO2 were monitored at 1, 3, 5 and 10 minutes of intubation. All intubations were smooth and gentle and were done within 15 seconds with appropriately sized endotracheal tube. Occurrence of ECG changes, if any, were noted. Patients were ventilated with oxygen and nitrous oxide using Bain's circuit. No additional anesthetic agents were given for first 10 minutes after intubation. No surgical stimulus was given till 10 minutes.

Maintenance of anesthesia was done with 50% O2 + 50% N2O, Injection propofol infusion 100 ug/kg/hr and inj. vecuronium 0.08 mg/kg i.v. as skeletal muscle relaxant till the end of surgery. Parameters like HR, SBP, DBP, MAP at 0, 1-, 3-, 5- and 10-minutes following laryngoscopy were recorded.

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Statistical analysis

Data so collected, tabulated, and coded in MS excel and was then analysed using SPSS, computer software version 16. Statistical analysis of data was done by using student's t-test for difference of means and chi-square test referred for p-value for their significance. Any p-value less than 0.05 ($p<0.05$) was taken as significant.

OBSERVATIONS AND RESULTS

A total of 80 patients were enrolled in the study and randomly allocated into two groups of 40 each. In both the groups, the maximum number of patients were from the age group of 20–21 years and above 41 years, ranging from 18-60 years. However, both the groups were comparable and found no significant difference with respect to demographic profile of the patients ($p>0.05$) as shown in table 1.

Table 1: Demographic profile of the patients

Demographic data		Group I	Group II
Age groups in years	≤20	02	06
	21 to 30	14	13
	31 to 40	10	08
	≥41	14	13
	Mean	35.48	34.50
Gender	Male	19	21
	Female	21	19

Table 2 show the hemodynamic parameters (HR, SBP, DBP, MAP) during laryngoscopy and intubation, in patients pretreated with injection lignocaine I.V. 3 minutes prior to laryngoscopy.

Table 2: Hemodynamic parameters in group I (lignocaine IV)

Parameters	Observations at different times of assessment (Mean±SD) (n=40)				
	0 min	1 min	3 min	5 min	10 min
HR	82.95±4.17	82.90±4.30	83.70±4.33	84.03±4.20	84.25±4.31
P value		0.599	<0.0001*	<0.0001*	<0.0001*
SBP	132.05±5.33	132.20±5.06	132.30±5.01	132.30±5.33	133.15±5.29
P value		0.474	0.281	0.342	0.001*
DBP	83.65±3.44	85.70±3.31	85.80±3.26	86.00±3.26	86.45±3.21
P value		<0.0001*	<0.0001*	<0.0001*	<0.0001*
MAP	99.78±2.66	101.20±2.47	101.30±2.52	101.43±2.52	102.02±2.55
P value		<0.0001*	<0.0001*	<0.0001*	<0.0001*

Group II patients received pregabalin 150 mg orally 1 hour prior to induction and it's hemodynamic parameters (HR, SBP, DBP, MAP) represented in table 3.

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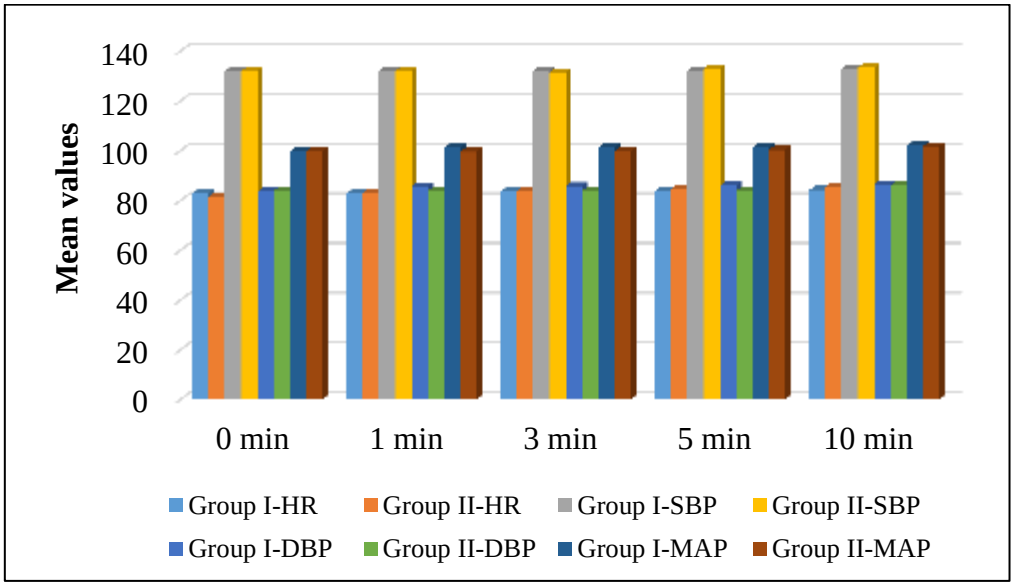
Table 3: Hemodynamic parameters in group II (Pregabalin oral)

Parameters	Observations at different times of assessment (Mean±SD) (n=40)				
	0 min	1 min	3 min	5 min	10 min
HR	81.55±5.14	83.13±5.03	84.00±4.99	84.75±4.98	85.58±4.89
P value		<0.0001*	<0.0001*	<0.0001*	<0.0001*
SBP	132.05±5.33	132.07±5.12	131.50±5.15	133.10±5.18	133.55±5.15
P value		0.893	0.039*	<0.0001*	<0.0001*
DBP	83.90±3.47	83.93±3.48	83.93±3.42	83.93±3.48	85.95±3.43
P value		0.812	0.864	0.844	<0.0001*
MAP	99.95±3.89	99.58±3.78	99.78±3.80	100.32±3.78	101.82±3.74
P value		0.774	0.237	0.004*	<0.0001*

Baseline HR was higher in group I than group II patients, but difference was statistically insignificant (p=0.819). HR increased in both groups following laryngoscopy, but the increase was statistically insignificant. When we see rising trend of HR in each group, group I was showing better control over HR at 1 minute. While comparing both drugs p>0.05, thus statistically no significant difference between two groups for controlling SBP. There was significant difference between two groups for attenuating rise in DBP at 1-, 3- and 5-minutes following laryngoscopy. From the data obtained, it was concluded that group II attenuates rise in DBP better than group I. MAP show statistically significant difference between two groups at 1- and 3-minutes following laryngoscopy (p=0.047 and 0.039 at 1 and 3 minutes respectively.). Thus, MAP was better controlled with group II, (Figure 1).

Figure 1: Comparison of haemodynamic parameters at different times in two groups



DISCUSSION

Hemodynamic pressor response to airway instrumentation i.e. direct laryngoscopy and intubation is hazardous complication of general anesthesia [9]. Pressor response to laryngoscopy and intubation is a sympathetic reflex, that is provoked by stimulation of

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orolaryngopharynx. This leads to increase in heart rate, blood pressure, intracranial tension, intraocular tension and dysarrhythmias. Various drugs have been used to minimize this stress response during intubation, but no modality was devoid of drawbacks and limitations. Few studies have compared oral pregabalin with placebo for pressure attenuation [10, 11], and still fewer have compared pregabalin with lignocaine [12, 13]– one of the widely used drugs for stress response attenuation.

In the present study, both the groups were comparable and found no significant difference with respect to demographic profile of the patients which is comparable with the study done by Talikoti AT et al [12] and Vadhanan P et al [13].

In group I, there was no significant increase in HR at 1 minute following laryngoscopy, (p=0.599). Increase in heart rate was statistically significant at 3, 5 and 10 minutes (p=<0.0001), however clinically insignificant (increase was less than 10 bpm). Thus, lignocaine prevents rise in HR after laryngoscopy. Similarly, there was no statistically significant rise in systolic BP till 5 min, but it was increased at 10 min which was statistically significant when compared with 0 minute (p=0.001), however again this was clinically insignificant (increase was less than 15 mmHg). Thus, lignocaine exerts better effect on SBP following laryngoscopy and intubation. Diastolic BP also increased significantly at 1 min (p<0.0001) and remained significantly high thereafter at 3 min, 5 min and 10 min (p<0.0001). Again, this increase was clinically insignificant as increase in DBP was less than 15 mmHg. Similar to DBP, MAP was also showing statistically significant increased at 1, 3, 5 and 10 min when compared with 0 minute, (p=<0.0001). As, i.v. preservative free lignocaine blocks the sodium channels in the cell membranes of the heart and reduces the rate of the rise of action potential and hence the conduction velocity of all His Purkinje system and in the atria and ventricular musculature. It also, has membrane stabilizing action so it is popularly used as anti-arrhythmic agent. This might be the reason for blunting of tachycardia following pressor response of laryngoscopy. Thus, results obtained in present study for lignocaine correlate with studies done by Talikoti AT et al [12] and Wilson IG et al [14].

In group II heart rate increased gradually from 1minute to 10 minutes, (p<0.0001 Vs 0 minute). Systolic BP decreased significantly at 3 min and increased at 5min and 10 min (p<0.0001 Vs 0 minute). Diastolic BP remained relatively constant at 1, 3 and 5 min but increased significantly at 10 minutes (p<0.0001 Vs 0 minute). There was no significant increase in MAP at 1 and 3 minutes. But MAP increased at 5 minutes (p=0.004 Vs 0 minute) and was maximum at 10 min (p<0.0001 Vs 0 minute). Similar to group I, the data from group II was showing statistically significant difference but when we see this data clinically, the rise in parameters were insignificant as rise in HR was less than 10 beats per minute, rise in SBP, DBP and MAP was <15 mmHg. These findings are correlated with the previous studies [12, 13].

When we compared groups I and II, both groups were comparable with respect to their values at 0 minute. HR (p=0.189), SBP(p=1.00), DBP(p=0.748) and MAP(p=0.824). It was found that group I and II were equally good at controlling HR following laryngoscopy and intubation upto 10 minutes. p value 0.830, 0.775, 0.484, 0.203 at 1,3,5 and 10 minutes respectively. Therefore, there was no significant difference between two groups. But when we saw values of HR of individual groups, it was found that group I has better control over

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 01, 2024

HR at 1 minute as compared to group II. Comparison for SBP showing statistically no significant difference between two groups as evident from p value at 1-, 3-, 5- and 10-minutes following laryngoscopy 0.913, 0.484, 0.485, 0.733 respectively. There was significant difference between group I and group II at 1-, 3- and 5-minutes following laryngoscopy while comparing for DBP. Thus, it was found that pregabalin is more efficient than lignocaine in controlling diastolic BP at 1(p=0.022), 3(0.014) and 5 (0.007) minutes. When comparing MAP, there was significant difference, at 1- and 3-minutes following laryngoscopy. Group II was more effective in controlling MAP at 1(p= 0.047) and 3(p=0.039) minutes following laryngoscopy and intubation, than group I. Thus, clinically both the drugs were equally effective for attenuating hemodynamic response to laryngoscopy and intubation. Both drugs attenuate rise in HR, SBP, DBP and MAP, but lignocaine (group I) was better for attenuating rise in HR and pregabalin (group II) was better for attenuation of rise in DBP and MAP. Similar findings are reported in the study conducted by Talikoti AT et al [12].

Both drugs have less side effects and more advantages. The most common adverse effect of pregabalin is dizziness and drowsiness, and for intravenous (preservative free) lignocaine is bradycardia and allergic reactions. Throughout the study period, we did not come across any adverse effect of pregabalin or injection lignocaine.

CONCLUSION

So, from the findings of present study we can say that I.V. lignocaine and oral pregabalin both drugs are better for attenuating hemodynamic response following laryngoscopy and intubation. Pregabalin is emerging as newer and safe drug as it leads to anxiolysis, analgesia and effective in attenuating rise in DBP and MAP following laryngoscopy and intubation. Whereas lignocaine has advantage of early onset and short duration of action. It has better control over HR as compared to pregabalin.

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