e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2022; 12(11); 69-77

Original Research Article

A Comparative Study between Nebulized Nitroglycerin and Lignocaine Nebulization for Attenuation of Haemodynamic Response to Laryngoscopy and Endotracheal Intubation during Elective Surgical Procedures: A Randomised Clinical Trial

Banani Ray[1], Sushil Kumar Nayak[2], Amitayu Nandi[3], Sujata Ghosh[4], Purba Haldar[5], Mausumi Niyogi[6]

[1]Senior Resident, Department of Anaesthesiology, Calcutta National Medical College & Hospital, Kolkata, West Bengal

[2]Associate Professor, Department of Anaesthesiology, Medical College Hospital, Kolkata, West Bengal

[3]Assistant Professor, Department of Anaesthesiology, Rampurhat Government Medical College & Hospital, Rampurhat, Birbhum, West Bengal

[4]Associate Professor, Department of Anaesthesiology, R G Kar Medical College & Hospital, Kolkata, West Bengal

[5]Professor, Department of Anaesthesiology, Bankura Sammilani Medical College & Hospital, Bankura, West Bengal

[6]Professor, Department of Anaesthesiology, Calcutta National Medical College & Hospital, Kolkata, West Bengal

Received: 28-09-2022 / Revised: 30-10-2022 / Accepted: 14-11-2022

Corresponding author: Dr Sujata Ghosh

Conflict of interest: Nil

Abstract

Introduction: Laryngoscopy and endotracheal intubation violates protective airway reflexes. This technique is found to have association with profound reflex sympatho-adrenal reflex by epi-pharyngeal and para-pharyngeal stimulation resulting in tachycardia, overshooting blood pressure, occasional disturbance in cardiac rhythm

Aims and Objective: Aim of the study was to find out the hemodynamic effect on patients receiving Nitroglycerine and Lignocaine nebulization and whether any of the study drugs was significantly more efficacious to attenuate the hemodynamic response followed by laryngoscopy and intubation.

Material and Methods: 50 patients aged between 18 to 45 years of both sex with ASA grading I & II and Malampatti grading I & II posted for elective surgical procedures under general anaesthesia were included in our study were randomly allocated in two different groups(n=50), Group L(lignocaine) and Group N(nitroglycerin). Group L patients were subjected to lignocaine nebulization for 3 minutes before induction, 4% Lignocaine nebulization 3mg/kg was administered to the patient in sitting position by asking the patient to inhale the drug for 3 minutes. Group N Patients were subjected to Nitroglycerin nebulization in a dose of 2.5 mg / kg / min for 3 minutes before induction. Hemodynamic parameters (HR, SBP, DBP and MAP) were recorded in the specific time intervals (preoperatively baseline, Pre intubation, immediate & 1, 3, 5 and 10 min after post intubation and operation was done as per schedule.

Results: Demographic variables taken here were Age, Sex, Weight, and ASA grading. All the variables were comparable with the p value < 0.001. . In group N heart rate was persistently increased in post intubation 1, 3, 5 minutes which was statistically significant with a decreasing trend and at 10 minutes interval it came to almost near baseline level. The SBP, DBP & MAP

variation in both groups were significant up to 3 minutes, but from 5 minute onward, the variation is not much significant.

Conclusion: Attenuation of heart rate is better with lignocaine nebulization but the attenuation of blood pressure is better with Nitroglycerin nebulization compared after direct laryngoscopy and intubation.

Keywords: Laryngoscopy, Endotracheal Intubation, Haemodynamic response, Attenuation, Nebulization, Lignocaine, Nitroglycerin

Introduction

Laryngoscopy and endotracheal intubation have paved a new era in the history of anesthesia and led to the introduction of safer anesthesia and for better control of airway and ventilation. Since the technique violates protective airway reflexes, this technique is found to have association with profound reflex sympatho-adrenal reflex by epi-pharyngeal and para-pharyngeal stimulation resulting in release of norepinephrine and epinephrine [1]. Due to this, certain cardiovascular response in the form of tachycardia, overshooting blood pressure, occasional disturbance in cardiac rhythm [2,3], rise in intracranial and intraocular pressure occur. In normotensive subjects these hemodynamic changes due to laryngoscopy are short lived [4] and coped by bodyphysiology and are of little significance. But this pressor response due to laryngoscopy can be detrimental in some cardiovascular diseases [5] like uncontrolled hypertension, coronary artery disease, diabetes mellitus, intracranial tumors, head injury with subdural hematoma or patient with coronary artery disease, cerebral hemorrhage or rupture of cerebral aneurysms. Sudden surge in plasma catecholamines in blood may lead to arrhythmia or ischemia, cerebral hemorrhage or rupture of cerebral aneurysms.

To limit the pressor response different pharmacological and nonpharmacological methods have been tried till date [6]. An array of pharmacological agents have been used to attenuate the hemodynamic responses to laryngoscopy and endotracheal intubation like lignocaine [7], Fentanyl, Remi-fentanyl, Alfentanil, Nifedipine, Magnesium sulfate, Dexmedetomidine, Clonidine, Nitroglycerin with varying results [8-10]. Previously there have been very less number of studies regarding nebulization of Nitroglycerine or lignocaine to attenuate the hemodynamic response. Lignocaine, acts as a local anesthetic and anaesthetize the oropharynx, nasopharynx and laryngopharynx. Lignocaine belongs to the group aminoethyl amide, that is a prototype of amide local anesthetic group. It is the most widely used short acting local anesthetic. Due to this patient feels less pain during laryngoscopy. Glyceryl trinitrate relaxes vascular smooth muscle with veno- dilation more than arteriolar dilation. This way it reduces the workload on heart and prevents the rise of blood pressure during laryngoscopy.

Here we have conducted the comparative study of the effectiveness, advantages, and disadvantages or adverse effects of the two agents via this route. Along with this idea we decided to conduct the present study to compare the effectiveness of nebulized nitroglycerin and nebulized lignocaine to attenuate the hemodynamic response following laryngoscopy and endotracheal intubation in two groups of adult patients of either sex undergoing elective abdominal surgeries under general anesthesia.

Aims and Objectives

Aim of the study was to find out the hemodynamic effect on patients receiving Nitroglycerine and Lignocaine nebulization. We also noted for adverse

effect of administration of these two drugs and whether any of the study drug was significantly more efficacious to attenuate the hemodynamic response followed by laryngoscopy and intubation and to find out the better one for the aforesaid purpose.

Materials and Methods

A randomized, prospective, single blind clinical study was conducted after taking approval from the Ethical cum Screening Committee of the institution during the time span of one and half year. Patients aged between 18 to 45 years of both sex wih ASA grading I & II and Malampatti grading I & II posted for elective surgical procedures under general anaesthesia were included in our study. A thorough clinical history, general survey, systemic examination, airway assessment and routine preoperative investigation was done and relevant findings were noted.

Patient with severe cardiovascular disease, history of coronary artery disease or uncontrolled diabetes or uncontrolled hypertension, respiratory disease , hepatic disease, altered sensorium, patient on alpha 2 agonist or beta blocker, difficult airway, Laryngoscopy andintubation time requiring more than 30 seconds or more than two attempt and failure to get informed consent were excluded from our study. Documented informed consent was taken from all patients.

On the night before operation patient were given tablet alprazolam 0.5 mg orally and at the morning of the day of surgery they were pre medicated with Pantoprazole 40 mg with sips of water. Continuous monitoring of heart rate (HR), noninvasivesystolic and diastolic blood pressure (SBP and DBP) and mean arterial pressure (MAP), continuous electrocardiography (ECG) monitoring and oxygen saturation (SpO2) was done before, during and after the procedure. 50 patients were randomly allocated in two different groups (n=50), Group L(lignocaine) and Group N(nitroglycerin). Randomization was achieved by closed envelops chosen by the patients before the procedure. Group L Patients were subjected to lignocaine nebulization for 3 minutes before induction, 4% Lignocaine nebulization 3mg/kg was administered to the patient in sitting position by asking the patient to inhale the drug for 3 minutes. Group N Patients were subjected to Nitroglycerin nebulization in a dose of 2.5 mg / kg / min for 3 minutes before induction. Followed by that induction was done with the same drug and laryngoscopy was done with the same procedure in all patients.

All patients were given 2mg/kg fentanyl before induction and 2mg/kg propofol followed by 0.5mg/kg Atracurium to facilitate endotracheal intubation. Using Macintosh blade, laryngoscopy was done and intubation done with appropriate size endotracheal tube. After successful endotracheal intubation, confirmation of correct placement of tube was done by bilateral chest auscultation and end tidal carbon di oxide monitoring. Maintenance of anaesthesia was done by 66% Nitrous oxide in oxygen followed by conjunction of sevoflurane at titrated MAC values.

Hemodynamic parameters (HR, SBP, DBP and MAP) were recorded in the specific time intervals (preoperatively baseline, Pre intubation, immediate & 1, 3, 5 and 10 min after post intubation (after confirming correct tube placement).

No surgical stimulation was provided during the study period and hemodynamic changes beyond the study period were not considered. At the end of the surgery, the patients were adequately reversed and monitored in the postoperative recovery room.

Statistical Analysis

The sample size had been calculated from results of previous studies. The collective raw data analysis was done by using SPSS version 20 software for windows 10. Unpaired t test was used to compare two means. P value less than 0.05 was considered statistically significant.

Results

Demographic variables taken here were Age, Sex, Weight, and ASA grading. All the variables were comparable with the p value < 0.001. There is no significant difference between two groups.

Table 1: Comparison of heart rates between and within the study groups at different points of time.

	GROUPS						P value	Significance
	GROUP L			GROUP N				
	Mean	Median	SD	Mean	Median	SD		
HR - baseline	74.58	75.00	3.21	75.04	75.00	3.17	0.471	Not Significant
HR pre intubation	74.94	75.00	3.11	95.24	95.00	2.70	<0.001**	Significant
HR after 1 min	75.08	75.00	3.05	93.48	93.00	2.84	<0.001**	Significant
HR after 3 min	74.94	75.00	3.37	85.54	86.00	3.04	<0.001**	Significant
HR after 5 min	74.44	74.50	2.98	84.50	84.00	3.22	<0.001**	Significant
HR after 10 min	74.46	74.50	3.21	74.46	74.50	3.21	1.000	Not Significant

When preoperative baseline heart rate was compared between the two groups, no statistically significant difference was found. After giving the induction agent before intubation, it showed a significant decrease in heart rate of both the groups. With analgesic fentanyl, before intubation, there was significant reduction of heart rate in group L, but in group N, increase in heart rate in seen, that was statistically significant. The same trend continued in all readings of HR till 10 minutes of post intubation. Post intubation HR in group L came to the baseline preoperative level in group L. In N group the heart rate was persistently raised in post intubation which was significant. After intubation next 1, 3, 5 minutes and 10 minutes period heart rate were less than preoperative baseline level in group L. In group N heart rate was persistently increased in post intubation 1, 3,5 minutes with a decreasing trend and at 10 minutes interval it came to almost near baseline level. Respective p values for 1 minute, 3 minute, 5minute and 10 minutes were <0.001, 0.001, 0.010, and all the values were statistically significant.

Table 2: Comparison of Systolic Blood Pressure between and within the study groups at different points of time.

	GROUPS						P value	Significance
	GROUP L			GROUP N				
	Mean	Median	SD	Mean	Median	SD		
SBP - PREOP BASELINE	114.78	115.00	3.59	115.42	116.00	2.70	0.390	Not significant
SBP - PRE-INTUBATION	115.10	115.00	3.27	105.00	105.00	3.32	<0.001**	Significant
SBP - AFTER 1 MIN	113.88	114.00	3.01	106.20	107.00	3.05	<0.001**	Significant
SBP - AFTER 3 MINS	114.58	114.50	3.48	105.24	105.00	3.03	<0.001**	Significant
SBP - AFTER 5 MINS	115.02	114.50	3.29	104.64	104.50	3.27	<0.001**	Significant
SBP - AFTER 10 MINS	114.60	114.00	3.22	114.50	114.00	3.19	0.917	Not significant

Table 3: Comparison of Diastolic Blood Pressure between and within the study groups at different points of time

	GROUPS						P value	Significance
	Group L			Group N				
	Mean	Median	SD	Mean	Median	SD		
DBP – Pre op Baseline	74.70	74.50	3.36	75.66	76.00	3.13	0.145	Not significant
DBP – Pre intubation	75.12	75.00	2.80	65.52	66.00	2.97	<0.001**	Significant
DBP – AFTER 1 min	74.60	74.50	3.00	63.86	64.00	2.74	<0.001**	Significant
DBP – AFTER 3 min	74.54	74.00	3.16	65.38	65.00	3.19	<0.001**	Significant
DBP – AFTER 5 min	74.64	74.50	3.09	64.92	64.50	3.07	<0.001**	Significant
DBP – AFTER 10 min	75.16	75.00	3.16	74.42	74.00	3.12	0.236	Not significant

Table 4: Comparison of Mean Blood Pressure between and within the study groups at different points

	GROUPS						P value	Significance
	Group L			Group N				
	Mean	Median	SD	Mean	Median	SD		
MAP – Pre op Baseline	88.06	88.17	2.53	88.91	89.33	2.33	0.099	Not significant
MAP – Pre intubation	88.45	88.67	2.19	78.68	78.67	2.30	<0.001**	Significant
MAP – AFTER 1 min	87.69	87.83	2.27	77.97	77.67	2.03	<0.001**	Significant
MAP – AFTER 3 min	87.89	87.17	2.53	78.67	78.33	2.07	<0.001**	Significant
MAP – AFTER 5 min	88,10	88.17	2.50	78.16	78.67	2.22	<0.001**	Significant
MAP – AFTER 10 min	88.31	88.33	2.43	87.78	87.67	2.05	0.252	Not significant

When the preoperative baseline SBP, DBD & MAP were compared between two groups, no statistically significant difference was found (p value=0.390). After giving the induction agent before intubation, we found a significant decrease in SBP, DBP & MAP in both groups, which was more prevalent in N group. (p value < 0.001). In the post intubation phase SBP, DBP and MAP remain below baseline in both groups which remains relatively less in group N (p value< 0.001), which is highly significant. In case of SBP, the p values for immediate post intubation,1 minute, 3minute, are <0.001, that is statistically significant. But p value of SBP recorded after 10 minutes of intubation was 0.917, which is not statistically significant. Which denotes the SBP variation in both groups significant up to 3 minutes, but from 5 minute onward, the variation is not much significant.

In case of DBP, the p values immediately after 1 minute and 3 minutes, and 5 minutes were<0.001, which makes the difference between both the group significant, but the p value after 10 minutes was 0.236 (>.001), which makes the difference between DBPs

of both the group are not significant at 10 minutes post intubation.

In case of MAP, the p values of 1 minute, 3 minutes were <0.001, which makes the difference between both the group significant, but the p value after10 minutes was>0.001, which makes the difference between both the groups no significant after 10 minutes of intubation.

Table 5: Comparison of SpO_2 between and within the study groups at different points of time

	GROUPS							Significance
	GROUP L			GROUP N			P value	
	Mean	Median	SD	Mean	Median	SD		
SpO_2 – Preop baseline	99.40	99.00	0.49	99.40	99.00	0.49	1.000	Not Significant
SpO_2 – Pre intubation	99.58	100.00	0.50	99.48	99.00	0.50	0.319	Not Significant
SpO_2 – After 1 min	99.50	99.50	0.51	99.40	99.00	0.49	0.317	Not Significant
SpO_2 – After 3 min	99.50	99.50	0.51	99.42	99.00	0.50	0.425	Not Significant
SpO_2 – After 5 min	99.64	100.00	0.48	99.58	100.00	0.50	0.541	Not Significant
SpO_2 – After 10 min	99.48	99.00	0.50	99.46	99.00	0.50	0.842	Not Significant

The two groups were statistically comparable with respect to pulse oximetry measurement. With the p value of >.001 the difference between both the groups was statistically not significant.

Regarding other post-operative complications, two patients in group L and no patient in group N suffered bradycardia. Intravenous Atropine 0.6 gm was administered to normalize the heart rate. 8 patients in group N complained of headache during immediate and early postoperative period which resolved with Paracetamol infusion. Postoperative hypotension was seen in one patient in group L, three patients in group N.

They were treated with intravenous colloid infusion. SpO_2 <92% was seen in two patients in group L, three patients in group N, which was treated with Oxygen 6L/min via facemask. None of them needed re-intubation or postoperative mechanical ventilation. 2 patients in each group complained of shivering in the recovery room which was corrected by covering the patient with warm blanket and oxygen supplementation. Postoperative nausea was complained by 2 patients in each groups L and 3 patients in group N, all of whom were treated with intravenous Ondansetron.

Discussion

The effects of laryngoscopy and intubation on the cardiovascular system were noted in 1940 by Reid LC and Brace DE [11]. They concluded that cardiac reflex could originate in trachea, larynx, bronchi and lungs. They termed the reflex vasovagal as both the afferent and efferent path of the reflex was assumed from Vagus nerve. S Singh and J.E. Smith *et al* in the year 2003 said these changes may be due to stimulation of cardio accelerator nerve fibers implying an increase in cardiac sympathetic tone rather than increase in vagal tone [12].

The main factor mainly influencing the cardiovascular changes associated with laryngoscopy and intubation are age, drugs, type and duration of procedure, hypoxiaand hypercarbia. With aging, variation of heart rate to stressful stimulus decreases

[13]. Marked fluctuations in hemodynamic response have also been reported in geriatric patients [14]. Therefore, patients with an optimum age range of 18 to 45 years, were selected for this study. As we know difficult intubation takes longer time and that will result in marked hemodynamic surge even in pre-medicated healthy individual patient with predicted difficult airway with higher Mallampati grade three and four were excluded from this study.

Lignocaine and GTN both are mainly metabolized by liver and lignocaine is excreted by kidney. Patients with septicemia, diabetes mellitus, autonomic dysfunction, altered sensorium, patient on beta blocker therapy, patient having hepatic disease or renal disease have been excluded from the study. Because if drug toxicity set in we cannot distinguish it in early stage. Mechanism of action of these two drugs are different.

Nitroglycerin acts as a potent vasodilator, it gets absorbed in the mucous membrane, reaches the blood flow and causes coronary vasodilation and causes reflex increase in myocardial contractility and heart rate. By causing systemic vasodilation it causes hypotension. Whereas lignocaine acts as a local anesthetic agent to the oropharynx which prevents sensory stimulation during laryngoscopy and prevents sympatho adrenal surge. In our study, Baseline heart rate was comparable in both the groups. After giving induction agent before performing intubation, there was significant decrease in heart rate in lignocaine group. In lignocaine group the reduction in heart rate was due to cardiac depressant effect of propofol and fentanyl. In nitroglycerin group, there was rise in heart rate. Glycerine tri nitrate (GTN), due to its direct coronary vasodilatory action causes a reflex increase in myocardial contractility and rise in heart rate. The decrease in blood pressure in group N was due to reflex increase in myocardial contractility caused by GTN. Difference between the heart rate was significant from pre-intubation upto 5 minutes post intubation followed by a decreasing trend. All the p values were statistically significant.

The decrease in BP in group N is very significant for all three parameters SBP, DBP and MAP. Since induction, up till 5 minutes after intubation patient remains hypotensive in group N. After that there is gradual rise in blood pressure from 5 to 10 minutes. For all three parameters we are measuring difference in between values of two groups for last recordings of 5and 10 minutes are not significant.

In both groups peak hemodynamic surge were observed in post intubation phase.Post intubation HR in L group was almost same with respect to baseline. Whereas group N there was 21.3% rise in HR at the same time. Their difference in HR was statistically highly significant (p value 0.001)). SBP, DBP and MAP differences in between two groups were nonsignificant 5minutes onwards. This finding shows that plasma catecholamine concentration comes down by 5 minutes after laryngoscopy. This finding is in support with the study by Montazeri *et al* (2011) [15].

In our study, few patients in both groups showed certain dysrhythmias during laryngoscopy and intubation on continuous ECG tracing. These included mostly sinus tachycardia and ventricular premature contractions. All though none of these dysrhythmias reached alarming levels during the study to require treatment and converted to normal sinus rhythm spontaneously. It has been shown by various authors that reflex autonomic responses provoked by laryngoscopy and endotracheal intubation could cause various types of dysrhythmias.

In the year 1995 Hwang JJ, *et al* [16] conducted a study about the use of intra nasal nitroglycerin to prevent pressor response during intubation in general anesthesia. But they concluded intranasal NTG does not attenuate the pressor response to laryngoscopy and tracheal intubation. Jain M, et. al. [17] in the year

2008 conducted a study for efficacy of topical lignocaine spray(10%) applied before the induction of anesthesia and concluded that it was an effective method for attenuating but not abolishing the pressor response to laryngoscopy and intubation without producing an increased risk of hypotension. Qureshi FM *et al* [18] in 2013 and Manjunath HG, *et al* [19] in 2015 did a clinical study with 10% lignocaine spray to show attenuation of hemodynamic response to direct laryngoscopy and intubation and concluded that 10% lignocaine spray is a simple and probably one of the most effective methods in attenuating hemodynamic response. In the year 2016 Kumari I, *et al* [20] found that NTG lingual spray in dose of 0.4 mg (1 spray) or 0.8 mg (2 sprays) was effective in attenuation of intubation induced hemodynamic response, in preventing significant rise in SBP, DBP and MAP compared to control group.

In the year 2017 Madhuri Gopal V *et al*. [21] conducted a comparative study of pressor response to laryngoscopy and intubation with oral spray of nitroglycerin and oropharyngeal spray of lignocaine and concluded that Lignocaine spray group patients who received 10 puffs (100 microgram) oropharyngeal spray 3 minutes before induction, there was a significantrise in the mean heart rate, SBP, DBP, mean arterial pressure occurred one minute following laryngoscopy and intubation than the patients receiving Nitroglycerine spray.

Conclusion

From our study we can conclude that attenuation of heart rate is better with lignocaine nebulization but the attenuation of blood pressure is better with Nitroglycerine nebulization compared after direct laryngoscopy and intubation. A few patients in both groups showed certain dysrhythmias during laryngoscopy and intubation on ECG monitoring. However, none of these dysrhythmias reach alarming levels or required intervention.

Serum catecholamines are the most important markers to access the sympathoadrenal stress response to any stimulus. One of the major limitations of the study is, we could not measure its level at various phases in each patient due to scarcity of resources in this study.

Acknowledgement

The authors would like to thank all patients who took part in the study and entire department of Anaesthesiology and operation theatre personnel.

References

1. Pernerstorfer T, Kraft P, Fitzgerald RD, Krenn CG, Chiari A, Wagner O, Weinstabl C. Stress response to tracheal intubation: direct laryngoscopy compared with blind oral intubation. Anaesthesia 1995; 50:17-22.
2. King BD, Hartris LC, Greifenstein FE, Elder JD, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anaesthesia. Anaesthesiology 1951; 12: 556-66.
3. Boralessa H, Senior DF, Whitman JC. Cardiovascular response to intubation. Anaesthesia 1983; 38: 623-7.
4. Forbes AM, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. Br J Anaesthesia 1970; 42: 618-24.
5. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. Anaesthesiology 1977; 47: 524-5.
6. Bukhar SA, Natasha I, Zargar J, *et al*. Pressor responses and intraocular pressure changes following insertion of laryngeal mask airway: Comparison with tracheal tube insertion. Indian J Anaesth 2003; 47(6): 473-5.
7. Gurulingappa, Aleem MA, Awati MN, Adarsh S. Attenuation of cardiovascular responses to direct laryngoscopes and intubation-A comparative study between IV bolus

fentanyl, lignocaine, and placebo (NS). Journal of clinical and Diagnostic Research. 2012 Dec;6(10):1749-52.
8. J Ashutosh, Pawar D, Bhosle P. Attenuation of pressor response by intravenous labetalol and its Comparison with intravenous lignocaine. Paripex-Indian Journal of Research. 2017 July; 6(7).
9. S Harbhej, Vichitvejpaisal P, G George Y, W Paul F. Comparative effects of lidocaine, esmolol, and nitroglycerin in modifying the hemodynamic response to laryngoscopy and intubation. Journal of Clinical Anaesthesia. 1995 Feb; 7(1): 5-8.
10. Gulabani M, Gurha P, Das P, Kulshreshtha N. Comparative analysis of efficacy of lignocaine 1.5 mg/kg and two different doses of dexmedetomidine (0.5 microgram/kg and 1 microgram/kg) in attenuating the hemodynamic pressure response to laryngoscopy and intubation. Anaesthesia Essays Res. 2015 jan-apr; 9(1): 5-14.
11. Reid, L.C. and Brace, D.E. (1940) Irritation of the Respiratory Tract and Its Reflex Effect upon Heart. Scientific Research Publishing Surgery, Gynecology & Obstetrics, 70, 157-162.
12. S Singh, J E Smith, Cardiovascular changes after the three stages of nasotracheal intubation. Br J Anaesth. 2003 Nov;91(5):667-71.
13. Solanki NM, Solanki RN, Patel RJ, GargA. Effects of dexmedetomidine to attenuate the sympathetic response of Laryngoscopy and intubation and perioperative hemodynamic stability in patients undergoing neurosurgery. 2016; 9(2): 235-240.
14. Bhagavan EH, Sikhakoli S. Efficacy of dexmedetomidine and esmolol in attenuation of pressor response during Laryngoscopy and Endotracheal Intubation. International Journal of Scientific Research. 2018 Apr; 7(4): 41-43.
15. 60. Montazeri K, Kashefi P, Honarmand A, Sefavi M, Hirmanpour A. Attenuation of the pressor response to direct Laryngoscopy and tracheal intubation: oral clonidine vs oral gabapentin premedication. J Res Med Sci. 2011 mar; 16(1): 377-379
16. J J Hwang 1, Y P Ko, R K Jen, Y W Hsu, C R Cheng, T T Wei, C Y Yeh. The use of intranasal nitroglycerin to prevent pressor responses during intubation in general anesthesia--a comparison of various doses Acta Anaesthesiol Sin. 1995 Dec;33(4):205-10
17. Jain M, Gurcoo S, Shora A, Qazi M, Dar B, Buchh V *et al*. Efficacy of Topical Lignocaine Spray (10%) Applied Before the Induction of Anaesthesia in Attenuating the Pressor Response to Direct Laryngoscopy and Endotracheal Intubation in Controlled Hypertensive Patients. The Internet Journal of Anaesthesiology. 2008(20)2.
18. Qureshi F M, Padmanabha S, Rahaman H, Imran S, Mohan P R. Efficacy and Optimal time of oropharyngeal topical 10% lignocaine spray before induction of anaesthesia in attenuating the pressor response to direct Laryngoscopy and Endotracheal Intubation. IOSR Journal of Dental and Medical Sciences. 2013 Sep-oct; 9(6): 57-63.
19. Manjunath H G, Ravi L. Attenuation of hemodynamic response to direct laryngoscopy and intubation using 10% Lignocaine spray: A clinical study. J of Evolution of Med and Dent sci. 2015 Jan; 4(4): 644-9.
20. Kumari I, Naithani U, Dadheech VK, Pradeep DS, Meena K, Verma D. Attenuation of pressor response following intubation: Efficacy of nitroglycerin lingual spray. 2016;32(1): 69-73.
21. V. Madhuri Gopal. Comparative study of pressor response to Laryngoscopy and intubation with oral spray of nitroglycerin and oropharyngeal spray of lignocaine. Sch. J. App. Med. Sci., 2017; 5(4D): 1463-69.