A Comparative Study of Intravenous Nitroglycerin With or Without Intravenous Lignocaine for Attenuation of Stress Responses to Endotracheal Intubation

Regmi NK\(^1\), Singh G\(^2\)

ABSTRACT

**Background:** Laryngoscopy and tracheal intubation lead to stress response which is characterized by transient rise in blood pressure and heart rate. This response is tolerated well in normal individuals but can lead to significant morbidity and mortality in patients with cardiovascular and cerebrovascular diseases. Search for the better drugs to suppress these responses is going on through decades. **Aim of Study:** To compare the effects of IV nitroglycerin alone and in combination with IV lignocaine, on attenuation of stress response to endotracheal intubation. **Material and Methods:** This is a randomized, double blind study conducted in 60 patients admitted for operation at NGMCH, between June 2018 to November 2018. Patients were of 16-60 years age groups and belonging to ASA group I and II. Patients were divided into two groups: Group I IV Nitroglycerin 500 mcg+ NS 3 ml. (n=30) and Group II IV Nitroglycerin 500 mcg+ IV Lignocaine 63 mg (n=30). Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) and Heart rate (HR) were measured and Rate Pressure Product (RPP) calculated. **Results:** Baseline values were comparable in both groups. Post Intubation, there was significant decrease in SBP at 0,1,3 and 5 minutes while DBP and MAP significantly decreased at 1, 3 and 5 minutes. Significant tachycardia was noted in both groups at 0,1and 3 minutes, and RPP remained unchanged in both groups. **Conclusion:** Nitroglycerin significantly decreases blood pressure, prevents rise in RPP but does not attenuate heart rate after endotracheal intubation. There is no benefit of adding IV lignocaine to IV nitroglycerin for attenuation of stress response to endotracheal intubation.

**Key Words:** Nitroglycerin, lignocaine, intubation, stress response.

INTRODUCTION:

Laryngoscopy and endotracheal intubation leads to an average increase in blood pressure by 40-50% and heart rate by 20%\(^6\). Although, these hemodynamic changes after intubation cause no significant morbidity in healthy individuals, these can lead to hypertensive crisis, pulmonary edema, cardiac dysrhythmias, myocardial ischemia, and cerebral hemorrhage in the presence of cardiovascular and cerebrovascular disease\(^7,8\).

A wide variety of pharmacological agents are used to attenuate the hemodynamic responses to endotracheal intubation, like lignocaine, fentanyl, alfentanil, remifentanil, nifedipine, beta-blockers, gabapentin, nitroglycerin, magnesium sulfate, verapamil, nicardipine, diltiazem with varying results\(^4\). Among these drugs, the advantage of using nitroglycerin (NTG) during intubation is that, while a desirable and transient hypotension is achieved, cardiac output is not likely to decrease\(^5\). In addition, it has cardioprotective effect\(^5\). Most of the studies have found that NTG successfully prevent increase in BP, although it does not attenuate heart rate\(^9,7,8\).

Lignocaine is class IB antiarrhythmic drugs commonly used for attenuation of haemodynamic response to laryngoscopy and intubation as it is devoid of cardiovascular side effects except when used in larger doses.\(^7\) Studies have shown that it significantly reduces heart rate post intubation\(^10,11\). On search of ideal drugs and technique to blunt these effects, some anesthesiologists are even combining two drugs based on their pharmacological action\(^11,12\). In this study we combined these cardioprotective and antiarrhythmic drugs.

**MATERIAL AND METHODS:**

This is a prospective, randomized, double blind study. This study was conducted from June 2018 to November 2018 in the Department of Anaesthesiology, Nepalgunj Medical College, after taking approval from Institution Review Committee. 60 patients were enrolled for the study. Patient of age 16 to 60 years, ASA physical status I and II, scheduled for surgery under general anaesthesia and giving consents for the study were taken as study samples. Patients with hypertension, ASA grade III and IV, patient suspected of difficult intubation and endotracheal intubation taking more than 30 seconds were excluded from the study.

All patients were admitted to the hospital at least a day before surgery and routine pre anesthetic checkup followed by premedication with diazepam 5 mg and pantoprazole 40 mg was done. On arrival in operation room pulse-oximeter, blood pressure, electrocardiogram, were applied and the patients' SBP, DBP, MAP, HR and RPP were measured and taken as baseline values. All patients received 0.2 mg glycopyrrolate and

1. Dr. Nabin Kumar Regmi
2. Dr. Grisuna Singh

**Address for correspondence:**
Dr. Nabin Kumar Regmi
Department of Anaesthesia
Nepalgunj Medical College and Teaching Hospital
Nepalgunj, Banke, Nepal
Email: nabinkums@gmail.com

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2 mg midazolam before induction. Fentanyl, Propofol and vecuronium were used for GA.

Patients were randomly divided to 2 groups in a double blind manner.
Group I: IV Nitroglycerin 500 mcg + 3 ml NS
Group II: IV Nitroglycerin 500 mcg + 63 mg Lignocaine (Volume= 3 ml)
Study drugs were given as bolus dose during induction of anaesthesia. Time just after intubation was taken as 0 minute.

In both groups there was significant decrease in SBP, DBP and MAP from their baselines. DBP 0 min and MAP 0 min were exception in both groups, as the decrease was not statistically significant. The highest decrease was observed at 3 minutes from intubation.

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<thead>
<tr>
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<th>Group I</th>
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<tr>
<td></td>
<td>N</td>
<td>Mean</td>
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<tr>
<td>SBP Baseline</td>
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<tr>
<td>DBP Baseline</td>
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<tr>
<td>MAP Baseline</td>
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<td>HR Baseline</td>
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<td>90.97</td>
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<tr>
<td>RPP Baseline</td>
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Table I: Comparison of Baseline Variables between the groups

In both groups there was significant decrease in SBP, DBP and MAP from their baselines. DBP 0 min and MAP 0 min were exception in both the groups, as the decrease was not statistically significant. The highest decrease was observed at 3 minutes from intubation.

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<td>N</td>
<td>Mean</td>
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<td>MAP Baseline</td>
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<tr>
<td>MAP 0 min</td>
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<td>MAP 1 min</td>
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<td>MAP 3 min</td>
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<td>MAP 5 min</td>
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Table II: Comparison of MAP of two groups from their baseline values.

**Statistical Analysis:**
Data was analyzed using SPSS 20. Independent sample t test, for comparison of variables among the groups and one sample t test, for comparison of variable within the groups were used. P value less than 0.05 was considered significant.

**RESULTS**
The mean age of group I and group II were, 34.37 and 33.03 respectively. The difference was statistically insignificant. There was no any significant difference on baseline variables (SBP, DBP, MAP, HR, RPP), between the groups.

**DISCUSSION:**
Reid and Brace in 1940 and by King et al in 1951 following laryngoscopy and intubation was documented by the circulatory response to laryngeal and tracheal stimulation. The circulatory response to laryngeal and tracheal stimulation is a sympathetic reflex, preventing increases in intracranial pressure, because of its theoretical advantages of suppressing cough response with response of NTG alone. NTG produce reduction in blood pressure but they do not blunt attenuating circulatory responses, reflex, preventing increases in intracranial pressure, excessive Excessive endotracheal intubation therapy are limitations to its use.
anaesthesia. Time just after intubation was taken as 0 minute. Study drugs were given as bolus dose during induction of

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<td></td>
<td>N</td>
<td>Mean</td>
<td>Std. Deviation</td>
<td>P Value</td>
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<tr>
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<td>HR 3 min</td>
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<tr>
<td>HR 5 min</td>
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<td>94.87</td>
<td>16.404</td>
<td>.203</td>
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Table III: Comparison of HR of two groups from their baseline values.

The pattern of change in heart rate was similar in both groups. Heart rate significantly increased just after intubation in both groups and gradually decreased. It reached to statistically insignificant level only on 5 min.

DISCUSSION:
The circulatory response to laryngeal and tracheal stimulation following laryngoscopy and intubation was documented by Reid and Brace in 1940 and by King et al in 1951. The response to laryngoscopy and intubation is a sympathetic reflex that is provoked by stimulation of the oro-laryngopharynx.

Dexmedetomidine although have good result for attenuation of intubation response, side effects like bradycardia and hypotension, necessitating need for pharmacological rescue therapy are limitations to its use. Short acting opioids appear to have a reliable and constant effect but they may contribute to truncal rigidity and prolong recovery time from general anaesthesia in addition to respiratory depression. Excessive negative chronotropic and inotropic action of the β-receptor blockers may reduce coronary perfusion and precipitate heart failure in susceptible patients. Vasodilators like intravenous NTG produce reduction in blood pressure but they do not blunt rise in heart rate. So, no single drugs can be concluded as ideal drugs for blunting intubation response. This is why in this chose to combine IV lignocaine with IV NTG and compare the response with response of NTG alone.

Nitroglycerine is an organic nitrate that acts principally on venous capacitance vessels and large coronary arteries to produce peripheral pooling of blood and decrease cardiac ventricular wall tension. Thus NTG may increase the coronary blood flow and oxygen delivery to the myocardium. NTG had been administered intranasally, or parenterally as a bolus or infusion to attenuate hemodynamic responses during laryngoscopy.

Lignocaine is an aminoethylamide and prototype of amide local anesthetic group. In 1961, Bromage showed that use of intravenous (IV) lignocaine blunted pressure response to intubation. Intravenous lidocaine has been popular probably because of its theoretical advantages of suppressing cough reflex, preventing increases in intracranial pressure, attenuating circulatory responses, and its antiarrhythmic properties.

In our study, demographic profile and baseline hemodynamic parameters i.e., SBP, DBP, MAP, HR and RPP were compared among both groups. Individual hemodynamic parameters in each group were compared with their baseline values. When compared to the baseline values, just after intubation (0 min), there was significant reduction in SBP, but no significant changes in DBP and MAP in both groups. In 1, 3 and 5 minutes...
there was significant reduction of blood pressure in both groups. At 5 minutes 20% (n=6) individuals in Group I and 23% (n=7) individuals in Group II had hypertension. The hypotension was managed with fast IV fluids and decreasing isoflurane, whereas 1 individuals from each group required 6 mg IV mephenetermine. Kumar N et al in their study found lower increase in SBP, DBP and MAP following administration of 2 mcg/kg NTG, but in our case hypotension have been associated because of higher drug dose, 500 mcg for all individuals.

In both groups, the heart rate was significantly greater at 0, 1and 3 minutes. It settled down to the baseline level at 5 min. Similar to this study, Kumari I et al in her study observed that NTG does not attenuate the rise in HR. Previous studies have also documented that NTG does not attenuate the rise in HR after intubation which can be attributed to reflex tachycardia produced by vasodilation.

There was no significant change in RPP from their baselines, in both groups. This study showed that adding lignocaine had no extra effect than NTG alone. This is consistent with studies done by Vanden Berg AA, Sawa D and Honjol NM. Padmawar S and Patil M also showed that IV lignocaine did not have any effect on the hemodynamic changes following intubation.

CONCLUSION
Nitroglycerin significantly decreases blood pressure, prevents rise in RPP but does not attenuate heart rate after endotracheal intubation. There is no benefit of adding IV lignocaine to IV nitroglycerin for attenuation of stress response to endotracheal intubation.

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