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Attenuation of stress response to laryngoscopy and intubation: Sublingual nitroglycerin spray vs intravenous fentanyl and sublingual nitroglycerin spray

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Abstract

Background and aim: Laryngoscopy and endotracheal intubation is associated with cardiovascular changes such as tachycardia and hypertension which may be detrimental to patients with limited cardiovascular reserve. Many pharmacological agents have been used to attenuate the stress responses but none has been found ideal. Our aim of this study is to compare the efficacy of sublingual Nitroglycerine spray alone and sublingual Nitroglycerine spray with intravenous Fentanyl to attenuate the stress response to laryngoscopy and endotracheal intubation.

Methods: A total of 90ASA I and II patients of age group 20-60 years scheduled for elective surgery under general anesthesia were randomly divided into 3 groups of 30 in each group. Group 1 received normal saline (control group), Group 2 received NTG sub-lingual spray (0.4mg/spray) two min. before induction, and Group 3 received inj. Fentanyl (2µg/kg) 5min before induction + NTG sub-lingual spray (0.4 mg/spray) 2min before induction. Vital parameters like HR,SBP,DBP and MAP before and after induction and thereafter at specified time interval following laryngoscopy and intubation were recorded and analyzed.

Results: Demographic characteristics and baseline parameters in both the groups were comparable. Significant differences in parameters like SBP,DBP, MAP and heart rate were recorded in between the groups after intubation.

Conclusions: Combination of intravenous Fentanyl plus Nitroglycerin spray is more potent than NTG spray alone in preventing the stress response following laryngoscopy and endotracheal intubation.

Keywords: Endotracheal intubation, Fentanyl, Nitroglycerine,stress response.

Introduction

Laryngoscopy and endotracheal intubation can cause dangerous hemodynamic stress response . A typical stress response can include increase in blood pressure, increase in heart rate, and an elevation of both epinephrine and norepinephrine levels.[1] These effects usually occur within seconds of intubation and last more than ten minutes. Usually they are tolerated well by healthy patients. However, these same effects can be dangerous in patients with preexisting conditions such as hypertension and coronary artery disease. A wide variety of pharmacological agents were used to attenuate the hemodynamic responses to laryngoscopy and endotracheal intubation like clonidine,dexmedetomidine,lignocaine, fentanyl, alfentanil, remifentanil, nifedipine, beta-blockers, gabapentin, magnesium sulfate,verapamil, nicardipin and diltiazem with varying results but none is ideal.[2,3]Among opioids fentanyl is commonly used as it is cost-effective and brings many other advantages.[4] Fentanyl is a μ-opioid receptor agonist that is characterized by high potency, rapid onset, and short duration of action.But fentanyl alone can not prevent stress response adequately.[5] Glyceryl trinitrate relaxes vascular smooth muscles with predominant venous dilation over arterial dilation. NTG had been administered intranasally and parenterally as a bolus or infusion to attenuate hemodynamic stress responses during laryngoscopy and intubation particularly in patients with coronary artery diseases.[6] Recently NTG lingual pump spray has been introduced, for spraying under the tongue.[7,8] Use of NTG spray for attenuating stress response of laryngoscopy and endotracheal intubation has been little evaluated. We conducted this study to evaluate the role of of NTG spray before intubation for attenuation of hemodynamic stress response to endotracheal intubation.Administration of NTG alone during pre-intubation may not be adequate to completely negate the hemodynamic response due to its tendency to produce tachycardia. So a combination of drug therapy may be able to better blunt this response adequately.[9] Till date, few studies have evaluated the combination of fentanyl and NTG spray with respect to their affect on hemodynamic stress response . So we have evaluated efficacy of NTG spray and NTG spray with fentanyl for prevention of stress response due to endotracheal intubation.

Methods

This was a prospective, randomized and controlled study, which was conducted in 90 patients. Patients ,aged 20-60 years of both sexes belonging to ASA grade I and II posted for elective non cardiac surgery requiring endotracheal intubation were enrolled in this study. A written informed consent was taken from all the patients.Patients belonging to ASA III and IV, patients with other co-morbid illness like diabetes, hypertension, respiratory disease, hepatic or renal derangements, patients on antipsychotic medication, and history of drug allergy were excluded from the study.

A detailed pre-anaesthetic evaluation was done and all routine investigations were checked. All patients were explained about the anaesthesia technique. All patients were given tablet Alprazolam 0.5 mg orally on the night before the operation and preoperative fasting for 8 hours was advised. Patients were randomly allocated and divided into three groups of 40 each. On arrival in operation theatre pulse-oximeter, noninvasive blood pressure and electrocardiogram were connected and the patient's HR, SBP, DBP, MAP and oxygen saturation (SpO_2) were recorded as baseline data. After securing a peripheral intravenous line, infusion of Ringer lactate (8 ml/kg) was started before induction. Patients were premedicated with glycopyrrolate (0.2 mg) and

nalbuphine (10 mg) intravenously.All the patients were preoxygenated for 3 min, and anesthesia was induced with propofol (2 mg/kg) and vecuronium Bromide 0.1mg/kg. Anesthesia was maintained with 66.66% N2O in O2 and isoflurane (0.5-1%) and vecuronium top-up doses as necessary. 90 patients were divided into following three groups.

- Group-1: Control group received normal saline infusion.
- Group-2:NTG sub-lingual spray (0.4 mg/spray) two min. before induction.
- Group-3: inj. Fentanyl (2µg/kg) 5min before + NTG sub-lingual spray (0.4 mg/spray) 2min before induction.

HR, SBP, DBP and MAP were recorded at T: Baseline(before premedication), T0: Just before intubation, T1: 1min after intubation, T3: 3 min after intubation, and T5: 5 min after intubation. Any incidence of hypotension (fall in SBP >20% from baseline), hypertension (rise in SBP >20% from baseline), bradycardia (fall in HR>20% from baseline), tachycardia (rise in HR >20% of baseline), arrhythmias, and ST-T changes etc. were observed and treated accordingly. Based on a pilot study a sample size of 5 per group with type I error of 0.05 and type II error of 0.20, for 25% difference in MAP between groups, sample size was calculated to be 25.So total of 90 patients were enrolled to include 30 in each group. The data were recorded on predesigned and pretested proforma, and was tabulated and master chart was prepared in Microsoft Excel 2007. Demographic data, heart Rate (HR), systolic BP, diastolic BP and mean arterial pressure (MAP) were tabulated as Mean and Standard deviation. Statistical significance was tested by ANNOVA test with Post hoc analysis. Paired student t-test was used for analyses within the group and unpaired Student t-test was used for comparison between the groups. All analysis was done by using two tailed test, with P-value of less than 0.05 was considered significant.

Results

Demographic characteristics of patients were comparable. No significant difference was observed among the groups (p >0.05).(table-1)

Table 1: Demographic Data

Variables		**Group1**	**Group2**	**Group3**
Age (years)		37.70±1	42.80±12.	40.1±12.
Weight (kg)		52.00±7.	54.43±6.2	53.57±5.
Sex	Male	16	12	17
	Female	14	18	13
ASA grade	I	12	13	20
	II	18	17	10
Type of surgery	Cholecystectomy	7	9	8
	Exploratory laparotomy	7	6	8
	Modified radical	6	6	7
	Pyelolithotomy	9	5	2
	Others	1	4	5
Duration of laryngoscopy(sec)		21.72±3.56	19.52±4.07	20.08±3.89

Fig1: Group comparison of heart rate(HR)

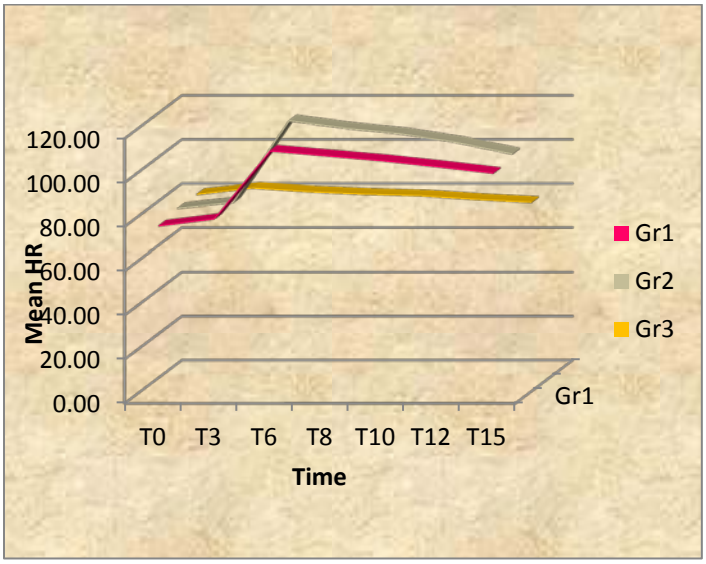
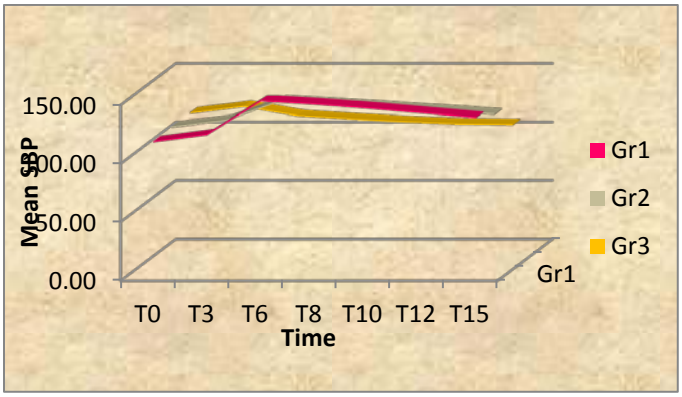


Fig2:Group comparison of systolic blood pressure(SBP)



Rise in heart rate,SBP,DBP and MAP in post-intubation periods were more in group 1 compared to group 2 and 3 which was statistically significant. (figure 1-4)

Fig3: Group comparison of diastolic blood pressure (DBP)

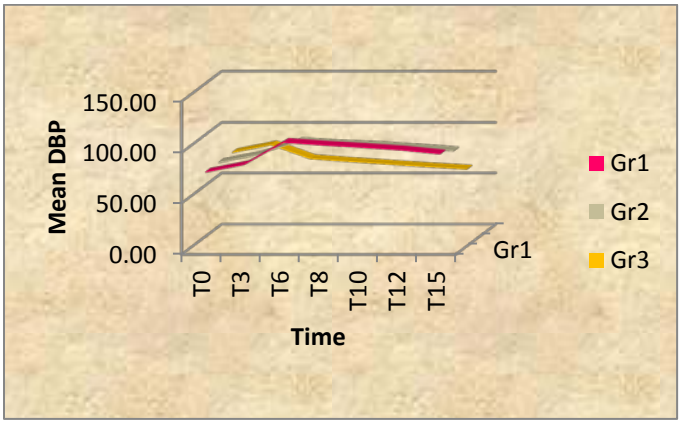


Fig4: Group comparison of mean arterial pressure(MAP)

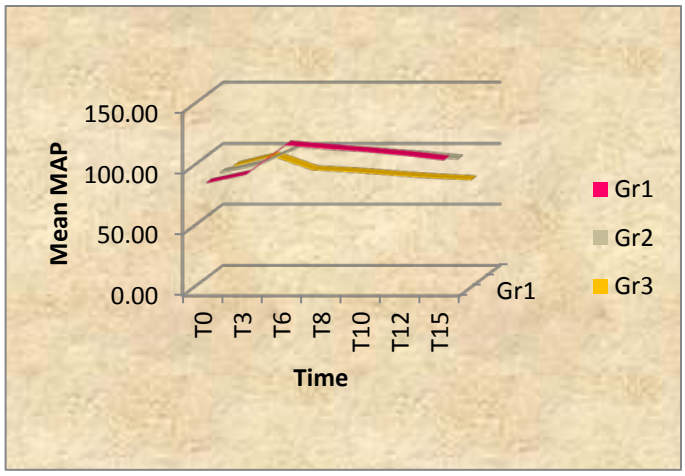
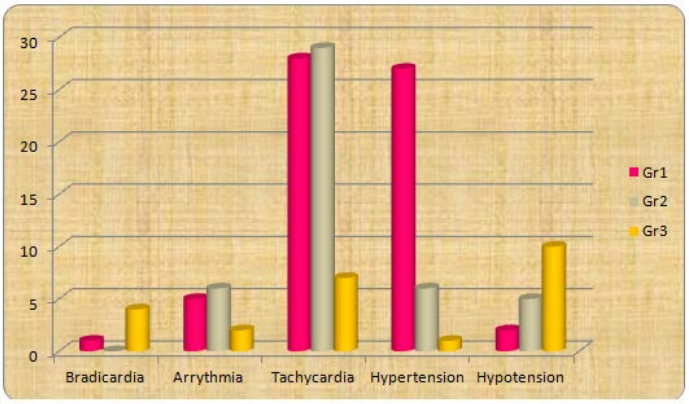


Fig5: Group comparison of adverse effects



Adverse effects like tachyarrhythmia and hypertension was seen in group 1 and group 2 in comparison to group 3 which was statistically significant. (figure 5)

Discussion

It has been shown that fentanyl can prevent elevation in HR, SBP, DBP, and MAP that result from endotracheal intubation. However, the use of fentanyl alone may not be sufficient to completely suppress hemodynamic stress response.[10,11,12] NTG was chosen to be used with fentanyl due to its ability to slowly decrease blood pressure and reduce the requirements of fentanyl. The mechanism of action for opioids like fentanyl includes the activation of the nitric oxide (NO)/cyclic-guanosine monophosphate (cGMP) pathway. NTG could serve as additional NO source thus possibly increase the effectiveness of fentanyl in attenuating the hemodynamic response during intubation.[13,14,15] We concluded that the attenuation of

stress response observed using the fentanyl-NTG combination was better than NTG spray alone. At all time intervals T-3 through T-15,HR,SBP, DBP and MAP in fentanyl-NTG group were lower than those of the control and NTG only group. This suggests that the use of NTG in conjunction with fentanyl increased the overall effectiveness of fentanyl on HR,SBP,DBP and MAP at specific time intervals. Few studies are in disagreement with our study. In a clinical trial where NTG was used in combination with fentanyl and pancuronium for anesthesia, the hemodynamics of the fentanyl-pancuronium and placebo groups were identical after induction.[16] Another study also concluded that combining NTG with fentanyl and pancuronium failed to attenuate hemodynamic pressor responses when the NTG dosage was 5 $\mu g/kg^{-1}/min^{-1}$ [17] These effects may be due to use of pancuronium for which we have used vecuronium. The principal advantage of using NTG is that, while a desirable and transient hypotension is achieved, cardiac output is not likely to decrease. Preload reduction and accompanying decrease in ventricular end-diastolic pressure reduces myocardial oxygen demand and increases endocardial perfusion by dilating the coronary vessels.NTG may increase the coronary blood flow and oxygen delivery to the myocardium.[18]Myocardial oxygen consumption (as measured by the pressure-rate product, tension-time index, and stroke-work index) is decreased by both the arterial and venous effects of NTG resulting in a more favourable supply-demand ratio. Previous studies have also found conclusions that were similar to our study's findings.[19,20] There is a lot of potential for the use fentanyl and NTG spray combine in preventing stress response. When administered in the proper dosage, combination of drugs like fentanyl and NTG spray could be used to produce better hemodynamic response which was confirmed in our study.

Conclusion

Combination of intravenous Fentanyl plus Nitroglycerin spray is more effective than NTG alone in attenuating the hemodynamic response following laryngoscopy and intubation without any major side effects. However, more studies in patients with hypertension and coronary artery diseases is required to prove its use fullness.

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