Original Article

4 INTRAVENOUS LIGNOCAINE AND INTRAVENOUS LIGNOCAINE PLUS NITROGLYCERINE LINGUAL SPRAY IN ATTENUATION OF HEMODYNAMIC RESPONSES TO TRACHEAL INTUBATION IN CONTROLLED HYPERTENSIVE PATIENTS: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL AUTHORS Kumari Indira[1],BugaliyaPradeep Kumar[2],BhagwaniDharmesh Kumar[3], Bedi Vikram[4], SinghalYogendra[5]GargAnkush Kumar[6]

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INTRAVENOUS LIGNOCAINE AND INTRAVENOUS LIGNOCAINE PLUS NITROGLYCERINE LINGUAL SPRAY IN ATTENUATION OF HEMODYNAMIC RESPONSES TO TRACHEAL INTUBATION IN CONTROLLED HYPERTENSIVE PATIENTS: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

Abstract

Aims and objectives: To evaluate the efficacy of nitroglycerine (NTG) lingual spray in attenuation of hemodynamic responses following laryngoscopy and intubation in controlled hypertensive patients.**Materials and method:** 60 patients scheduled for elective surgeries,

requiring endotracheal intubationwere randomized in two groups (30 patients in each group).Group C the control group received lignocaine 1.5 mg/kg intravenously and Group S the study groupreceived lignocaine 1.5 mg/kg intravenous plus one metered spray (400µg) of nitroglycerine (NTG) lingually after induction.**Results:** The changes in heart rate were comparable in both groups. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) significantly increased in group C when compared to group S from baseline values ($P<0.05$, $P<0.05$ and $P<0.01$ respectively). Mean rate pressure product **(**RPP) rose significantly from baseline following laryngoscopy and tracheal intubation in both groups. Maximum rise in RPP was 44.18% in group C at 1min as compared to 26.3% in group S at 2min. However,this difference was statistically not significant. **Conclusion:** The present study failed to demonstrate any significant reduction in the pressor response to laryngoscopy and intubation as measured by RPP in controlled hypertensive patient by addition of NTG spray to lignocaine when compared to lignocaine alone. However, the addition of one puff of (400 µg) NTG spray to lignocaine may offer some benefit in patients at an increased risk ofadvanced cardiovascularevents dueto transient decreasein MAP.

Key words: Nitroglycerine, Laryngoscopy, Intubation, Hypertensive patients, Pressor response.

Introduction

The sympathetic response to laryngoscopy and Endotracheal intubation is a well-knownproblem that has been challenging anaesthesiologists for several decades.[1]The resultant tachycardia and hypertension from this response pose an enhanced risk to patients with systemic hypertension and may result in left ventricular failure , arrhythmias and myocardial infraction.[2]

A number of agents have been evaluatedforobtundation of the response,with varying degree of success.[3]

Nitroglycerine (NTG) causes dilatation of the arterioles and post capillary vessels.This causes reduction in systolic, diastolic and mean arterial pressure and is therefore useful for attenuating thepressor response to intubation.NTGlingual spray isametered dose spray which delivers400µg puffs in form of droplets on or under the tongue.It has successfully been used to bluntthepressorresponse in normotensive patients,[4]however there is not much literature on its use in hypertensive patients.

The present study was planned to evaluate the effect of NTG spray in attenuating the pressor response in controlled hypertensive patients.

Materials And Methods

The study was carried out in a thousand beded tertiary care teaching hospital. The institutional ethical committee clearance was obtained prior to commencement of the study. An informed, written consent was taken from each participant prior to enrolling them in study.

This study was designed as a prospective, double blinded,Randomised control trial.Sixty patients of either sex, aged 40-60 yrs, belonging to ASA(American Society of Anaesthesiology) physical status II with hypertension, controlled on medication (BP<140/90mmHg) and posted for elective surgery under general anaesthesia requiring endotracheal intubation were included and those with anticipated difficult airway, morbid obesity, ASA physical grade III or higher, history of coronary artery diseases (CAD), cardiac arrhythmia,neuromuscular disease, known allergy to anaesthetic or any other drug and those taking phosphodiesterase inhibitorswere excluded from the study.

The calculated sample size was based on a pilot study,in which we found that the mean BP immediately after intubation rose by 24 mmHg in the lignocaine 1.5 mg/kg intravenously over a period of 5-10 seconds as compared to 8 mmHg in lignocaine plus NTG (400µg per spray), difference of 16 mmHg seen. The standardized difference for the two groups was 0.88. For the study to have a power 90% with a type 1 error of <0.05%, we needed 55 patients in two groups. Therefore we decided to include 30 patients in each group to compensate for dropouts.

Sixty patients were allocated randomly in 2 groups (30 patients in each group) using anopaque sealed envelope technique and a computer generated sequence of random numbers, opened just before the start of surgery.The patients in control group(group C) were scheduled to receive inj. Lignocaine (Xylocard,ASTRA ZENECA INDIA LTD) 1.5 mg/kg intravenously over a period of 5-10 seconds and patients in study group (Group S) were scheduled to receive Lignocaine(Xylocard,ASTRA ZENECA INDIA LTD) 1.5 mg/kg intravenously over a period of 5-10 seconds plus one metered spray (400µg per spray) of Nitroglycerine (NITROCIN,SAMARTH PHARMA PVT.LTD)lingualy.

After a detailed pre anaesthetic evaluation, all patients were kept NBM for at least 6 hours before surgery. On night before surgery tablet alprazolam 0.5 mg and ranitidine 150 mg were given. All antihypertensive drugs were continued up to the morning of surgery except ACE inhibitors. Routine monitoring consisting of ECG, BP, &pulse oximetry were used and patient's base line HR, SBP, DBP, MAP and SPO_2 were recorded.

After taking peripheral intravenous line, crystalloid infusion (8ml/kg) was started and premedication was done with glycopyrrolate (0.2mg), ondansetron (4mg) and fentanyl (2mcg/kg) intravenously. Preoxygenation wasdone for 3 min and anaesthesia induced with injection

propofol (2mg / kg) until loss of verbal response and muscle relaxation done with rocuronium (0.9mg/kg) over a 15 seconds period.Immediately after induction lignocaine (1.5 mg/kg) was given intravenously in control group C and lignocaine (1.5 mg/kg) intravenously plus nitroglycerine one metered dose (onthe tongue) in study group S. After 60sec laryngoscopy was attempted by an experienced anaesthesiologist. If laryngoscopy time exceeded 30 seconds or multiple attempts were required for intubation, patient was excluded from study.

After confirmation of endotracheal tube position with help of $EtCO_2$ measurement, anaesthesia was maintained using 60% N_2O in 40%O_2, isoflurane and intermittent doses of rocuronium.

SBP, DBP, MAP and HR were recorded as baseline (T_1), just before intubation (i.e. 60 sec after NTG spray) (T_2), immediately after intubation (T_3), at 1min (T_4), 2min (T_5), 5min (T_6), and 10min (T_7) after intubation.The surgery was allowed to commence thereafter. This was done to negate the influence of surgical stimulus on hemodynamic parameters. Rate pressure product (RPP) was calculated at each time interval by multiplying SBP and HR.

Data were analysed using MS Excel and EpiInfo 6 system. The data related to patient distribution according to age, weight, indication for surgery, type of surgery were presented as number (proportion) and compared by using Pearson chi-square test. All parameters like HR, SBP, DBP, MBP and RPP were expressed as mean±SD and compared using student t-test and Pearson's chi-square test.

Results

The patients in both groups were comparable in age, weight, gender, distribution of surgeries and duration of laryngoscopy.

A significant increase in HR occurred in Group S at1 min 104.77±14.9 and 10 min 107.37±13.3when compared to Group C at 1 min 112.7±13.9 and 10 min 93.63±7.72 post laryngoscopy(P=0.710 and 0.004 respectively).**Fig.1**

The mean arterial pressure was significantly greater in Group C 1 min 111.93±7.27 and 2min 109.07±6.84 when compared to Group S at 1min 106.17±4.36 and 2 min 103.63±3.99 (P=0.007 and 0.004 respectively).**Fig.2**

There was no significant difference in the RPP amongst the two groups at all period of observation (Table 1).

	RPP(Mean±SD)		P value
Time interval	Group C (n=30)	Group S (n=30)	C/S
T_1: Baseline (Before Premedication)	11480±1167.1	11414±1372.6	0.387

T_2: Before Intubation (1 min after induction & study drug)	11646±1357.9	11667±1961.6	0.052
T_3: Just after Intubation (0 Min.)	13985±1977.51	13233±2122.9	0.705
T_4: 1 Min after Intubation	16553±2725.3	14310±2232.7	0.288
T_5: 2 Min after Intubation	15748±2651.2	14413±2037.5	0.162
T_6: 5 Min after Intubation	13620±1591.2	13991±1876.9	0.378
T_7: 10 Min after Intubation	12338±1196.9	13689±1683.3	0.071

(Data are expressed in mean±SD, range; test used-student t test)

Table 1:Comparison of changes in rate pressure product (RPP) at various time intervals in Group C and S

Discussion

Laryngoscopy and tracheal intubation are universally recognized as one of the most noxious stimuli occurring during general anaesthesia and surgery and result in exaggerated sympathetic response (an increase in blood pressure, tachycardia and blood sugar) due to catecholamine release.

Hypertensive patients show an enhanced hemodynamic response to laryngoscopy and tracheal intubation. However, regardless of the preoperative blood pressure control, many patients with hypertension display an accentuated hypotensive response to induction of

anaesthesia, followed by an exaggerated hypertensive response to endotracheal intubation. This response was first described by Reid and Brace in 1940.[5] In normotensive individuals, the average increase in blood pressure is 40-50% while that in the heart rate is 20%, the peak effect occurring one minute after tracheal intubation.[6]

Several potential life threatening conditions including myocardial ischemia and cerebrovascular accident can be reduced by attenuation of this response with use of several pharmacological agents (eg. local anaesthetic like lignocaine,[7] alfentanil,[8] fentanyl,[8] remifentanil,[8] nifedipine,[9] betablockers,[3]verapamil,[10]diltiazem,[10] gabapentin,[11] magnesium sulphate,[12] nicardipine[13)]. All of these techniques have disadvantages related to either cardiovascular or respiratory depression; none directly inhibits the release of catecholamines.

Lignocainealso has direct myocardial depressant effect, peripheral vasodilating effect and the effect on synaptic transmission.[7,14]

Glyceryltrinitrate (NTG) is a vasodilator predominantly venous over arterial dilation. Due to venodilation it decreases the preload and blunts the hypertensive response of intubation reflex.In the patients with low cardiac output and moderately elevated vascular resistance it seems to be the best choice.[14]

NTG has been administered by intranasal route,[16] intravenous bolus[17] and i.v. infusion[18,19]to attenuate tracheal intubation induced hypertensive response and favourable results have been reported.Recently NTG lingual pump spray, or pen spray have been introduced, for spraying on to or under tongue. Its use has been recommended during an anginal attack; it may also be used 5 to 10 min prior to engaging in activities which might provoke an acute attack. NTG spray is easy to use and seems cost effective because there are approximately 70 metered sprays of NTG per pen spray.[20]

The present study was an attempt to find out the effectivity of NTG spray in blunting the pressor response to intubation in hypertensive patients.

In order to eliminate the pressor response to surgical stimuli, the surgery was allowed to commence 10 min after intubation.This ensured that the haemodynamic changes reflected were only due to laryngoscopy and intubation.

Furthermore lignocaine was administered in both groups to ensure that all patients were given the benefit of obtundation of the pressor response.A significant increase in HR occurred in Group S at 1 min 104.77±14.9 and 10 min 107.37±13.3when compared to Group C at 1 min 112.7±13.9 and 10 min 93.63±7.72 post laryngoscopy(P=0.710 and 0.004 respectively).

The mean arterial pressure was significantly greater in Group C 1 min 111.93±7.27 and 2 min 109.07±6.84 when compared to Group S at 1min 106.17±4.36 and 2 min 103.63±3.99 (P=0.007 and 0.004 respectively).

We have used the RPP as a measure of pressor response because it is the index which best correlates with myocardial O_2 consumption (MVO2) and is therefore the critical one in defining response of coronary circulation to myocardial metabolic demands. RPP is also an important indicator of ventricular functional status.

Usually, invasive methods are used to determine the oxygen consumption (VO2max) of an organ by collecting blood sample and subjecting it for blood gas analysis which is a tedious, time consuming and risky process. But determination of RPP is a very handy, non-invasive, simple, reliable and reproducible method of knowing VO2max and serving the same purpose.

The present study has shown that the use of NTG spray along with lignocaine does not result in sustained suppression of the pressor response to laryngoscopy and when compared with lignocaine alone.

However the use of the NTG did result in decrease in MAP at 1 and 2 min post laryngoscopy when compare to lignocaine alone, along with increase in HR at 1 min.The increase in HR and decrease in MAP can be explained by the pharmacological action of NTG confirm to earlier findings reported by Fassoulaki[16] and Dich-Nielsen et al.[21]

Similar results were also reported by Mikawa et al[18]they concluded that a single, rapid IV dose of nitroglycerin is a simple, practical, effective, and safe method to attenuate the hypertensive response to laryngoscopy and tracheal intubation whereasGrover et al [22]found no change in HR post laryngoscopy and intubation in hypertensive patients pretreated with intranasal NTG .This may be because all in their study were on B-blockers.

Our study did not find any reduction in RPP in NTG group when compared to control group.These finding differ from those of Mikawa et al[18] and Dich-Nielsen et al [21]both of whom have reported a significant reduction in the increase in RPP associated with laryngoscopy and tracheal intubation by the use of I.V. or topical NTG. However it must be kept in mind that the patients enrolled in their studies were normotensive while in our study were hypertensive.This may indicate towards differential effect of NTG on normotensive and hypertensive patients.

One limitation of the present study is the use of Non-invasive method of measuring BP.The use of invasive BP monitoring might have brought to light any possible existing difference in the two groups that we have failed to find.

Conclusion

The present study failed to demonstrate any significant reduction in the pressor response to laryngoscopy and intubation as measured by RPP in controlled hypertensivepatients by addition of NTG spray to lignocaine when compared to lignocaine alone.

However,the addition of one puff of(400 µg) NTG spray to lignocaine may offer some benefit in patients at an increased risk of advanced cardiovascular events due to a transient decrease in MAP.

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