Original Article

# Assessment of the effect of two different doses of intranasal nitroglycerine spray on attenuation of haemodynamic stress response to pneumoperitoneum in laparoscopic surgeries: A randomised, double-blinded study

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## ABSTRACT

**Background and Aims:** The stress response to pneumoperitoneum can be deleterious due to its effects on haemodynamics, thereby increasing the morbidity. We intended to compare different doses of nitroglycerine nasal spray to obtund these responses and to look for any side effects. **Methods**: After ethical committee clearance and clinical trials registration, 70 patients scheduled for laparoscopic cholecystectomy were recruited. Random allocation was done into two groups by a computer generated randomisation table. Group N4 (n = 35) received 400 μg nitroglycerine and group N8 (n = 35) received 800 μg nitroglycerine with an intranasal spray 2 min prior to pneumoperitoneum. All the haemodynamic parameters were monitored at regular intervals. **Results:** The heart rate was comparable between the groups except at 6 and 10 min of pneumoperitoneum but showed significant increase from baseline within the groups. Mean arterial pressure (MAP) was statistically significant between the groups, being higher in group N4. Within group N4, MAP was significantly low only at 2 min, 4 min of pneumoperitoneum (101.69 ± 12.34 at baseline versus 93.31 ± 8.07 at 2 min and 97.54 ± 9.07 mm Hg at 4 min) and increased significantly at 30 min of pneumoperitoneum (101.69 ± 12.34 at baseline versus 105.66 ± 12.35 mm Hg) and hence, MAP was observed to be around baseline throughout the rest of intraoperative period. Within group N8, there was a significant decrease in mean, systolic and diastolic blood pressure from baseline at most of the time intervals. **Conclusion:** 800 μg of intranasal nitroglycerine effectively obtunds the hypertensive response associated with pneumoperitoneum as compared to 400 μg without significant side effects.

**Key words:** Blood pressure, heart rate, laparoscopic, nasal sprays, nitroglycerin, pneumoperitoneum

## INTRODUCTION

Laparoscopy is a minimally invasive procedure with clinical advantages like better visualisation of surgical field, shorter hospital stay and early ambulation due to lesser perioperative complications. However, carbon-dioxide ($CO_2$) insufflation induces haemodynamic instability such as decrease in cardiac output, increased mean arterial pressure (MAP) and increase in systemic vascular resistance.[1,2] It also leads



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to decrease in thoracic and pulmonary compliances, pulmonary hypertension, increase in preload due to increased intra-abdominal pressure and hypercapnia. So, anaesthetic risks can increase especially in elderly and in cardiac patients.[1]

To reduce the haemodynamic changes and pathophysiologic influences due to pneumoperitoneum, proper maintenance of preload and systemic vascular resistance is required and agents including vasodilators, high dose opioids, calcium channel blockers, beta blockers and alpha-2 agonists have been selectively used.[2-4]

Nitroglycerine, an organic nitrate is a venous and arteriolar dilator that releases nitric oxide and causes relaxation of vascular smooth muscles. Dilation of larger veins promotes peripheral pooling of blood thereby reducing preload. At higher doses, arterial relaxation reduces systemic vascular resistance and hence, the afterload. Various preparations of nitroglycerine are available for its therapeutic use such as tablets which can be used orally, sublingually or through buccal route, transdermal ointments or patches, sublingual spray and intravenous formulations. Sublingual spray has been used in this study in the form of nasal spray as organic nitrates are absorbed well from mucous membranes.

Literature search revealed studies done on intranasal nitroglycerine, to attenuate hypertensive response of laryngoscopy and intubation.[5,6] But there are no studies which have used intranasal nitroglycerine to prevent haemodynamic response of pneumoperitoneum. Hence, this study aimed to investigate the effect of two different doses of nitroglycerine on haemodynamic changes associated with pneumoperitoneum.

Our primary objective was to compare 400 μg and 800 μg of intranasal nitroglycerine spray to attenuate hypertensive response associated with pneumoperitoneum in laparoscopic surgeries. Secondary objective was to look for any side effects of the study drug.

## METHODS

This prospective, randomised, double-blinded study was performed in our tertiary care referral centre under the tenets of the declaration of Helsinki after obtaining written informed consent and approval from the institutional ethics committee (BMCRI/PS/254/2020-21). The trial was registered in the clinical trial registry (CTRI/2021/03/032461) and was conducted from July 2021 to September 2021. A detailed pre-anaesthetic evaluation was done. We included 70 patients aged between 18 and 50 years belonging to American Society of Anesthesiologists (ASA) physical classes I and II with body mass index 19-25 kg/m$^2$ undergoing elective laparoscopic cholecystectomy. Patients who refused to participate, had anaemia, systolic blood pressure (SBP) less than 90 mm Hg or MAP less than 50 mm Hg, allergy to nitrates or those who were on phosphodiesterase inhibitors, antihypertensives or sympathomimetics, history of upper respiratory tract infection within the past two weeks or those with known pathologies of the nasal passages were excluded from the study.

The patients were kept nil by mouth for 8 hours prior to surgery. After obtaining informed consent, all patients received tablet alprazolam 0.25 mg and tablet ranitidine 150 mg on the night prior to surgery.

On arrival in the operation theatre, standard anaesthesia monitors were attached and baseline haemodynamic parameters such as heart rate (HR), SBP, diastolic blood pressure (DBP), MAP, oxygen saturation and skin surface temperature were noted. Injection midazolam 0.03 mg/kg, injection glycopyrrolate 0.004 mg/kg, injection fentanyl 2 μg/kg, injection ondansetron 0.15 mg/kg were administered intravenously (IV) as premedication. Patients were pre-oxygenated with 100% oxygen for 3 min and induced with injection propofol 2 mg/kg IV. Injection vecuronium 0.1 mg/kg was administered with neuromuscular monitoring. Injection 2% preservative-free lignocaine 40 mg IV was given 90 seconds prior to laryngoscopy. The trachea was intubated and connected to ventilator (DatexOhmedaAvance S5™, General Electric Healthcare, Finland) with end tidal $CO_2$ monitoring. Maintenance was with 50% oxygen and air, isoflurane (1 to 1.4 minimum alveolar concentration) with intermittent doses of injection vecuronium 0.03 mg/kg IV.

Group allocation was done by computer generated random numbers and the numbers were entered in sequentially numbered sealed opaque envelopes. These envelopes were opened by a principal investigator (PI) and the PI administered nitroglycerine to the patients. The group allocation

was not revealed to the attending anaesthesiologist who was involved in monitoring the patient. Group N4 received one metred spray (400 μg) of nitroglycerine intra nasally and group N8 received two metred sprays (800 μg) of nitroglycerine intra nasally. Nitrocin spray (Samarth pharmacy Private Limited., Mumbai, India) was used. The spray was administered 2 min prior to the creation of pneumoperitoneum in the nostril where the nasogastric tube was not inserted.

$CO_2$ insufflation was done in the supine position and subsequently, the operating table was tilted 10-15 degrees in the reverse Trendelenburg position with a left lateral tilt. The rate of insufflation of $CO_2$ by surgeons was initiated at 1 litre/minute, then increased up to 5 litres/minute and maintained to achieve an intra-abdominal pressure of 15 mm Hg throughout the procedure.

All parameters were noted at baseline and intraoperatively, every 2 min for the first 15 min and then every 15 min till the end of surgery. If there was no response to the study drug or if the HR or SBP was >20% of baseline or DBP >100 mm Hg, additional doses of fentanyl (25 μg) were administered or the concentration of inhalational agent was increased. Occurrence of hypotension (fall in SBP >20% from baseline), any arrhythmia, flushing of skin, cyanosis, desaturation, bronchospasm and postoperative headache were looked for and treated accordingly. Injection paracetamol 1 g IV was infused slowly. Injection neostigmine 0.05 mg/kg and injection glycopyrrolate 0.01 mg/kg were administered and extubation was done after confirming complete recovery by clinical observations and train of four counts.

Based on our pilot study on 10 patients, after 2 min of pneumoperitoneum, MAP in group N4 was 90.17 ± 11.70 mmHg and in group N8 was 80.67 ± 14.15 mm Hg. With a minimum expected difference between the two groups of 9.5 mm Hg and for 95% confidence interval and 80% power, the sample size was found to be 30 in each group. 35 patients were included in each group to compensate for drop outs (15%).

Collected data was entered in Microsoft Excel and was exported into Statistical Package for Social Sciences version 24.0. All parameters followed normal distribution. Chi-square test was used for association of qualitative variables (gender, ASA class). Continuous variables (HR and blood pressure) were compared between the two groups using unpaired t-test. Repeated measures of analysis of variance (ANOVA) test were used for intragroup comparisons at different time intervals. If repeated measures of ANOVA were found significant, results were subjected to post-hoc test. Numerical data were expressed as mean ± standard deviation and categorical data were expressed as ratio. Level of statistical significance was considered at 0.05 and highly significant if $P$ was < 0.001.

## RESULTS

Out of 192 patients who were screened for eligibility, 70 patients were enroled for the study by simple random sampling [Figure 1]. The demographic parameters including age, gender, body mass index and duration of surgery were comparable between the two groups [Table 1].

There was significant difference in mean MAP between the two groups at almost all intervals after drug administration, being significantly on lower side from baseline in group N8. Within group N4, there was statistical significance in mean MAP only at 2, 4 and 30 min after pneumoperitoneum. There was no significant difference in MAP compared to baseline value at other intervals [Table 2].

There was significant difference in mean SBP between the two groups at all intervals after administration of the study drug, being on much lower side in group N8 compared to group N4. Within group N8, there was significant decrease in mean SBP from baseline throughout. Within group N4, mean SBP initially lesser than baseline values after drug showed steady increase from 10 min to 60 min following pneumoperitoneum [Table 3].

There was significant difference in mean DBP between the two groups at all intervals after drug administration, being lower in group N8 than in group N4. Within

**Table 1: Comparison of demographic parameters**

| | Group | | *P* |
|---|---|---|---|
| | N8 Mean±SD | N4 Mean±SD | |
| Age (in years) | 46.77±6.25 | 43.57±7.37 | 0.054 |
| BMI (kg/m$^2$) | 22.57±2.37 | 21.60±2.12 | 0.075 |
| Gender (Male: Female) | 15:20 | 16:19 | |
| Duration of surgery (min) | 89.57±21.71 | 85.43±16.03 | 0.367 |

N8 – Group N8, N4 – Group N4, SD – Standard Deviation, BMI – Body mass index

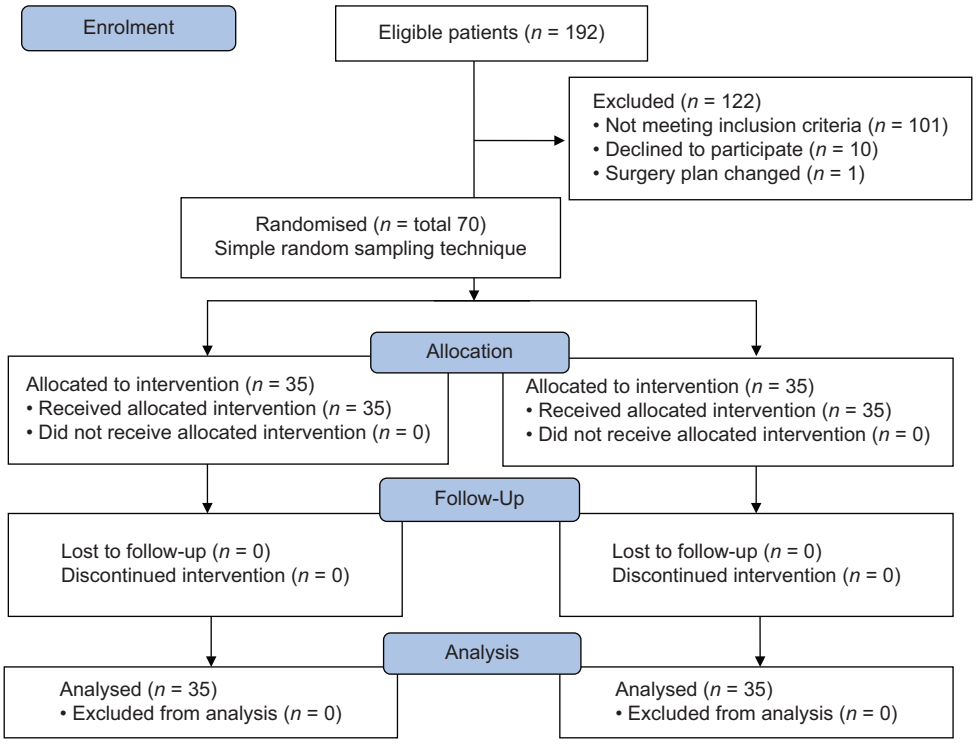


**Figure 1:** Consolidated standards of reporting trials (CONSORT) flow diagram. n:number

**Table 2: Mean arterial pressure comparison between two groups at different time intervals**

| MAP (In mm Hg) | Group | | | | *P*‡ |
|---|---|---|---|---|---|
| | N8 | | N4 | | |
| | Mean±SD | *P*† | Mean±SD | *P*† | |
| Baseline | 97.11±9.875 | | 101.69±12.34 | | 0.092 |
| After Intubation | 92.54±15.06 | 0.124 | 111.17±18.83 | 0.022* | <0.001* |
| After NTG | 85.91±11.79 | <0.001* | 97.09±14.67 | 0.200 | 0.001* |
| 2 min after pneumoperitoneum | 80.66±7.44 | <0.001* | 93.31±8.07 | <0.001* | <0.001* |
| 4 min | 84.37±9.28 | <0.001* | 97.54±9.07 | 0.017* | <0.001* |
| 6 min | 83.14±7.55 | <0.001* | 99.97±10.14 | 0.497 | <0.001* |
| 8 min | 88.09±7.68 | <0.001* | 102.29±10.53 | 0.804 | <0.001* |
| 10 min | 88.71±7.05 | <0.001* | 101.14±11.63 | 0.642 | <0.001* |
| 12 min | 88.31±9.32 | <0.001* | 104.51±8.15 | 0.078 | <0.001* |
| 14 min | 91.37±10.42 | 0.001* | 105.31±9.55 | 0.054 | <0.001* |
| 30 min | 94.40±14.73 | 0.194 | 105.66±12.35 | 0.008* | 0.001* |
| 45 min | 92.43±11.61 | 0.023* | 104.94±9.43 | 0.105 | <0.001* |
| 1 hour | 90.17±8.77 | 0.001* | 99.14±9.28 | 0.272 | <0.001* |
| Post op | 95.06±12.14 | 0.390 | 102.46±9.28 | 0.721 | 0.006* |

MAP – Mean Arterial Pressure, N8 – Group N8, N4 – Group N4, NTG - Nitroglycerine, SD – Standard Deviation, Post op – Postoperative period. †Within Group ‡Between group *Statistically significant

group N8, there was significant decrease in mean DBP compared to baseline at all the intervals except after intubation till 14 min after pneumoperitoneum. Within group N4, there was significant decrease in DBP at 2 min and increase at 30 min after pneumoperitoneum only [Table 4].

There was no significant difference in mean HR between the two groups at all the intervals except at the 6$^{th}$ and 10$^{th}$ min after pneumoperitoneum, being on the higher side in group N4 at these intervals. Within both the groups, there was increase in mean HR from the baseline throughout [Table 5].

Two patients in group N8 (both with tachycardia between 2 min to 8 min of administration of nitroglycerine) and two patients in N4 group (one manifested with tachycardia around 4 min of administration of nitroglycerine, and the other one had high BP recordings around 35 min of nitroglycerine

**Table 3: Systolic blood pressure comparison between two groups at different time intervals**

| SBP (In mm Hg) | Group | | | | $P^{\ddagger}$ |
|---|---|---|---|---|---|
| | N8 | | N4 | | |
| | Mean±SD | $P^{\dagger}$ | Mean±SD | $P^{\dagger}$ | |
| Baseline | 130.40±7.834 | | 131.60±6.175 | | 0.479 |
| After intubation | 121.11±15.79 | 0.003* | 139.49±19.50 | 0.040* | <0.001* |
| After NTG | 117.54±17.20 | 0.001* | 122.54±15.22 | 0.004* | 0.202 |
| 2 min after pneumoperitoneum | 105.77±11.27 | <0.001* | 123.51±9.76 | <0.001* | <0.001* |
| 4 min | 102.11±12.44 | <0.001* | 127.26±9.89 | 0.058 | <0.001* |
| 6 min | 106.37±8.78 | <0.001* | 132.74±8.98 | 0.583 | <0.001* |
| 8 min | 110.14±6.21 | <0.001* | 134.57±10.26 | 0.134 | <0.001* |
| 10 min | 110.34±6.61 | <0.001* | 135.94±12.00 | 0.041* | <0.001* |
| 12 min | 111.57±12.14 | <0.001* | 136.29±15.08 | 0.060 | <0.001* |
| 14 min | 118.29±9.94 | <0.001* | 136.00±10.35 | 0.007* | <0.001* |
| 30 min | 123.46±14.94 | <0.001* | 138.60±11.31 | <0.001* | <0.001* |
| 45 min | 119.11±13.62 | <0.001* | 136.57±9.86 | 0.009* | <0.001* |
| 1 hour | 117.54±15.01 | <0.001* | 128.00±6.30 | 0.002* | <0.001* |
| Post op | 122.46±17.33 | 0.009* | 134.49±16.46 | 0.332 | 0.004* |

SBP – Systolic Blood Pressure, N8 – Group N8, N4 – Group N4, NTG – Nitroglycerine, SD – Standard Deviation, Post op – Postoperative period. †Within Group ‡Between group *Statistically significant

**Table 4: Diastolic blood pressure comparison between two groups at different time intervals**

| DBP (In mm Hg) | Group | | | | $P^{\ddagger}$ |
|---|---|---|---|---|---|
| | N8 | | N4 | | |
| | Mean±SD | $P^{\dagger}$ | Mean±SD | $P^{\dagger}$ | |
| Baseline | 84.83±11.90 | | 85.83±11.63 | | 0.723 |
| After Intubation | 86.86±13.91 | 0.474 | 96.51±21.45 | 0.020 | 0.029* |
| After NTG | 78.14±11.75 | 0.039* | 83.94±13.66 | 0.571 | 0.061 |
| 2 min after pneumoperitoneum | 71.11±9.02 | <0.001* | 78.34±10.68 | <0.001* | 0.003* |
| 4 min | 72.37±8.96 | <0.001* | 85.03±9.33 | 0.661 | <0.001* |
| 6 min | 70.86±9.09 | <0.001* | 85.37±10.62 | 0.848 | <0.001* |
| 8 min | 73.46±8.41 | <0.001* | 88.40±14.19 | 0.293 | <0.001* |
| 10 min | 76.80±6.33 | <0.001* | 85.83±13.98 | 1.000 | 0.001* |
| 12 min | 76.60±10.09 | <0.001* | 87.60±13.44 | 0.363 | <0.001* |
| 14 min | 76.17±9.40 | <0.001* | 88.91±11.87 | 0.119 | <0.001* |
| 30 min | 82.89±13.08 | 0.218 | 91.14±8.99 | <0.001* | 0.003* |
| 45 min | 81.69±12.89 | 0.134 | 88.29±11.77 | 0.308 | 0.029* |
| 1 hour | 79.89±8.39 | 0.020* | 84.20±7.86 | 0.402 | 0.030* |
| Post op | 82.31±11.29 | 0.333 | 88.40±11.65 | 0.235 | 0.030* |

DBP – Diastolic Blood Pressure, N8 – Group N8, N4 – Group N4, NTG – Nitroglycerine, SD – Standard Deviation, Post op – Postoperative period. †Within Group ‡Between group *Statistically significant

spray) were treated with additional doses of fentanyl. There were no significant differences between the groups in haemodynamic variables measured during the postoperative period. No significant adverse effects associated with nitroglycerine were observed.

## DISCUSSION

The results of the present study showed that blood pressure and HR during the intraoperative period was near baseline values in group N8 compared to group N4.

The stress response to pneumoperitoneum can have deleterious effects due to alteration in haemodynamics. Maintaining HR and blood pressure near baseline levels with the advancements in anaesthetic techniques and dosing regimens is the need of the hour. Drugs used should preferably have short duration of action as the trend is moving towards enhanced recovery protocols in terms of both surgical and anaesthetic techniques.[7,8] Nitroglycerine which is known to have a short half-life and quicker onset has been utilised in the current study by virtue of its action on reduction of the systemic vascular resistance and hence, the afterload. Control group has not been used as there has been previous literature proving that nitroglycerine has effects on the HR and blood pressure and is being used in hospitalised patients with angina, hypertension and heart failure in areas other than anaesthesia.[9,10] The doses used in

**Table 5: Heart rate comparison between two groups at different time intervals**

| Heart Rate (In per minute) | Group | | | | $P^{\ddagger}$ |
|---|---|---|---|---|---|
| | N8 | | N4 | | |
| | Mean±SD | $P^{\dagger}$ | Mean±SD | $P^{\dagger}$ | |
| Baseline | 85.63±11.035 | | 90.46±12.006 | | 0.084 |
| After intubation | 110.23±22.07 | <0.001* | 101.34±18.96 | <0.001* | 0.075 |
| After NTG | 102.29±23.12 | <0.001* | 106.74±18.60 | <0.001* | 0.377 |
| 2 min after pneumoperitoneum | 101.11±19.40 | <0.001* | 103.37±19.53 | <0.001* | 0.629 |
| 4 min | 99.71±17.11 | <0.001* | 106.40±16.77 | <0.001* | 0.103 |
| 6 min | 95.54±16.38 | <0.001* | 103.74±15.59 | <0.001* | 0.035* |
| 8 min | 95.46±15.45 | <0.001* | 99.80±15.36 | <0.001* | 0.242 |
| 10 min | 92.94±17.23 | 0.004* | 101.40±14.18 | <0.001* | 0.028* |
| 12 min | 95.17±15.72 | 0.001* | 102.09±14.40 | <0.001* | 0.059 |
| 14 min | 97.60±13.85 | <0.001* | 96.86±12.83 | 0.010* | 0.817 |
| 30 min | 93.89±18.21 | 0.009* | 97.37±11.67 | 0.001* | 0.344 |
| 45 min | 97.80±21.44 | 0.008* | 100.71±14.46 | <0.001* | 0.507 |
| 1 hour | 101.69±20.67 | 0.001* | 102.66±17.28 | <0.001* | 0.832 |
| Post op | 104.11±19.16 | 0.004* | 98.86±15.25 | <0.001* | 0.208 |

N8 – Group N8, N4 – Group N4, NTG – Nitroglycerine, SD – Standard Deviation, Post op – Postoperative period. †Within Group ‡Between group *Statistically significant

our study have been used in previous studies as nasal spray effectively to attenuate haemodynamic changes to laryngoscopy and intubation.[5,6,11]

Literature search revealed that none of the studies have evaluated nitroglycerine with regards to pneumoperitoneum response. Intranasal route is one of the most convenient and easy routes of administration under anaesthesia. Different routes of administration of nitroglycerine can variably hinder absorption of the drug. The presence of surgical drapes intra-operatively, the endotracheal tube or oral airway as well as temperature probe may render topical or sublingual administration difficult. Also, premedication with antisialagogues inhibits the dissolution and absorption through sublingual route. Though the IV route is rapidly acting, the preparation and standardisation of the solution might be expensive. The nasal route circumvents hepatic first pass metabolism, is easily accessible to the anaesthesiologist during anaesthesia for administration, non-invasive, easier to administer and has quicker onset of action. Some of the physiological barriers to intranasal drug absorption include viscosity of nasal mucous, mucociliary clearance and permeability of the nasal epithelium.[12]

Vyas *et al*. and Kumari *et al*. used 400 µg and 800 µg nitroglycerine spray to attenuate pressure response following intubation.[5,6] Similar doses have been evaluated in the current study to blunt haemodynamic effects due to pneumoperitoneum. Vyas *et al*.[5] administered 400 µg, 800 µg and 1200 µg nasal spray to attenuate the intubation response and observed maximum fall in blood pressure and increase in HR with 1200 µg. No other adverse effects have been noted by them. They found that 400 µg and 800 µg of intranasal nitroglycerine is more effective for attenuating the haemodynamic response to intubation. The current study shows similar findings with 400 µg and 800 µg for pneumoperitoneum response whereas aforementioned studies have used nitroglycerine to attenuate intubation response. To obtund pneumoperitoneum response for laparoscopic surgeries of duration around 1 hour, such low doses of nitroglycerine can be beneficial.

Hajian *et al*.[13] studied the effect of bolus doses of 1 µg/kg and 2 µg/kg IV nitroglycerine to reduce haemodynamic responses to laryngoscopy and intubation. They observed that the most marked blood pressure decrease from the baseline was seen in the group receiving 2 µg/kg dose of nitroglycerine without much of a difference in HR between the groups. We differed in using intranasal nitroglycerine wherein peak blood concentration is attained at 2 minutes and declines rapidly within 15 min. It has a plasma half-life of around 1 to 4 min and its biologically active metabolites having half-life of 30-40 min. Same has been noted by us as there was significant decrease in mean DBP and MAP only at 2 min, 4 min after pneumoperitoneum and there is subsequent steady increase in blood pressure around baseline in group N4. Whereas in group N8, both decreased significantly after administration of nitroglycerine upto 15 min and at

60 min possibly due to higher dose and consequently longer duration.

Varshney *et al*.[11] compared the effects of nitroglycerine and lignocaine spray on the oropharynx to attenuate the pressor response during laryngoscopy and endotracheal intubation. They observed the greatest decrease in mean SBP values in the nitroglycerine group at 2-4 min. Also, intergroup comparison at 1–5 min revealed that the highest decrease in the mean rate pressure product (RPP) was in the nitroglycerine group compared to the lignocaine group, indicating a decrease in the myocardial oxygen consumption. Nitroglycerine group patients by virtue of the peripheral vasodilatory property of nitroglycerine had reflex tachycardia. There was a sustained decrease in MAP in the nitroglycerine group compared to other groups, with significant results noted after 4 min. The current study did not determine RRP but similar results have been noted with MAP and SBP.

A Cochrane review included 27 randomised controlled trials which compared nitrates versus no treatment, placebo or other pharmacological interventions in reducing cardiac risk in patients undergoing non-cardiac surgeries. The review concluded that nitrates did not improve cardiac mortality. Few trials mentioned in it had participants with tachycardia, hypotension and headache as adverse effects of nitrates.[14] We did not observe any significant side effects as the bioavailability of nitroglycerine by intranasal route used by us might be lesser than intravenous or sublingual route.

The limitations of the study are that invasive blood pressure monitoring was not done and hence beat to beat variability of MAP could not be monitored. Also, objective monitoring of depth of anaesthesia could not be done due to logistic issues. The sample size is small.

Future research can be diverted toward determining the frequency of administration of 800 μg nitroglycerine via the intranasal route for sustained effect in long duration surgeries as this dose is short acting.

## CONCLUSION

Haemodynamic variables like HR and blood pressure were more stable with 800 μg compared to 400 μg of intranasal nitroglycerine after the creation of pneumoperitoneum. Hence, use of intranasal 800 nitroglycerine helps better in suppressing the hypertensive response to pneumoperitoneum.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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