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# Clonidine Versus Nitroglycerin Infusion in Laparoscopic Cholecystectomy

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## ABSTRACT

**Background and Objectives:** Laparoscopic surgery offers the advantages of minimally invasive surgery; however, pneumoperitoneum and the patient's position induce pathophysiological changes that may complicate anesthetic management. We studied the effect of clonidine and nitroglycerin on heart rate and blood pressure, if any, in association with these drugs or the procedure, as well as the effect of these drugs, if any, on end-tidal carbon dioxide pressure and intraocular pressure.

**Methods:** Sixty patients (minimum age of 20 years and maximum age of 65 years, American Society of Anesthesiologists class I or II) undergoing laparoscopic cholecystectomy were randomized into 3 groups and given an infusion of clonidine (group I), nitroglycerin (group II), or normal saline solution (group III) after induction and before creation of pneumoperitoneum. We observed and recorded the following parameters: heart rate, mean arterial blood pressure, end-tidal carbon dioxide pressure, and intraocular pressure. The mean and standard deviation of the parameters studied during the observation period were calculated for the 3 treatment groups and compared by use of analysis of variance tests. Intragroup comparison was performed with the paired *t* test. The critical value of *P*, indicating the probability of a significant difference, was taken as $< .05$ for comparisons.

**Results:** Statistically significant differences in heart rate were observed among the various groups, whereas comparisons of mean arterial pressure, intraocular pressure, and end-tidal carbon dioxide pressure showed statistically significant differences only between groups I and III and between groups II and III.

**Conclusion:** We found clonidine to be more effective than nitroglycerin at preventing changes in hemodynamic parameters and intraocular pressure induced by carbon dioxide insufflation during laparoscopic cholecystectomy. It was also found not to cause hypotension severe enough to stop the infusion and warrant treatment.

**Key Words:** Laparoscopy, Pneumoperitoneum, Clonidine, Nitroglycerin.

## INTRODUCTION

Laparoscopic surgical procedures, having the benefits of minimally invasive surgical procedures, are being successfully performed and accepted worldwide.[1,2] However, pneumoperitoneum and the position of the patient required for laparoscopy induce pathophysiological changes that may potentially complicate anesthetic management.[3,4] Knowledge of the pathophysiological consequences of increased intra-abdominal pressure is important for the anesthesiologist to achieve better perioperative management.

Clonidine is an imidazoline compound and a selective $\alpha_2$-adrenergic receptor agonist. It is currently the only drug in this group available for use in anesthetic practice. Clonidine is lipid soluble and is absorbed rapidly and almost completely after oral administration, with peak plasma concentrations occurring at 60 to 90 minutes. The cardiovascular effects of clonidine probably involve both $\alpha_2$-adrenergic receptors and imidazoline receptors, and its administration leads to decreases in heart rate and arterial pressure. Clonidine decreases the requirements for both intravenous and volatile anesthetics.

The normal range of intraocular pressure (IOP) is 10 to 22 mm Hg, and IOP is maintained by several factors. Some of these factors are venous congestion of the orbital veins and the volume of intraocular fluid, such as blood and aqueous humor, as well as semisolid structures, which include the lens, the vitreous, and intraocular tumors.[5] The many physiological changes that occur during laparoscopic surgery cause increases in IOP. These changes include increases in blood pressure, end-tidal carbon dioxide ($EtCO_2$) pressure, and central venous pressure,

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which are the result of the increase in intrathoracic pressure and postural changes.[6]

The effects of nitroglycerin on the eye and specifically on IOP have been investigated, with diverse results. Various investigators have reported on the use of nitrates in healthy persons and glaucomatous patients.[7–10] Hessemer and Schmidt[8] found a minimal drop in IOP by using oral nitrates. Chronic nitrate treatment causes retinal venous dilatation and leads to improvement in perfusion of the retina and optic nerve head in patients with glaucoma.[9] In addition, Wizemann and Wizemann[10] reported that the use of systemic nitrate therapy lowers IOP both in glaucoma patients and in healthy persons. The effect was dose dependent. Jantzen et al[11] suggested the use of intravenous nitroglycerin to prevent IOP increases resulting from succinylcholine in anesthetized patients.

We designed this randomized controlled study to observe changes in heart rate, blood pressure, $EtCO_2$ pressure, and IOP (if any) associated with these drugs or the procedure itself. The study included patients undergoing laparoscopic cholecystectomy and receiving clonidine or nitroglycerin and aimed (1) to observe changes in heart rate and blood pressure, if any, associated with these drugs or the procedure and (2) to study the effect of these drugs, if any, on $EtCO_2$ pressure and IOP.

## MATERIALS AND METHODS

After we obtained ethical committee approval, as well as written informed consent forms, 60 patients (American Society of Anesthesiologists class I or II) undergoing elective laparoscopic cholecystectomy were included in the study. We excluded patients who were aged <20 years or >65 years, had acute or chronic eye disease, had preexisting ocular hypertension, or had chronic obstructive lung diseases.

The patients were randomly divided into 3 groups by use of a computer-generated table. Group I received clonidine infusion at a rate of 1.5 $\mu g \cdot kg^{-1} \cdot h^{-1}$, group II received nitroglycerin infusion at a rate of 0.8 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (48 $\mu g \cdot kg^{-1} \cdot h^{-1}$), and group III received 0.9% normal saline solution infusion at a rate of 0.2 $mL \cdot kg^{-1} \cdot h^{-1}$.

All patients were premedicated with tablets of alprazolam, 0.5 mg, and ranitidine, 150 mg, orally on the night before surgery and again 2 hours before surgery. In the operating theater, monitors showing heart rate, electrocardiogram, noninvasive blood pressure, oxygen saturation, and $EtCO_2$ pressure were connected and baseline readings were recorded. Before the induction of anesthesia, patients were given intravenous fentanyl, at a dose of 3 $\mu$g/kg; glycopyrrolate, 0.2 mg; and ondansetron, 4 mg. After preoxygenation, patients underwent induction with an injection of propofol, 2 mg/kg. Endotracheal intubation was performed after the administration of vecuronium at a dose of 100 $\mu$g/kg of body weight. Infusion was started after induction and before creation of pneumoperitoneum. Anesthesia was maintained with oxygen, $N_2O$, Nitrous Oxide isoflurane, and intermittent fentanyl at a dose of 1 $\mu$g/kg.

The rate of infusion was reduced to half if the mean arterial blood pressure value decreased by 20% of the baseline value; the rate of infusion was increased to double if the mean arterial blood pressure value increased by 20% of the baseline value. The infusion was stopped if the mean arterial blood pressure value became <60 mm Hg. In all the patients, the infusion was stopped before anesthesia reversal. Ringer lactate solution was administered intravenously at a rate of 15 mL/kg in the first hour, followed by 7.5 $mL \cdot kg^{-1} \cdot h^{-1}$ until the end of surgery, in all patients.

We observed the following parameters: heart rate, mean arterial blood pressure, $EtCO_2$ pressure, and IOP. We observed heart rate and mean arterial blood pressure just before induction and after induction, as well as every 5 minutes thereafter until reversal. $EtCO_2$ pressure was observed every 5 minutes after induction until reversal. IOP was measured before induction, at the start of the infusion, and 15 minutes after the infusion with a Schiotz tonometer.

### Statistical Analysis

The mean and standard deviation of the parameters studied during the observation period were calculated for the 3 treatment groups and compared by use of analysis of variance tests. Intragroup comparison was performed with the paired $t$ test. $P < .05$ was taken as significant.

## RESULTS

There were no significant differences among the 3 groups with respect to age and sex. **Table 1** shows the patients' heart rates at different time intervals in the 3 groups. The comparison of heart rate between groups I and II showed a statistically significant difference after 15 minutes onward, up to reversal. The comparison of heart rate between groups I and III showed a statistically significant difference at 5 minutes after intubation up to reversal. The comparison of heart rate between groups II and III showed a statistically significant difference at 5 minutes after intubation up to 30 minutes.

**Table 2** shows intergroup comparisons of mean arterial pressure. The intergroup comparison of mean arterial pressure between groups I and II showed no significant difference. The comparison of mean arterial pressure between groups I and III showed a significant difference at 5 minutes after intubation up to reversal. The comparison of mean arterial pressure between groups II and III showed a significant difference at 5 minutes after intubation up to reversal.

**Table 1.**
Intergroup Comparison of Heart Rate

| Time Interval | Heart Rate (beats/min) | | | Group I vs Group II | | Group I vs Group III | | Group II vs Group III | |
|---|---|---|---|---|---|---|---|---|---|
| | Group I (n = 20) | Group II (n = 20) | Group III (n = 20) | *q* Value | *P* Value | *q* Value | *P* Value | *q* Value | *P* Value |
| Before induction | 77.75 ± 16.739 | 72.15 ± 16.339 | 74.75 ± 12.777 | 5.600 | .628 | 3.000 | >.999 | 8.600 | .248 |
| At intubation | 79.30 ± 14.030 | 74.05 ± 15.662 | 80.32 ± 9.152 | 5.250 | .578 | 5.621 | .521 | 12.500 | .115 |
| 5 min | 75.10 ± 14.607 | 77.80 ± 15.504 | 87.50 ± 11.431 | 2.700 | >.999 | 12.400 | .020[a] | 10.215 | .025[a] |
| 10 min | 72.00 ± 13.700 | 79.75 ± 15.103 | 89.80 ± 10.260 | 7.750 | .150 | 10.325 | .017[a] | 9.658 | .019[a] |
| 15 min | 69.60 ± 13.808 | 81.85 ± 14.908 | 90.65 ± 6.492 | 12.250[a] | .008[a] | 14.015 | <.001[a] | 10.548 | .004[a] |
| 20 min | 67.50 ± 12.955 | 84.75 ± 14.607 | 91.00 ± 6.924 | 17.250[a] | <.001[a] | 15.205 | <.001[a] | 10.750 | .019[a] |
| 25 min | 66.16 ± 12.180 | 87.89 ± 14.847 | 91.85 ± 6.920 | 21.737[a] | <.001[a] | 14.012 | <.001[a] | 12.045 | .007[a] |
| 30 min | 62.17 ± 11.907 | 89.21 ± 11.517 | 92.94 ± 7.701 | 27.048[a] | <.001[a] | 15.601 | <.001[a] | 11.273 | .013[a] |
| 35 min | 65.25 ± 11.708 | 94.33 ± 12.349 | 93.50 ± 12.111 | 29.083[a] | <.001[a] | 15.021 | <.001[a] | 4.315 | .233 |
| 40 min | 63.80 ± 14.990 | 94.20 ± 17.541 | 94.75 ± 12.367 | 30.400[a] | .029[a] | 15.261 | <.001[a] | 4.450 | >.999 |
| Reversal | 66.85 ± 10.624 | 95.45 ± 14.862 | 94.30 ± 8.564 | 28.600[a] | <.001[a] | 15.450 | <.001[a] | 3.515 | .231 |

[a]Statistically significant.

**Table 2.**
Intergroup Comparison of Mean Arterial Pressure

| Time Interval | Mean Arterial Pressure (mm Hg) | | | Group I vs Group II | | Group I vs Group III | | Group II vs Group III | |
|---|---|---|---|---|---|---|---|---|---|
| | Group I (n = 20) | Group II (n = 20) | Group III (n = 20) | *q* Value | *P* Value | *q* Value | *P* Value | *q* Value | *P* Value |
| Before induction | 81.70 ± 8.974 | 80.30 ± 8.467 | 80.25 ± 6.154 | 1.400 | >.999 | 2.200 | >.999 | 3.600 | .528 |
| At intubation | 81.90 ± 8.143 | 82.85 ± 7.876 | 82.20 ± 6.740 | 2.250 | >.999 | 1.100 | >.999 | 1.350 | .508 |
| 5 min | 78.40 ± 7.535 | 76.25 ± 7.853 | 83.12 ± 7.146 | 2.150 | >.999 | 4.869 | .037[a] | 5.238 | .021[a] |
| 10 min | 76.30 ± 7.183 | 73.47 ± 7.947 | 83.62 ± 5.088 | 2.826 | .661 | 11.625 | <.001[a] | 14.054 | <.001[a] |
| 15 min | 74.30 ± 6.906 | 71.65 ± 7.191 | 84.65 ± 7.257 | 2.650 | .732 | 7.350 | .006[a] | 10.000 | <.001[a] |
| 20 min | 71.90 ± 6.719 | 69.89 ± 7.845 | 85.55 ± 6.525 | 2.005 | >.999 | 13.650 | <.001[a] | 15.655 | <.001[a] |
| 25 min | 69.68 ± 6.675 | 67.58 ± 8.553 | 89.25 ± 6.340 | 2.105 | >.999 | 19.566 | <.001[a] | 21.671 | <.001[a] |
| 30 min | 68.33 ± 6.257 | 68.40 ± 7.179 | 92.35 ± 6.051 | 0.067 | >.999 | 24.020 | <.001[a] | 23.953 | <.001[a] |
| 35 min | 65.25 ± 5.751 | 66.44 ± 6.839 | 93.67 ± 5.715 | 1.194 | >.999 | 28.417 | <.001[a] | 27.222 | <.001[a] |
| 40 min | 62.80 ± 4.147 | 62.40 ± 4.775 | 99.00 ± 6.000 | 0.400 | >.999 | 36.200 | <.001[a] | 36.000 | <.001[a] |
| Reversal | 65.50 ± 6.152 | 64.10 ± 6.340 | 99.20 ± 6.296 | 1.400 | >.999 | 33.700 | <.001[a] | 35.100 | <.001[a] |

[a]Statistically significant.

**Table 3** shows intergroup comparisons of IOP. The intergroup comparison of IOP between groups I and II showed no significant difference. The comparison of IOP between groups I and III showed a significant difference at 15 minutes onward, up to reversal. The mean IOP between groups II and III showed a significant difference at 15 minutes onward, up to reversal.

**Table 4** shows intergroup comparisons of $EtCO_2$ pressure. The intergroup comparison of $EtCO_2$ pressure between groups I and II showed no statistically significant difference. The comparison of $EtCO_2$ pressure between groups I and III showed a statistically significant difference after 15 minutes onward, up to reversal. The mean $EtCO_2$ pressure between groups II and III showed a statistically significant difference after 15 minutes onward, up to reversal.

## DISCUSSION

Laparoscopic cholecystectomy is the standard of care for gallstone disease and one of the most commonly performed surgical procedures. It involves abrupt hemodynamic changes due to carbon dioxide ($CO_2$) pneumoperitoneum, increased intra-abdominal pressure, and the position of the patient during the procedure.

**Table 3.**
Intergroup Comparison of IOP

| Time Interval | IOP (mm Hg) | | | Group I vs Group II | | Group I vs Group III | | Group II vs Group III | |
|---|---|---|---|---|---|---|---|---|---|
| | Group I (n = 20) | Group II (n = 20) | Group III (n = 20) | *q* Value | *P* Value | *q* Value | *P* Value | *q* Value | *P* Value |
| Before induction | 16.10 ± 2.900 | 16.55 ± 2.625 | 17.10 ± 1.744 | 2.450 | .062 | 1.300 | .158 | 0.550 | >.999 |
| At intubation | 17.00 ± 2.239 | 18.20 ± 2.745 | 18.35 ± 1.309 | 2.312 | .057 | 2.384 | .067 | 0.150 | >.999 |
| 15 min | 14.50 ± 2.685 | 16.00 ± 2.362 | 19.10 ± 2.447 | 1.500 | .189 | 4.600 | <.001[a] | 3.100 | .001[a] |
| 30 min | 14.00 ± 2.898 | 15.07 ± 2.018 | 21.78 ± 2.861 | 1.071 | .952 | 7.778 | <.001[a] | 6.706 | <.001[a] |
| Reversal | 14.05 ± 2.305 | 14.85 ± 2.110 | 23.20 ± 3.122 | 0.800 | .976 | 9.150 | <.001[a] | 8.350 | <.001[a] |

[a]Statistically significant.

**Table 4.**
Intergroup Comparison of $EtCO_2$ Pressure

| Time Interval | $EtCO_2$ Pressure (mm Hg) | | | Group I vs Group II | | Group I vs Group III | | Group II vs Group III | |
|---|---|---|---|---|---|---|---|---|---|
| | Group I (n = 20) | Group II (n = 20) | Group III (n = 20) | *q* Value | *P* Value | *q* Value | *P* Value | *q* Value | *P* Value |
| 5 min (before pneumoperitoneum) | 40.35 ± 3.29 | 40.50 ± 2.328 | 38.75 ± 2.124 | 0.150 | >.999 | 1.600 | .173 | 1.750 | .116 |
| 10 min | 38.80 ± 2.56 | 39.30 ± 2.155 | 40.05 ± 2.417 | 0.500 | >.999 | 1.250 | .306 | 0.750 | .968 |
| 15 min | 37.35 ± 2.19 | 37.50 ± 1.960 | 40.90 ± 2.511 | 0.150 | >.999 | 3.550[a] | <.001[a] | 3.400[a] | <.001[a] |
| 20 min | 35.50 ± 1.88 | 36.05 ± 1.820 | 42.80 ± 2.191 | 0.550 | >.999 | 7.300[a] | <.001[a] | 6.750[a] | <.001[a] |
| 25 min | 35.42 ± 1.60 | 35.26 ± 1.593 | 43.80 ± 2.215 | 0.158 | >.999 | 8.379[a] | <.001[a] | 8.537[a] | <.001[a] |
| 30 min | 34.67 ± 1.31 | 34.93 ± 1.859 | 45.06 ± 1.952 | 0.262 | >.999 | 10.392[a] | <.001[a] | 10.130[a] | <.001[a] |
| 35 min | 35.12 ± 1.26 | 35.11 ± 1.167 | 46.17 ± 3.371 | 0.014 | >.999 | 11.042[a] | <.001[a] | 11.056[a] | <.001[a] |
| 40 min | 33.80 ± 1.05 | 34.20 ± 1.304 | 48.25 ± 2.754 | 0.400 | >.999 | 14.450[a] | <.001[a] | 14.050[a] | <.001[a] |
| Reversal | 34.40 ± 1.21 | 34.85 ± .988 | 44.68 ± 2.496 | 0.450 | >.999 | 10.284[a] | <.001[a] | 9.834[a] | <.001[a] |

[a]Statistically significant.

Knowledge of the potential problems is essential for optimal anesthetic care of patients undergoing laparoscopic surgery. The choice of anesthetic technique for upper abdominal laparoscopic surgery is mostly limited to general anesthesia with muscle paralysis, tracheal intubation, and intermittent positive-pressure ventilation. Tracheal intubation and intermittent positive-pressure ventilation ensure airway protection and control of pulmonary ventilation to maintain eucapnia.

Hemodynamic changes associated with pneumoperitoneum are profound hypertension and tachycardia. Pneumoperitoneum, along with the head-up position, leads to significant hemodynamic changes, that is, an increase in mean arterial pressure and systemic vascular resistance (SVR) and a decrease in cardiac output. $CO_2$ insufflation during pneumoperitoneum leads to an increase in $EtCO_2$ pressure and IOP. These hemodynamic changes can be detrimental especially in patients with significant cardiac risk, and hence it is desirable to find specific pharmacologic agents to prevent these hemodynamic changes. This study was undertaken to compare the hemodynamic and IOP effects of clonidine and nitroglycerin infusion during laparoscopic cholecystectomy.

This study was performed in 60 patients with American Society of Anesthesiologists physical status I or II divided randomly into 3 groups. In group I we used a clonidine infusion at a rate of 1.5 $\mu g \cdot kg^{-1} \cdot h^{-1}$, and a statistically significant ($P < .05$) fall in heart rate was seen 10 minutes after intubation and onward, up to reversal. Clonidine decreases the heart rate by parasympathetic stimulation. Our findings support those of Malek et al,[12] who used 150 $\mu g$ of clonidine as an intravenous infusion and intramuscularly as premedication for maintenance of hemodynamic stability during pneumoperitoneum. Yu et al[13] used 150 $\mu g$ of oral clonidine as premedication and concluded that clonidine preserves heart rate variability for patients undergoing laparoscopic cholecystectomy. Moreover, Tripathi et al[14] reported that the hemodynamic derangements that occur during pneumoperitoneum can be effectively attenuated by premedicating with clonidine.

In our study 13 of the 20 patients in the clonidine group (65%) had an increased heart rate after intubation due to the intubation response. At 10 minutes after intubation and onward, a fall in heart rate occurred and this was statistically significant ($P < .05$). In our study we observed that the onset of action of clonidine occurred at >5 minutes. The fall in heart rate was highly statistically significant at 20 to 30 minutes because clonidine reaches its peak plasma concentration after 30 minutes. At reversal, a slight increase in heart rate was seen because the infusion was stopped before reversal.

Group II received nitroglycerin infusion at a rate of 0.8 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (48 $\mu g \cdot kg^{-1} \cdot h^{-1}$). A statistically significant ($P < .05$) rise in heart rate was seen just after intubation up to reversal. The onset of action observed in our study was 1 to 3 minutes. Nitroglycerin is a vascular smooth muscle relaxant. In our study we used a low-dose nitroglycerin infusion. Low concentrations of nitroglycerin preferentially dilate the veins more than the arterioles. Venodilation decreases left and right ventricular chamber size and end-diastolic pressures but results in little change in SVR. This causes a fall in mean arterial pressure, and the heart rate might increase in response to a decrease in blood pressure.

Our findings support those of Vatner et al,[15] who concluded that intravenous nitroglycerin caused substantial coronary vasodilatation before any change in systemic hemodynamics occurred. Lahtela and Sotaniemi[16] concluded that in healthy subjects, the heart rate began to increase after 1 minute of sublingual administration. The heart rate became normalized within 30 minutes. Moon et al[17] found partially successful hemodynamic effects with nitroglycerin infusion during laparoscopic surgery.

In the placebo group we used normal saline solution. There was a statistically significant ($P < .05$) rise in heart rate just after intubation up to reversal. At the time of intubation, the increase in heart rate might have occurred because of the intubation response. After that, the rise in heart rate was due to pneumoperitoneum. Pneumoperitoneum-induced hypercarbia might cause sympathetic stimulation, which leads to an increased heart rate (**Table 4**).

A statistically significant ($P < .05$) difference in heart rate between the clonidine and nitroglycerin groups was seen after 15 minutes of intubation up to reversal because clonidine decreases heart rate whereas nitroglycerin increases heart rate (**Table 1**).

When we compared the clonidine group with the placebo group, we observed a statistically significant difference in heart rate after intubation up to reversal. At the time of intubation, both groups showed a rise in heart rate. This rise in heart rate might have been due to the intubation response. Clonidine decreases the heart rate by stimulating parasympathetic outflow, which may contribute to the slowing of the heart rate as a consequence of increased vagal tone and diminished sympathetic drive. In contrast, in group III, from 5 minutes onward, the rise in heart rate

was due to sympathetic stimulation as a consequence of pneumoperitoneum (**Table 1**).

At the time of intubation, a rise in heart rate due to the intubation response was seen with nitroglycerin infusion and with saline solution infusion. A statistically significant difference in mean heart rate between the nitroglycerin group and placebo group was seen at 5 minutes after intubation up to 30 minutes. Although nitroglycerin caused an increase in heart rate, it restricted the increase in heart rate compared with the placebo group (**Table 1**).

Both clonidine infusion and nitroglycerin infusion in the tested doses led to a significant decrease in mean arterial pressure to the preinfusion level. The decreases in mean arterial pressure by these two drugs were similar (**Table 2**). Clonidine produces a fall in blood pressure associated with decreased cardiac output and SVR. Our findings are consistent with those of Sung et al,[18] who used oral clonidine as premedication and suggested that clonidine provides perioperative hemodynamic stability.

Nitroglycerin is a vasodilator, active on both arteries and veins. An increase in mean arterial pressure and SVR can be attenuated with nitroglycerin. Nitroglycerin infusion is a relatively simple and adjustable technique for relaxing the vascular smooth muscle, and it rapidly produced marked hemodynamic improvement during laparoscopic surgery, presumably mainly as a result of a decrease in afterload. In the group receiving nitroglycerin infusion, the infusion was stopped in 3 of 20 patients (15%) because the mean arterial pressure fell to <60 mm Hg. All 3 patients were women. None of the patients receiving clonidine infusion in our study had hypotension severe enough to warrant treatment.

In the normal saline solution group, there was a significant rise in mean arterial pressure; this may have been due to the intubation response, hypercarbia, or baroreceptor stimulation due to reduced venous return and cardiac output combined with the reverse Trendelenburg position and pain (**Table 2**). The rise in mean arterial blood pressure was significantly higher in the placebo group than in the clonidine and nitroglycerin groups.

In all 3 groups there was a rise in preinfusion but postintubation IOP. This rise might have been due to the intubation response. Both clonidine and nitroglycerin led to a fall in IOP. This fall in IOP was the same with both drugs (**Table 3**). Clonidine decreases IOP by a central mechanism. Our findings are consistent with those of Innemee et al,[19] who administered the drug by different routes and concluded that clonidine decreases IOP.

Nitroglycerin prevents an increase in SVR and modulating aqueous humor dynamics, by which it decreases IOP. Our findings support those of Sen et al,[20] who concluded that low-dose nitroglycerin infusion during the period of pneumoperitoneum might be effective at decreasing IOP during laparoscopic cholecystectomy.

In our placebo group a significant rise in IOP persisted up to reversal. This rise in IOP might have occurred because of $CO_2$ insufflation.

Both clonidine infusion and nitroglycerin infusion led to a significant decrease in $EtCO_2$ pressure that persisted up to reversal. The decrease in blood pressure can decrease lung perfusion, and this may lead to a fall in $EtCO_2$ pressure. However, it has been proved that neither drug has any direct effect on $EtCO_2$ pressure. In the placebo group a significant ($P < .05$) rise in $EtCO_2$ pressure persisted up to reversal due to pneumoperitoneum.

Our study showed that clonidine is more effective than nitroglycerin at preventing changes in hemodynamic parameters and IOP induced by $CO_2$ insufflation during laparoscopic cholecystectomy. Earlier studies showed similar results, but this type of comparative study was lacking. However, the patient population of our study is very small, so generalization of our results to other populations needs further validation.

## CONCLUSION

We found that clonidine is a more effective drug for preventing the hemodynamic changes due to laparoscopic cholecystectomy. Clonidine decreases heart rate, mean arterial blood pressure, and IOP, whereas nitroglycerin causes an increase in heart rate and decreases mean arterial blood pressure and IOP. Both the clonidine and nitroglycerin groups showed a fall in $EtCO_2$ pressure. Nitroglycerin caused a fall in mean arterial blood pressure <60 mm Hg in 3 of 20 patients, whereas no such fall was seen in the clonidine group.

The observations of our study suggest that clonidine is more effective than nitroglycerin at preventing changes in hemodynamic parameters and IOP induced by $CO_2$ insufflation during laparoscopic cholecystectomy. It also does not cause hypotension severe enough to stop the infusion and warrant treatment.

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