Comparison of Clonidine and Dexmedetomidine on Cardiovascular Stability in Laparoscopic Cholecystectomy

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INTRODUCTION

Laparoscopic surgery is a modern surgical technique involving insufflation of gas (usually CO₂) into the peritoneal cavity, under pressure, to separate the organs from the abdominal cavity.¹ Laparoscopic cholecystectomy has revolutionized gall bladder surgeries and it has now become the gold standard for the treatment of cholelithiasis. Since the introduction of diagnostic laparoscopic procedures in early 1970’s and the first laparoscopic cholecystectomy procedures in late 1980’s, laparoscopy has expanded impressively both in scope and volume. Increasing the success of laparoscopic surgery can be attributed to the fact that it results in multiple benefits compared with open procedures such as reduced trauma to the patient, disturbance of homeostasis, morbidity, mortality, recovery time, and hospital stay with a consequent reduction in healthcare costs.

Despite multiple benefits, all laparoscopic surgeries are challenging from an anesthesia point of view, mainly due to significant alteration of hemodynamics, resulting in:

- Reduced trauma to the patient
- Disturbance of homeostasis
- Morbidity
- Mortality
- Recovery time
- Hospital stay

In order to control these hemodynamic changes, numerous agents and combinations of agents have been used. However, the search for an ideal agent to control hemodynamic instability during laparoscopic cholecystectomy has been on.

Abstract

Introduction: Laparoscopic cholecystectomy has revolutionized gall bladder surgeries and it has now become the gold standard for the treatment of cholelithiasis. Despite multiple benefits, all laparoscopic surgeries are challenging from an anesthesia point of view, mainly due to significant alteration of hemodynamics. Numerous agents and combination of agents have been used in an effort to minimize the hemodynamic instability during this period, but search for an ideal agent to control this instability in hemodynamics is still on. In this study, it has been attempted to compare the beneficial effect of the two α₂ agonists, clonidine and dexmedetomidine, in maintaining perioperative parameters like mean arterial pressure (MAP) and heart rate (HR).

Purpose: To assess the efficacies of clonidine and dexmedetomidine in maintaining hemodynamic stability during laparoscopic cholecystectomy.

Materials and Methods: Patients were randomly divided into three groups, who received 0.9% normal saline infusion, 3 mcg/kg/h of clonidine infusion, and 0.2 mcg/kg/h of dexmedetomidine infusion, intravenously. Intraoperative hemodynamic stability was assessed by monitoring HR, MAP and requirement of isoflurane in the three groups.

Results: Clonidine and dexmedetomidine caused significant reductions in intraoperative HR, MAP and requirement of isoflurane when compared to the control (normal saline) group. Clonidine caused a significant reduction in HR when compared to dexmedetomidine. No significant differences were observed in MAP and requirement of isoflurane between the two drugs.

Conclusion: Both clonidine and dexmedetomidine favorably alter the intraoperative hemodynamics during laparoscopic cholecystectomy. Clonidine decreased intraoperative HR more than dexmedetomidine.

Key words: Clonidine, Dexmedetomidine, Hemodynamic stability, Inhalational agent sparing effect, Laparoscopic cholecystectomy
from the combined effects of pneumoperitoneum, patient position, and hypercapnia from the absorbed \( CO_2 \). Pneumoperitoneum creation raises the intra-abdominal pressure (IAP) and is immediately followed by an increased plasma renin activity and increase in plasma norepinephrine and epinephrine levels. There is also an increase in the circulating blood volume, which is due to the shifting of blood from the splanchnic capacitance blood vessels to the systemic circulation. All these changes collectively lead to an elevated arterial pressure, increased systemic and pulmonary vascular resistance, and decreased cardiac output. These hemodynamic responses are well tolerated in otherwise healthy individuals, but in patients with hypertension, coronary heart disease, cerebrovascular disease, and intracranial aneurysm; these transient changes can result in potentially deleterious effects such as left ventricular failure, pulmonary edema, myocardial ischemia, ventricular dysrhythmias, and cerebral hemorrhage.\(^2\)\(^3\)

Numerous agents and combination of agents have been used in an effort to minimize the hemodynamic instability during this period. Volatile agents such as isoflurane and sevoflurane\(^3\) have been used with limited success in maintaining hemodynamic stability as volatile agents decrease surgical stimulus induced catecholamine secretion. Opioids have traditionally been used for blunting the perioperative stress response during general anesthesia. General anesthesia has been supplemented on occasions with intraoperative infusions of propofol, due to its intrinsic ability to inhibit catecholamine secretion, and infusions of nitroglycerine or beta blockers, to control perioperative stress. Combined general with epidural anesthesia\(^4\) is yet another strategy employed by anesthesiologists to control perioperative hemodynamic instability with limited success. But search for an ideal agent to control this instability in hemodynamics is still on.

\( \alpha_2 \) agonists produce diverse responses, including analgesia, anxiolysis, sedation, and sympatholysis, each of which has been reported to be useful in the treatment of patients with surgical and chronic pain. The Food and Drug Administration has approved two novel \( \alpha_2 \) adrenergic agonists, clonidine and dexmedetomidine, for intravenous administration.\(^5\)

Clonidine, with elimination half-life of 6-10 h, is a centrally acting selective partial \( \alpha_2 \) agonist (220:1 \( \alpha_2 \) to \( \alpha_1 \)). It is known to induce sedation, decrease anesthetic drug requirement and improve perioperative hemodynamics by attenuating blood pressure and heart rate (HR) responses to surgical stimulation, and protect against perioperative myocardial ischemia. It provides sympathoadrenal stability and suppresses renin-angiotensin activity. There are studies indicating benefits of using clonidine for maintenance of hemodynamic stability in laparoscopic cholecystectomy.

Dexmedetomidine, with elimination half-life of 2-3 h, is a highly selective and potent \( \alpha_2 \) agonist (1620:1 \( \alpha_2 \) to \( \alpha_1 \)), and is seven to ten times more selective for \( \alpha_2 \) receptors compared to clonidine, and has a shorter duration of action. Dexmedetomidine is considered full agonist at \( \alpha_2 \) receptors as compared to clonidine, which is considered a partial agonist. Similar to clonidine, dexmedetomidine, also attenuates the hemodynamic response to tracheal intubation, decreases plasma catecholamine concentration during anesthesia and decreases perioperative requirements of inhaled anesthetics.\(^6\)

Laparoscopic cholecystectomy is a routinely performed surgery and it is desirable to have a stable intraoperative hemodynamic status. Hence, in this study, it has been attempted to compare the beneficial effect of the two \( \alpha_2 \) agonists, clonidine and dexmedetomidine, in maintaining perioperative parameters like mean arterial pressure (MAP) and HR.

**MATERIALS AND METHODS**

The study entitled “Comparison of clonidine and dexmedetomidine on cardiovascular stability in laparoscopic cholecystectomy” was carried on 120 American Society of Anesthesiologists (ASA) Grades I and II patients of either sex with comparable characteristics in the Department of Anaesthesiology, Critical Care and Pain Management, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India.

The study was conducted after obtaining approval from the ethical, academic committee and a written, informed consent from the patients.

The study was conducted in three groups comprising 40 patients each.

1. **Group 1** (control group): Received 0.9% normal saline infusion
2. **Group 2** (clonidine group): Received 3 mcg/kg/h of clonidine in 0.9% normal saline
3. **Group 3** (dexmedetomidine group): Received 0.2 mcg/kg/h of dexmedetomidine in 0.9% normal saline.

**Exclusion Criteria**

1. Patient refusal
2. Patients with known hypersensitivity to the drugs used in the study
3. Patients less than 18 years or more than 60 years of age
4. ASA Grades III and IV patients
5. Patients with cardiac disorders
6. Patients with hepatic dysfunction
7. Patients with renal dysfunction
8. Hypertensive patients
9. Patients with basal HR less than 55 bpm
10. Pregnant and lactating patients.

Furthermore, surgeries lasting for more than 120 min were not considered in the study.

The study drug was provided as prefilled and coded identical 20 mL syringes containing study drugs, as per the randomization protocol, in dilutions of:
1. Normal saline 0.9% - 20 ml
2. Clonidine - 20 ml (30 mcg/mL)
3. Dexmedetomidine - 20 ml (2 mcg/mL).

The investigators involved in the study did not know about the content of the drug infusion syringes. Patients were explained about the study but did not know which drug was used. The study drug prefilled and coded syringes were obtained on the day of the surgery from a third person not directly involved in the study. Randomization was ensured by picking up a chit from a pool of 120 chits to decide which drug to administer to a particular patient.

Preanesthetic check-up, comprising detailed history and thorough physical examination, of all the patients was done 1 day before the surgery. The following investigations were performed:
• Hemoglobin, packed cell volume
• Total leukocyte count, differential leukocyte count, Erythrocyte sedimentation rate
• Platelet count
• Prothrombin time, partial thromboplastin time
• Random blood sugar
• Kidney function test
• Liver function test
• Serum electrolytes
• Electrocardiogram (ECG)
• Chest X-ray (posterioranterior view).

Two intravenous lines of 18 G and 20 G were secured on any two convenient veins on the left and the right hand, respectively. The 20 G line was used to administer the infusion of drugs under study, while the 18 G line was used to administer intravenous (IV) fluids and all the other drugs.

The monitoring of the patient was started 15 min before the induction and was continued into the post-operative room until 15 min after the extubation. It comprised monitoring the HR, systolic and diastolic blood pressures, MAP, ECG, oxygen saturation and capnography.

After shifting to the operation theatre and attaching all the monitors, the patient was pre-medicated using injection ondansetron 0.08 mg/kg IV, injection glycopyrrolate 4 mcg/kg IV and injection fentanyl 1.5 mcg/kg IV. The anesthesia was induced using injection propofol 2 mg/kg IV. The trachea was then intubated using the appropriate sized cuffed oral endotracheal tube, facilitated with the help of injection vecuronium 0.08 mg/kg IV. The anesthesia was maintained on O₂:N₂O (50%:50%) and variable rate of isoflurane 0.2-0.4% v/v. Incremental dosage of injection vecuronium was used for muscle relaxation, as and when required. End-tidal carbon dioxide was monitored intraoperatively and kept between 25 and 30 mm of Hg.

The study drug infusion, in prefilled coded 20 ml syringe, was started 10 min before creation of pneumoperitoneum, using infusion pump, at the rate of 0.1 mL/kg body weight/hour, and the code number of the study drug syringe was noted down in the proforma. The IAP was maintained at 14 mmHg. The drug infusion and was stopped when the pneumoperitoneum was resolved back to the status quo ante.

Throughout the procedure, any change in the MAP of over 20% of the basal value was countered by varying the rate of isoflurane. HR less than 50 beats per minute was treated by administering Injection Atropine 0.6 mg.

After the surgery, the residual neuromuscular blockade was reversed using injection neostigmine 0.05 mg/kg IV and injection glycopyrrolate 0.01 mg/kg IV. The trachea was extubated and patient shifted to the post-operative recovery room.

Assessment
The following parameters were assessed in the case studies:
• HR
• MAP
• ECG changes.

Additional parameters included:
• Requirement of isoflurane
• Requirement of atropine
• Total surgery time
• Total anesthesia time.

The MAP and HR were monitored at the following junctures:
1. In the pre-operative room
2. 5 min before induction
3. Start of drug infusion
4. Creation of pneumoperitoneum
5. Thereafter every 5 min till the pneumoperitoneum is resolved
6. After reversal
7. In the post-operative room.
**Statistical Analysis**

Statistical analysis was performed using the SPSS statistical package (version 17.0; SPSS). Continuous variables, including hemodynamic over time within the groups, were analyzed using repeated measures analysis of variance (ANOVA) followed by Bonferroni’s *post hoc* testing. Statistical comparisons among the groups were performed using ANOVA. If the *F* value was significant and variance was homogeneous, Tukey’s multiple comparison test was used to assess the differences between the individual groups; otherwise, Tamhane’s T2 test was used. Nominal or categorical data between the three groups were analyzed and compared using the Chi-square test. *P* < 0.05 was considered statistically significant.

**RESULTS**

There was no statistically significant difference between the groups with regard to age distribution, weight distribution (Table 1), sex distribution (Table 2), surgery time, and anesthesia time (Table 3) with *P* > 0.05 among the groups.

**HR (Table 4)**

*Group 1 (control) versus Group 2 (clonidine)*

HR in Group 1 increased significantly, compared to Group 2 at 5, 10, 15, 20, 25, 30, 35 and 40 min after the creation of pneumoperitoneum; at the end of pneumoperitoneum; after reversal; and postoperatively (*P* < 0.05).

*Group 2 (clonidine) versus Group 3 (dexmedetomidine)*

The decrease in HR appeared more in Group 2 at all intervals, compared to Group 3, but the decrease was found to be statistically significant only at 25, 30 and 35 min after creation of pneumoperitoneum; and postoperatively (*P* < 0.05), when HR was found to be more in Group 3.

**MAP (Table 5)**

*Group 1 (control) versus Group 2 (clonidine)*

MAP in Group 1 increased significantly when compared to Group 2 at 5, 10, 15, 20, 25, 30, 35, 40 and 45 min after the creation of pneumoperitoneum; at the end of pneumoperitoneum; after reversal; and postoperatively (*P* < 0.05).

*Group 1 (control) versus Group 3 (dexmedetomidine)*

MAP in Group 1 was significantly higher, compared to Group 3 after creation of pneumoperitoneum; 5, 10, 15, 20, 25, 30, 35, 40 and 45 min after the creation of pneumoperitoneum.

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**Table 1: Age and weight distribution**

<table>
<thead>
<tr>
<th>Age and weight</th>
<th>Mean±SD</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 1 versus Group 2</th>
<th>Group 1 versus Group 3</th>
<th>Group 2 versus Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>38.15±12.16</td>
<td>40.13±12.79</td>
<td>41.70±11.01</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>58.73±6.62</td>
<td>55.60±8.96</td>
<td>56.10±5.34</td>
</tr>
</tbody>
</table>

*P* value

| Group 1 versus Group 2 | 0.743 |
| Group 1 versus Group 3 | 0.386 |
| Group 2 versus Group 3 | 0.828 |

SD: Standard deviation

**Table 2: Sex distribution**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Frequency (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>Female</td>
<td>30 (75)</td>
<td>33 (82.5)</td>
</tr>
<tr>
<td>Male</td>
<td>10 (25)</td>
<td>7 (17.5)</td>
</tr>
<tr>
<td>Total</td>
<td>40 (100)</td>
<td>40 (100)</td>
</tr>
</tbody>
</table>

SD: Standard deviation

**Table 3: Duration of surgery and duration of anesthesia**

<table>
<thead>
<tr>
<th>Duration</th>
<th>Mean±SD</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 1 versus Group 2</th>
<th>Group 1 versus Group 3</th>
<th>Group 2 versus Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of surgery (min)</td>
<td></td>
<td>49.25±4.74</td>
<td>50.13±6.25</td>
<td>51.75±5.72</td>
<td>0.765</td>
<td>0.118</td>
<td>0.400</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>70.13±5.13</td>
<td>71.25±5.75</td>
<td>72.00±5.97</td>
<td>0.645</td>
<td>0.299</td>
<td>0.822</td>
<td></td>
</tr>
</tbody>
</table>

SD: Standard deviation
pneumoperitoneum; at the end of pneumoperitoneum; after reversal; and postoperatively \((P < 0.05)\).

**Group 2 (clonidine) versus Group 3 (dexmedetomidine)**

There was no statistically significant difference in MAP between the two groups. MAP between the two groups was found to be comparable.

**Requirement of Isoflurane (Table 6)**

All the patients in Group 1 (100%); 3 patients in Group 2 (7.5%); and 4 patients in Group 3 (10%) required isoflurane concentration of more than 1%, during the intraoperative period. Patients in Group 1 had significantly increased requirements, compared to Group 2 and Group 3 \((P < 0.05)\).

**Requirement of Atropine (Table 7)**

None of the patients in Group 1 (0%); 5 patients in Group 2 (12.5%); and 3 patients in Group 3 (7.5%) required intraoperative Atropine for the treatment of Bradycardia. There was no statistically significant difference in the requirement of Atropine among the three groups \((P > 0.05)\).

**Perioperative ECG Changes**

No perioperative ECG changes were seen in any of the patients included the study.

### Table 4: HR

<table>
<thead>
<tr>
<th>HR</th>
<th>Mean±SD</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>Baseline</td>
<td>87.80±8.57</td>
<td>86.80±8.31</td>
</tr>
<tr>
<td>5 min before induction</td>
<td>90.18±8.82</td>
<td>89.03±7.97</td>
</tr>
<tr>
<td>Start of drug infusion</td>
<td>91.03±8.95</td>
<td>91.10±8.04</td>
</tr>
<tr>
<td>Pneumoperitoneum</td>
<td>90.90±8.70</td>
<td>89.13±8.37</td>
</tr>
<tr>
<td>5 min</td>
<td>95.20±9.48</td>
<td>85.88±8.06</td>
</tr>
<tr>
<td>10 min</td>
<td>99.88±10.45</td>
<td>81.35±8.03</td>
</tr>
<tr>
<td>15 min</td>
<td>100.03±8.66</td>
<td>76.75±7.28</td>
</tr>
<tr>
<td>20 min</td>
<td>98.25±9.24</td>
<td>75.23±8.35</td>
</tr>
<tr>
<td>25 min</td>
<td>97.45±9.15</td>
<td>73.83±8.95</td>
</tr>
<tr>
<td>30 min</td>
<td>96.63±9.35</td>
<td>72.06±9.86</td>
</tr>
<tr>
<td>35 min</td>
<td>99.22±9.05</td>
<td>71.36±11.66</td>
</tr>
<tr>
<td>40 min</td>
<td>98.78±10.39</td>
<td>73.00±9.85</td>
</tr>
<tr>
<td>45 min</td>
<td>103.50±6.36</td>
<td>80±11.04</td>
</tr>
<tr>
<td>50 min</td>
<td>86.50±20.21</td>
<td>68.00±0</td>
</tr>
</tbody>
</table>

SD: Standard deviation, HR: Heart rate

### Table 5: MAP

<table>
<thead>
<tr>
<th>MAP</th>
<th>Mean±SD</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>Baseline</td>
<td>73.73±5.15</td>
<td>94.08±5.68</td>
</tr>
<tr>
<td>5 min before induction</td>
<td>97.05±4.74</td>
<td>96.25±4.81</td>
</tr>
<tr>
<td>Start of drug infusion</td>
<td>96.86±4.54</td>
<td>94.50±5.19</td>
</tr>
<tr>
<td>Pneumoperitoneum</td>
<td>99.80±4.92</td>
<td>97.38±5.20</td>
</tr>
<tr>
<td>5 min</td>
<td>104.55±4.63</td>
<td>96.83±6.18</td>
</tr>
<tr>
<td>10 min</td>
<td>110.50±4.43</td>
<td>91.90±9.00</td>
</tr>
<tr>
<td>15 min</td>
<td>116.65±4.35</td>
<td>87.43±10.82</td>
</tr>
<tr>
<td>20 min</td>
<td>113.28±5.17</td>
<td>88±11.49</td>
</tr>
<tr>
<td>25 min</td>
<td>110.65±4.49</td>
<td>87.45±11.46</td>
</tr>
<tr>
<td>30 min</td>
<td>107.91±5.77</td>
<td>85.59±10.17</td>
</tr>
<tr>
<td>35 min</td>
<td>106.83±5.35</td>
<td>85±10.51</td>
</tr>
<tr>
<td>40 min</td>
<td>106.11±5.37</td>
<td>83.55±7.62</td>
</tr>
<tr>
<td>45 min</td>
<td>110±4.11</td>
<td>82.60±5.22</td>
</tr>
<tr>
<td>50 min</td>
<td>0±0</td>
<td>86.50±0.71</td>
</tr>
<tr>
<td>End of pneumoperitoneum</td>
<td>103.55±5.59</td>
<td>86.00±9.56</td>
</tr>
<tr>
<td>Reversal</td>
<td>108.45±5.88</td>
<td>97.65±6.39</td>
</tr>
<tr>
<td>Post-operative</td>
<td>93.93±5.34</td>
<td>89.71±5.15</td>
</tr>
</tbody>
</table>

SD: Standard deviation, MAP: Mean arterial pressure
DISCUSSION

Baseline Comparison
Baseline comparison between the three study groups revealed that the groups were comparable with respect to age, sex, weight, total surgery time, and total anesthesia time. There was no statistically significant variation in these baseline characteristics among the three groups.

Clonidine versus Control
Statistically significant differences were observed in the HR, MAP and requirement of isoflurane between control (Group 1) and clonidine (Group 2) groups. The HR and MAP were found to be lower in Group 2, and the patients in Group 2 required lesser isoflurane.

No statistically significant difference was observed in the requirement of atropine between the two groups.

Dexmedetomdine versus Control
Statistically significant differences were observed in the HR, MAP and requirement of isoflurane between control (Group 1) and dexmedetomdine (Group 3) groups. The HR and MAP were found to be lower in Group 3, and the patients in Group 3 required lesser isoflurane.

No statistically significant difference was observed in the requirement of atropine between the two groups.

Clonidine versus Dexmedetomdine
Although decrease in HR appeared more in clonidine group (Group 2), compared to dexmedetomdine group (Group 3), at all the intervals, but the difference was found to be statistically significant only at 25, 30, and 35 min after creation of pneumoperitoneum; and postoperatively ($P < 0.05$).

No statistically significant difference was found in MAP, requirement of isoflurane and requirement of atropine between the two groups.

Ghignone et al.\textsuperscript{7} reported less than 20% intraoperative fluctuation in both HR and blood pressure of the preinduction values; and blunting of the cardiovascular response to intubation effectively, in patients receiving clonidine 5 mcg/kg orally, 90 min before induction. They found consistently lower HR; and mean, systolic, and diastolic blood pressures in the clonidine group ($n = 12$) when compared to the control group ($n = 12$), during the intraoperative period. These results are in agreement with that of the present study. The blunting of the cardiovascular response to intubation was not seen in the current study as the study drug infusion was started after intubation and induction of anesthesia.

Hall et al.\textsuperscript{8} compared the dose-response relationship of 1 h infusions of clonidine 1, 2, and 4 mcg/kg/h; and placebo in 8 healthy individuals. MAP decreased by 13% of the baseline value in clonidine 4 mcg/kg/h group, 1 h after starting the infusion. In the current study, MAP decreased by 12.20%, 50 min after starting the clonidine infusion. The effect of 150 mcg of oral clonidine, 90 min before induction, was studied by Singh and Arora\textsuperscript{9} in 50 patients undergoing laparoscopic cholecystectomy. It was found that the perioperative mean arterial blood pressure and HR were significantly lower in clonidine group at all time points. The study also demonstrated a significant decrease in the requirement of isoflurane in the clonidine group. Results of the present study are similar except for the fact that significant lowering of MAP and HR were not seen at all time points, but only after creation of the pneumoperitoneum. This could be attributed to the fact

<table>
<thead>
<tr>
<th>Requirement of isoflurane</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 1 versus Group 2</th>
<th>Group 1 versus Group 3</th>
<th>Group 2 versus Group 3</th>
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</thead>
<tbody>
<tr>
<td>No</td>
<td>0 (0)</td>
<td>37 (92.5)</td>
<td>36 (90)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>1.000</td>
</tr>
<tr>
<td>Yes</td>
<td>40 (100)</td>
<td>3 (7.5)</td>
<td>4 (10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>40 (100)</td>
<td>40 (100)</td>
<td>40 (100)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Requirement of atropine</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>(P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>40 (100)</td>
<td>35 (87.5)</td>
<td>37 (92.5)</td>
<td>0.055</td>
</tr>
<tr>
<td>Yes</td>
<td>0 (0)</td>
<td>5 (12.5)</td>
<td>3 (7.5)</td>
<td>0.241</td>
</tr>
<tr>
<td>Total</td>
<td>40 (100)</td>
<td>40 (100)</td>
<td>40 (100)</td>
<td>0.712</td>
</tr>
</tbody>
</table>
that clonidine was administered 90 min before induction in the said study, while it was administered after induction in the present study. Isoflurane sparing effect of clonidine was also observed in the present study.

Aantaa et al.\textsuperscript{10} conducted a study, to define the interaction between intravenous infusion of dexmedetomidine and isoflurane in 49 women undergoing abdominal hysterectomy using minimum alveolar concentration (MAC) of isoflurane as the measure of anesthetic potency. The study included 49 women, randomly allocated to receive either a placebo infusion \((n = 16)\) or a two staged infusion of dexmedetomidine with target plasma concentration of 0.3 ng/mL \((n = 17)\) or 0.6 ng/mL \((n = 16)\). It was found that the MAC of isoflurane was 0.85\% end tidal in the control group, 0.55\% end tidal with the low-dose dexmedetomidine and 0.45\% end tidal with high-dose dexmedetomidine. Similar results were observed regarding the isoflurane-sparing effect of dexmedetomidine in the current study.

Bhattacharjee et al.\textsuperscript{11} studied the effects of dexmedetomidine infusion (0.2 mcg/kg/h) for hemodynamic stability in 60 patients undergoing laparoscopic cholecystectomy and found that MAP and HR in dexmedetomidine group were significantly less after intubation and throughout the period of pneumoperitoneum. Similar results were obtained in the present study.

Taittonen et al.\textsuperscript{12} administered clonidine 4 mcg/kg and dexmedetomidine 2.5 mcg/kg 40-50 min before the anticipated induction of anesthesia in 30 ASA I patients and observed that HR and MAP were lower in clonidine and dexmedetomidine groups when compared to placebo group. These results are comparable to those obtained in the current study.

**CONCLUSION**

Laparoscopic cholecystectomy is a routinely performed surgery and it is desirable to have a stable intraoperative hemodynamic status by avoiding hypertension, hypotension, or tachycardia. Opioids; volatile agents such as isoflurane and sevoflurane; nitroglycerine; beta blockers; etc., have been used to control perioperative stress during laparoscopy. However, the search for an ideal agent is still on. Of late, \(\alpha_2\) adrenergic agonists have generated interest in this regard. Hence, the present study was conducted to establish and compare the beneficial effect of two \(\alpha_2\) agonists, clonidine and dexmedetomidine, in maintaining perioperative cardiovascular stability during laparoscopic cholecystectomy.

On the basis of observations made during study, following conclusions were drawn:

1. Intraoperative HR was significantly lower in clonidine and dexmedetomidine groups, compared to the control group.
2. Intraoperative HR was significantly lower in clonidine group, compared to dexmedetomidine group.
3. There was no statistically significant difference in the requirement of atropine among the three groups, indicating that there was no significant rise in the episodes of bradycardia associated with the use of either clonidine or dexmedetomidine.
4. Intraoperative blood pressure (MAP) was significantly lower in clonidine and dexmedetomidine groups, compared to the control group.
5. There was no statistically significant difference in intraoperative blood pressure (MAP) between clonidine and dexmedetomidine groups.
6. Requirement of isoflurane was significantly lower in clonidine and dexmedetomidine groups, compared to the control group, indicating the inhalational agent sparing effects of the two drugs.
7. There was no statistically significant difference in the requirement of isoflurane between clonidine and dexmedetomidine groups.
8. There were no ECG changes associated with the use of the two study drugs.
9. Thus, both clonidine and dexmedetomidine favorably alter the intraoperative hemodynamics and maintain cardiovascular stability during laparoscopic cholecystectomy. In the doses used in the current study, clonidine decreased intraoperative HR more than dexmedetomidine.

**REFERENCES**


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