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# Effects of Oral Clonidine versus Oral Pregabalin Premedication on Post-operative Recovery Profile: A Randomized Double-Blind Study

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## ABSTRACT

**Background:** Post-operative recovery optimization remains a crucial aspect of modern anesthetic practice. This study compared the effects of oral clonidine versus pregabalin premedication on post-operative recovery profiles.
**Methods**: In this prospective, randomized, double-blind study, 75 ASA I patients undergoing laparoscopic cholecystectomy were randomly allocated to receive either oral clonidine 5µg/kg (n=25), pregabalin 150mg (n=25), or placebo (n=25) before surgery. Post-operative parameters including pain scores, sedation levels, hemodynamic stability, and analgesic requirements were monitored for 4 hours.
**Results**: Pregabalin demonstrated superior pain control with 100% of patients maintaining VAS ≤4 versus 72% in clonidine and 24% in placebo groups ($p<0.001$). Clonidine provided better hemodynamic stability, maintaining lower heart rates (71.00±3.51 vs 83.20±5.76 beats/min in placebo, $p<0.001$) and mean arterial pressure (82.64±2.30 vs 93.60±6.61 mmHg in placebo, $p<0.001$) at 240 minutes. Sedation patterns differed significantly, with pregabalin showing deeper sedation (RSS 3 in 88%) compared to clonidine (RSS 2 in 96%).
**Conclusion**: Both medications demonstrated distinct advantages in different aspects of recovery, suggesting the need for individualized premedication selection based on specific recovery priorities.

***Keywords:*** *Post-operative Recovery; Clonidine; Pregabalin; Pain Management; Hemodynamic Stability; Sedation; Laparoscopic Cholecystectomy; Premedication; Visual Analogue Scale; Ramsay Sedation Score.*

## INTRODUCTION

The postoperative period represents a critical phase in surgical patient care, characterized by complex physiological responses to surgical stress and anesthesia [1]. Optimizing postoperative recovery through effective premedication strategies has become increasingly important in modern anesthetic practice, particularly in the context of enhanced recovery protocols and ambulatory surgery programs [2]. Among the various premedication options available, clonidine and pregabalin have emerged as promising agents with potential benefits extending beyond the immediate perioperative period.

Postoperative pain management remains a significant challenge, with studies indicating that approximately 40% of surgical patients experience moderate to severe acute postoperative pain despite current analgesic strategies [3]. This inadequate pain control not only affects patient comfort but can also lead to delayed recovery, prolonged hospital stays, and increased healthcare costs [4]. Furthermore, acute postoperative pain has been identified as a significant risk factor for the development of chronic postsurgical pain, emphasizing the importance of effective early interventions [3].

Clonidine, an α2-adrenergic agonist, has been traditionally used for its sympatholytic properties and its ability to reduce

anesthetic requirements [5]. Beyond these established effects, research has demonstrated its potential in improving postoperative outcomes through multiple mechanisms. Studies have shown that preoperative clonidine can reduce postoperative pain scores, decrease analgesic requirements, and provide extended periods of hemodynamic stability [6]. Its sedative properties may also contribute to reduced preoperative anxiety, an important factor in patient satisfaction and recovery.

Pregabalin, initially developed for neuropathic pain management, has gained attention in perioperative medicine due to its unique pharmacological profile [7]. As a gabapentinoid that modulates calcium channel activity, pregabalin has demonstrated efficacy in reducing postoperative pain intensity and opioid consumption [8]. Additionally, its anxiolytic properties and potential to prevent central sensitization make it an attractive option for perioperative pain management strategies [9].

While both medications have shown promise individually, direct comparisons of their effectiveness in managing postoperative recovery parameters are limited. Understanding their relative efficacy in controlling pain, maintaining hemodynamic stability, and influencing sedation levels is crucial for developing optimal premedication protocols.

Furthermore, the impact of these agents on overall recovery profiles and patient satisfaction needs comprehensive evaluation [10].

The present study aims to compare the effects of oral clonidine versus pregabalin premedication on postoperative recovery parameters, including pain scores, hemodynamic stability, sedation levels, and analgesic requirements. This investigation seeks to provide evidence-based guidance for selecting appropriate premedication strategies to optimize postoperative recovery.

## AIMS AND OBJECTIVES

The primary aim of this study was to evaluate and compare the effects of oral clonidine and pregabalin premedication on postoperative recovery profiles in patients undergoing laparoscopic cholecystectomy. The study specifically focused on comparing postoperative sedation levels, hemodynamic stability, pain control, and analgesic requirements between the study groups. Additionally, the study aimed to assess the preoperative anxiolytic and sedative effects of both medications to determine their impact on the overall recovery process.

## MATERIALS AND METHODS

### Study Design

This prospective, randomized, double-blind, comparative study was conducted at Narayana Health City, Bommasandra, Bengaluru from April 2017 to May 2018 after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrollment in the study.

### Sample Size Calculation

The sample size was calculated based on a previous study by Shirin Parveen et al, which reported postoperative sedation scores. Using the reported values of $2.2 \pm 0.41$ in the oral clonidine group and $2.73 \pm 0.55$ in the oral pregabalin group, with a confidence level of 95% ($\alpha = 0.05$) and power of 95% ($\beta = 0.05$), the minimum required sample size was calculated to be 25 patients per group. To account for potential dropouts, a total of 75 patients were included in the study, with equal distribution among three groups.

### Study Population and Selection Criteria

The study included ASA grade I patients between 18 to 50 years of age of both genders who were scheduled for elective laparoscopic cholecystectomy under general anesthesia.

Exclusion criteria encompassed patients with medical comorbidities including hypertension, ischemic heart diseases, arrhythmia, renal, respiratory, cerebral diseases, asthma, and epilepsy. Patients with anticipated difficult intubation, allergies to study medications, those taking sedatives or hypnotics, and pregnant women were also excluded. Additionally, patients who did not provide consent were excluded from the study.

### Randomization and Blinding Process

Patient randomization was accomplished using a computer-generated random number list. From approximately 200-250 eligible cases identified during the study period, 75 cases were selected by enrolling every third eligible and willing patient. The selected patients were randomly divided into three equal groups of 25 each. The study maintained double-blinding throughout, with both patients and anesthesiologists unaware of the treatment allocation. The hospital pharmacy prepared identical capsules containing either pregabalin, clonidine, or placebo, and a doctor not involved in the perioperative evaluation administered the capsules according to the randomization sequence.

**Drug Administration and Monitoring Protocol**

Patients in Group A received oral clonidine 5µg/kg, Group B received oral pregabalin 150 mg, and Group C received a placebo (B complex capsule), all administered 60 minutes prior to surgery. All patients received standard premedication with 5mg oral diazepam the night before surgery and 40mg pantoprazole on the day of surgery.

**Postoperative Assessment**

Postoperative monitoring was conducted in the Post Anesthesia Care Unit (PACU) for four hours. Sedation levels were assessed using the Ramsay Sedation Scale at regular intervals. Pain was evaluated using the Visual Analog Scale (VAS) on arrival and during the second hour. Analgesics were administered when the VAS score exceeded 4. Hemodynamic parameters including heart rate, blood pressure, and mean arterial pressure were recorded every 15 minutes for the first two hours and every 30 minutes for the subsequent two hours. Patients were monitored for adverse effects and the need for rescue analgesics. Discharge from PACU was based on achieving an Aldrete score greater than 9.

**Statistical Analysis**

Data analysis was performed using SPSS statistical package version 17. Statistical measures included calculation of mean, standard deviation, and p-values. The ANOVA test was used for quantitative variables, while Yate's and Fisher's chi-square tests were employed for qualitative variables. A p-value less than 0.05 was considered statistically significant.

## RESULTS

Demographic characteristics were comparable across all three groups. The mean age of patients in the clonidine, pregabalin, and placebo groups was 40.5±8.17, 38.48±6.2, and 41.12±5.7 years respectively, with no significant statistical difference between groups. Gender distribution showed male predominance across all groups: clonidine (72%), pregabalin (80%), and placebo (84%).

Post-operative heart rate showed significant differences between groups throughout the observation period ($p<0.001$). At 1 minute post-operative, the clonidine group demonstrated significantly lower heart rates (74.04±4.59 beats/min) compared to pregabalin (82.36±3.45 beats/min) and placebo (93.28±7.70 beats/min) groups. This trend continued throughout the observation period, with the clonidine group maintaining lower heart rates. By 240 minutes, both clonidine (71.00±3.51 beats/min) and pregabalin (70.60±2.48 beats/min) groups showed similar heart rates, significantly lower than the placebo group (83.20±5.76 beats/min).

Post-operative sedation scores revealed distinct patterns between groups. During the first hour, all patients (100%) in the clonidine group maintained RSS 2, while the pregabalin group showed predominantly RSS 3 (88%), with only 12% at RSS 2. The placebo group demonstrated lower sedation levels, with 48% at RSS 1 and 52% at RSS 2. During the second hour, the clonidine group maintained stable sedation with 96% at RSS 2, while pregabalin group continued to show deeper sedation (88% at RSS 3).

Pain control, as assessed by VAS scores, showed superior results in the pregabalin group. During the first hour, 100% of pregabalin patients maintained VAS scores ≤4, compared to 72% in the clonidine group and only 24% in the placebo group. This trend continued into the second hour, with pregabalin maintaining 100% of patients at VAS ≤4, while clonidine decreased to 52% and placebo to 12%.

Analgesic requirements correlated with pain scores. In the first hour, only 4% of patients in the clonidine group and none in the pregabalin group required rescue analgesia, compared to 48% in the placebo group. During the second hour, analgesic requirement increased slightly in the clonidine group (16%), while the pregabalin group maintained zero requirement, and the placebo group showed 20% requirement.

Hemodynamic parameters showed consistent patterns across groups. Systolic blood pressure remained significantly lower in the clonidine group throughout the observation period, starting at 113.96±2.95 mmHg at 1 minute and maintaining stability through 240 minutes (111.68±3.98 mmHg). The pregabalin group showed intermediate values, while the placebo group maintained higher readings throughout ($p<0.001$).

Diastolic blood pressure and mean arterial pressure followed similar trends. The clonidine group maintained the lowest values throughout the observation period, with final readings at 240 minutes of 70.32±3.06 mmHg (DBP) and 82.64±2.30 mmHg (MAP), significantly lower than both pregabalin and placebo groups ($p<0.001$).

**Table 1: Post-operative Heart Rate (beats/min) in PACU**

| Time | Clonidine Group (n=25) | Pregabalin Group (n=25) | Placebo Group (n=25) | p-value |
|---|---|---|---|---|
| 1 min | 74.04±4.59 | 82.36±3.45 | 93.28±7.70 | <0.001 |
| 15 min | 74.08±4.77 | 81.44±3.46 | 90.72±5.66 | <0.001 |
| 30 min | 73.68±4.08 | 81.92±3.69 | 88.16±5.31 | <0.001 |
| 60 min | 71.32±1.88 | 79.36±3.41 | 87.28±7.00 | <0.001 |
| 120 min | 68.24±13.08 | 74.52±2.87 | 86.12±6.75 | <0.001 |
| 240 min | 71.00±3.51 | 70.60±2.48 | 83.20±5.76 | <0.001 |

**Table 2: Post-operative Sedation Scores**

| Group | First Hour | | | Second Hour | | |
|---|---|---|---|---|---|---|
| | RSS 1 | RSS 2 | RSS 3 | RSS 2 | RSS 3 | RSS 4 |
| Clonidine | 0 (0%) | 25 (100%) | 0 (0%) | 24 (96%) | 1 (4%) | 0 (0%) |
| Pregabalin | 0 (0%) | 3 (12%) | 22 (88%) | 3 (12%) | 22 (88%) | 0 (0%) |
| **Group** | **First Hour** | | | **Second Hour** | | |
| Placebo | 12 (48%) | 13 (52%) | 0 (0%) | 25 (100%) | 0 (0%) | 0 (0%) |

**Table 3: Visual Analogue Score Distribution**

| Time | Group | VAS ≤4 | VAS >4 |
|---|---|---|---|
| First Hour | Clonidine | 18 (72%) | 7 (28%) |
| | Pregabalin | 25 (100%) | 0 (0%) |
| | Placebo | 6 (24%) | 19 (76%) |
| Second Hour | Clonidine | 13 (52%) | 12 (48%) |
| | Pregabalin | 25 (100%) | 0 (0%) |
| | Placebo | 3 (12%) | 22 (88%) |

**Table 4: Postoperative Analgesic Requirements**

| Time | Group | No Analgesia | Required Analgesia |
|---|---|---|---|
| First Hour | Clonidine | 24 (96%) | 1 (4%) |
| | Pregabalin | 25 (100%) | 0 (0%) |
| | Placebo | 13 (52%) | 12 (48%) |
| Second Hour | Clonidine | 21 (84%) | 4 (16%) |
| | Pregabalin | 25 (100%) | 0 (0%) |
| | Placebo | 20 (80%) | 5 (20%) |

**Table 5: Post-operative Systolic Blood Pressure (mmHg) in PACU**

| Time | Clonidine Group (n=25) | Pregabalin Group (n=25) | Placebo Group (n=25) | p-value |
|---|---|---|---|---|
| 1 min | 113.96±2.95 | 122.56±2.06 | 129.88±4.26 | <0.001 |
| 15 min | 112.52±2.74 | 122.56±3.12 | 128.32±5.40 | <0.001 |
| 30 min | 110.76±2.72 | 122.28±2.96 | 126.88±6.43 | <0.001 |
| 60 min | 111.04±3.64 | 118.36±2.25 | 124.84±8.49 | <0.001 |
| 120 min | 110.84±3.54 | 114.00±3.08 | 123.60±8.33 | <0.001 |
| **Time** | **Clonidine Group (n=25)** | **Pregabalin Group (n=25)** | **Placebo Group (n=25)** | **p-value** |
| 240 min | 111.68±3.98 | 110.88±2.78 | 123.40±8.33 | <0.001 |

**Table 6: Post-operative Diastolic Blood Pressure (mmHg) in PACU**

| Time | Clonidine Group (n=25) | Pregabalin Group (n=25) | Placebo Group (n=25) | p-value |
|---|---|---|---|---|
| 1 min | 71.36±2.98 | 84.40±3.01 | 81.24±7.30 | <0.001 |
| 15 min | 70.80±3.10 | 82.80±3.18 | 79.96±7.87 | <0.001 |
| 30 min | 69.80±2.73 | 82.56±2.95 | 79.80±7.35 | <0.001 |
| 60 min | 69.32±2.99 | 80.48±2.27 | 80.00±7.60 | <0.001 |

| | | | | |
|---|---|---|---|---|
| 120 min | 69.32±2.89 | 74.76±2.83 | 78.96±5.91 | <0.001 |
| 240 min | 70.32±3.06 | 70.92±2.08 | 79.24±6.64 | <0.001 |

**Table 7: Post-operative Mean Arterial Pressure (mmHg) in PACU**

| Time | Clonidine Group (n=25) | Pregabalin Group (n=25) | Placebo Group (n=25) | p-value |
|---|---|---|---|---|
| 1 min | 85.16±3.27 | 96.52±2.87 | 97.32±5.28 | <0.001 |
| 15 min | 83.84±2.32 | 95.72±2.66 | 95.48±6.24 | <0.001 |
| 30 min | 82.64±1.75 | 95.20±2.70 | 95.12±6.37 | <0.001 |
| 60 min | 81.80±1.84 | 92.80±1.84 | 95.00±6.58 | <0.001 |
| 120 min | 82.20±1.95 | 87.44±2.59 | 93.52±6.42 | <0.001 |
| 240 min | 82.64±2.30 | 83.84±2.01 | 93.60±6.61 | <0.001 |

## DISCUSSION

This study evaluated the post-operative recovery profiles following premedication with oral clonidine versus pregabalin in patients undergoing laparoscopic cholecystectomy.

The findings demonstrated distinct advantages for both medications in different aspects of post-operative recovery.

The superior pain control observed in the pregabalin group (100% of patients maintaining VAS ≤4) aligns with Mishriky et al.'s meta-analysis [11], which reported significant reduction in post-operative pain scores with pregabalin premedication (mean difference -0.59; 95% CI -0.83 to -0.35). The minimal requirement for rescue analgesia in the pregabalin group supports Zhang et al.'s findings [12], where pregabalin reduced 24-hour opioid consumption by 13.4mg morphine equivalents (95% CI: -18.7 to -8.1).

Post-operative sedation patterns differed significantly between groups. The predominant RSS 3 sedation level (88%) in the pregabalin group correlates with White et al.'s study [13], which reported increased sedation scores with 150mg pregabalin compared to placebo ($p<0.001$). The more moderate sedation profile observed with clonidine (96% at RSS 2) mirrors findings by Kumar et al. [14], suggesting a more favorable balance for early recovery.

Hemodynamic stability was notably better in the clonidine group, maintaining lower heart rates and blood pressure throughout the observation period. These findings support Blaudszun et al.'s systematic review [15], which demonstrated sustained hemodynamic control with α2-agonists in the post-operative period. The gradual convergence of hemodynamic parameters between clonidine and pregabalin groups by 240 minutes reflects similar observations by Gupta et al. [16].

## CONCLUSION

Based on this comprehensive analysis of post-operative recovery profiles, both pregabalin and clonidine demonstrated distinct advantages in different aspects of recovery. Pregabalin 150mg showed superior pain control with 100% of patients maintaining VAS scores ≤4 and requiring no rescue analgesia, though with deeper sedation levels (RSS 3 in 88% of patients). Clonidine 5μg/kg provided better hemodynamic stability with more moderate sedation (RSS 2 in 96% of patients), but slightly less effective pain control. These findings suggest that the choice between these premedications should be tailored to individual patient needs, considering the primary post-operative concerns.

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