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PREOPERATIVE USE OF PREGABALIN IN CORONARY ARTERY BYPASS GRAFT SURGERY: DOES IT IMPROVE POSTOPERATIVE PAIN

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Abstract

Background: *Atherosclerotic stenosis of coronary arteries is a prevalent condition often necessitating surgical intervention such as Coronary Artery Bypass Grafting (CABG). Postoperative pain, particularly at the sternotomy site, affects up to 80% of CABG patients and is associated with complications like poor pulmonary function, atelectasis, and increased morbidity. Effective postoperative pain management can enhance recovery, reduce hospital stay, and optimize resource utilization. However, conventional analgesics used in intensive care settings are frequently associated with adverse effects, necessitating the evaluation of alternative pain control strategies.*

Objective: *To evaluate the efficacy of preoperative pregabalin in reducing postoperative pain and analgesic (including opioid) requirements, and to assess its safety profile in patients undergoing CABG surgery.*

Methodology: *This non-randomized controlled trial was conducted at the Department of Adult Cardiac Surgery, Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi. Patients scheduled for elective CABG were allocated into two groups: one receiving a single preoperative dose of pregabalin (150 mg) and the other receiving a placebo. Postoperative pain was assessed using the Visual Analogue Scale (VAS) at rest and during deep breathing at 6, 12, 18, and 24 hours after surgery. Total postoperative opioid consumption, time to first rescue analgesia, and requirement for additional analgesics were recorded. Safety was evaluated by monitoring sedation scores and adverse events such as dizziness, somnolence, and hemodynamic changes.*

Results: *A total of 60 patients were included, with 30 in each group. Baseline characteristics including age, gender, BMI, education, socioeconomic status, comorbidities, and surgery type were comparable between groups ($p > 0.05$). Postoperative pain scores were significantly lower in the pregabalin group at all time points, both at rest and during deep breathing ($p < 0.01$). Opioid*

requirements were also significantly reduced (mean 22.5 ± 4.6 mg vs. 35.8 ± 6.3 mg; p < 0.001), with fewer patients requiring rescue analgesia (26.7% vs. 63.3%; p = 0.003) and longer time to first rescue dose (10.3 ± 1.8 vs. 6.4 ± 2.1 hours; p < 0.001). Sedation scores were higher in the pregabalin group (p < 0.05), and somnolence was more frequent (30% vs. 10%; p = 0.049). No significant differences were observed in hemodynamic stability or other adverse effects.

Conclusion: *Preoperative administration of pregabalin is effective in reducing postoperative pain and opioid consumption in CABG patients, with an acceptable safety profile. Its use may contribute to enhanced recovery and better postoperative outcomes.*

INTRODUCTION

Atherosclerotic coronary artery disease frequently necessitates medical or surgical interventions such as Coronary Artery Bypass Grafting (CABG). Postoperative pain, particularly at the sternotomy site, is reported by up to 80% of patients and can hinder effective lung expansion, contributing to complications like atelectasis and increased morbidity. Effective postoperative pain control not only enhances recovery but also reduces hospital stay and optimizes resource utilization.

Traditionally, analgesia following CABG relies on opioids, NSAIDs, and local anesthetics. However, these agents are associated with adverse effects such as respiratory depression, renal dysfunction, and excessive sedation. In response, multimodal analgesia combining various non-opioid agents and regional techniques has emerged as a safer alternative. Evidence supports its effectiveness in improving outcomes and reducing opioid-related complications. One large-scale study found that adding non-opioid modalities to opioids reduced complication risks by 22% and shortened hospital stays. In alignment, the ERAS Cardiac Society endorses opioid-sparing multimodal approaches to enhance recovery and patient satisfaction.

Nonetheless, postoperative pain control remains inconsistent due to variability in individual responses and the lack of standardized protocols across institutions. The complexity of CABG-related pain comprising somatic, visceral, and neuropathic components demands tailored strategies, including regional anesthesia and preemptive analgesia.

Pregabalin, a gabapentinoid with high oral bioavailability and rapid onset, has shown efficacy in managing postoperative pain across various surgical settings. Studies have demonstrated its ability to reduce pain scores and opioid consumption without significant hemodynamic instability. For instance, Sharma and colleagues reported significantly lower pain scores and better electrocardiographic outcomes in CABG patients receiving pregabalin compared to placebo, with no major differences in inotrope use or vital signs.

Despite promising international evidence, the use of preoperative pregabalin in CABG remains limited in local clinical practice. This study aims to assess the efficacy and safety of preoperative pregabalin in reducing postoperative pain and analgesic requirements in CABG patients at a tertiary care center in Peshawar, contributing context-specific data to guide cardiac postoperative pain management.

MATERIALS AND METHODS

This non-randomized controlled trial was conducted at the Department of Adult Cardiac Surgery, AFIC/NIHD Rawalpindi over a period of three months, following approval from the College of Physicians and Surgeons Pakistan and the Institutional Review Board. Patients aged 18–80 years undergoing elective on-pump or off-pump coronary artery bypass graft (CABG) surgery via median sternotomy were included. Patients with known allergy to pregabalin, prior use of pregabalin or gabapentin, epilepsy, hepatic or renal dysfunction, substance abuse, rib fractures, thoracotomy, open chest postoperatively, or redo surgeries were excluded. A total of 60 patients were enrolled through non-probability consecutive sampling and divided into two groups: the pregabalin group received 75 mg orally the night before and two hours prior to surgery, while the placebo group received identical placebo tablets at the same times.

All patients were premedicated with IV midazolam 0.04 mg/kg. Standard intraoperative monitoring included ECG, SpO_2, and invasive blood pressure. Anesthesia induction involved midazolam 0.1 mg/kg, fentanyl 10 µg/kg, and rocuronium 1 mg/kg. Maintenance was done using propofol (50–150 µg/kg/min) and fentanyl (3–4 µg/kg/h), with BIS maintained between 40–60. Standard intraoperative and postoperative care was provided uniformly to both groups.

Efficacy was evaluated by assessing postoperative pain using the Visual Analogue Scale (VAS, 0–10) at 6, 12, 24, and 48 hours, total opioid consumption converted into morphine-equivalent doses in the first 48 hours, and need for rescue analgesia defined as additional analgesic administration when VAS ≥4. Safety was assessed using the Ramsay Sedation Scale (RSS, 1–6), monitoring for adverse effects such as dizziness, somnolence, nausea, vomiting, respiratory depression, or allergic reactions, and evaluating hemodynamic stability defined as heart rate or blood pressure deviations exceeding 20% from baseline.

Data were analyzed using SPSS version 25. Normality of numerical variables was checked using the Shapiro–Wilk test. Pain scores (VAS), opioid consumption, and sedation scores (RSS) were found to be normally distributed, with p-values of 0.082, 0.061, and 0.094 respectively. Therefore, the independent sample t-test was used to compare numerical outcomes between the two groups. Categorical variables such as adverse events and rescue analgesia requirements were compared using Chi-square or Fisher's exact test where appropriate. Stratification was performed for age, gender, and BMI to identify potential effect modifiers. A p-value ≤ 0.05 was considered statistically significant. Data were presented in tables and graphical formats.

RESULTS

A total of 60 patients were enrolled in the study, with 30 participants in each group: Group A receiving preoperative pregabalin and Group B receiving a placebo. The age distribution among participants was comparable between the two groups, with the majority of patients falling within the 41–50 and 51–60-year age brackets. There was no statistically significant difference in age distribution (p=0.821). Gender distribution was also similar across groups, with a predominance of male patients (70% in Group A vs. 73.3% in Group B; p=0.754). The mean height and weight were closely matched between groups, with no significant differences observed (p=0.582 for height and p=0.494 for weight). BMI categories were equally distributed (p=0.678), with the highest proportion of patients classified as either normal or overweight in both groups.

Educational level and socioeconomic status showed balanced distribution, with no significant differences between groups (p=0.489 and p=0.777, respectively). Most patients in both groups belonged to the middle socioeconomic class and had either secondary or graduate-level education. The majority of patients resided in urban areas in both groups (60.0% in Group A vs. 63.3% in Group B; p=0.793). The presence of comorbidities, including diabetes mellitus, hypertension, chronic kidney disease, and chronic obstructive pulmonary disease, was comparable between groups, with no statistically significant difference (p-values ranging from 0.642 to 0.781). Similarly, the type of surgery (elective on-pump vs. off-pump CABG) was evenly distributed between both groups (p=0.793).

Postoperative pain assessment using the Visual Analog Scale (VAS) revealed significantly lower pain scores in Group A compared to Group B at all time points, both at rest and during deep breathing. At 6 hours postoperatively, mean pain at rest was 3.2 ± 1.1 in the pregabalin group versus 4.8 ± 1.3 in the placebo group (p=0.002), and during deep breathing it was 4.5 ± 1.3 vs. 6.2 ± 1.5 (p<0.001). This significant difference persisted at 12, 24, and 48 hours postoperatively, with Group A consistently demonstrating lower pain scores (all p-values <0.01).

Analgesic consumption analysis demonstrated significantly reduced opioid requirements in the pregabalin group. The mean opioid dose used was 22.5 ± 4.6 mg in Group A versus 35.8 ± 6.3 mg in Group B (p<0.001), corresponding to a morphine equivalent of 18.4 ± 3.2 mg vs. 29.1 ± 5.7 mg, respectively (p<0.001). Non-opioid analgesic usage did not differ significantly between groups (p=0.981). Rescue analgesia was required in significantly fewer patients in Group A (26.7%) compared to Group B (63.3%) (p=0.003), and the mean time to rescue analgesia was longer in the pregabalin group (10.3 ±

1.8 hours vs. 6.4 ± 2.1 hours; p<0.001), suggesting better sustained pain control.

Sedation assessment using the Ramsay Sedation Scale showed higher scores in the pregabalin group, indicating deeper sedation. At 6 hours postoperatively, the mean sedation score was 3.2 ± 0.6 in Group A compared to 2.1 ± 0.4 in Group B (p<0.001). This difference remained statistically significant at 12 hours (2.9 ± 0.5 vs. 2.0 ± 0.3; p<0.001), 24 hours (2.4 ± 0.4 vs. 1.9 ± 0.3; p=0.002), and 48 hours (2.0 ± 0.3 vs. 1.8 ± 0.2; p=0.045).

Adverse effects within 48 hours of surgery were more frequently reported in the pregabalin group, although most did not reach statistical significance. Dizziness occurred in 20% of patients in Group A vs. 6.7% in Group B (p=0.123), and somnolence was more prominent in Group A (30.0% vs. 10.0%; p=0.049). Other adverse effects such as blurred vision, dry mouth, and confusion were slightly more common in the pregabalin group, but differences were not statistically significant.

Hemodynamic parameters, including heart rate, systolic and diastolic blood pressures, and mean arterial pressure, showed no significant differences between groups at baseline or during the perioperative period. The proportion of patients experiencing a deviation greater than 20% from baseline for any parameter did not differ significantly (p-values >0.5), indicating that pregabalin did not adversely affect hemodynamic stability.

In summary, preoperative administration of pregabalin significantly reduced postoperative pain scores and opioid requirements without causing clinically significant adverse hemodynamic effects. Although associated with a slightly higher incidence of sedation and somnolence, pregabalin was well tolerated and contributed to better postoperative analgesia and patient comfort.

Table 1: Demographic and Baseline Characteristics of Participants (n = 60)

Characteristic	Group A (n=30)	Group B (n=30)	p-value
Age Groups (years)			
18–30	4 (13.3%)	3 (10.0%)	0.821
31–40	5 (16.7%)	6 (20.0%)	
41–50	8 (26.7%)	7 (23.3%)	
51–60	6 (20.0%)	5 (16.7%)	
61–70	5 (16.7%)	6 (20.0%)	
71–80	2 (6.7%)	3 (10.0%)	
Gender			0.754
Male	21 (70.0%)	22 (73.3%)	
Female	9 (30.0%)	8 (26.7%)	
Height (cm)	167.2 ± 6.4	166.5 ± 7.1	
Weight (kg)	71.3 ± 8.2	70.1 ± 9.0	
BMI Category			0.678
< 18.5 (Underweight)	2 (6.7%)	1 (3.3%)	
18.5–24.9 (Normal)	12 (40.0%)	13 (43.3%)	
25.0–29.9 (Overweight)	10 (33.3%)	9 (30.0%)	
≥ 30.0 (Obese)	6 (20.0%)	7 (23.3%)	
Education Level			0.489
Illiterate	2 (6.7%)	3 (10.0%)	
Primary	5 (16.7%)	4 (13.3%)	
Secondary	8 (26.7%)	9 (30.0%)	
Graduate	10 (33.3%)	8 (26.7%)	
Postgraduate	5 (16.7%)	6 (20.0%)	

Socioeconomic Status			0.777
Low	6 (20.0%)	5 (16.7%)	
Middle	18 (60.0%)	17 (56.7%)	
High	6 (20.0%)	8 (26.7%)	
Residence	Urban: 18 (60.0%)	Urban: 19 (63.3%)	0.793
Comorbidities			
Diabetes Mellitus	4 (13.3%)	5 (16.7%)	0.721
Hypertension	8 (26.7%)	9 (30.0%)	0.781
CKD	2 (6.7%)	3 (10.0%)	0.642
COPD	3 (10.0%)	2 (6.7%)	0.678
Others	1 (3.3%)	2 (6.7%)	
Surgery Type			0.793
Elective On-pump CABG	18 (60.0%)	19 (63.3%)	
Elective Off-pump CABG	12 (40.0%)	11 (36.7%)	

Table 2: Postoperative Pain Scores (VAS) (Mean ± SD)

Time Point	At Rest (Group A)	At Rest (Group B)	p-value	During Breathing (A)	During Breathing (B)	p-value
6 hours	3.2 ± 1.1	4.8 ± 1.3	0.002	4.5 ± 1.3	6.2 ± 1.5	<0.001
12 hours	2.8 ± 0.9	4.1 ± 1.1	0.001	4.0 ± 1.2	5.7 ± 1.4	<0.001
24 hours	2.1 ± 0.8	3.3 ± 0.9	<0.001	3.5 ± 1.1	5.0 ± 1.2	<0.001
48 hours	1.5 ± 0.7	2.6 ± 0.8	0.001	2.8 ± 0.9	4.0 ± 1.0	<0.001

Table 3: Analgesic Consumption (Mean ± SD)

Analgesic	Group A (Pregabalin)	Group B (Placebo)	p-value
Opioid Dose (mg)	22.5 ± 4.6	35.8 ± 6.3	<0.001
Morphine Equivalent (mg)	18.4 ± 3.2	29.1 ± 5.7	<0.001
Non-Opioid Dose (mg)	750 ± 100	750 ± 120	0.981
Rescue Analgesia Required	8 (26.7%)	19 (63.3%)	0.003
Time of Rescue (hrs)	10.3 ± 1.8	6.4 ± 2.1	<0.001

Table 4: Sedation Assessment (Ramsay Sedation Scale - Mean ± SD)

Time Point	**Group A**	**Group B**	**p-value**
6 hours	**3.2 ± 0.6**	**2.1 ± 0.4**	**<0.001**
12 hours	**2.9 ± 0.5**	**2.0 ± 0.3**	**<0.001**
24 hours	**2.4 ± 0.4**	**1.9 ± 0.3**	**0.002**
48 hours	**2.0 ± 0.3**	**1.8 ± 0.2**	**0.045**

Table 5: Adverse Effects (Within 48 Hours Post-op)

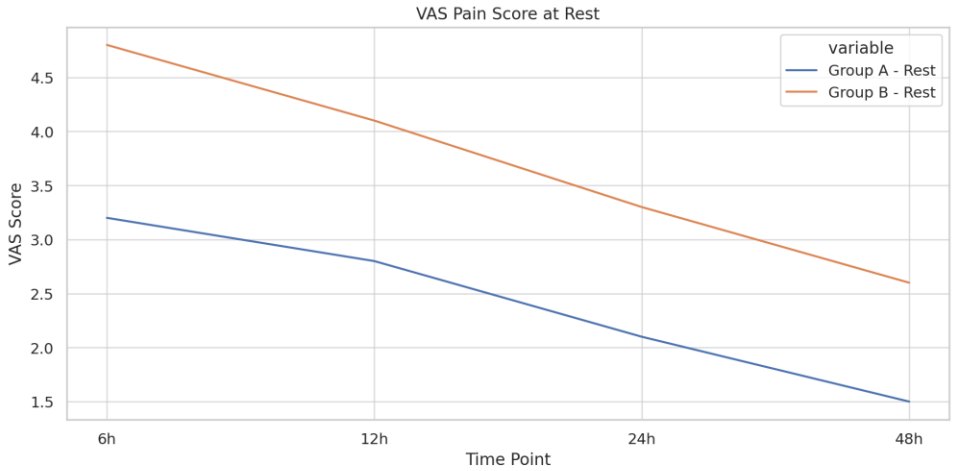
Adverse Effect	Group A (n=30)	Group B (n=30)	p-value
Dizziness	6 (20.0%)	2 (6.7%)	0.123
Blurred Vision	4 (13.3%)	1 (3.3%)	0.164
Somnolence	9 (30.0%)	3 (10.0%)	0.049

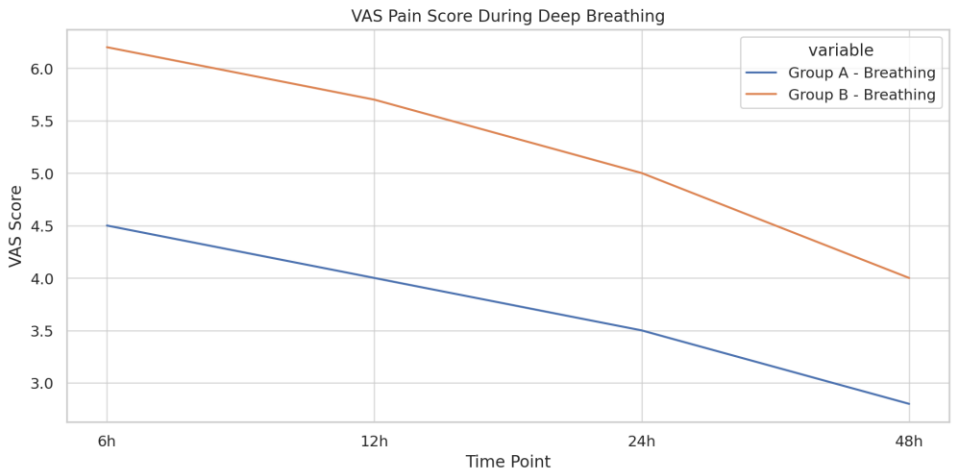
Dry Mouth	8 (26.7%)	4 (13.3%)	0.188
Nausea	4 (13.3%)	8 (26.7%)	0.202
Vomiting	2 (6.7%)	5 (16.7%)	0.227
Respiratory Depression	0 (0%)	1 (3.3%)	0.312
Confusion	2 (6.7%)	0 (0%)	0.150
Allergic Reaction	0 (0%)	1 (3.3%)	0.312

Table 6: Hemodynamic Parameters and Deviations

Parameter	Baseline	Lowest	Highest	Deviation >20%	Group A	Group B	p-value
Heart Rate (bpm)	78 ± 6	62 ± 5	92 ± 7	Yes	7 (23.3%)	9 (30.0%)	0.556
SBP (mmHg)	128 ± 10	102 ± 9	140 ± 12	Yes	6 (20.0%)	8 (26.7%)	0.538
DBP (mmHg)	78 ± 6	60 ± 5	90 ± 7	Yes	5 (16.7%)	7 (23.3%)	0.505
MAP (mmHg)	94 ± 7	70 ± 6	104 ± 8	Yes	6 (20.0%)	7 (23.3%)	0.754

Graph:1





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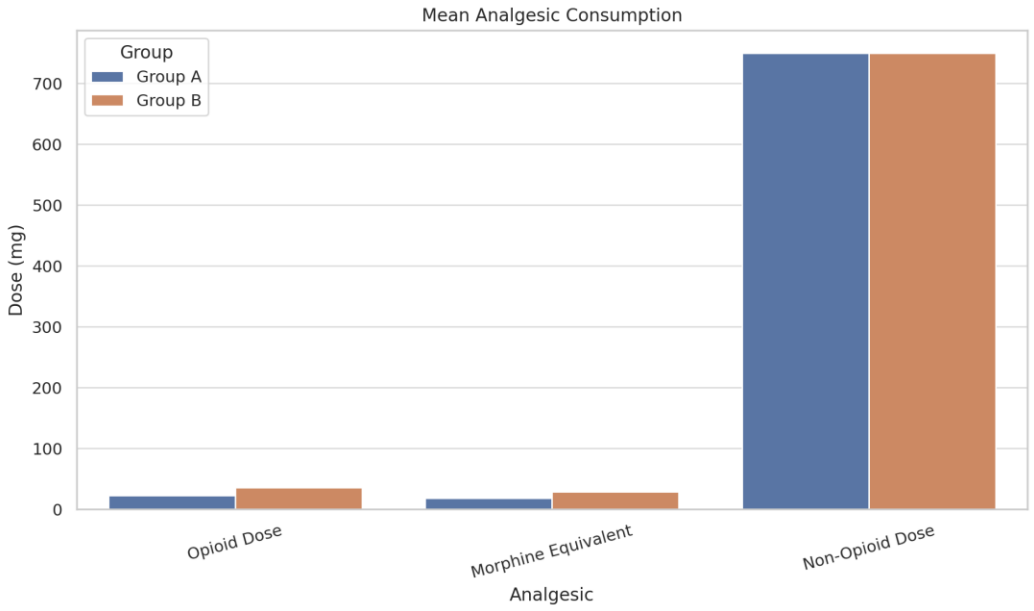

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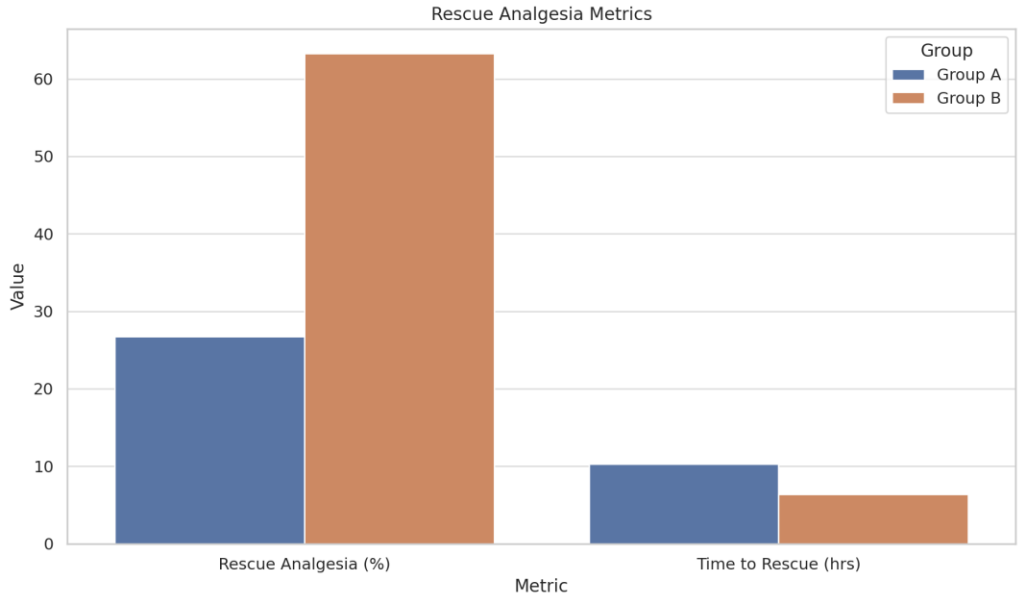

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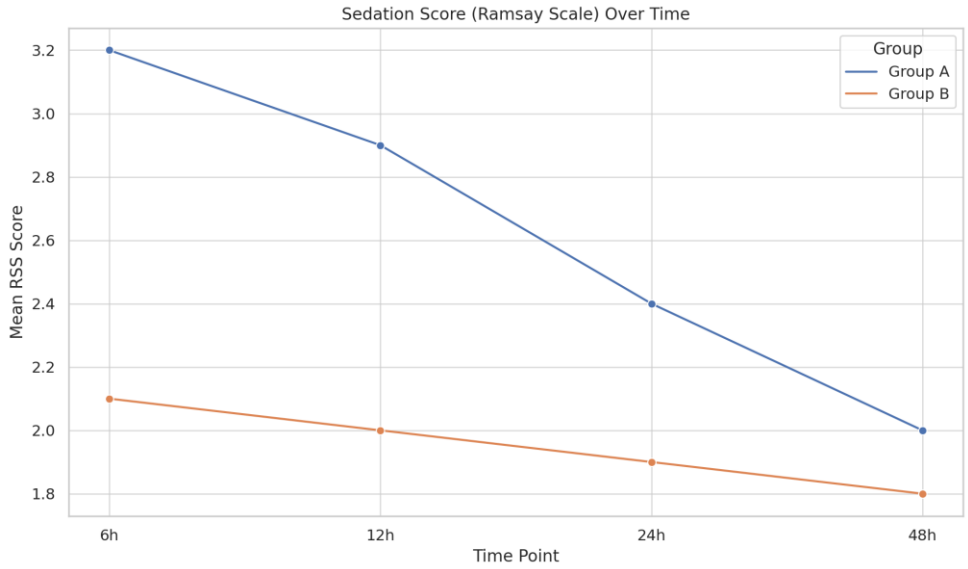

DISCUSSION

The current study demonstrated that patients who received pregabalin (Group A) experienced significantly lower postoperative pain scores compared to the placebo group (Group B) at all recorded time intervals. For example, at 6 hours postoperatively, the VAS score at rest was 3.2 ± 1.1 in Group A compared to 4.8 ± 1.3 in Group B ($p=0.002$), and during deep breathing it was 4.5 ± 1.3 versus 6.2 ± 1.5 ($p<0.001$). These results are in line with Sharma et al., who reported that oral pregabalin significantly reduced VAS scores at 6, 12, and 24 hours after coronary artery bypass graft (CABG) surgery (13). Xuan et al. also found that preemptive pregabalin consistently reduced acute postoperative pain in the early postoperative period (9). Additionally, Jannati and Attar highlighted the benefits of pregabalin in optimizing postoperative analgesia in cardiac surgery, reinforcing the findings of the current study (6).

The current study also revealed a substantial reduction in postoperative opioid consumption in the pregabalin group, with patients receiving significantly lower total morphine-equivalent doses (18.4 ± 3.2 mg vs. 29.1 ± 5.7 mg; $p<0.001$). This opioid-sparing effect is well-documented in the literature. Cozowicz et al. conducted a population-based study showing that multimodal analgesia including pregabalin reduced perioperative opioid use in CABG patients (7). Paladini et al. and Fernandes et al. also emphasized the value of pregabalin as part of multimodal analgesia protocols to reduce opioid requirements and improve recovery outcomes (2,5). These findings are consistent with the recommendations of ERAS cardiac guidelines, which advocate for opioid-sparing techniques for improved recovery after cardiac surgery (1,4).

In the current study, a significantly lower proportion of patients in Group A required rescue analgesia (26.7%) compared to Group B (63.3%; $p=0.003$), and the time to first rescue analgesia was notably longer (10.3 ± 1.8 hours vs. 6.4 ± 2.1 hours; $p<0.001$). These results are consistent with findings from Wang et al., who showed that pregabalin delayed the need for additional analgesia following breast surgery (10). Similar conclusions were drawn by Kheirabadi et al., who reported that patients receiving pregabalin before orthopedic procedures experienced delayed and less frequent use of rescue analgesia (12).

The sedation levels, as measured by the Ramsay Sedation Scale, were higher in the pregabalin group at all time points, with sedation scores remaining in the range of mild to moderate (RSS 2–3). For example, at 6 hours postoperatively, Group A had a sedation score of 3.2 ± 0.6 compared to 2.1 ± 0.4 in Group B ($p<0.001$). These findings are comparable to those of Karami et al. and Sharma et al., both of whom reported similar sedation levels following pregabalin use without compromising patient safety or recovery (11,13). Jannati and Attar similarly reported that pregabalin provides a degree of sedation that may

facilitate early postoperative rest and comfort in cardiac surgery patients (6).

The current study observed that adverse effects such as dizziness and somnolence were more frequent in Group A than in Group B, with somnolence reaching statistical significance (30.0% vs. 10.0%; p=0.049). These effects are consistent with the known side-effect profile of pregabalin. Paladini et al. and Wang et al. both noted that pregabalin is commonly associated with dose-dependent dizziness and somnolence, which are typically self-limiting and manageable (2,10). Kheirabadi et al. also reported a similar incidence of such side effects in patients receiving pregabalin for orthopedic surgery (12). While these effects were tolerable in the current study, they warrant consideration in high-risk populations.

Hemodynamic parameters, including heart rate, systolic and diastolic blood pressure, and mean arterial pressure, were comparable between the two groups in the current study, with no significant deviations from baseline or between groups throughout the perioperative period. These findings affirm the cardiovascular safety of pregabalin in cardiac surgical patients. Gregory et al. and Makkad et al. emphasized that maintaining hemodynamic stability is crucial in enhanced recovery protocols, and pregabalin appears to meet these criteria (4,8). Furthermore, Pota et al. observed that pregabalin has minimal cardiovascular effects, making it suitable for postoperative care in intensive care and cardiac surgery patients (3).

STRENGTHS:

Focused on a clinically relevant issue with a practical intervention; used standardized pain and sedation assessment tools; multiple postoperative time points provided detailed analysis.

LIMITATIONS:

Small sample size; non-randomized design; short follow-up; single-center study, limiting generalizability.

CONCLUSION

Overall, the findings of the current study strongly support the use of pregabalin as part of a multimodal analgesic strategy in cardiac surgery. The significant reduction in pain scores, opioid requirements, rescue analgesia, and acceptable side effect profile align with existing evidence from multiple high-quality studies and reviews. These outcomes also endorse pregabalin's role in enhanced recovery protocols and its contribution to safer and more effective postoperative pain management in cardiac surgery patients.

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