Preoperative Anxiety Among Cardiac Surgery Patients and Its Impact on Major Adverse Cardiac Events and Mortality– A Randomized, Parallel-Group Study

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ABSTRACT

Background: Patients undergoing elective cardiac surgery often experience pre-operative anxiety. Preoperative anxiety influences surgical outcome. There are very few studies which have assessed the impact of clonidine and Gabapentin in the treatment of anxiety especially in Indian populations and its implications on major adverse cardiac events (MACE) and 30 days mortality.

Materials and Methods: Adult patients aged 18 to 80 years old who were scheduled to have an elective coronary artery by-pass graft (CABG) were included in the study. Those who satisfied the inclusion criteria were given either Gabapentin (800 mg) or Clonidine (300 mcg) 90-120 minutes before the induction. State trait anxiety inventory (STAI) was used to assess anxiety in baseline and taking just before operating room. The primary endpoint was a reduction in the STAI associated with the study drug, while the secondary endpoint was the incidence of MACE in the perioperative period (30 days), which included composite episodes of non-fatal cardiac arrest, chaotic rhythm, acute myocardial infarction, congestive heart failure, cardiac arrhythmia, angina, and death.

Results: A total of 75 patients were considered for the statistical analysis. The demographic and clinical features of the study participants were similar in both groups. Nearly 75-80% of participants had severe anxiety in the preoperative period while 10-20% had moderate anxiety. While both the drugs showed a reduction in the anxiety levels, the clonidine group fared better (statistically insignificant). The incidence of MACE was similar in both groups.

Conclusion: The preoperative anxiety levels were high among cardiac surgery patients. Both clonidine and gabapentin were equally effective in reducing the levels of preoperative anxiety. Preoperative STAI scores in the range of 32-53 is not associated with MACE and 30-day mortality among cardiac surgery patients.

Keywords: Anxiety, clonidine, gabapentin, major adverse cardiac events, perioperative

INTRODUCTION

Patients undergoing elective cardiac surgery often experience pre-operative anxiety.⁵ Anxiety is a distressing emotion that can cause patients undergoing coronary artery bypass surgery to delay planned procedures. Such delays may turn out to be fatal. Millions of patients are given sedatives before surgery to help them relax, but the decision to do so is often based on institutional habit and practice.

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Preoperative anxiety influences surgical outcomes affect mental wellbeing and induce hypertension, tachycardia, and increased surgical bleeding, among others. These are crucial factors to consider in cardiac surgery which can precipitate sudden myocardial infarction in patients with critical coronary artery narrowing.[3] Cultural variations also contribute to anxiety; therefore, western data cannot be directly adapted to the Indian population. There is only one study that examines the prevalence of preoperative anxiety in Indian patients undergoing cardiac surgery, and it found that approximately half of those undergoing cardiac surgery have preoperative anxiety.[3] Although several studies have revealed the presence of anxiety associated with surgery,[4,5] not many have assessed the impact of clonidine and gabapentin in the treatment of anxiety and its implications on major adverse cardiac events and mortality.

The present study is carried out to assess the baseline anxiety levels in the Indian cardiac surgical population, the impact of clonidine and gabapentin in reducing preoperative anxiety, and the role of preoperative anxiety in causing major cardiac adverse events (MACE) and 30-day mortality.

**MATERIALS AND METHODS**

The study included adult patient’s aged between 18-80 years that were scheduled to undergo elective coronary artery by-pass graft (CABG) under general anesthesia to treat triple vessel disease. The study was carried out at a tertiary care teaching hospital between January 2020 and January 2021. All the patients included in the study gave informed written consent and the research was approved by the institute’s ethics committee. The trial was prospectively registered in clinical trial registry India vide infra CTRI/2020/12/029860.

All patients aged more than 80 years and below 18 years, pregnant, lactating, and menstruating females, patients suffering from drug/alcohol abuse, chronic pain, psychiatric diseases, peripheral vascular disease, were excluded from the study. Also, patients concomitantly on gabapentin, clonidine, sedatives, hypnotics, antidepressants, alpha-blockers, methyldopa, benzodiazepines, MAO inhibitors or drugs with effect on the nervous system and patients with severe renal or hepatic diseases were excluded from the study.

Randomization methods

Eighty similar-looking opaque boxes were randomly divided into two equal groups of 40 each (group A and B) and the code name A/B was mentioned on top of the boxes. The pharmacist was asked to separate the tablets of gabapentin (800 mg; 2 tablets of 400 mg each), and Clonidine (300 mcg; 3 tablets of 100 mcg each) into two equal groups of 40 each and load them separately into the boxes and sealed them to enable randomization.

The patients were randomized by a computer-generated table into two equal groups A/B so that group A patient received all the tablets from the box labelled as group A and patients in group B received all the tablets from the box labelled group B.

All patients were assessed a day before the surgery, and the state trait anxiety inventory (STAI) form was explained to them. STAI is the study instrument to measure preoperative anxiety. The STAI anxiety score was measured in the ward on the morning of surgery and just before taking the patient into the operation room.

The drug from the closed envelope was drawn and given to the patient by the ward nurse with sips of water, 90-120 min before induction. The identity of the tablet was not revealed to the patient. No other premedication was given other than the study drugs. Upon arrival in the operating room, STAI scale was again measured and anesthesia procedure followed standard operating institutional protocols.[6]

The primary endpoint of the study was a reduction in anxiety scale (STAI) associated with the study drug and the secondary endpoint was the incidence of MACE in the perioperative period (30 days) that included composite episodes of non-fatal cardiac arrest, chaotic rhythm, acute myocardial infarction, congestive heart failure, cardiac arrhythmia, angina, and death.[7]

**Statistical analysis**

The Statistical Package for Social Sciences (SPSS) version 16.0.0 for Windows (SPSS Inc., Chicago, IL, USA) and open epi software by CDC version 3.01 updated 2013/04/06 were used to analyze data.

**RESULTS**

From the total of 85 patients who were enrolled in the study, 10 patients were lost to follow-up or data was not available. The remaining 75 patients were included in the statistical analysis. The patients were randomized into two equal groups (37 each). The two groups were compared using the Chi-square test for categorical variables and the Student’s t-test for continuous variables. The primary endpoint of the study was a reduction in anxiety scale (STAI) associated with the study drug and the secondary endpoint was the incidence of MACE in the perioperative period (30 days) that included composite episodes of non-fatal cardiac arrest, chaotic rhythm, acute myocardial infarction, congestive heart failure, cardiac arrhythmia, angina, and death.

**Table 1: Demographic and clinical characteristics of patients**

| Patient characteristic | Group A | Group B | P     |
|------------------------|---------|---------|-------|
| Age (years) (Mean±SD)  | 38.7±11.2| 35.9±12.8| 0.27 (NS)* |
| Gender M:F             | 22:15   | 16:22   | 0.25 (NS)** |
| Weight (kg) (Mean±SD)  | 54.65±6.18| 55.03±6.31| 0.37 (NS)* |
| Number of grafts       | 3.12±1.1 | 3.11±1.21|       |
| Left Ventricular Ejection Fraction | 42.12±10.11 | 41.11±9.86 |       |

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[1] Mudgalkar, et al.: Preoperative anxiety and major adverse cardiac events

[2] CTNR/2020/12/029860.
Table 2: Classification of patients with baseline STAI score in both groups

| Variable                        | Group A (n=37) | Group B (n=38) | Z score | P       |
|--------------------------------|----------------|----------------|---------|---------|
| Mild anxiety STAI score <30    | 2 (2.7%)       | 1 (2.63%)      | 0.612   | 0.54    |
| Moderate anxiety STAI score 30-45 | 5 (13.51%)     | 8 (21.05%)     | -0.86   | 0.389   |
| Severe anxiety STAI score >45  | 30 (81.08%)    | 29 (76.21%)    | 0.50    | 0.61    |

Table 3: Baseline mean anxiety levels before and after the treatment

| Group   | n=37 n=38 | Mean ± SD | T statistics | F statistics | Df | P     |
|---------|-----------|-----------|--------------|--------------|----|-------|
| Before drug (baseline) | 69.2±16.5 68.4±14.7 | 1.25 | 36,37 | 0.4876 |
| Before shifting to OT | 53.1±15.9 32.4±11.8 | 1.81 | 36,37 | 0.07504 |

P<0.05 is considered as significant. Two sample independent T test.

Nearly 75-80% of participants had severe anxiety in the preoperative period while 10-20% had moderate anxiety. Very few (less than 5%) patients in both groups had low levels of anxiety as shown in Table 2.

The baseline anxiety score in Group A (gabapentin) was 69.2 ± 16.5, while in Group B (clonidine) it was 68.4 ± 14.7. The anxiety score revealed a 30% reduction in Group A as compared to a 50% anxiety reduction in Group B. Although the difference was observed in absolute values, there was no statistical significance (P value = 0.075). The data on anxiety levels among the two study groups are presented in [Table 2].

The occurrence of MACE was calculated in both groups after a follow-up of 30 days. Only one patient in Group A developed acute myocardial infarction and died of severe left ventricular dysfunction after a week of surgery. A patient in Group B developed congestive heart failure with severe left ventricular dysfunction, However, the patient responded well to diuretics, beta-blockers, and anti-anginal treatment and survived. On follow-up, the patient revealed a reduced quality of life. The incidence of MACE in both groups is mentioned in Table 4.

**DISCUSSION**

During the perioperative period, anxiety is a common phenomenon. Several studies have found that perioperative anxiety is linked to an eventful surgical outcome. Preoperative anxiety is a typical occurrence that can harm a variety of perioperative parameters.

Our study corroborates with the findings of previous researchers that anxiety is common among cardiac surgery patients. Almost every patient in our study was anxious about surgery, with the incidence of moderate and severe anxiety is nearly 92%. This indicates a definitive need for preoperative psychological counseling of the patients, wherein the patients are reassured about the surgery. The provision of information, relaxation techniques, sensory approaches, behavioral instructions, cognitive interventions, and emotion- and hypnosis-based techniques were generally described as effective in minimizing postoperative pain, and the length of the hospital stay. The cardiac surgical patients suffer from significant psychological stress, and currently, there is no specific intervention recommended in the literature to treat/manage such patients. Therefore, the current study was undertaken to assess the impact of two different medications on preoperative anxiety.

The study observed the effects of clonidine and gabapentin on preoperative anxiety among cardiac surgery patients. While both the drugs showed a reduction in the anxiety levels, the clonidine group fared better (statistically insignificant) as noted by the decrease in the anxiety levels from severe to moderate levels.

Though few previous studies assessed association of preoperative depression and postoperative mortality, none of the previous studies investigated the association of MACE in cardiac surgery and its relation to preoperative anxiety. The present study is the first of its kind that has attempted to assess the impact of preoperative anxiety on MACE and 30 day mortality. Considering the results of the present study it can be concluded that severe preoperative anxiety may not be associated with MACE and 30 days mortality.

Preoperative anxiety was linked to a lower quality of life and cognitive performance, a greater need for information, poorer memory and attention, longer hospitalization, depressive symptoms, and increased physical disability as evidenced by the results of a previous meta-analysis on this topic. However, this study revealed no correlation of survival rate with preoperative anxiety.

The current study’s findings have implications in the field of cardiac surgery. The first and most important is
that patients have access to the knowledge they need to adjust to the negative effects of hospitalization and deal effectively with medical and surgical treatments. Patients gain greatly from concentrated and systematic attempts to psychologically prepare them.

The observations drawn from the results of the current study indicate the fact that medical practitioners have overlooked the psychological consequences of the disease, treatment, and the impacts of hospitalization and surgery. Therefore, it is important to give more emphasis on these factors that enable patients to recover faster and lead an improved quality of life after hospitalization and surgery.

**CONCLUSION**

The preoperative anxiety levels were high among cardiac surgery patients. Both clonidine and gabapentin were equally effective in reducing the levels of preoperative anxiety. Preoperative STAI Scores between 32 and 53 is not associated with MACE and 30-day mortality among cardiac surgery patients.

**Limitation**

This is a single-center research, and larger multi-center studies with a larger sample size are needed to correctly quantify the influence of anxiety and MACE after 30 days. Because there have been no previous studies linking preoperative anxiety to 30-day MACE, a power analysis could not be undertaken, and this study can serve as a pilot study for future research.

**Declaration of patient consent**

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

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**Conflicts of interest**

There are no conflicts of interest.

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