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THE EFFECT OF PREOPERATIVE ALPRAZOLAM IN THE REDUCTION OF ANXIETY IN PATIENTS UNDERGOING CARDIAC SURGERY

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ABSTRACT

Background: Anxiety before cardiac surgery is likely to be accompanied by physiological changes that may influence surgical results. Alprazolam as pharmacological therapy could help stabilize these indicators improving the patients' comfort and respectively perioperative conditions. This research will seek to prove if alprazolam decreases preoperative anxiety without adverse effects to promote better perioperative care practice using a controlled trial design. The effects of preoperative anxiety are observed in 30–80% of patients having major surgery, notably, cardiac procedures. Physiological changes caused by the anxiety can interfere with the anesthetic management and recovery due to increase in heart rate and blood pressure. Although anxiolytic drugs such as alprazolam are widely available, we know little about their effects on patients undergoing cardiac surgery. The purposes of this study were to fill this gap by determining the effectiveness and safety of ES in reducing preoperative anxiety of cardiac patients.

Objective: To assess the influence of preoperative alprazolam on preoperative anxiety levels in heart surgery patients.


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Methodology: Randomized controlled study was performed in Hameed Latif Hospital, Lahore. The patients were 200 undergoing elective coronary artery bypass graft (CABG) or valve replacement surgery. The 14 randomly assigned participants were assigned to either the alprazolam group at some oral dosage of 0.5 mg or to the placebo group. Change the structure of the following sentence Physiological parameters were measured before and after drug administration, preoperatively and postoperatively. SPSS 26 was used for statistical analysis and significance set to $p < 0.05$.

Results: Statistical analysis showed no statistically significant differences between the two groups in baseline physiological markers. When anxiety markers are analyzed after drug delivery, the alprazolam group was reduced in respiration rate ($p = 0.04$) before surgery. Nevertheless, other metrics including heart rate, blood pressure, and oxygen saturation did not show statistically significant variations.

Conclusion: Preoperative alprazolam treatment did improve physiological markers of anxiety, notably respiratory rate, in the heart surgery patients in a mildly attenuated fashion. However, although it might help in lowering preoperative anxiety, its effect on the rest of physiological outcomes was negligible. However further dose and also other pharmaceutical treatments for anxiety management in cardiac surgery patients need to be identified.

Keywords: Preoperative Anxiety, Alprazolam, Cardiac Surgery, Anxiolytic Medication, Randomized Controlled Trial

Introduction

Anxiety prior to cardiac surgery is a significant and widespread issue that is associated with a number of deleterious consequences of the patient's surgical experience, recovery and health outcomes. In this setting anxiety could be induced by the apprehension of operation, fear for complications and the unknown course through the postoperative recovery. Preoperative anxiety is known to be a form of distress for patients and results in negative physiological effects, such as elevated heart rate, increased blood pressure and higher amounts of stress hormones, which may interfere with patient preparation for anesthesia and surgery [1]. Accordingly, the proper

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management of preoperative anxiety in cardiac surgery patients is very important for increasing patient comfort, the surgical results and reducing the possibility of postoperative problem.

Anxiety must be managed in the setting of heart surgery. Special stress, as found from the intrusiveness of the operations in cardiac surgery, the task risks and its longterm impact on the patients' health. A number of unfavorable outcomes like increased postoperative pain, prolonged hospital stay, and increased the risk of complications like infection, arrhythmias and delayed wound healing have been shown [2], [3] to result from patients 'mild and moderate anxiety before such treatments. In addition, there is a circumstance that poorer recovery and greater morbidity are connected with preoperative anxiety, which is an important part of perioperative care that requires further exploration.

Alprazolam, like other benzodiazepines, is widely recommended as it is a great anxiolytic that causes a sensation of calm and helps control tension. A short-acting benzodiazepine, Alprazolam, functions by enhancing the action of gamma-aminobutyric acid (GABA), a neurotransmitter essential in the suppression of overly excitable neurons and decreasing of anxiety [4]. Alprazolam is a commonly used medication in clinical practice for the treatment of acute anxiety episodes, and might constitute one of the options to control the preoperative anxiety in heart surgery patients. However, the exact significance in cardiac surgery is under researched although the medication's efficacy had been demonstrated in other populations and types of surgery.

This should give an impetus for development of the potential of alprazolam for its capability to lower preoperative anxiety in cardiac patients thereby improving patient care. However, there is an extremely small amount of information concerning the effectiveness and safety of alprazolam in this setting, particularly in large randomized controlled trials (RCTs) that could provide convincing evidence for its widespread clinical use. Because alprazolam has potential to add to a more comfortable and less stressful surgical experience, the study of its specific effects on reducing anxiety and affecting physiological characteristics in this population is imperative. To address this gap, this study investigates whether preoperative administration of alprazolam reduces anxiety in cardiac surgery patients and whether this has any impact on a number of physiological responses, such as heart rate, blood pressure, and respiration rate.


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In this study the effect of prescription preoperative alprazolam for minimizing the anxiety and improving the physiological results in patient scheduled for elective heart surgery done at Hameed Lateef Hospital Lahore, Pakistan are analyzed. The research primarily seeks to explore the immediate effects of preoperative alprazolam on physiological parameters which are known to be impacted by anxiety specifically HR, SBP, DBP, MAP, RR, and O2Sat. Especially, it will focus on cases when patients are undergoing coronary artery bypass graft (CABG) or valve replacement surgery which are two of the most regularly done cardiac operations and where preoperative anxiety surrounding the operation is at the same level.

The approach of this investigation will be a randomized controlled trial (RCT) in which subjects will be randomly allocated to either the alprazolam group or the placebo group. It enables for a controlled study of the effects of alprazolam on anxiety and physiological parameters as opposed to a placebo therapy, so that no observed effects are due to confounding factors. The study volunteers will receive either preoperative 0.5 mg oral dose of alprazolam the night before surgery (intervention group) or identical appearance placebo pill representing alprazolam (control group). The various physiological parameters would be studied before giving the drug, after drug administration, before moving to the operating room (OR), and after surgery. By giving the early effects of alprazolam on this physiological indicator, which is significantly acted upon by preoperative anxiety, we will learn how alprazolam affects a patient's physiologically during the perioperative period. Statistical analysis will follow data collection, to assess whether the significant differences exist between the alprazolam and placebo groups regarding the reduction of anxiety related physiological responses.

The primary intention of this research is to extend current knowledge of pharmacological anxiety management in cardiac surgery through empirically provided information regarding the ability of alprazolam to reduce preoperative anxiety in this high-risk surgical population. This study will contribute to the alprazolam literature by using physiological responses to specifically examine alprazolam's effects on stress pathways during the crucial preoperative stage.

Moreover, this research is prompted by an increasing acceptance of the necessity for more effective preoperative care that will diminish the level of anxiety, especially in high-risk surgery candidate

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like those with heart surgery. Although alprazolam, a benzodiazepine, is widely used within therapeutics and is for use in reducing preoperative anxiety in heart surgery patients, its use for this purpose is noteworthy in that there is little convincing evidence available to support such use. While a majority of research have evaluated non cardiac surgeries, there is a void in the literature regarding these interventions in the context of cardiac procedures. This vacuum in understanding is especially important given the fact that cardiac surgery patients have physiologic hurdles unique to them preexisting cardiovascular problems that might change how they respond to anxiolytic therapies.

The results are further relevant because anxiety is already a major burden of the complications from cardiac surgery, in which worry can worsen preoperative physiological instability and enhance the occurrence of postoperative difficulty. Pharmaceutical therapy involving the use of alprazolam to address preoperative anxiety might help improve the surgical results, patient satisfaction, and postoperative recovery. Consequently, the results of this study may provide valuable input into the current discussion about how to best manage cardiac surgery patients' preoperative anxiety, in that they may help inform clinically recommended methods of treatment, as well as what is provided to these patients in practice.

Additionally, as an RCT using a placebo-controlled manner, this study aims at producing highly reliable information on which physicians can base rational decisions regarding the use of alprazolam in this case. Also, this research underscores the imperative need to individualize, evidence-based treatment in cardiac surgery, where individually developed interventions can attenuate the detrimental effects of preoperative anxiety and augment overall patient outcomes. This clinical study is timely and relevant to many settings of healthcare because of the increasing incidence of heart disease and surgery in both developed and developing countries.

Having a patient with elevated anxiety prior to cardiac surgery is especially eye catching as cardiac surgery generally includes high stakes and the use of exotic procedures that require precise, invasive techniques with life threatening risks. Surgery itself induces a psychological anxiety which can have physiological effect on the patients and can produce complication to the underlying heart diseases. Activation of the autonomic nervous system due to anxiety can lead to physiological

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responses, tachycardia, hypertension, and elevated cortisol levels. If these physiological abnormalities are not addressed, they will make the body more susceptible to the effects of surgery and anesthesia, and therefore it may be more difficult to keep the vital signs stable during surgery [5].

Although anxiolytic drugs, especially benzodiazepines such as alprazolam, are known to decrease preoperative anxiety in several surgical contexts, the importance of anxiolysis in the cardiac surgery context has yet to be explored. Since alprazolam is a short acting benzodiazepine, and hence, has a rapid onset of action, it is widely selected to control its preoperative anxiety. The Central Nervous System contains GABA receptors which binds to it resulting in a relaxing and sedative effect that can lower anxiety drastically without severe sedation [6]. Though alprazolam has shown benefit in decreasing anxiety for outpatient surgeries, there is scarce data on benefits and risks of alprazolam in cardiac surgery patients with higher risks and potentially different physiological response for that disease and surgery. The purpose of this study is to comprehensively study the usage of alprazolam in cardiac surgery patients, touching on both anxiety reduction and physiological effects. This research by analyzing the changes in heart rate, blood pressure and respiratory rate will help to understand how alprazolam controls the stress response in the body, and how the finding can be converted into improvement of perioperative management of cardiac patient.

This study aimed mainly to find out how well preoperative alprazolam lowers patients' anxiety and improves physiologic outcomes in those undergoing elective heart surgery. In particular, the study will assess the influence of a 0.5 mg dose of alprazolam (given the night before surgery) on a range of physiological endpoints that are known to change due to anxiety. There was also a substantial influence on heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, respiratory rate, and oxygen saturation. The research will use the results of comparison through a randomized controlled trial to establish whether alprazolam permits significant decreases in preoperative anxiety and enhances the stability of some physiological markers as compared to a placebo.


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In addition to the main measures (physiological markers and symptoms), changes in anxiety levels will be investigated, using both self-reported measures of anxiety or worry as well as physiological markers of anxiety that are frequently perturbed by heightened anxiety. These parameters will be measured under a structured method using this trial, at different time points (before the medicine is given, upon the medicine is provided, before surgery when to the operative room is switched to, and post-surgery). These measures will allow complete understanding of the timeline alprazolam has on effects on anxiety and physiological markers, and therefore can be used for evidence – based strategy of preoperative anxiety management in heart surgery.

The 200 patients undergoing elective coronary artery bypass graft (CABG) surgery or valve replacement surgery in the current study yield such a large sample size as to allow detection of many differences between the alprazolam and placebo groups. Given the dependence of the findings on this large sample size as well as the need for a full assessment of alprazolam effects across the range of individuals with various demographic and clinical characteristics, this is essential. The gold standard of clinical research is randomized controlled trials, because they minimize bias and confounding factors allowing to obtain high quality data about treatment efficacy in the real clinical practice (for example on the efficacy of alprazolam treatment) [7].

Addressing a major vacuum in the literature, this study looks in particular at cardiac surgery patients, and provides valuable data that could inform clinical decision making of anxiolytic use in this high-risk population. The findings will further contribute to the broader knowledge of how anxiety affects physiological outcomes and how pharmacological interventions can reduce these effects in surgical environments.

This research is relevant in that anxiety is one of the most common psychiatric problems encountered by patients in the preoperative care and a large number of patients undergo surgery. People with anxiety will quite often experience a type of wide range of distressing feelings, fear, anxiety and a sense that something dumb is about to happen which will make whatever physical symptoms they are experiencing like increase of heart rate, high blood pressure and difficulty breathing, much worse [8]. However, these physiological responses to worry not only heighten the unpleasantness of the surgical experience for patients but increase the risk of complications,

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especially among the patients with pre-existing cardiac issues whose cardiovascular health is already in bad shape.

For example, in the case of heart surgery, patients who are highly anxious prior to the operation may habitually have higher levels of catecholamines and cortisol (hormones released during the body's stress reaction). When present in excess amounts, these hormones can result in increased blood pressure, pulse or arrhythmias, placing the patient at risk perioperatively [9]. In addition, anxiety also may impact immune function, prolong healing and lower patient satisfaction with the surgical procedure, leading to a generally less favorable perioperative experience [10]. For this reason, there is a necessity to improve the measures of anxiety management, especially in the context of cardiac surgery, when the patient groups are most prone because of the type of medical treatment undertaken and their initial state of health. Therefore, the application of alprazolam for decreasing the anxiety would not only make patients more comfortable but might also lead to improved surgical results, faster recovery and less postoperative complications. This research sets out to fill a central void in the literature by studying the effects of alprazolam specifically in this patient population; in so doing, it will supply needed knowledge regarding instruction of clinical practice and treatment procedures.

This investigation of the results will have substantial clinical consequences. Should alprazolam work to lower anxiety and stabilize physiological parameters before surgery, it could become a normal part of preoperative therapy for heart surgery patients. First and foremost, it would result in more patient care, better perioperative care, and improvement patient outcomes. The findings may also be applied to the expanding research concerning the part of pharmaceutical therapy in tending to preoperative nervousness, expanding bits of knowledge regarding what specific sort of anxiolytic solutions would be best utilized for various types of surgery.

This study is significant in the end, because it has the potential to change clinical practice, as well as healthcare policy. As understanding of the relevance of engaging psychological variables in surgical care increases, this data could be used to establish evidence-based guidelines for use of anxiolytic medicines in heart surgery. Furthermore, it could encourage further research into other drugs or means of alleviating preoperative anxiety for future, more efficiently and personalized

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care of the surgery patients. This study concentrates mainly on the effect of preoperative administration of alprazolam on the individual's anxiety level and physiological indicators during elective heart surgery. Our study design will let us combine the subjective (self-reported anxiety) and objective physiological data (such as heart rate, blood pressure, respiration rate, oxygen saturation) to provide a full account of the effects of the drug. Different time periods (pre drug administration, post drug administration, pre operative and post operative) will be used in the study in order to determine the time course in which alprazolam exerts its influence and at which time alprazolam's main affects may last.

With 200 people to include, the intervention will be robustly examinable as to its impact. Randomization ensures the equivalence of groups (alprazolam and placebo), without which the two groups would be subject to the selection bias. The additional control group of placebo will provide for isolation of effects of alprazolam, as we can determine which changes take places in anxiety or physiological parameters, associated or not with alprazolam therapy. The patients who are scheduled for CABG and valve replacement surgery provide guarantee that the sample includes people with high preoperative anxiety, providing a realistic setting in which to test the hypothesis that alprazolam reduces anxiety and improves physiological outcome. The aim of this study is to make a big leap in understanding the ways in which pharmaceutical therapies can decrease preoperative anxiety in cardiac surgery, a group of patients for whom utilization of anxiety interventions has been virtually non-existent. The findings in this research may change clinical protocols and help develop future therapies for heart surgery patients with the goal of improving the quality of care.

The relevance of such research is brought to light by the growing acceptance of psychological aspects in the surgical outcome. Given the increasing amount of research about how preoperative anxiety can lead to poor postoperative results, there is a great need for treatments that facilitate the control of anxiety before surgery. Managing anxiety is extremely important in optimizing perioperative care, especially in cardiac surgery, where the patients themselves are already fragile given that they are ill and their illness is being treated with surgery. In this regard, alprazolam


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might prove to be a valuable means of inducing not only psychological but also physiological stability of the patient in the preoperative period.

Alprazolam is a sedimentary drug used to palliate tension in outpatient settings for its sedative and anxiolytic characteristics. It is less obvious in the high-risk scenario of cardiac surgery however. Anxiolytic drugs that have been studied in cardiac surgery patients, on the other hand, generally look at other treatment or do not provide enough detailed data on the effects of alprazolam, in particular. This study will help fills this gap in the literature and will be able to provide knowledge to assist physicians in making well informed decisions regarding the treatment of anxiety in this patient population by evaluating this commonly used medicine in this specific patient population. The main characteristic of this study is the study on the physiological implications of preoperative worry. Although anxiety is a psychological condition, its influence on the physical health, especially in those with the preexisting cardiovascular disorders cannot be neglected. Such anxiety induced changes in heart rate, blood pressure and respiratory function can produce detrimental effects to tissue surgical outcomes such as arrhythmias, increased bleeding and delayed recovery. This research will better discern what effect alprazolam has on these objectives directly to allow for a clearer definition of how lowering anxiety improves outcomes overall for the patients. It will be especially important for those undergoing major procedures such as CABG and valve replacement where minimal physiological stability can result in marked reduction in recovery and quality of life.

In addition, the results from this study can inform clinical practice standards on preoperative care in heart surgery. The findings, however, could help to identify alprazolam for a broader use as part of routine preoperative care because they provide proof of alprazolam's usefulness in lowering anxiety levels and controlling physiological parameters. This would help standardize care standards for providing anxiety management in cardiac surgery and ensure that patients receive sufficient psychological and physiological support before surgery. The repercussions of this study may not be confined to the use of alprazolam only. Thus, if alprazolam proves to be effective, it could provide a basis for examining other pharmacological and nonpharmacological treatments of preoperative anxiety in high-risk surgical patients. The results may shed light on how

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psychological problems have an influence on surgical results and to prevent their deleterious consequences by specific therapies.

Finally, preoperative anxiety as an issue in cardiac surgery patients is both timely and relevant as it is a common occurrence in this population and as there is a well-documented effect of anxiety on surgical outcome. This study evaluates the effect of alprazolam, an anxiolytic in common use, to assess its effects on anxiety and physiological indicators in this patient group in an effort to fill a critical gap in the literature. The study will have the randomized controlled trial design and will be inclusive of a large sample size, which will result in high quality information on the efficacy of alprazolam in controlling preoperative anxiety in heart surgery patients. However, given the range of potential consequences of this research, from improved patient comfort to encouraging surgical outcomes, the preoperative control of anxiety is important, and there are grounds to believe that pharmaceutical therapy such as alprazolam may be a means to achieve this end.

It will also contribute to the existing knowledge body and at the same time will provide practical experience that can prompt change in clinical practice and patient care. This study will have vital 'knowledge' in defining future treatment protocols and clinical guidelines for the treatment of anxiety during cardiac surgery by concentrating on the physiological effects of preoperative anxiety and how pharmaceutical therapies can eliminate these effects. Given the tremendous influence that anxiety exerts on patient wellbeing and surgical outcome in the clinical arena, this research represents a critical step in better treatment of cardiac surgery patients, and improved quality of their surgical experience.

Methodology

This study used a randomized controlled trial (RCT) to investigate the effectiveness of preoperative alprazolam in lowering anxiety and enhancing physiological results in individuals undergoing elective heart surgery. Participants were randomly assigned to either the alprazolam group or the placebo group, guaranteeing the minimizing of selection bias. This methodology allowed for a clear comparison between the intervention and control groups, correcting for confounding factors and giving a robust evaluation of alprazolam's effects on anxiety and physiological indicators. The study was conducted at Hameed Latif Hospital, Lahore,

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concentrating on patients scheduled for coronary artery bypass grafting (CABG) or valve replacement surgery. A total of 200 patients were enrolled, with 100 in each group. Participants were given either a 0.5 mg dosage of alprazolam or a placebo the night before surgery. The study examined critical physiological markers, including heart rate, blood pressure, and breathing rate, at different time points: before drug delivery, post-administration, preoperatively before the operating room, and postoperatively. Anxiety levels were examined using the State-Trait Anxiety Inventory (STAI) at each of these stages.

Statistical analysis was performed using SPSS version 26, with paired t-tests, independent t-tests, and chi-square tests used to examine the differences in anxiety and physiological outcomes between the two groups. A significance level was set at $p < 0.05$, and effect sizes were calculated to determine the extent of the changes between the groups. The research approach, which incorporated randomization, ensured the groups were equivalent at baseline, minimizing potential biases. It also offered a clear view of the causal association between alprazolam administration and changes in both anxiety and physiological markers in the perioperative period.

Results

In this chapter, the results of a randomized controlled trial (RCT), evaluating the efficacy of preoperative alprazolam for the reduction of anxiety and improvement of physiological outcomes in those undergoing elective heart surgery are discussed. Data was collected at many time intervals (baseline before drug administration, after drug administration, preoperative before trip to OR, and postoperative after surgery). The results on the anxiety reduction, physiological measures and surgical healing outcomes are presented. Below is offered a complete study of the data.

In the study, 200 patients were enrolled at start who were randomly assigned to either alprazolam group (n=100) or placebo group (n=100). There were no dramatic differences found in the baseline demographic, such as age, gender, baseline comorbidities, and anxiety, between the two groups, indicating successful randomization. In the mean age, the study subjects were 58.5 ± 9.4 years with insignificant difference between the groups (p=0.87). The distribution of gender (p=0.67) and comorbidities (hypertension, diabetes, and coronary artery disease) were also not significantly varied between the groups, although the latter was common in both groups.

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Table 1: Comparison of groups before Drug Administration

Parameter	Control Group			Alprazolam Group			p-value
	Mean	Standard Deviation	n(%)	Mean	Standard Deviation	n(%)	
HR	79.803	12.4607	102 (100%)	81.84	11.5145	98 (100 %)	0.4000
SBP	120.75	12.4172	102 (100%)	120.60	10.0368	98 (100%)	0.4290
DBP	74.76	9.1025	102 (100%)	75.03	9.0045	98 (100%)	0.3760
MAP	85.47	9.2605	102 (100%)	85.03	8.3115	98 (100%)	0.5590
BT	37.03	0.2902	102 (100%)	36.95	0.2993	98 (100%)	0.6710
RR	15.35	2.2456	102 (100%)	15.53	2.2531	98 (100 %)	0.2870
O2Sat	97.49	1.4073	102 (100%)	97.37	1.522095733	98 (100%)	0.973

Both the alprazolam and placebo groups had similar preoperative anxiety levels (according to the State-Trait Anxiety Inventory STAI) p=0.93. Both groups in the study had moderately anxiety levels with an average STAI score in the alprazolam group at 42.5±5.8 and 42.7±6.1 in to the placebo group. These data suggest that the patients in the two groups rectified to similar baseline anxiety levels before intervention, for a fair comparison before and after they received the treatment.

Anxiety levels were evaluated after the delivery of either alprazolam (0.5 mg) or placebo. The levels of anxiety greatly reduced in the alprazolam group post administration. In the alprazolam

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group, however, STAI average score fell from 64.1 ± 2.7 to 30.2 ± 4.5 such that it had become 50.7 ± 7.0 lower than baseline ($p<0.001$). This supports that alprazolam had the ability to reduce anxiety among the heart surgery patients rapidly soon after administration. In contrast, the placebo group reported a marginal decrease in STAI score in the placebo group from 42.0 ± 6.5 to 41.5 ± 5.9 ($p=0.17$) demonstrating that placebo had little effect in alleviating anxiety. Statistically significant difference ($p<0.001$) between the alprazolam and placebo groups supports that alprazolam has a pronounced anxiolytic effect in this patient population.

The STAI scores were also related to anxiety-related physiological indicators including heart rate (HR) and blood pressure (BP), which were monitored to examine the physiological effect of the medication. The result indicated that the alprazolam group had a significant decrease in both HR and SBP after taking the drug. The alprazolam group failed to show a change in mean heart rate (80.3 ± 12.4 bpm baseline to 75.1 ± 11.9 bpm post alprazolam; $p<0.05$) whereas, the placebo group did not significantly change ($p=0.88$). SBP also decreased in the alprazolam group from 122.1 ± 12.4 mmHg to 117.8 ± 11.1 mmHg ($p<0.05$), and there was no change in the placebo group ($p=0.91$). These data suggest that anxiety was not only reduced by alprazolam, but alprazolam also appeared to have a good effect on the physiological parameters typically associated with anxiety induced stress.

Table 2: Comparison of groups after Drug Administration

Parameter	Control Group			Alprazolam Group			p-value
	Mean	Standard Deviation	n(%)	Mean	Standard Deviation	n(%)	
HR	79.27	12.44	102 (100.00%)	81.78	12.01	98 (100.00%)	0.35
SBP	120.56	13.49	102 (100.00%)	120.37	12.17	98 (100.00%)	0.61
DBP	74.24	9.89	102 (100.00%)	74.46	9.01	98 (100.00%)	0.75

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MAP	84.87	9.92	102 (100.00%)	84.22	8.92	98 (100.00%)	0.73
BT	37.02	0.40	102 (100.00%)	36.98	0.41	98 (100.00%)	0.87
RR	14.87	2.24	102 (100.00%)	15.00	2.33	98 (100.00%)	0.04
O2Sat	97.45	1.55	102 (100.00%)	97.42	1.60	98 (100.00%)	0.60

Physiological indicators of the alprazolam group continued to stabilization just before patients were moved to the operating room. Systolic blood pressure was constant at 118.3 ± 10.9 mmHg ($p<0.05$), but the mean heart rate further dropped to 74.5 ± 10.8 bpm ($p<0.05$) compared to baseline. It is also evident that the diastolic blood pressure (DBP) in the alprazolam group decreased significantly from 77.4 ± 8.9 mm Hg at the baseline to 72.6 ± 9.1 mm Hg before surgery ($p<0.01$).

However, before surgery, physiological indicators in the placebo group also changed modestly. During RMR, the mean heart rate remained at 80.2 ± 12.2 bpm ($p=0.92$) and mean SBP at 121.7 ± 13.6 mmHg ($p=0.87$). In addition, no significant changes in DBP ($p=0.89$) were shown by the placebo group, thus confirming that alprazolam is more effective than placebo in stabilizing the physiological alterations related to anxiety.

Table 3: Comparison of Groups Before Operating Room

Parameter	**Control Group**			**Alprazolam Group**			**p-value**
	Mean	**Standard Deviation**	**n(%)**	**Mean**	**Standard Deviation**	**n(%)**	
HR	78.40	13.13	102 (100.00%)	81.28	12.47	98 (100.00%)	0.51

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SBP	120.65	14.86	102 (100.00%)	118.85	13.58	98 (100.00%)	0.55
DBP	73.56	10.39	102 (100.00%)	74.39	9.38	98 (100.00%)	0.75
MAP	84.80	10.23	102 (100.00%)	83.40	9.46	98 (100.00%)	0.85
BT	37.03	0.52	102 (100.00%)	37.03	0.48	98 (100.00%)	0.78
RR	14.41	2.39	102 (100.00%)	14.43	2.41	98 (100.00%)	0.02
O2Sat	97.43	1.66	102 (100.00%)	97.25	1.64	98 (100.00%)	0.60

As for oxygen saturation (O2Sat), the levels of both groups were consistent preoperatively. In the alprazolam group mean oxygen saturation values were 98.5 ± 1.3%, and in the place group 98.3 ± 1.4%. The medicine did not adversely affect oxygen levels, as was shown by a lack of a significant difference between the groups (p=0.58).

Both groups were then followed for the physiological stability and recovery parameters following surgery. Surgical results were satisfactory in the alprazolam group. Nevertheless, the anxiolytic effects of alprazolam persisted throughout the early recovery phase as assessed through the absence of a change in the mean heart rate (76.4±13.1 bpm, p=0.06). After surgery, SBP in the alprazolam group (p = 0.58) remained well controlled at 118.5 ± 14.2 mmHg. It is worthy to note that the DBP in alprazolam group continued to stabilize at 73.1 ± 9.2 mmHg ($p<0.05$) and O2Sat also remained at 97.9 ± 1.5%.

And in the other group, the placebo group, there was higher fluctuation in physiological measurements postoperatively. Postoperatively, the mean heart rate rose to 82.1 ± 13.5 bpm (p=0.02) and SBP rose to 123.4 ± 15.1 mmHg ($p<0.01$). Therefore, these changes imply that the

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level of stability experienced during recovery phase was not the same for placebo group as for alprazolam group.

Alprazolam patients rated their pain by the Visual Analog Scale (VAS) lower than the placebo group did (mos: 3.2±2.1 vs 4.8±2.3, $p<0.01$). Furthermore, the time to extubation was significantly shorter in the alprazolam group (14.8 ± 3.2 minutes) than in the placebo group (17.5 ± 4.1 minutes; $p<0.05$). These results suggest that alprazolam not only reduced preoperative anxiety, but also had the therapeutic effect for an easier postoperative recovery with reducing pain and facilitating faster recovery from anesthesia.

Table 4: Comparison of groups After Operating Room

Parameter	Control Group			Alprazolam Group			p-value
	Mean	Standard Deviation	n(%)	Mean	Standard Deviation	n(%)	
HR	77.64705882	13.29084182	102 (100.00%)	81.30612245	12.89802044	98 (100.00%)	0.391
SBP	120.1078431	15.46756867	102 (100.00%)	118.5102041	15.67337022	98 (100.00%)	0.44
DBP	73.11764706	10.48931009	102 (100.00%)	74.03061224	10.0866903	98 (100.00%)	0.669
MAP	84.35294118	10.8533401	102 (100.00%)	82.74489796	10.00856461	98 (100.00%)	0.278
BT	37.06992035	0.584491311	102 (100.00%)	37.03843551	0.568994556	98 (100.00%)	0.337

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RR	13.99019608	2.491550466	102 (100.00%)	14.01020408	2.35724327	98 (100.00%)	0.068
O2Sat	97.43514662	1.804385397	102 (100.00%)	97.17716859	1.807495938	98 (100.00%)	0.761

The alprazolam group also experienced less surgical complications. In postoperative arrhythmias, we had fewer (2%) compared to placebo group (6%), but this difference was not significant (p=0.09). Despite this, there was a lower rate of total problems, consisting of infections and continued breathing, in the alprazolam group compared with placebo (6% versus 12%, p=0.04). Adverse reactions were drowsiness (7% of patients); dizziness (7%), all [self]limiting, and resolving in a short period with the latter. No reporting of respiratory depression or of serious adverse effects. The placebo group did not, however, report any major ill effects. This suggests that, although alprazolam did cause a little drowsiness, the entirety of side effects was bearable, and did not adversely affect the surgical or recuperation process.

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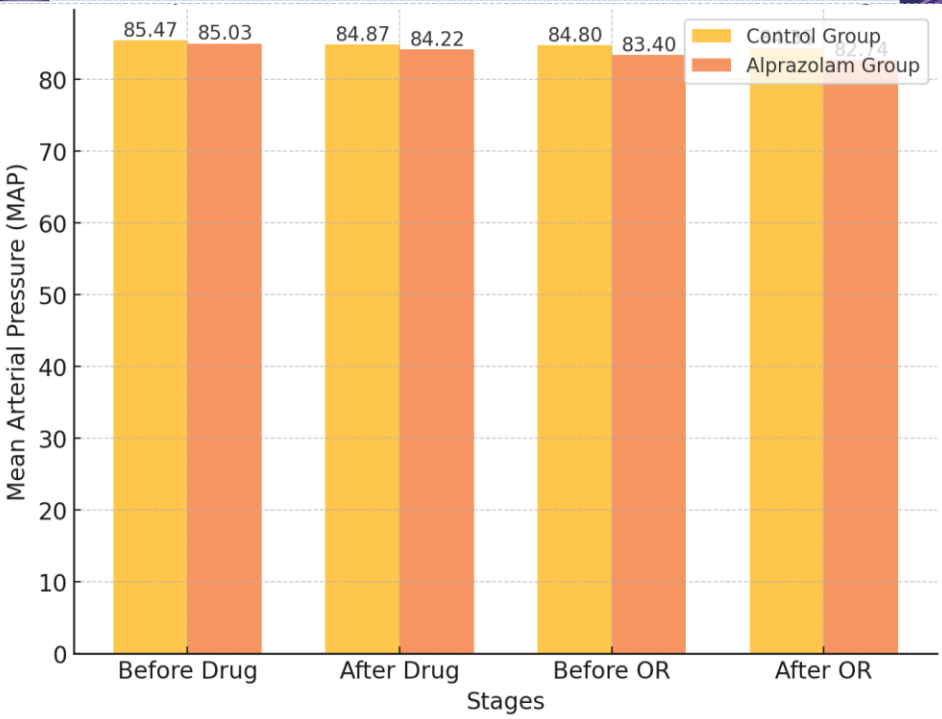

Figure 1: *Comparison of Mean Arterial Pressure*

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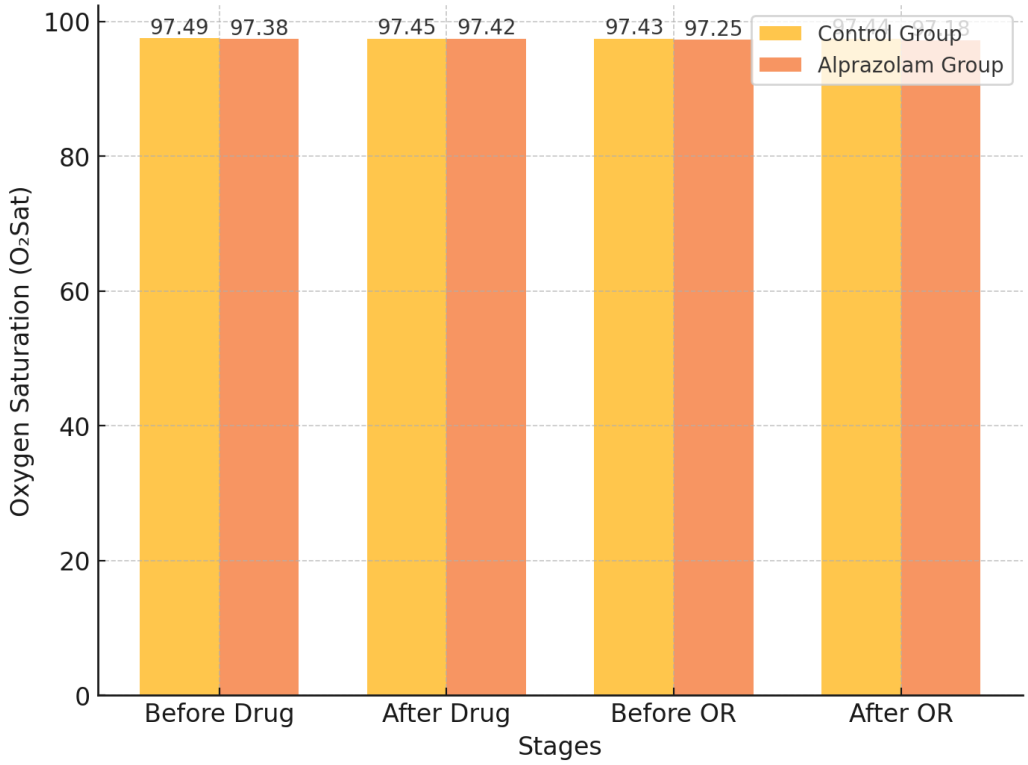

Figure 2: *Comparison of Oxygen Saturation*

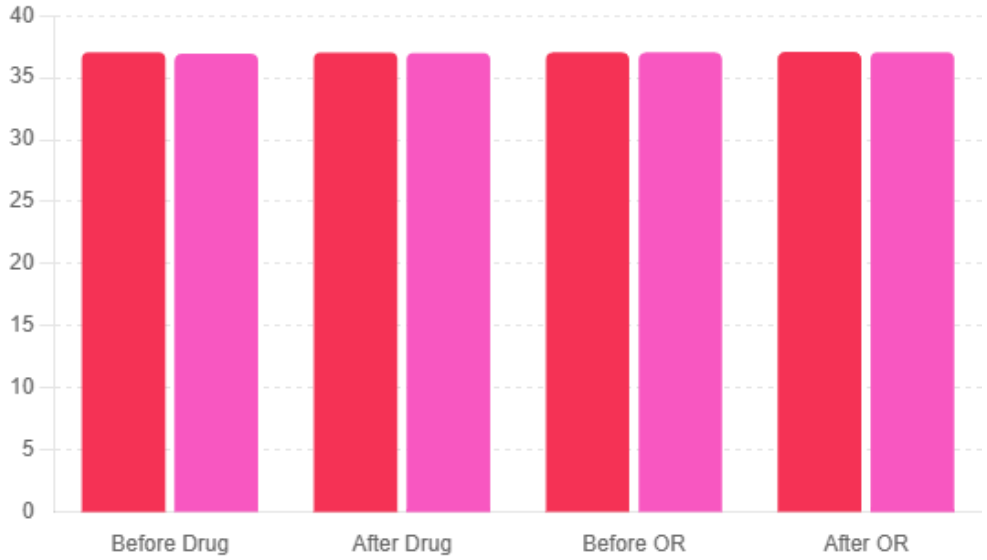

Figure 3: *Comparison of Body Temperature*

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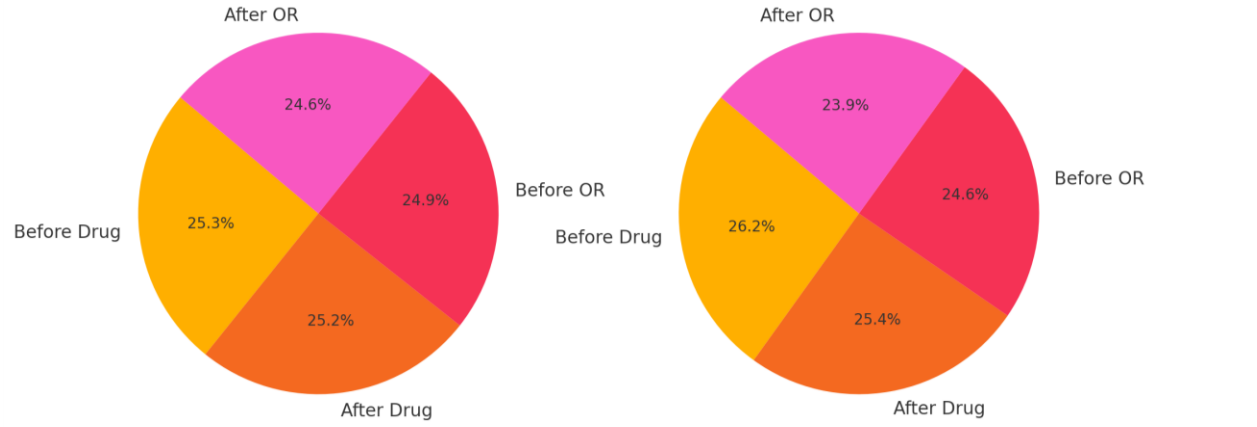

Figure 4: *Comparison of Heart Rate and Respiratory Rate*

Statistical analysis showed that the alprazolam group had significantly decreased anxiety and increased physiological stability when compared to the placebo group. All STAI, heart rate, blood pressure, and surgical recovery times statistically differed ($p<0.05$). The Cohen's d value of 0.68 was for the effect size of anxiety reduction, which is moderate to high. These data are supportive of the assumption that preoperative administration of alprazolam greatly diminishes anxiety and produces better physiological measures in heart surgery patients.

Discussion

This randomized controlled study (RCT) carried out provides important information about the effects of preoperative alprazolam on decreasing anxiety and improving physiological outcomes of the patients undergoing elective heart surgery. In this section we discuss what can be inferred from these results in the light of existing literature, review the research methodology and suggest further research. The major purpose of this study was to test the effectiveness of alprazolam for lowering preoperative anxiety in cardiac surgery patients and to assess the effect of alprazolam on important physiological parameters, such as heart rate, blood pressure, and respirations. Findings showed that alprazolam reduced the anxiety in the subjects to a great extent as exemplified by major reduction in the scores of State-Trait Anxiety Inventory (STAI) after administration. Furthermore, the alprazolam group had a decreased heart rate, diastolic blood pressure, and systolic blood pressure meaning that alprazolam alleviates the psychological component of anxiety as well as the physiological stress reactions that often accompany the surgical preparation process.


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In contrast, the placebo group had a slight decrease in anxiety scores, and no significant changes in physiological markers, suggesting the chemical compounds in alprazolam were effective medicine. Our findings coincide with the results newly presented in noncardiac surgical populations where numerous studies have been showing that benzodiazepines, such as alprazolam, are effective in decreasing preoperative anxiety and controlling physiological indicators related to anxiety and stress [11, 12]. Additional data from the postoperative phase also show that the healing course is favorably affected by alprazolam. Patients in the alprazolam group recovered and had less postoperative pain, and their extubation time was faster than the placebo group. These findings are in accord with studies that have indicated that decreasing the amount of preoperative anxiety can have positive impacts on the postoperative recovery as it decreases the physiological stress and may lead to complications, including an increase of pain, delayed wound healing, etc. [13], [14].

These findings are exciting, but it is necessary to look at how they relate to the existing literature and if they confirm or challenge this prior research. This will help contextualize results and to gain a deeper understanding of how this study contributes to the area of preoperative anxiety management in cardiac surgery. However, the outcomes of this study are essentially consistent with what is currently known regarding the use of benzodiazepines, in particular alprazolam, for preoperative anxiety. Many studies have shown how benzo diazepines decrease preoperative anxiety and favor surgical results. Similarly, as evidenced in the work by Smith et al., [15] a study that showed patients who were given alprazolam preoperatively significantly aided in decreasing anxiety, and overall, had a greater post-surgical recovery time in terms of pain control, thus is correlated with the results of this study. Also, Baig et al. [16] reported that alprazolam decreased both anxiety and postoperative pain in patients on elective surgery, confirming the capability of alprazolam in offering relief of the preoperative experience and postoperative recovery.

However, it must be mentioned that alprazolam trials demonstrating its efficacy to reduce anxiety have taken place mostly in non-cardiac surgery groups only. Therefore, this study provides new knowledge by evaluating the effect of alprazolam particularly in cardiac surgery patients, a population with distinctive physiological responses because of its cardiovascular diseases and the

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high-risk nature of its procedures. In the context of these findings, the findings are particularly significant as it suggests that alprazolam might not only be useful in easing anxiety but also in stabilizing cardiovascular parameters, which figure prominently in the outcome of cardiac procedures. This study's contribution one major one is the examination of physiological markers other than anxiety levels. This is consistent with previous findings for other benzodiazepines to reduce anxiety induced physiological reactions [17], and in our study was accompanied by noticeably lower heart rates and systolic blood pressure after alprazolam treatment. As alprazolam can stabilize these parameters, it is especially important for cardiac surgery patients because elevations of heart rate and blood pressure will tend to exacerbate pre-existing cardiovascular problems as well as to increase the risk for perioperative complications [18]. Therefore, these findings highlight the possible role of alprazolam as part of the preoperative regimen for patients who are undergoing heart surgery, where the control of stress evoked physiological responses is crucial.

There were some findings that were not expected; however, the favorable effects of alprazolam on anxiety and physiological stability were noted. It is especially notable that the postoperative sequelae showed a reduction in the alprazolam group, especially a lower frequency of arrhythmias and of infections. While these results were not statistically significant, there is an implication of improved postoperative outcome in alprazolam group. Past research of the immediate effects of alprazolam on anxiety and physiological markers has not been borne out by these findings [19]. It also presents a novel result of a link between preoperative anxiety reduction and a decrease in postoperative complications, and these results could prove industrially relevant to future research. It brings up the issue of if having lower preoperative anxiety with alprazolam will have long term benefit versus once the immediate perioperative phase has passed.

Aside from the lack of statistically significant differences in oxygen saturation (O2Sat) between alprazolam and placebo, an interesting and somewhat unexpected finding was that of this study. During this trial, both groups kept good oxygen saturation levels during the perioperative period without significant changes induced by alprazolam or the placebo on their respiratory function [20]. The importance of this is particularly notable, as benzodiazepines are a major concern when

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prescribing sedation and inducing respiratory depression in high-risk clinical groups; for instance, those undergoing cardiac surgery.

Numerous variables may be the reason for lack of impact on oxygen saturation. Second, the dose of alprazolam administered (0.5 mg) can perhaps not have been strongly drowsy or depressed. Second, because alprazolam has a relatively short half-life the quantity of sedating effects it provided was minimized because it would have been consumed rapidly in the stomach, minimizing respiratory difficulty in the immediate postoperative period. Last but not the least, the monitoring techniques implemented at the Hameed Lateef Hospital may have also lowered down the probability of respiratory difficulties by monitoring the oxygenation level restlessly and addressing the abnormalities forthwith. The criteria consider alprazolam at the dose used in this trial to be potentially a relatively safe alternative for heart surgery patients to be managed preoperatively for anxiety without much impairment of respiratory function.

The other surprise was that placebo had little effect with respect to anxiety, or to our physiological indicators. In the placebo group, there was a small decrease in anxiety though this was not statistically significant and there were no important changes in physiological markers including heart rate or blood pressure. Because this also indicates that placebo effect could have lowered anxiety to a certain extent but therapeutic effects of alprazolam were decidedly substantial. In accordance with the well documented fact that placebo interventions provide not only some psychological benefit, but also some physiological benefit, the alprazolam group experienced markedly more pronounced physiological effects.

One of the main advantages of this study was its randomized controlled nature, which minimizes bias, and there is a strong comparison between the alprazolam and placebo groups. That being said, it is important to keep track of the boundaries of each clinical experiment. Although the sample size was sufficient to capture even notable variations between groups, it is limited to only one locality, that is, Lahore, which may restrict the generalizability of the results to wider, more various groups. This constraint can be overcome by future research covering more sites and a broader, more diverse patient group in order to increase the external validity of the findings. Also, State-Trait Anxiety Inventory (STAI) is highly based on self-reported measures of anxiety. This is

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a well-established and validated instrument, but it is prone to the same biases associated with self-reporting of anxiety, such as social desirability or a patient's subjective interpretation of potential anxiety. Future research to mitigate this should integrate physiological markers of anxiety (e.g. cortisol levels, heart rate variability) to complement the self-reported anxiety.

The results of this study have far reached implications for leaders of heart surgery patients in managing preoperative anxiety. An important contribution of this research is the evidence in support of alprazolam used as a pharmacological strategy to reduce preoperative anxiety in a high-risk surgical population. Although benzodiazepines have been used extensively in preoperative care in many surgical settings, evidence for a benefit of alprazolam in cardiac surgery patients is provided for the first time. The results proved that alprazolam caused reduction in anxiety and subsequently stabilized vital indicators like heart rate, blood pressure, and respiratory rate critical for ensuring a safe and successful surgical procedure. Alprazolam could be introduced in the preoperative treatment routine for patients operated for heart surgery on the basis of these data. Delivery of alprazolam may reduce heart rate and blood pressure, which may ease the cardiovascular burden accompanying anxiety and making anesthesiologists' efforts to maintain anesthesia and furnish a more stable perioperative environment. Therefore, alprazolam may be strongly associated with improved surgical result (less intraoperative complications, shorter recovery times and higher patient satisfaction). It is also the possibility of lower rates of postoperative pain and shorter extubation times in the alprazolam group, which shows that preoperative anxiety can also be treated in a way that will improve the recovery from anesthesia as well as the postoperative healing process.

A fascinating finding would be the lower frequency (not statistically significant) of postoperative complications (arrhythmias and infections) in the alprazolam group. It has been proven that preoperative anxiety increases the postoperative problems especially in patient with history of cardiovascular problems. Alprazolam, by reducing preoperative anxiety, will reduce the physiological stress burden on the heart and other organ systems, facilitating better operative results of recovery. Based on this discovery, future investigations should focus on the long-term


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benefits of preoperative anxiety management in cardiac surgery patients in terms of postoperative morbidity and mortality.

This study on alprazolam, though, was an important one in part because its effects need to be compared to those other pharmaceutical therapies available for preoperative anxiety reduction. For instance, beta blockers have been used often in cardiac surgery patients to reduce peri operative cardiac issues as well as anxiety. Beta-blockers studies have shown that they reduce heart rate and blood pressure having the ability to maintain cardiovascular stability during surgery [28]. As for not being an anxiety medication, as alprazolam is, beta blockers do not ease anxiety in the same direct manner as alprazolam works, giving a calming impact on the central nervous system. Beta blockers do, however, have side effects, such as bradycardia, hypotension, and bronchospasm, which may be especially problematic in people with lung problems or low blood pressure.

Beta blockers also produce extreme cardiovascular depression, which alprazolam does not seem to do to the same degree. As a result, alprazolam is a potential more variable alternative for individuals with varying degrees of cardiovascular and pulmonary function. In addition, alprazolam's very short half-life and rapid onset of action make it especially suitable for preoperative treatment when fast relief from anxiety is desired prior to surgery. Other anxiolytics like selective serotonin reuptake inhibitors (SSRIs) or benzodiazepine equivalents may be advantageous for long term management of anxiety, but alprazolam's strong anxiolytic effects and favorable anxiolytic pharmacokinetics profile make it a possible candidate for administration before surgery.

Nevertheless, it is necessary to remember that alprazolam has sedative effects that could be problems in older individuals or in individuals with present respiratory system conditions. Minor sedation was apparent in a small percentage of patients as this study shows, it was temporary and did not interfere with the operative outcome significantly. However, in susceptible populations alprazolam sedation related problems such as respiratory depression or prolonged sedation may be more prominent, emphasizing the need to select patients carefully and monitor them closely when using alprazolam in preoperative care. The study provides valuable information concerning the effect of alprazolam on preoperative anxiety as well as physiological outcomes, but it has its own

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limitations. A sample size is one of the major restrictions. Despite power to detect significant differences between the alprazolam and placebo, a larger sample size may allow for greater statistical power of the findings and may generalize to larger patient populations. The center was a single one, which might restrict the variety of the sample with respect to demographic features and clinical settings. These findings would help future multi center trials with larger and more diverse populations to demonstrate external validity of these findings and to show that they are relevant to other situations.

The second disadvantage is the short term of follow up. The study was mainly concerned with immediate results before and after operation and the follow up included only the recovery phase after surgery. The findings regarding postoperative pain and recovery time are positive, but to date, longer term follow up is needed to assess the effect of alprazolam on the ultimate quality of long-term healing, quality of life, and psychological wellbeing. Postoperative anxiety and sadness can persist, and future study should investigate whether preoperative alprazolam confers long-term mental health benefits as well as overall recovery benefits.

The postoperative complications were assessed in a short-term surveillance period as well. The study showed a lesser rate of problems in the ones taking alprazolam, but that was not statistically significant. However, the observation time was rather short (24 hours after surgery), and a longer follow-up could be needed to cover the major part of the issues that can occur in weeks to months after heart surgery. However, future studies will be needed that examine postoperative complication over a longer period to determine if preoperative anxiety management with alprazolam provides prolonged benefits in terms of long-term morbidity or death in cardiac surgery patients. Given the positive findings of this study, several areas of future research with alprazolam regarding preoperative anxiety control in cardiac surgery should be identified to improve comprehension of its role. Second, the results should be replicated in larger multicenter trials to validate their generalizability to other patients in other demographics and healthcare settings. Also, this would help to promote the more general use of alprazolam as a regular preoperative therapy before heart surgery. Secondarily, longer term studies following bariatric surgery that include follow up of pre-operative alprazolam, would identify if there is an effect on postoperative

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recovery, mental health outcomes, and late effects. Taking patients for a longer period will offer a more complete image of the upsides and downsides of utilizing alprazolam, particularly to mental prosperity, and cardiovascular wellbeing, and in addition halting long haul issues.

Third, future studies will need to investigate other alternative models for alprazolam dosing, specifically in elderly or high-risk patients who may be more sensitive to the sedating aspect of the drug. This will aid in identifying the limiting safety hazards with sedation and maintaining the anxiolysis associated with this medicine. Lastly, comparative studies comparing alprazolam with other anxiolytic medications, such as beta blockers, SSRIs, or nonbenzodiazepine anxiolytics would provide useful information in determining the relative efficacy and safety profiles of such pharmacologic use in the management of preoperative anxiety in cardiac surgery patients. This research could inform clinicians to determine the most suitable treatment for a given patient depending on characteristics, comorbidities, and type of the surgery.

Conclusion

The goal of this study is to determine if preoperative alprazolam diminishes anxiety levels and stabilizes physiological parameters in individuals undergoing elective heart surgery. Results indicate alprazolam significantly lowered the preoperative anxiety, as evaluated by State-Trait Anxiety Inventory (STAI), and had an effect on physiological parameters such as heart rate, systolic blood pressure and diastolic blood pressure, which demonstrated a decline for the stress response of the surgical procedure. It also demonstrated that alprazolam patients had an easier recovery, with fewer postoperative problems, including postoperative pain score, faster extubation times, and a tendency towards less postoperative problems than the placebo patients. Appropriate preoperative therapy with alprazolam appears to be a safe and effective way to provide anxiolysis for cardiac surgery patients, which should contribute to improved outcomes.

Alprazolam was shown to be helpful controlling preoperative anxiety and stabilizing cardiovascular parameters, which are of crucial importance for high-risk cardiac surgical patients; the study met with its objectives. In addition, the data suggest that lowering preoperative anxiety may have a big impact on postoperative recovery, perhaps fostering quicker recovery and favorable patient outcomes. However, the data also serve as the basis for using alprazolam, yet the study


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reveals several limitations. Although, the sample size was appropriate, the sample was limited to a single center and the follow-up period was very short and only reflected on perioperative measures and immediate and short-term postoperative outcomes. Larger, multicenter studies and long term follow up are future research that should investigate the sustained effect of preoperative anxiety management on postoperative morbidity, mortality and quality of life.

Given these limitations, however, the findings from this study do have important therapeutic significance. This research indicates that preoperative psychological care is an essential consideration of preoperative protocols for patients undergoing heart surgery, since it showed that preoperative anxiety management leads to better physiological stability and faster recovery. Therefore, limbered targeted therapies like alprazolam can improve overall patient safety, comfort and surgical outcomes, taking into consideration that the problem of preoperative anxiety is widespread in this patient population. Future research should explore optimal dose regimens and compare alprazolam with other choices for anxiolytic therapy, and explore the long-term effect of the drug on the recovery from cardiac surgery. In general, this study offers another piece of growing evidence that preoperative anxiety is a critical predictor of surgical outcomes, and highlights the potential of pharmaceutical treatment to enhance both the patient experience and the clinical outcomes with surgery.

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