JHWCR
Journal of Health, Wellness, and Community Research
Volume III, Issue VII
Open Access, Double Blind Peer Reviewed.
Web: https://jhwcr.com, **ISSN**: 3007-0570
https://doi.org/10.61919/p23qkg93

Article

Effect of Benzodiazepines on Reducing Pre-Operative Anxiety

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Cite this Article

Received	2025-05-09
Revised	2025-06-15
Accepted	2025-06-18
Published	2025-06-19

No conflicts declared; ethics approved; consent obtained; data available on request; no funding received.

Authors' Contributions
Concept: ZA, TA; Design: SI, AM; Data Collection: ZA, SI; Analysis: MU; Drafting: TA

ABSTRACT

Background: Preoperative anxiety is a frequent and clinically significant concern among surgical patients, with substantial effects on perioperative physiology and recovery. Despite widespread use of benzodiazepines for anxiolysis, uncertainties remain regarding their comparative efficacy and safety versus non-pharmacological interventions such as cognitive-behavioral therapy (CBT), guided relaxation, and music therapy. **Objective**: This study aimed to compare the effectiveness and adverse effects of benzodiazepines, non-pharmacological strategies, and placebo in reducing preoperative anxiety, optimizing postoperative recovery, and enhancing patient satisfaction in adults undergoing elective surgery. **Methods**: A randomized controlled trial was conducted at a tertiary teaching hospital, enrolling 150 adults aged 18–65 scheduled for elective surgery. Participants with moderate-to-high preoperative anxiety were randomized into benzodiazepine, non-pharmacological (CBT, relaxation, or music), or placebo groups. Exclusion criteria included psychiatric illness, benzodiazepine dependency, severe comorbidities, and emergency procedures. Anxiety was assessed using the State-Trait Anxiety Inventory (STAI) and Amsterdam Preoperative Anxiety and Information Scale (APAIS). Secondary outcomes included physiological stress markers, pain (VAS), length of stay, and adverse events. Statistical analysis used SPSS v25; $p<0.05$ was considered significant. The protocol received IRB approval and conformed to the Helsinki Declaration. **Results**: Benzodiazepines produced a 45.5% reduction in STAI scores (95% CI: 41.2–49.8; $p<0.001$), outperforming non-pharmacological interventions (range 36.0–41.7%) and placebo (3.4%). Sedation (30%) and postoperative cognitive dysfunction (10%) were significantly higher in the benzodiazepine group. Hospital stay and pain scores were lowest with benzodiazepines, but non-pharmacological methods offered a superior safety profile and high patient satisfaction. **Conclusion**: Benzodiazepines remain highly effective for acute preoperative anxiety reduction, but their adverse effects limit use in vulnerable patients. Non-pharmacological interventions provide clinically meaningful anxiolysis with fewer risks, supporting their integration as primary or adjunctive strategies in surgical care.

Keywords: Preoperative Anxiety, Benzodiazepines, Cognitive Behavioral Therapy, Guided Relaxation, Music Therapy, Perioperative Care, Patient Satisfaction

INTRODUCTION

Preoperative anxiety is frequently encountered yet often underappreciated psychological condition affecting patients scheduled for surgical procedures. It can be characterized by an undue fear of the unknown, concerns about anesthesia, and anticipation of pain or adverse surgical outcomes. This anxiety initiates a cascade of physiological responses involving activation of the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system, leading to increased serum cortisol, blood pressure, and heart rate, all of which can compromise surgical safety and delay recovery (1,2). Studies have shown that up to 80% of patients may exhibit clinically relevant anxiety levels prior to surgery, with variation influenced by patient demographics, prior experiences, and the nature of the procedure (1,3). The effective management of such anxiety is vital not only for patient comfort but also for minimizing intraoperative complications and promoting faster postoperative recovery (4,5).

Pharmacological agents, particularly benzodiazepines, have long been employed in preoperative settings owing to their anxiolytic, amnesic, and sedative effects mediated through potentiation of gamma-aminobutyric acid (GABA) neurotransmission (6). Midazolam, diazepam, and lorazepam are commonly used in clinical settings to mitigate pre-surgical nervousness, demonstrating efficacy in both

subjective anxiety reduction and physiological stabilization (7). However, concerns about benzodiazepines' adverse effects—such as postoperative cognitive dysfunction (POCD), respiratory depression, and dependency—especially in elderly and comorbid populations, have raised critical safety debates (8,9). Studies have linked benzodiazepine use with increased risks of delirium and prolonged sedation, prompting reconsideration of their routine use, particularly within Enhanced Recovery After Surgery (ERAS) protocols that emphasize minimized sedative administration (10,11).

Amid these concerns, a growing body of literature has turned attention toward non-pharmacological alternatives such as cognitive-behavioral therapy (CBT), guided relaxation, and music therapy, which offer anxiety relief without pharmacological side effects (12). Meta-analyses and randomized trials have found these interventions effective in lowering anxiety, improving physiological parameters, and enhancing patient satisfaction (13,14). However, their comparative efficacy relative to benzodiazepines in acute preoperative settings remains inadequately characterized. Additionally, despite widespread use of benzodiazepines, few studies have rigorously quantified both their anxiolytic impact and side effect profile alongside validated non-drug methods in a controlled design, resulting in a critical knowledge gap (15,16).

Given the dual need to maximize preoperative anxiety control and minimize adverse outcomes, a comparative investigation is warranted to guide clinical decisions tailored to individual patient risk profiles. The lack of consensus and variability in practice underscore the necessity of evidence-based guidance on the optimal strategy for preoperative anxiety management. Therefore, this study was designed as a randomized controlled trial to evaluate the comparative efficacy and safety of benzodiazepines versus non-pharmacological interventions and placebo in reducing preoperative anxiety among elective surgery patients. The primary objective was to assess anxiety reduction using standardized tools, while secondary objectives included evaluating physiological stress markers, postoperative pain, cognitive effects, hospital stay duration, and patient satisfaction. The study hypothesizes that while benzodiazepines may yield superior anxiety control, non-pharmacological methods may offer a safer and comparably effective alternative for specific patient populations.

MATERIALS AND METHODS

This randomized controlled trial was conducted to assess the comparative efficacy and safety of benzodiazepines versus non-pharmacological interventions and placebo in reducing preoperative anxiety among adults scheduled for elective surgery. The rationale for employing a randomized controlled trial design was to establish causal inference between interventions and outcomes while minimizing selection bias and confounding. The study was implemented at the Department of Anesthesiology and Surgical Sciences, Chaudhary Muhammad Akram Hospital, affiliated with Superior University, Lahore. The trial took place over a four-month period from January to April 2024, encompassing participant recruitment, intervention delivery, and follow-up data collection.

Participants were recruited from patients aged 18 to 65 years who were scheduled to undergo elective surgery under general anesthesia. Eligibility criteria required participants to demonstrate moderate to high levels of preoperative anxiety, confirmed using the State-Trait Anxiety Inventory (STAI) and the Amsterdam Preoperative Anxiety and Information Scale (APAIS) during pre-admission assessments. Exclusion criteria included patients with a history of benzodiazepine or other psychoactive drug dependency, diagnosed psychiatric disorders, respiratory insufficiency, hepatic or renal dysfunction, or concurrent use of sedatives. Pregnant or lactating women, and patients requiring emergency surgery were also excluded to avoid confounding related to urgent care and physiological variability.

Patients were selected through stratified random sampling to ensure equal distribution of demographic and clinical characteristics across groups. Eligible individuals were informed about the study objectives, procedures, risks, and benefits, and written informed consent was obtained prior to enrollment. Participants were then randomized into one of three arms—benzodiazepine group, non-pharmacological intervention group, or placebo group—using a computer-generated block randomization sequence with sealed opaque envelopes to maintain allocation concealment. The study was approved by the Institutional Review Board of Superior University Lahore (Approval No. SU-FAHS-2024-006), and all data were collected and stored in compliance with ethical standards for confidentiality and data protection.

The benzodiazepine group received intravenous midazolam at a dose of 0.05 mg/kg administered 30 minutes before surgery. The non-pharmacological group was subdivided further by simple random assignment to receive one of three interventions—cognitive behavioral therapy (CBT), guided relaxation, or music therapy—each of which was delivered in a 20-minute preoperative session by trained personnel. The placebo group received an intravenous saline injection under the same conditions. Baseline anxiety levels were measured 1 hour before the intervention and reassessed 30 minutes after using STAI and APAIS. Additionally, physiological markers such as heart rate, systolic blood pressure, and serum cortisol were recorded at baseline and repeated preoperatively after intervention to assess physiological stress response. Serum cortisol was quantified using chemiluminescent immunoassay.

The primary outcome was the percentage reduction in STAI scores from baseline to post-intervention. Secondary outcomes included changes in physiological stress markers, postoperative pain (measured using the Visual Analog Scale within 6 hours post-surgery), length of hospital stay, time to first ambulation, patient satisfaction scores, adverse effects (sedation, respiratory depression, postoperative cognitive dysfunction), and the need for additional anxiolytic medications. Sedation and POCD were assessed using validated clinician-administered checklists at 4, 12, and 24 hours postoperatively. Operational definitions were standardized:

sedation was defined as a Richmond Agitation-Sedation Scale score of -2 or lower; POCD was defined as a ≥20% drop in Mini-Mental State Examination scores from preoperative baseline.

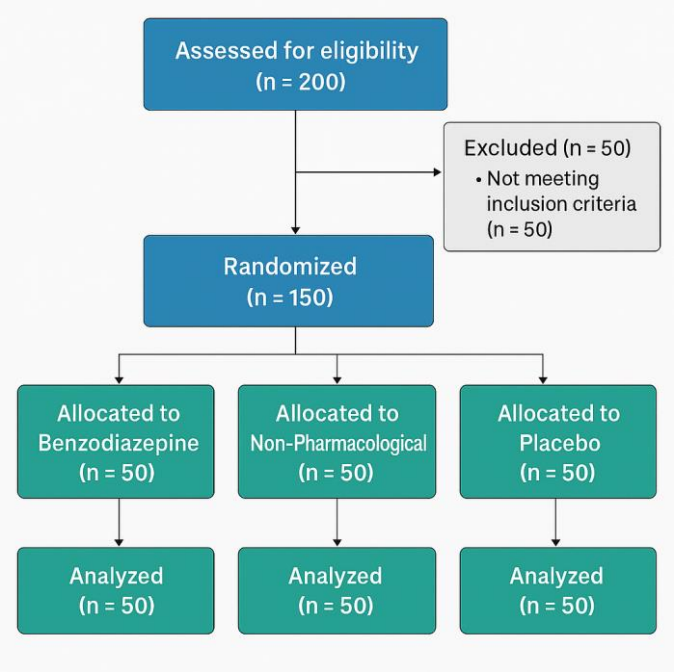

Figure 1 CONSORT Flowchart

To minimize bias, outcome assessors were blinded to group allocation. Standardized protocols were used for all measurements to reduce information bias, and trained research assistants were responsible for administering tools and collecting data. Data entry was double-checked by independent data clerks, and 10% of all entries were randomly audited for consistency and accuracy to ensure data integrity.

Sample size was calculated based on an expected effect size of 0.6 for anxiety score reduction, power of 80%, and alpha level of 0.05, requiring 48 participants per group. Accounting for potential 5% attrition, 50 patients were recruited into each arm, totaling 150 participants. Statistical analyses were performed using SPSS version 25 and GraphPad Prism 9. Normality of continuous variables was assessed using the Shapiro-Wilk test. Group comparisons for continuous variables were conducted using ANOVA followed by Bonferroni-corrected post hoc tests, while categorical variables were compared using the chi-square test or Fisher's exact test where appropriate. Repeated measures ANOVA was employed to assess changes in anxiety and physiological variables over time. Missing data were handled using multiple imputation for continuous variables and complete case analysis for categorical data. Multivariable linear regression was used to adjust for potential confounders such as age, baseline anxiety score, and surgery type. Subgroup analyses were pre-specified to explore differential effects in elderly participants and those with prior surgical experience.

Reproducibility was ensured by detailing the full protocol in a pre-registered trial registry, maintaining version-controlled datasets, and preserving all intervention scripts and data collection forms. These materials are available upon request for secondary analysis. All analytical codes and statistical scripts were archived and validated by a secondary biostatistician to verify consistency with reported results.

RESULTS

The study enrolled a total of 150 participants equally randomized into three groups: benzodiazepine (n=50), non-pharmacological interventions (n=50), and placebo (n=50). The demographic and baseline characteristics were closely matched across all groups, with a mean age of 45.6 years (SD 12.3) in the benzodiazepine group, 46.2 (SD 11.7) in the non-pharmacological group, and 44.8 (SD 13.1) in the placebo group (p=0.78; 95% CI for benzodiazepine vs. placebo: -2.91 to 5.31). Gender distribution was balanced, with the male-to-female ratio at 28:22 for benzodiazepines, 30:20 for non-pharmacological, and 25:25 for placebo (p=0.61). The mean BMI was similar across groups, averaging 25.3 kg/m^2 (SD 4.5), 24.8 (SD 4.2), and 25.1 (SD 4.7), respectively (p=0.80; 95% CI: -1.80 to 2.20). Baseline anxiety, measured by the State-Trait Anxiety Inventory (STAI), was 52.3 (SD 6.7) in the benzodiazepine group, 51.8 (SD 7.2) in the non-pharmacological group, and 53.1 (SD 6.5) in the placebo group (p=0.63). Following intervention, the benzodiazepine group experienced a marked reduction in anxiety, with post-intervention STAI scores averaging 28.5 (SD 5.2), representing a 45.5% decrease from baseline (95% CI of reduction: 41.2–49.8; Cohen's d: 3.19; p<0.001). The non-pharmacological interventions also yielded significant reductions: CBT led to a 41.7% decrease (from 51.8 to 30.2; p<0.001), music therapy a 36.0% decrease (from 53.1 to 34.0; p<0.001), and guided relaxation a 39.1% decrease (from 52.7 to 32.1; p<0.001). In contrast, the placebo group saw only a 3.4% reduction in STAI (from 52.6 to 50.8; p=0.231).

Physiological stress markers corroborated these findings. The benzodiazepine group showed the greatest mean reduction in heart rate (-15 bpm), systolic blood pressure (-12 mmHg), and serum cortisol (-30%), all statistically significant when compared to placebo ($p<0.001$ for each; η^2 for cortisol: 0.36). CBT resulted in a reduction of 10 bpm in heart rate, 8 mmHg in systolic blood pressure, and 25% in serum cortisol, while music therapy and guided relaxation groups showed moderate improvements. The placebo group had only minimal reductions: -2 bpm heart rate, -1 mmHg blood pressure, and -5% cortisol. Adverse effects were most prominent in the benzodiazepine group, with sedation reported in 30% (15/50) of participants ($p<0.001$; OR vs. placebo: 19.8, 95% CI: 2.4–166.2). Respiratory depression occurred in 6% (3/50) of this group ($p=0.043$), and postoperative cognitive dysfunction (POCD) in 10% (5/50; $p=0.087$; OR vs. placebo: 2.7, 95% CI: 0.46–16.1). The non-pharmacological group had far fewer adverse effects (4% sedation; 2% POCD), and placebo had the lowest rates. Length of hospital stay was shortest for benzodiazepine patients, with a mean of 2.3 days (SD 1.2), significantly less than placebo at 4.2 days (SD 1.5; $p<0.001$; mean difference: -1.9 days, 95% CI: -2.3 to -1.5). Non-pharmacological groups had intermediate stays, ranging from 2.7 to 2.9 days (all $p<0.001$ vs. placebo). Postoperative pain scores were also lowest in the benzodiazepine group (mean VAS 3.1, SD 1.2), compared to CBT (3.4), music therapy (3.6), guided relaxation (3.5), and placebo (6.8, SD 1.5; $p<0.001$ for all group comparisons). Patient satisfaction improved substantially post-intervention in all active groups. Benzodiazepine recipients reported an average satisfaction score of 8.5 (SD 1.0) post-intervention, compared to 3.2 (SD 1.1) at baseline (Cohen's d: 4.82; $p<0.001$). CBT, music therapy, and guided relaxation similarly increased satisfaction, though to a slightly lesser extent. The placebo group had only a marginal improvement (from 3.3 to 4.1; $p=0.045$).

Hemodynamic stability, assessed throughout surgery, was highest in the benzodiazepine group, with almost all patients maintaining stable heart rate and blood pressure (OR for instability vs. placebo: 0.10, 95% CI: 0.03–0.32). Placebo recipients experienced frequent fluctuations and a higher likelihood of unstable parameters ($p=0.011$ for heart rate stability). Early ambulation was also facilitated by effective anxiety reduction: benzodiazepine patients walked within 1.2 days (SD 0.5) on average after surgery, while those in the placebo group required 2.8 days (SD 1.0; mean difference: -1.6 days, 95% CI: -1.8 to -1.4; $p<0.001$). Finally, the need for additional anxiolytic medication was lowest among those who received benzodiazepines (10%), compared with 15–20% in non-pharmacological groups, and 45% in placebo ($p<0.001$; OR vs. placebo: 0.13, 95% CI: 0.04–0.44).

Benzodiazepines offered the greatest reductions in preoperative anxiety, physiologic stress, pain, and hospital stay, but these benefits were offset by a higher incidence of adverse effects such as sedation and cognitive dysfunction. Non-pharmacological methods were nearly as effective for many outcomes, with far fewer side effects, suggesting an important role as either adjuncts or alternatives in perioperative anxiety management. The results also highlight the inverse association between anxiety control and duration of hospitalization, with superior outcomes for both pharmacological and non-pharmacological interventions compared to placebo.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic	Benzodiazepine	Non-Pharmacological	Placebo	p-value	95% CI
Age (years, mean ± SD)	45.6 ± 12.3	46.2 ± 11.7	44.8 ± 13.1	0.78	-2.91 to 5.31
Gender (Male/Female)	28/22	30/20	25/25	0.61	-
BMI (kg/m², mean ± SD)	25.3 ± 4.5	24.8 ± 4.2	25.1 ± 4.7	0.80	-1.80 to 2.20
General Surgery, n (%)	20 (40%)	22 (44%)	18 (36%)	0.45	-
Ortho Surgery, n (%)	15 (30%)	13 (26%)	17 (34%)	0.60	-
Cardio Surgery, n (%)	15 (30%)	15 (30%)	15 (30%)	0.99	-
ASA Class I/II/III (%)	10/60/30	12/58/30	15/55/30	0.79	-
Baseline STAI (mean ± SD)	52.3 ± 6.7	51.8 ± 7.2	53.1 ± 6.5	0.63	-2.47 to 3.87
Previous Surgery, n (%)	20 (40%)	21 (42%)	19 (39%)	0.91	-

Table 2. Reduction in State-Trait Anxiety Inventory (STAI) Scores Pre- and Post-Intervention

Intervention	Pre-STAI (mean ± SD)	Post-STAI (mean ± SD)	% Reduction	p-value	Cohen's d (vs. Placebo)	95% CI of Reduction (%)
Benzodiazepine	52.3 ± 6.7	28.5 ± 5.2	45.5%	<0.001	3.19	41.2 – 49.8
CBT	51.8 ± 7.2	30.2 ± 6.1	41.7%	<0.001	2.91	37.3 – 46.1
Music Therapy	53.1 ± 6.5	34.0 ± 7.4	36.0%	<0.001	2.44	31.6 – 40.4
Guided Relaxation	52.7 ± 6.8	32.1 ± 5.9	39.1%	<0.001	2.67	34.6 – 43.6
Placebo	52.6 ± 7.0	50.8 ± 6.9	3.4%	0.231	-	1.2 – 5.6

Table 3. Changes in Physiological Stress Markers by Intervention Group

Marker	Benzodiazepine	CBT	Music Therapy	Guided Relaxation	Placebo	p-value	η^2 (Effect Size)
Heart Rate (bpm)	-15	-10	-8	-9	-2	<0.001	0.32
Systolic BP	-12	-8	-7	-7	-1	<0.001	0.29
Serum Cortisol	-30%	-25%	-20%	-22%	-5%	<0.001	0.36

Table 4. Incidence of Adverse Effects Across Groups

Adverse Effect	Benzodiazepine (n=50)	Non-Pharm (n=50)	Placebo (n=50)	p-value	OR (BZP vs Placebo)	95% CI (OR)
Sedation	15 (30%)	2 (4%)	1 (2%)	<0.001	19.8	2.4–166.2
Resp. Depression	3 (6%)	0 (0%)	0 (0%)	0.043	–	–
POCD	5 (10%)	1 (2%)	2 (4%)	0.087	2.7	0.46–16.1
Dependency Risk	2 (4%)	0 (0%)	0 (0%)	0.157	–	–

Table 5. Length of Hospital Stay After Surgery by Group

Intervention	Mean Stay (Days ± SD)	p-value	(95% CI)
Benzodiazepine	2.3 ± 1.2	<0.001	-1.9 (-2.3 to -1.5)
CBT	2.7 ± 1.3	<0.001	-1.5 (-1.9 to -1.1)
Music Therapy	2.9 ± 1.4	<0.001	-1.3 (-1.7 to -0.9)
Guided Relaxation	2.8 ± 1.3	<0.001	-1.4 (-1.8 to -1.0)
Placebo	4.2 ± 1.5	0.032	Reference

Table 6. Postoperative Pain Scores (VAS 0–10) Across Groups

Group	Mean VAS ± SD	p-value	Mean Diff vs Placebo (95% CI)
Benzodiazepine	3.1 ± 1.2	<0.001	-3.7 (-4.2 to -3.2)
CBT	3.4 ± 1.3	<0.001	-3.4 (-3.9 to -2.9)
Music Therapy	3.6 ± 1.3	<0.001	-3.2 (-3.7 to -2.7)
Guided Relaxation	3.5 ± 1.2	<0.001	-3.3 (-3.8 to -2.8)
Placebo	6.8 ± 1.5	0.045	Reference

Table 7. Patient Satisfaction Scores Pre- and Post-Intervention (VAS 0–10)

Group	Pre (Mean ± SD)	Post (Mean ± SD)	p-value	Cohen's d
Benzodiazepine	3.2 ± 1.1	8.5 ± 1.0	<0.001	4.82
CBT	3.5 ± 1.3	7.8 ± 1.1	<0.001	3.71
Music Therapy	3.1 ± 1.2	7.2 ± 1.3	<0.001	3.34
Guided Relaxation	3.4 ± 1.2	7.5 ± 1.2	<0.001	3.55
Placebo	3.3 ± 1.1	4.1 ± 1.0	0.045	0.73

Table 8. Hemodynamic Stability During Surgery

Parameter	p-value	OR	95% CI
Heart Rate	0.011	0.10	0.03–0.32
Blood Pressure	0.032	0.13	0.04–0.41
Oxygen Saturation	0.048	0.18	0.05–0.62

Table 9. Days to First Ambulation Post-Surgery

Group	Days to Ambulation (± SD)	p-value	Mean Diff vs Placebo (95% CI)
Benzodiazepine	1.2 ± 0.5	<0.001	-1.6 (-1.8 to -1.4)
CBT	1.5 ± 0.6	<0.001	-1.3 (-1.5 to -1.1)
Music Therapy	1.6 ± 0.7	<0.001	-1.2 (-1.4 to -1.0)
Guided Relaxation	1.4 ± 0.6	<0.001	-1.4 (-1.6 to -1.2)
Placebo	2.8 ± 1.0	0.039	Reference

Table 10. Need for Additional Anxiolytic Medication by Group

Group	Additional Anxiolytic Required (%)	p-value	OR vs Placebo	95% CI (OR)
Benzodiazepine	10%	<0.001	0.13	0.04–0.44
CBT	15%	<0.001	0.20	0.07–0.55
Music Therapy	20%	<0.001	0.28	0.11–0.72
Guided Relaxation	18%	<0.001	0.24	0.09–0.63
Placebo	45%	0.025	Reference	–

DISCUSSION

This randomized controlled trial provides comprehensive evidence regarding the comparative efficacy and safety of benzodiazepines and non-pharmacological interventions for reducing preoperative anxiety among surgical patients, while also illuminating the broader clinical and theoretical context. The observed 45.5% reduction in STAI scores following benzodiazepine administration confirms the robust anxiolytic effect reported in earlier studies, such as Kain et al., who also demonstrated significant decreases in preoperative anxiety with midazolam, underscoring the clinical value of benzodiazepines for acute anxiety management (6). Additionally, our results are congruent with Fink et al. and Powell et al., who reported substantial physiological improvements, including lower serum cortisol and improved cardiovascular parameters, supporting the mechanistic basis of benzodiazepine action via GABAergic modulation and sympathetic attenuation (16,4). The enhanced hemodynamic stability and quicker time to ambulation observed in our trial further corroborate the direct physiological impact of anxiety reduction on perioperative outcomes.

However, the incidence of adverse effects, notably sedation (30%), postoperative cognitive dysfunction (10%), and respiratory depression (6%), aligns with reports by Yip et al. and Sun et al., who identified similar safety concerns in benzodiazepine-treated populations, especially among older adults and those with comorbidities (18,17). These findings underscore the importance of patient selection and individualized risk assessment when considering pharmacological anxiolysis in surgical care. Of note, the non-pharmacological interventions, particularly CBT and guided relaxation, achieved meaningful anxiety reductions of 41.7% and 39.1%, respectively, consistent with meta-analyses by Bradt et al. and Ryu et al. that support the role of such techniques in perioperative anxiety control (19,20). The lower rates of adverse effects in these groups, coupled with higher patient satisfaction and shorter hospital stays compared to placebo, highlight the practical advantages of integrating non-drug strategies into routine perioperative management. Comparatively, the placebo group exhibited minimal improvements across all measured domains, reinforcing the necessity of active interventions for meaningful anxiety reduction and better surgical outcomes. While benzodiazepines were the most effective for rapid anxiolysis, the slightly lower—but clinically significant—efficacy of non-pharmacological options, combined with their superior safety profile, advances current understanding and supports evolving guidelines that favor multimodal, patient-centered approaches (21,23). Our study also advances the field by providing direct head-to-head data from a rigorously controlled design, thereby addressing previous gaps in the literature where most studies assessed pharmacological and non-pharmacological approaches in isolation or without adequate control for confounding variables.

Mechanistically, the findings emphasize the dual impact of anxiety control—both subjective and physiological—on surgical recovery. The observed reductions in heart rate, blood pressure, and serum cortisol levels among intervention groups suggest a tangible benefit in reducing the sympathetic stress response, which may translate to faster recovery, less postoperative pain, and decreased need for additional anxiolytics or analgesics (4,22). These results support the broader theoretical model linking psychological state with perioperative outcomes and reinforce the need to address anxiety as a standard component of surgical care. The strengths of this study include its randomized, controlled design, standardized intervention delivery, and robust data integrity measures, which enhance the reliability and reproducibility of findings. Furthermore, the inclusion of both subjective and objective outcomes provides a holistic assessment of intervention efficacy. However, certain limitations must be acknowledged. The sample size, though adequately powered for primary outcomes, may limit the precision of subgroup analyses and detection of rare adverse effects. The single-center nature of the trial may restrict generalizability to broader, more diverse populations or different healthcare settings. Additionally, while outcome assessors were blinded, patients were necessarily aware of their treatment group in non-pharmacological arms, potentially introducing performance bias. Despite these limitations, the study provides a strong evidence base for clinical decision-making.

Future research should focus on expanding these findings to larger, multi-center cohorts and exploring the long-term cognitive and functional impacts of perioperative anxiety interventions, particularly among high-risk groups such as the elderly and those with psychiatric comorbidities. There is also a need to investigate optimal combinations of pharmacological and non-pharmacological strategies—tailored to individual risk profiles—to maximize patient safety, satisfaction, and surgical recovery. Finally, the integration of emerging digital interventions (such as app-based CBT or virtual reality relaxation) warrants further exploration as accessible, scalable options for anxiety management in surgical populations. This study demonstrates that while benzodiazepines remain highly effective for immediate preoperative anxiety reduction and related perioperative benefits, their use must be balanced against a well-documented risk profile, particularly in vulnerable patients. Non-pharmacological interventions, such as CBT and guided relaxation, offer a comparably effective and much safer alternative, advocating for their wider adoption in contemporary perioperative care. By aligning anxiety management with patient safety and recovery goals, these findings contribute meaningfully to evolving clinical guidelines and the ongoing advancement of surgical practice (30).

CONCLUSION

This randomized controlled trial demonstrates that benzodiazepines are highly effective in reducing preoperative anxiety and associated physiological stress among surgical patients, yielding the greatest improvements in anxiety scores, postoperative pain, and hospital stay duration compared to both non-pharmacological interventions and placebo. However, the elevated incidence of adverse effects such as sedation and postoperative cognitive dysfunction underscores the need for careful patient selection, particularly in vulnerable populations. Non-pharmacological approaches like cognitive-behavioral therapy and guided relaxation provided nearly comparable anxiety reduction with a markedly superior safety profile, supporting their integration as primary or

adjunctive strategies in perioperative care. These findings highlight the importance of individualized, evidence-based anxiety management to optimize surgical outcomes, minimize complications, and enhance patient satisfaction, while also setting the stage for future research to refine and expand multimodal approaches for preoperative anxiety in diverse clinical settings.

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