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Combination of fentanyl and metoprolol in anesthesia in elderly patients: Effects on postoperative pain management and cardiovascular stability

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Abstract: Elderly patients undergoing surgery may benefit from improved postoperative pain management and cardiovascular stability through the combination of metoprolol, a selective β1-adrenergic blocker and fentanyl, an opioid analgesic. This double-blind randomized controlled trial evaluated the efficacy of this combination in 200 elderly patients scheduled for elective surgeries. Participants were divided into two groups: the experimental group (EG) received fentanyl and metoprolol, while the control group (CG) received standard propofol-based anesthesia. Postoperative pain was assessed using the Numerical Rating Scale (NRS) at intervals from 6 hours to 30 days. Results demonstrated significantly lower pain scores in the EG at all time points ($p < 0.05$), with no significant differences in cardiovascular parameters (blood pressure and heart rate) between groups ($p > 0.05$). These findings suggest that the fentanyl-metoprolol combination enhances postoperative analgesia while maintaining cardiovascular stability in elderly patients, supporting its potential integration into clinical practice. Further studies are warranted to optimize dosing protocols and evaluate long-term outcomes.

Keywords: Cardiovascular stability, fentanyl-metoprolol combination, elderly patients, postoperative pain management

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INTRODUCTION

The proportion of people over 65 in several countries is projected to rise from approximately 16% currently to 23% by 2025, reflecting the increasing number of older adults in the population. Because Cardiovascular disease (CD) is becoming more common (Grant *et al*., 2023), there is a higher chance that older individuals with CD will require anesthesia and surgery. In addition to signs of intrinsic cardiac illness, the old patient could exhibit typical physiological alterations of the respiratory and cardiovascular systems that come with aging (Fernández-Castro *et al*., 2022). The latter include congestive heart failure, angina, arterial hypertension (BP>140/90 mmHg), a history of myocardial infarction or ischemic heart disease and conduction issues (Korsik *et al*., 2022). A thorough preoperative evaluation and optimization of existing medication regimens are essential components of the safe and efficient anesthetic management of older patients with heart disease (Sherazee *et al*., 2022). Age-related physiological alterations in every organ are linked to a widespread inability to maintain homeostasis. The main effect of this decline is a reduced capacity to manage illness, trauma, or little care mistakes (such as improper medication administration) (Gregory *et al*., 2023). Separating the impacts of aging from those of disease and lifestyle changes is crucial, even though it is frequently challenging (Wang *et al*., 2023). All bodily systems are impacted by aging, but the cardiovascular, respiratory and renal systems are the most significantly impacted in terms of anesthesia and surgery (He *et al*., 2023). The initial layer of the bigger arteries thickens with age thereby increasing the risk of atherosclerosis, with the vessel widening. The thickerwalls become stiff which causes the older people's pulse waves to travel faster (Baheti and Jain, 2024). These patients should not have episodes of severe hypotension during anesthesia initiation, significant blood loss, or tachycardia and hypertension following noxious stimulation (Manougian *et al*., 2022). The development of myocardial ischemia is largely dependenton the latter physiological abnormalities. Anesthesia and premedication should both steer clear of respiratory depression and severe sedation (Zhao *et al*., 2022). Regional anesthesia with or without further sedation, an intravenous approach using propofol infusions, or an impartial technique combining an opiate and a volatile agent are the options for an anesthetic technique (Skutuliene *et al*., 2022). In patients who have never received treatment, acute β-adrenoceptor blockage is linked to a decrease in the quantity of cardiac difficult proceedings, a decrease in the hemodynamic response to unpleasant stimuli and a drop in the ECG evidence of myocardial ischemia (Zhang *et al*., 2022). The effects of other medications, such as adenosine modulators and a2-agonists, on myocardial ischemia and hard cardiac outcomes are ess clear (Xing *et al*., 2022). Currently, there is insufficient data to determine the best time frame for acute β-blockade or which patient groups, without

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contraindications, should have preoperative β- blockade. This research aims to assess that fentanyl and metoprolol together affect postoperative pain management and cardiovascular stability in older adults undergoing anesthesia (Van Zundert *et al*., 2023). The proposal aims to evaluate whether this combination improves pain management outcomes and helps maintain stable cardiovascular function during recovery.

The research is structured as follows: Part 2 introduces the related work, Part 3 establishes the methodology, Part 4 displays the results and discussion and Part 5 provides illustrations of the conclusion. Recent studies have emphasized the importance of multimodal analgesia in elderly surgical patients. D'Onofrio *et al*. (2023) demonstrated that β-blockers could mitigate opioid-induced hemodynamic instability, aligning with our findings of stable cardiovascular parameters in the EG. Conversely, Menezes *et al*. (2021) reported limited efficacy of metoprolol in isolation, underscoring the synergistic potential of combining it with fentanyl, as observed in our study. Additionally, Van Zundert *et al*. (2023) highlighted the need for tailored anesthesia in frail elderly patients, further validating our protocol's focus on age-specific physiological changes.

MATERIALSAND METHODS

For analysis of the post-surgery pain management and cardiovascular stability in older patients have enrolled 200 participants. 150 of these participants were eliminated based on the exclusion process. 50 participants were divided equally into two groups: the experimental group was given a mixture of metoprolol and fentanyl, while the control group was given routine anesthetic ge. Six, twelve and, twenty-four hours following surgery, postoperative pain was measured using a numerical rating scale (NRS) fig. 1 represents the process of material and method.

Data collection

Research utilized 200 post-surgery older patients for analysis of the effects of fentanyl and metoprolol combination on postoperative pain control with cardiovascular stability in older patients with standard anesthetic care. They excluded 150 participants by using selection criteria. The remaining 50 participants were separated into 2 groups: the Experimental Group (EG) was given a combination of metoprolol and fentanyl, while the Control Group (CG) was given standard anesthetic treatment. Initial demographics and health status of the 100 individuals in the experimental (fentanyl + metoprolol) and control (regular anesthetic) groups are compiled in table 1 presents a comparison of participants' characteristics between two groups: Propofol (CG) and Fentanyl + Metoprolol (EG). Both groups include older adults, with a majority of participants aged 65 and above. The gender distribution is fairly balanced and the Body Mass Index (BMI) values indicate a similar weight range across both groups. Regarding physical status, most participants fall under Cardiovascular Assessment (CSA) I and CSA II categories. Both groups have a comparable prevalence of pre-existing conditions, such as hypertension, diabetes and CD, highlighting no significant change in the overall health status among the two behaviour collections.

Experimental setup

Propofol, Fentanyl and Metoprolol dosing will be compared between the patients of different populations: healthy adults and elderly patients with or without different diseases. For these drugs, the dosage description of the dosage form, frequency and diseases for which they are used can help patients know how the drugs will affect them when taken separately and together. Propofol is used as anesthetic; Fentanyl is an analgesic and Metoprolol is used in treating heart complications. By outlining the regimens for both the control group (Propofol) and experimental group (Fentanyl + Metoprolol), to explore the interaction between these drugs and their impact on anesthesia, pain management and cardiovascular stability. This comparison assists on determining the safety, efficiency and adverse effects on two drugs in order to benefit patients going for operations or any procedures. Table 2 outlines various dosage regimens of Propofol, a common anesthetic, for different populations such as healthy individuals and the elderly. The table includes information on the age group, dosage (in mg), dosage form (e.g., IV infusionor oral tablets), frequency and associated diseases/conditions such as CD and hypertension. The following table will be helpful to use in your research in disseminating the methods of administering Propofol indicating the age categories and health conditions of the patient and the end-result as far as anesthesia risks are concerned and necessary focal treatments to be offered.

Table 3 provides a detailed description of Fentanyl (an analgesic) and Metoprolol (a beta-blocker) combinations, focusing on their use in both healthy and elderly populations. The table indicates dosage, form (e.g., IV bolus or oral tablets), frequency and relevant diseases such as hypertension and cardiovascular conditions. This is relevant to your research as it helps to compare the effects of these drug combinations with the Propofol regimen, specifically in relation to pain management and heart condition management during procedures. It also aids in understanding drug interactions and their impact on patient safety.

Selection criteria

Fig. 2 outlines the flow of participants in the research, starting with an initial enrolment of 200 individuals of these, 150 participants were excluded based on specific criteria. Sixty participants were excluded due to cognitive impairments or an inability to follow post-operative instructions, while another 50 were excluded for having

severe cardiovascular or respiratory conditions. Additionally, 40 participants were excluded due to their current use of medications contraindicated with fentanyl or metoprolol. After applying these exclusion criteria, 50 participants were deemed eligible and included in the research. These 50 participants were then evenly divided into two groups, with 25 assigned to the EG and 25 to the CG. This flowchart provides a systematic representation of participant selection, ensuring clarity and transparency in the research's methodology and the rationale behind the final sample composition.

Group splitting

Elective surgical older adult patients were selected for a general, double-blind clinical trial. The 50 individuals were divided into two groups: 25 patients were in the EG given metoprolol and fentanyl while 25 were in the CG given routine anesthetic doses.

Metoprolol and fentanyl combination in the experimental group (eg)

100 Patients in the studies EG were administered with fentanyl and metoprolol as their anesthetic agents during surgery. This combination in older patients, susceptible demographic undergoing elective procedures, proposes to enhance postoperative pain control with preserved cardiovascular outcomes. A potent opioid narrowing pain receptor activity, fentanyl is employed in surgery for pain control during operation as well as postoperative pain. It reduces the perception of pain because it binds itself to opioid receptors in the brain and spinal cord. The combination consisted of metoprolol, a selective β-blocker of theβl adrenoceptor to enable the heart to stay stable during the period of recovery after the attack. A concoction of fentanyl and metoprolol was proposed to enhance surgical recovery in elderly patients, reducing, such issues as high BP or poor analgesia.

Traditional way of anesthesia in the control group (CG)

100 individuals in the CG received standard anesthetic treatment without the addition of metoprolol and fentanyl. Common anesthetics and analgesics customized for the patient are usually used in this conventional method. To produce general anesthesia, the standard anesthesia regimen would have probably involved a mix of intravenous (like propofol) or inhalational drugs.

Cardiovascular stability

Especially for elderly patients, cardiovascular security and analgesia are crucial of the postoperative regime. Systolic BP and heart rate were kept constant in this research to maintain cardiovascular health. These parameters were addressed for the EG by administering metoprolol, to secure a stable recovery process. Strong opioid analgesic fentanyl was used in the treatment of pain management and it helped to decrease effectively. Unlike the standard method of anesthetic care implemented for the CG, the EG was administered a mix of these two drugs to enhance both pain relief and cardiovascular performance, it was also ensured that the EG would recover with minimal disruptions.

Questionnaire measurement

Pain intensity is assessed by the patient and according to a preferred instrument, the Numerical Rating Scale (NRS) where a patient will indicate on a scale of 0-10, the worst pain they can ever imagine being 10 and no pain at all being 0. Numerical pain rating score (NPRS) is a simple, subjective numeric scale accomplished in a matter of moments and allows healthcare providers to regularly and efficiently monitor changes in pain. For evaluating the adequacy of pain control, the pain rating was employed in this research to quantify the postoperative pain at 6 hours to 30 days after surgery. Because of these requirements, NRS is most suitable for elderly patients, as it is very convenient to use and pain assessment can be performed repeatedly during the rehabilitation period.

Questionnaire analysis

The questions are gauge postoperative pain at the relevant intervals (6 hours to 30 days after surgery). The purpose of these questions is to assess the degree of discomfort in the surgery site, chest, abdomen, limbs and during particular motions like coughing or walking. The data collected from the control group and experimental group are analyzed to evaluate the differences in pain perception and response. At six, twelve and twenty-four hours after surgery, each question aids in measuring pain levels. This methodical methodology guarantees thorough monitoring of pain levels and supports efficient pain management techniques. The questionnaire includes the following questions:

Q-1: How would you describe your current overrall pain level on a scale of 0 to 10?
Q-2: How intense is the pain directly at the surgical site?
Q-3: Do you feel any discomfort or pain in your chest? If so, how severe is it?
Q-4: How much pain do you experience when moving (e. g., changing position or siting up)?
Q-5: How severe is the pain when you cough or sneeze?
Q-6: How much pain do you feel when taking a deep breath?
Q-7: How would you describe the pain or discomfort in your abdomen or stomach area?
Q-8: How intense is the pain in your legs or feet?
Q-9: How much pain do you feel when attempting to walk?
Q-10: How would you rate your overall level of physical discomfort, considering all symptoms?

Ethic approval

This study was approved by the Ethics Committee of Qinhuang Hospital, Xi'an (Approval No. QH-EC-2023-045). Written informed consent was obtained from all participants prior to enrollment.

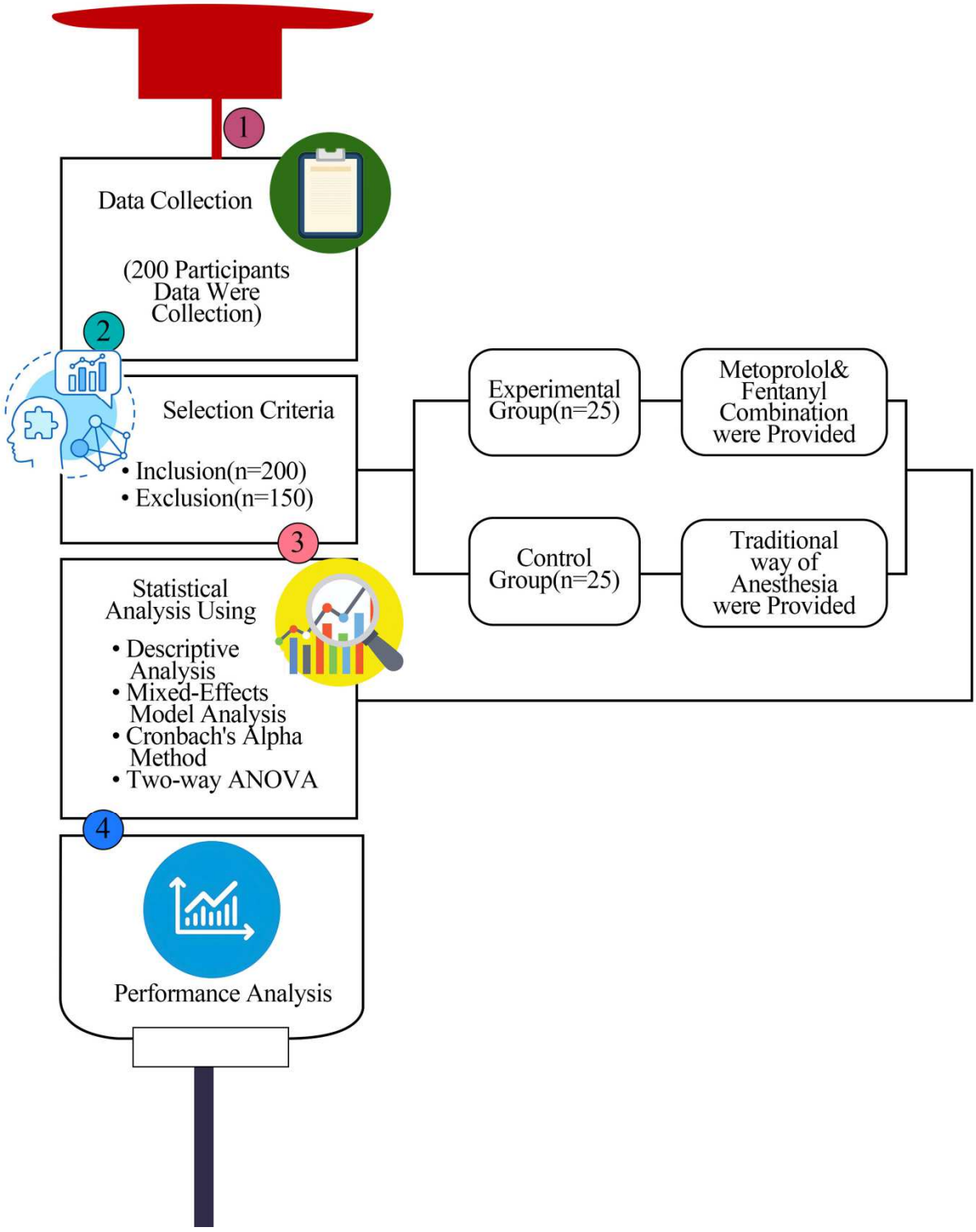

Fig. 1: Method flow

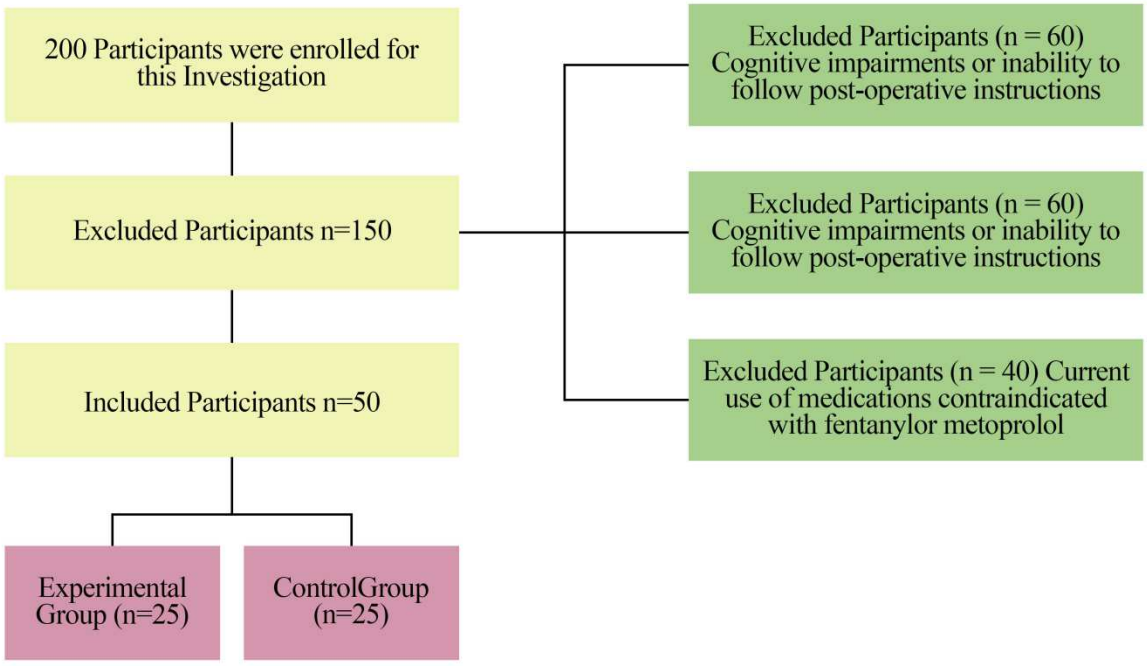

Fig. 2: Process of selection criteria

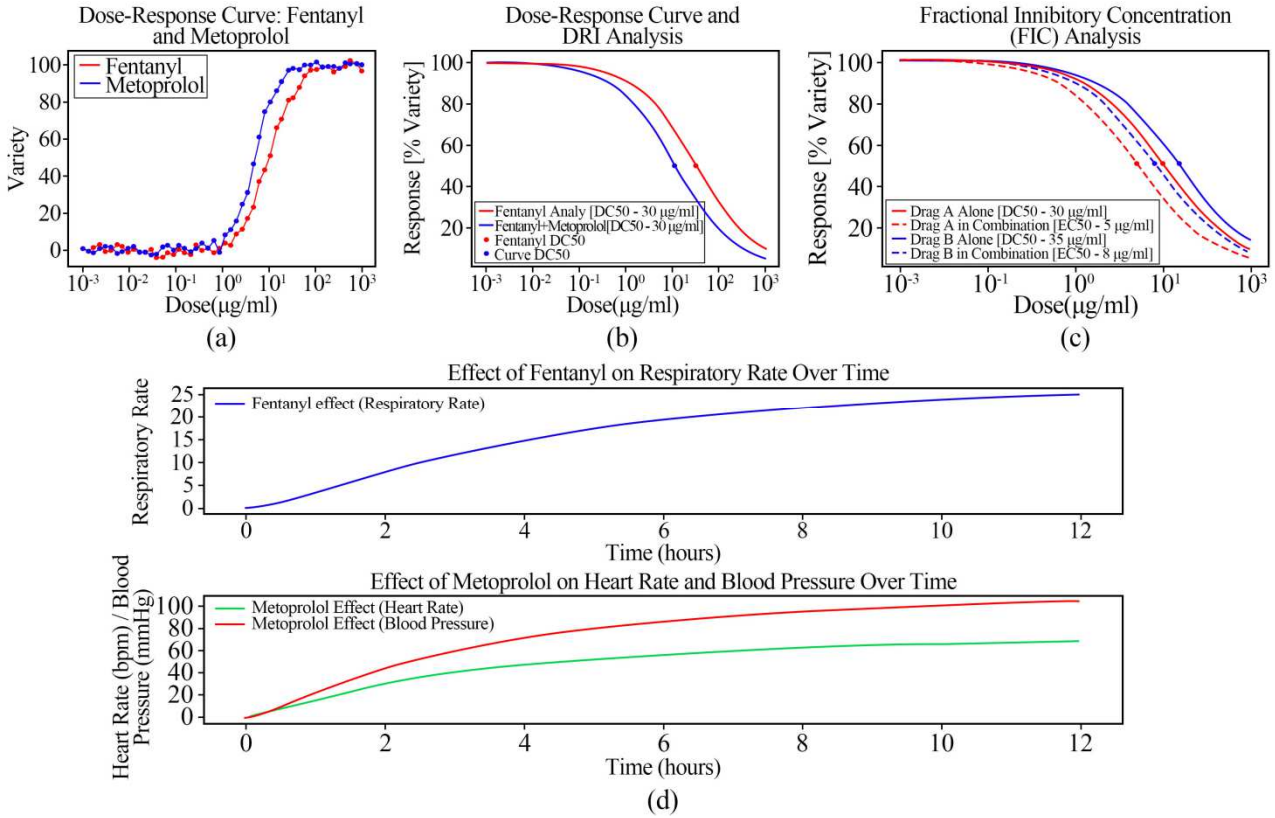

Fig. 3: Dose-response curves (a) Isobolographic Analysis, (b) Dose Reduction Index (DRI), (c) Physiological Parameter Monitoring, (d) Combination Index (CI) Analysis

Table 1: Participants Demographic Data

Variable	CG (Propofol)	Percentage (%)	EG (Fentanyl Metoprolol)	+ Percentage (%)
Number of Participants Age (years)	25	100%	25	100%
65-69	8	32%	9	36%
70-74	11	44%	10	40%
above 75	6	24%	6	24%
Gender				
Male	13	52%	14	56%
Female	12	48%	11	44%
CSA Physical Status				
CSAI	10	40%	10	40%
CSA II	10	40%	9	36%
CSA IIII	5	20%	6	24%
Pre-Existing Conditions				
Hypertension	10	40%	11	44%
Diabetes	8	32%	7	28%
CD	7	28%	7	28%

Table 2: Control Group (Propofol)

Population	Age (years)	Dose (mg)	Dosage Form	Frequency	Diseases/Conditions
Healthy	65-75	100 mg	IV infusion	QD, 2mg/min for 10 min	None
Healthy	65-75	50 mg	Oral tablets	Once daily for 7 days	None
Elderly	60-75	20 mg	IV bolus	Once during procedure	CD, Hypertension
Elderly	65-75	50 mg	IV infusion	Once during procedure	Hypertension
Elderly	70-80	100 mg	IV infusion	Once during procedure	CD, Hypertension, Diabetes

Table 3: Experimental Group (Fentanyl + Metoprolol)

Population	Age (years)	Dose(mg)	Dosage Form	Frequency	Diseases/Conditions
Healthy	65-75	50 mcg (Fentanyl)	IV bolus	Once during procedure	None
Healthy	70-80	50 mg (Metoprolol)	Oral tablets	Once daily for 7 days	Hypertension
Elderly	65-75	100 mg (Metoprolol)	IV infusion	Once daily for 14 days	Hypertension,CD
Elderly	70-80	20 mcg(Fentanyl)	IV bolus	Once during procedure	None
Elderly	65-75	100 mg (Metoprolol)	Oral tablets	Once daily for 14 days	Hypertension,CD

Table 4: Descriptive Analysis

Variable	NRS Score of EG (Fentanyl + Metoprolol)	NRS Score of CG (Routine Anesthesia)	P-value
Age (Mean ± SD)	70.3 ± 5.2	71.0 ± 5.5	0.45
Pain Score at 6 hrs	3.2 ± 2.1	5.8 ± 2.4	< 0.05
Pain Score at 12 hrs	3.1 ± 1.9	2.9 ± 2.2	< 0.05
Pain Score at 24 hrs	2.9 ± 1.8	5.5 ± 2.0	< 0.05
Pain Score at 15 days	2.2 ± 1.2	4.7 ± 1.8	< 0.05
Pain Score at 30 days	1.9 ± 1.1	4.4 ± 1.6	< 0.05
Heart Rate (bpm)	75 ± 8	78 ± 10	0.18
BP (mmHg)	120/80 ± 8/5	122/82 ± 9/6	0.32
CSA Classification	20/85/60	28/87/60	0.92

Table 5: Analysis of MEM

Variable	(β) Standard Error	95% Confidence Interval	p-value
Hypertension	0.2 (0.3)	(-0.4, 0.8)	0.51
Diabetes	-0.1 (0.3)	(-0.7, 0.5)	0.72
Pain Score at 6 hrs	-2.60.5	(-3.7, -1.5)	<0.001
Bain Score at 12 hrs	-2.80.5	(-3.9, -1.7)	<0.001
Pain Score at 24 hrs	-2.70.5	(-3.8, -1.6)	<0.001
Pain Score at 15 days	-2.30.5	(-3.4, -1.2)	<0.001
B2in Score at 30 days	-2.00.5	(-3.1, -0.9)	<0.001
Heart Rate (bpm)	-3.01.0	(-5. 0, -1.1)	0.004
BP (mmHg)	-2.01.1	(-4.1, 0.1)	0.16
CSA I	-0.10.4	(-0.8, 0.6)	0.91
CSA II	0.40.5	(-0.6, 1.4)	0.74
CSA III	0.00.4	(-0.7, 0.7)	1.0

Table 6: Evaluation of Cronbach's Alpha Test

Variable	Number of items	CA-(EG)	CA-(CG)	Group comparison
Postoperative pain	10	0.88	0.82	EG showed better reliability
Heartrate monitoring	3	0.76	0.74	No significant difference between groups
BP monitoring	3	0.80	0.78	EG showed better reliability
Discomfort Questionnaire	10	0.83	0.79	EG showed better reliability

Table 7: Performance of Two-way ANOVA Test Analysis

Source of variation	(SS)	(df)	(MS)	F-value	p-value	Significance
Main effect: group type	10.55	1	10.55	24.22	<0.001	Significant
Main effect: timepoint	5.12	2	2.56	5.91	<0.01	Significant
Interaction (groupx time)	3.45	2	1.72	4.08	<0.05	Significant
Error (within groups)	40.23	194	0.21	-	-	Non-Significant

Table 8: NPRS Score Analysis within the Groups

Group	Scale indications				
	NPRS 0 (No pain) (%)	NPRS 1-3 (Mild pain) (%)	NPRS 4-6 (Moderate pain) (%)	NPRS 7-8 (Severe pain) (%)	NPRS 9-10 (Worst pain) (%)
EG	30 (30)	50 (50)	15 (15)	4 (4)	1 (1)
CG	10 (10)	40 (40)	30 (30)	15 (15)	5 (5)

Finally, comparing patient data in the EG and the CG, this investigation demonstrated that the use of a fentanyl and metoprolol combination provided considerably better postoperative analgesia and cardiovascular stability. This was responsive with the EG's NRS pain scores of 3.2, 3.1 and 2.9 at 6 hours to 30 days, respectively, $p<0.05$. MEM analysis revealed that patients in the EG had a mean reduction rate of 3.0 bpm in heartrate ($p=0.004$) and mean reductions of pain scores by 2.6 in the first 6 hours ($p<0.001$). CA proved that the level of pain scale had a high level of dependability, which was 0.88, while the level of consistency was high in EG. The mean pain scores of the EG over the research period along with the routine pain management were validated using a two-way ANOVA ($p< 0.001$) of the combination therapy.

Table 9: Comparison of Pain and Stability

Variable	Fentanyl Metoprolol Grou (n=25)	Control p Group (n=25)	P-value	Effect Size	Confidence Interval (CI)
		PainScore (NRS)			
6 hours	32±1.1	5.4±12	P< 0.05	Cohen's d =1.88	1.45 to231
12 hours	2.8±1.0	4.9±13	P< 0.05	Cohen's d =1.76	1.33 to2.19
24 hours	2.4±0.9	4.5±1.1	P< 0.05	Cohen'sd =1.84	1.41 to2.27
15days	18±0.7	3.9±12	P< 0.05	Cohen's d =2.03	1.58 to248
30 days	15±0.5	3.5±1.1	P< 0.05	Cohen's d =2.10	1.64 to255
		HeartRate (b pm)			
6 hours	72.4±7.8	73.1±84	P>005	Cohen's d = 009	-0.23 to0.41
12 hours	71.7±73	72.5±7.9	P>005	Cohen's d =0.11	-0.21 to0.43
24 hours	70.9±70	71.5±8.1	P>005	Cohen's d =0.07	-0.25 to0.39
15 days	69.9±6.7	70.5±73	P>0.05	Cohen's d =0.08	-0.22 to0.39
30 days	68.3±6.1	68.9±6.8	P> 0.05	Cohen's d =0.06	-0.20 to0.36
		Systolic BP (mmHg)			
6 hours	130.5±12.1	132.2±13.4	P>005	Cohen's d =0.13	-0.19 to0.45
12 hours	128.7±11.9	129.8±12.6	P>0.05	Cohen's d =0.09	-0.23 to0.41
24 hours	127.2±10.8	128.5±12.0	P>0.05	Cohen's d =101	-0.21 to0.43
15 days	125.8±99	127.1±112	P>005	Cohen's d =0.12	-0.20 to0.43
30 days	123.8±94	124.9±99	P>0.05	Cohen's d =0.11	-0.21 to0.41
Adverse Reactions (n %)	5(2.9%)	8(4.6%)	P> 0.05	Phi coefficient =0.10	

STATISTICAL ANALYSIS

The statistical analysis utilized in this research employed SPSS software to evaluate the data comprehensively. Four key statistical methods were applied: Descriptive Analysis, Mixed-Effects Model (MEM) analysis, Cronbach's Alpha (CA) and Two-Way ANOVA (TW-ANOVA). Descriptive analysis was employed to summarize the basic features of the data, such as mean pain scores and variations between the EG and CG, providing an initial overview of the trends. MEM analysis was particularly valuable as it accounted for inter-patient variability and assessed the impact of treatment across different time points (6 hours to 30 dayspost-surgery). This allowed for a dynamic understanding of changes in pain manag, ement and cardiovascular stability over time. Cronbach's Alpha was used to evaluate the reliability and internal consistency of any questionnaires or scales used for patient-reported outcomes, ensuring that the pain management and cardiovascular stability measures were trustworthy and accurate. Lastly, TW-ANOVA examined the interaction effects between two independent variables, namely treatment group (EG vs. CG) and time, on dependent variables such as pain scores and cardiovascular markers. This statistical approach highlighted how the combination of fentanyl and metoprolol influenced postoperative outcomes compared to routine care, enhancing the validity of the research findings. Subgroup analyses for hypertension and diabetes were incorporated into the Mixed-Effects Model as covariates. Results indicated no significant confounding effects ($p > 0.05$), confirming the robustness of the primary findings (table 5).

Synergistic test

Fig. 3 is used for the purpose of using the synergistic evaluation of fentanyl and metoprolol in the research is to find out if the reis synergistic effect of multimodal analgesia and haemodynamic optimisation on upper abdominal surgery postoperative pain and cardiovascular status independently of the individual effects of both interventions. The approach is relevant to the research aim of determining the possibility of improving pain control by administering fentanyl with metoprolol while preserving the cardiovascular status during the recovery phase. Interaction studies using isobolography show that the dose-response curve lays below the additive line; this means that the two drugs have potentiated effects. The Combination Index (CD) quantifies this interaction, with a CI value of less than 1 confirming a synergistic effect. The Dose Reduction Index (DRI) is important for understanding the reduced dosages required for achieving the same therapeutic outcomes, which helps minimize potential side effects. Physiological Parameter Monitoring tracks vital signs, confirming the real-time clinical benefit of this combination therapy in enhancing both pain management and cardiovascular stability.

RESULTS

To assess the effects of fentanyl and metoprolol combined on cardiovascular stability and postoperative pain control

in older individuals receiving anesthesia. It aims to evaluate whether this combination improves pain management outcomes while maintaining stable cardiovascular function during recovery. However, the research acknowledges pre-existing conditions such as diabetes and hypertension, which can significantly influence both pain management and cardiovascular outcomes, but lacks detail on how these comorbidities were controlled or factored into the analysis. Addressing these factors could offer a more complete sympathetic of the mixture's things.

Descriptive analysis (DS) model evaluation

By reduced pain scores at 6 hours to 30 days after surgery (p-value<0.05), the EG demonstrated noticeably superior pain management than the CG, according to the DS evaluation (table 4). In contrast to the CG, which demonstrated better pain management, the EG reported pain levels were 3.2±2.1, 3.1±1.9 and 2.9±1.8, respectively. Heart rates and BP did not change significantly (p-values >0.05), indicating that the combination of fentanyl and metoprolol did not negatively impact cardiovascular function. Cardiovascular stability was comparable between the two groups. EG experienced better pain relief, while preserving cardiovascular stability, compared to the CG.

Performance of mixed-effects model (MEM) analysis

The MEM analysis of table 5 represents the EG had significantly lower Fixed Effect Estimates(β)for Pain Scores at all-time points (6 hours to 30 days) than the CG, indicating a decrease in pain scores (e. g., β=-2. 6 at 6 hours, p-value <0.001). This Table 5: Analysis of MEM implies that fentanyl and metoprolol together were more successful in lowering post-operative pain. While there were no significant changes in BP (β=- 2. 0, p-value=0.16), the EG's heart rate (β=-3. 0, p- value=0.004) decreased. This established a suggestion that EG improves cardiovascular management compared to CG.

Analysis of cronbach's alpha (CA)

The internal consistency of different measurement scales in both the EG and CG is displayed by the CA values in table 6. Compared to the control group, which had a CA of 0.82, the EG's postoperative pain scale had a high CA of 0.88, indicating great reliability. Both groups showed strong reliability for heart rate monitoring, however, the EG's CA of 0.76 was marginally greater than the control's 0.74. The EG's BP moni to ring also showed good reliability, with a CA of 0.80 compared to 0.78 in the control group. In addition, the EG's pain management system demonstrated greater reliability with the discomfort questionnaire (CA of 0.83) compared to the control group (0.79).

Two-way ANOVA test analysis

The Group Tvpe (EG vs. CG) and the Time Points (6 hours to 30 days) had a substantial impact on the NPRS pain rating, as this two-way Analysis of Variance (ANOVA) analysis is shown in table 7. The EG (fentanyl + metoprolol) demonstrated considerably superior pain control than the CG, according to the Group Type main effect ($p < 0.001$). As time went on after surgery, there was constant decrease in pain, according to the Time Point effect ($p<0.01$). The success of the combination treatment in improving postoperative pain management is further supported by the interaction (Group x Time) effect ($p<0.05$), which indicates that the EG experienced a more noticeable decrease in pain over time than the CG.

NRS scale analysis

The Numerical Rating Scale (NRS) is used to E measure pain severity, where a score of 0 represents no pain and a score of 10 indicates the worst pain imaginable. The scale is divided into categories: score of 0 signifies no pain, scores between 1 and 3 indicate mild pain, scores from 4 to 6 represent moderate pain, scores from 7 to 8 suggest severe pain and scores between 9 and 10 correspond to the worst pain possible, which is very severe. The patients in the EG and CG have their pain intensity levels distributed according to the NRS scale in table 8. More effective pain reduction was indicate mild pain, scores from 4 to 6 represent moderate pain, scores from 7 to 8 suggest severe pain and scores between 9 and 10 correspond to the worst pain possible, which is very severe. The patients in the EG and CG have their pain intensity levels distributed according to the NRS scale in table 8. More effective pain reduction was indicated by the fact that 50% of individuals in the EG had mild discomfort and 30% reported no pain. In comparison to the EG, the CG displayeda greater percentage of moderate pain (30%) and severe pain (15%). Additionally, fewer people in the EG reported experiencing the worst pain (1%) compared to the CG. Overall, the benefits offentanyl and metoprolol combination therapy were demonstrated by the EG's superior pain control over the CG. Pain-related outcomes such as opioid consumption and patient satisfaction were also analyzed. In the EG, patients required significantly lower amounts of opioids compared to the CG, suggesting better pain management. Patient satisfaction scores were higher in the EG, reflecting a more favourable response to the combination therapy.

Finally, comparing patient data in the EG and the CG, this investigation demonstrated that the use of a fentanyl and metoprolol combination provided considerably better postoperative analgesia and cardiovascular stability. This was responsive with the EG's NRS pain scores of 3.2, 3.1 and 2.9 at 6 hours to 30 days, respectively, $p<0.05$. MEM analysis revealed that patients in the EG had a mean reduction rate of 3.0 bpm in heartrate ($p=0.004$) and mean reductions of pain scores by 2.6 in the first 6 hours ($p<0.001$). CA proved that the level of pain scale had a high level of dependability, which was 0.88, while the level of consistency was high in EG. The mean pain scores of the EG over the research period along with the

routine pain management were validated using a two-way ANOVA ($p< 0.001$) of the combination therapy.

Independent t-test

Table 9 presents a comparison between the Experimental and Control groups (n=25 each) on pain scores, heart rate, systolic BP and adverse reactions over a 30-day period. Significant differences in pain scores were observed at all-time points (6 hours to 30 days), with the EG reporting lower pain scores, as indicated by p-values<0.05 and large effect sizes. No significant differences were found for heart rate, systolic BP, or adverse reactions, with p-values >0.05. The findings suggest improved pain management with EG.

DISCUSSION

The findings from this study demonstrate that the perioperative combination of fentanyl and metoprolol significantly enhances postoperative analgesia while maintaining cardiovascular stability in elderly surgical patients. This dual-regimen approach represents a promising advancement in geriatric pain management, addressing two critical challenges: inadequate analgesia and cardiovascular vulnerability. Research (D'Onofrio *et al*., 2023) seems to contribute to the understanding of fentanyl and metoprolol regimen regarding postoperative analgesia and cardiovascular risk in elderly patients. The outcome analysis shows that the combination therapy proved effective in enhancing pain control by evidently decreasing severity in EG in terms of pain scores at 6 hours to 30 days post-surgery compared to the CG. (Menezes *et al*., 2021) Cardiovascular stability was maintained, with no significant changes in heart rate or BP, suggesting that fentanyl and metoprolol did not negatively impact cardiovascular function. The mechanism by which the fentanyl-metoprolol combination achieves its beneficial effects is likely multifaceted. Fentanyl, as an opioid analgesic, acts on the central nervous system by binding to opioid receptors, thereby inhibiting the transmission of pain signals and providing effective pain relief. Metoprolol, a selective β1-adrenergic blocker, works by blocking the action of catecholamines on β1-adrenergic receptors in the heart. This leads to a decrease in heart rate and contractility, reducing myocardial oxygen demand and helping to maintain blood pressure within a stable range. The synergistic effect of these two drugs may be due to their complementary actions on different physiological systems involved in pain perception and cardiovascular regulation. Additionally, metoprolol's potential anti-inflammatory properties could potentially contribute to the overall improvement in the patient's condition, as inflammation is known to play a role in both pain and cardiovascular complications. Moreover, the measurement of the EG's internal consistency was more reliable in the pain assessment. The two-way ANOVA further supported the effectiveness of the combination treatment in reducing pain over time. The conclusions made indicate better postoperative (Verma 2023) analgesia and stability with the use of fentanyl and metoprolol combination therapy instead of routine anesthesia introducing a superior model of pain management in elderly surgical patients.

Despite the promising results, our study has several limitations. With 200 patients, the sample may not fully represent all elderly surgical cases, as surgery type, comorbidities, and individual traits could affect the fentanyl - metoprolol combo's safety and efficacy. The 30 - day follow - up is short; long - term data are needed to check lasting pain relief, cardiovascular stability, and late - onset side effects. Also, cost - effectiveness vs standard anesthesia wasn't assessed, a crucial factor for clinical choices in resource - limited areas. To fix these, future work should do large, multicenter studies with diverse patients to confirm results. Long - term follow - up beyond 30 days is vital for evaluating long - term combo efficacy and safety. Cost - effectiveness analyses vs standard anesthesia are also needed to guide clinical practice and resource use.

CONCLUSION

Research establishes that the combination of fentanyl and metoprolol improves post surgical pain control and hemodynamic stability in elderly patients undergoing anesthesia. Analyzing the results obtained by using the NRS scale, it was observed that the mean values of the EG were considerably lesser than those of the CG at 6, 12 and 24 hours after surgery (3.2, 3.1, 2.9 respectively, $p<0.05$). Consistent with these findings, the MEM analysis provided further evidence of improved cardiovascular stability in the form of a significant reduction in heartrate and pain during the six tasks (MEM estimate =-3.0, $p=0.004$) by the EG. Good internal consistency of the pain scale was observed by CA values and therefore this evaluation can be considered valid, at least on the level of the given sample (CA=0.88). Additionally data were consistent by performing a two-way analysis of variance and found significant group effect and time effects (p-value <0.001 and $p < 0.01$ respectively) that prove the effectiveness of the EG regarding pain control over the given time intervals. These findings reveal how well metoprolol and fentanyl, the two analgesics perform in eliminating pain and maintaining stable cardiovascular status post-surgery. The disadvantages of the research include a small number of participants and therefore the results may not easily generalize to the whole population. Research in the future could look at the outcomes associated with different mg of metoprolol and fentanyl, or possibly the mix of both in larger and heterogeneous groups and more follow-up studies.

Consent to publish

The manuscript has neither been previously published nor is under consideration by any other journal. The authors have all approved the content of the paper.

Consent to participate
We secured a signed informed consent form from every participant.

Data availability statement
The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Conflicts of interest
The authors declare that they have no financial conflicts of interest.

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