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A COMPARATIVE OBSERVATIONAL STUDY OF EFFICACY AND SAFETY OF DEXMEDETOMIDINE-KETAMINE VERSUS FENTANYL-MIDAZOLAM COMBINATION FOR POSTOPERATIVE SEDATION IN PATIENTS UNDERGOING ELECTIVE OFF PUMP CORONARY ARTERY BYPASS GRAFT SURGERY

Anaesthesiology

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ABSTRACT

Background: Dexmedetomidine and ketamine are anesthetic agents which are frequently used for sedation and analgesia in intensive care units after procedures such as coronary artery bypass grafting (CABG). This study compared the efficacy of dexmedetomidine-ketamine (DK) combination versus fentanyl-midazolam (FM) combination for sedation after off-pump CABG surgery. **Methods:** Forty two patients undergoing elective off-pump Coronary Artery Bypass graft were divided into two separate groups - DK group received dexmedetomidine 0.3 mcg/kg + ketamine 0.25 mg/kg IV bolus followed by infusions for 1 hour, while FM group received fentanyl 1 mcg/kg/hr + midazolam 0.02 mg/kg/hr infusions for 1 hour postoperatively. The primary outcomes were time to extubation, time of weaning, duration of ICU stay and hemodynamic changes. Secondary outcome was depth of sedation and was compared between groups. **Results:** The mean time to extubation was significantly shorter in the DK group (283.3± 16.53) compared to FM group (296.0± 22.45), P=0.0451. Time to weaning in DK group (222.9± 15.86) was lower than FM group (234.5± 27.38) however, the findings did not demonstrate statistical significance. (P=0.1008) and the length of ICU stay were similar (44.67± 2.106) in FM group as compared to (43.71± 1.454) in DK group (P=0.0968). Heart rate and mean arterial pressure were observed to be lower in the DK group at most time points by 5-10%. Ramsay sedation scores were comparable and adequate in the two groups. **Conclusion:** Dexmedetomidine-ketamine provided faster extubation compared to fentanyl-midazolam for sedation after CABG surgery, with favorable hemodynamic effects but similar sedation quality and ICU course. The combination may be a viable alternative for post-operative sedation.

KEYWORDS

Fentanyl; Midazolam; Dexmedetomidine; Ketamine; Safety (CABG- Coronary Artery Bypass Grafting, DK- Dexamedetomidine-Ketamine, FM- Fentanyl-Midazolam)

INTRODUCTION

Following cardiac surgery, a number of complications can arise, potentially increasing mortality rates and extending hospital stays. Careful management during and after surgery is crucial to prevent these adverse events. Tachycardia, a primary cause of post-coronary artery bypass graft (CABG) myocardial ischemia, can be mitigated through appropriate sedation and pain management.[1]

Dexmedetomidine, a highly selective alpha-2-adrenoreceptor agonist, provides sedation by stimulating central nervous system receptors without affecting the GABA system.[8] It offers effective sedation with minimal impact on respiratory function and hemodynamics, making it suitable for use during ventilator weaning and extubation.[2] Its unique properties, including analgesic effects and the ability to produce sleep patterns similar to natural sleep, have made it a preferred choice for sedation in intensive care units (ICUs).[3,4]

Ketamine, a nonbarbiturate derivative, interacts with N-methyl-d-aspartate and sigma opioid receptors to produce dissociative anesthesia, pain relief, and amnesia. It maintains hemodynamic stability through its effects on nitric oxide production and cardiovascular function.[5]

Midazolam, a commonly used intravenous sedative, offers rapid onset and relatively quick recovery in comparison to others benzodiazepines. However, its use may be limited due to its poor analgesic properties and potential for respiratory depression.[6]

Fentanyl, a synthetic opioid, is widely used for perioperative and postoperative pain management, with substantially higher potency compared to morphine.[7] While the combination of fentanyl and midazolam for postoperative sedation and analgesia has been well-studied, the comparative efficacy and safety of dexmedetomidine-ketamine versus fentanyl-midazolam combinations in post-CABG patients have not been directly examined.

It is possible that dexmedetomidine-ketamine combination can be proved to be better than fentanyl-midazolam combination owing to previously described advantages. In this direction we investigated this effect in patients undergoing elective off pump Coronary artery bypass graft surgery. In our study we used null hypothesis that there is no difference in the time of extubation, time of weaning, duration of ICU stay and hemodynamic changes between Dexmedetomidine-Ketamine and Fentanyl-Midazolam combination in patients after elective off pump CABG surgery.

Aim Of The Study

The study aims to conduct a comparison in the efficacy and safety of Dexmedetomidine- Ketamine versus Fentanyl-Midazolam combination for post operative sedation in patients undergoing elective off pump Coronary artery bypass graft surgery.

Objective Of The Study

1. To compare the time of extubation, time of weaning, duration of ICU stay in patient undergoing elective off pump Coronary artery bypass graft surgery when using Dexmedetomidine-Ketamine versus Fentanyl-Midazolam combination for post-operative sedation
2. To observe Heart rate and Mean Arterial Pressure in response to Dexmedetomidine- Ketamine and Fentanyl-Midazolam combination in patient after elective off pump Coronary artery bypass graft surgery to assess the safety of both group of drugs.

Primary Outcome

To find out the time of extubation, time of weaning, duration of ICU stay and hemodynamic changes in response to the use of Dexmedetomidine-Ketamine versus Fentanyl-Midazolam combination in patients after elective off pump CABG surgery.

Secondary Outcome

To compare the depth of sedation in response to the use of Dexmedetomidine-Ketamine versus Fentanyl-Midazolam combination in patients after elective off pump CABG surgery.

MATERIALS AND METHODS

Source of Data

The institute"s ethical committee approved this observational study. Forty two randomly assigned patients belonging to the age group of 30-60 years who were hospitalised at A.J institute of medical sciences and research centre, Mangalore at least a day prior to the day of surgery and who were expected to undergo elective off pump coronary artery bypass graft over a period of 24 months (from July 2022-2024) were encompassed in the study.

Study Design

It was an observational, comparative, analytical study. Patients were allocated non randomized based on convenience method and the data was recorded by the observer.

Selection Criteria

All patients who were scheduled for elective off-pump CABG surgery

and belonged to the physical status American Society of Anesthesiologists (ASA) classes 3 and 4 were included. We excluded all patients with poor LV dysfunction, Left ventricle ejection fraction <45%, neurologic disease, hepatic or renal diseases or insufficiencies, known allergy to any medication used in the study, respiratory disorders and acute myocardial infarction.

Sample Size

On the basis of a study conducted by Mohgahd MM et al, in order to detect a mean difference of 17.6 minutes to detect mean time of extubation between the groups assuming 95% confidence, 90% power with a pooled standard deviation (SD) of 69 units, the sample size estimated for the study was 19.4 ≈ 19 in each group. Further assuming 10% attrition rate, final sample size estimated for the study was 21 in each group. Hence a total of 42 patients were recruited for the study.

STUDY PROCEDURE AND METHODOLOGY

Prior to the day of surgery, we performed a detailed pre-anaesthetic assessment and noted the demographic details, baseline vitals and laboratory investigations. We obtained a written informed consent from all the included patients. All our patients were pre-medicated with Tablet Alprazolam 0.25mg and Tablet Pantoprazole 40mg on the Night prior to surgery. We advised our patients to remain nil per oral for solids for at least 8 hours, semi-solids for a duration of 4 hours and clear liquids for a period of 2 hours. No opiods were used for the purpose of premedication Of the 42 patients, 21 each were included in the groups Group FM(Group1): patients who received Fentanyl-Midazolam[FM] for sedation postsurgery in ITU Group DK(Group 2) : patients who received Dexmedetomidine-Ketamine [DK] for sedation post-surgery in ITU.

Induction Sequence:

Induction was carried out as per cardiac anaesthesia department protocol. After shifting the patient inside the operating room noninvasive blood pressure, saturation probe and electrocardiogram monitoring with 5 leads were attached and baseline values were recorded. 14 Guage Intravenous Cannula secured. IV fluid started. By giving local infiltration by seldinger technique right Internal jugular vein Central venous catheter was secured. Radial and Femoral arterial lines were secured.

All the patients were preoxygenated with 100% oxygen for 3 minutes and intravenous fentanyl 2 mcg/ kg was injected. Anaesthesia was induced with intravenous Etomidate 0.2- 0.4mg/kg and loss of response to verbal stimuli was confirmed. On confirming the ability to bag and mask ventilate, patient neuromuscular blockade was achieved with intravenous rocuronium 0.6 mg/kg and anaesthesia deepened with isoflurane.

Consultant Anaesthesiologist did direct laryngoscopy and endotracheal intubation. After tracheal intubation, mechanical ventilation was initiated. Low-flow technique (fresh gas flow of 1 L/min) using anaesthesia machine to achieve normocapnia was used. Inspired and expired gas concentration of O2, carbon dioxide (CO2) and isoflurane was measured using smart anaesthetic gas monitoring system. Trans Esophageal Echocardiograph was placed. Hemodynamic parameters was maintained within 20% of the basal values with dopamine, phenylephrine, and glyceryltrinitrate, as required. Intraoperative hypothermia was prevented by the use of warm airflow, warming blanket and warm intravenous fluids. Blood loss and urine output was monitored. After the procedure was done. Patient was shifted to Intensive.

Thoracic care unit with ET tube insitu connected to bains circuit with Oxygen of 10L/min. In ITU patient was connected to Mechanical Ventilator.

FM group of patients were sedated using Fentanyl 1mcg/kg/hr + Midazolam 0.02mg/kg/hr infusion for 1 hour through two separate infusion pumps

DK group of patients were sedated using Ketamine 0.25mg/kg IV bolus + Dexmedetomidine 0.3mcg/kg IV bolus through a burette set over 5 minutes followed by Ketamine 0.25mg/kg/hr + Dexmedetomidine 0.3mcg/kg/hr infusion for 1 hour through two separate infusion pumps.

Sedation level was assessed using Ramsay Sedation Scale.

Ramsay 0- If awake,
Ramsay 1 – anxious, agitated, or restless;
Ramsay 2 – cooperative, oriented, tranquil;
Ramsay 3 – responsive to commands only. Moreover, if asleep
Ramsay 4 – brisk response to light glabellar tap or loud auditory stimulus
Ramsay 5 – sluggish response to light glabellar tap or loud auditory stimulus Ramsay 6 – no response to light glabellar tap or loud auditory stimulus.

The duration of infusion was for 1 hour in ITU. Our study continues without infusions after 1 hour and patients were continued on mechanical ventilation. The time of weaning from mechanical ventilation, time of extubation and duration of ICU stay were noted. The patient's Heart rate, Mean arterial blood pressure and Ramsay sedation scores were noted pre sedation and at 10,30 minutes, 1,2,4 hours.

PARAMETERS STUDIED AND MEASURES OF OUTCOME

Time of extubation, time of weaning from mechanical ventilation, duration of ICU stay. Heart rate, mean arterial blood pressure and ramsay sedation scores pre sedation and at 10,30 minutes, 1,2,4 hours post operatively.

Demographic data

Side effects or complications, if any.

Study Hypothesis-

H0 – Null hypothesis – There is no difference in the time of extubation, time of weaning, duration of ICU stay and hemodynamic changes between Fentanyl-Midazolam and Dexmedetomidine-Ketamine combination in patients after elective off pump CABG surgery
H1 – Alternative hypothesis – Dexmedetomidine-Ketamine has a decreased time of extubation, time of weaning, duration of ICU stay and more favourable hemodynamics than Fentanyl-Midazolam combination in patients after elective off pump CABG surgery
H2 – Alternative hypothesis – Fentanyl-Midazolam has a decreased time of extubation, time of weaning, duration of ICU stay and more favourable hemodynamics than Dexmedetomidine- Ketamine combination in patients after elective off pump CABG surgery.

Statistical Analysis

Statistical analysis was performed using GraphPad Prism 10 on data from 42 subjects. Data normality was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Continuous variables were analyzed using an unpaired t-test with Welch's correction, while repeated measures ANOVA or Kruskal-Wallis tests were used for serial comparisons within groups. Tukey's multiple comparison test was applied for parametric data, and categorical variables were analyzed with Chi-square or Fisher's exact tests. Pearson's test ($P < 0.1$) was used for correlations, and $P < 0.05$ was considered statistically significant.

Age, weight, ASA grade, blood transfusions, diabetes mellitus, total vecuronium dose, and ejection fraction were included in multivariate analysis. Predictors that did not fit the model were excluded, and multicollinearity was checked using variance inflation factors (VIF), with VIF < 3 considered optimal. Models were deemed adequate if the Goodness of Fit test had a $P > 0.05$.

OBSERVATION AND RESULTS

The result of our study is as follows :

Table 1. Comparison Of Age Between Two Groups:

	N	Mean ± SD	SE of mean	P value
Group 1	21	59.71±8.18	1.786	0.7097
Group 2	21	60.81±10.59	2.311	

Inference:- Age was comparable between two groups. The mean age for Group 1 was 59.71±8.18 and for Group 2 was 60.81±10.59.

Table 2. Comparison Of Sex Distribution Between Two Groups

	Group 1	Group 2
Male	57.14	66.66
Female	42.85	33.33

Comparison of sex distribution between two groups. The values are represented as percentages. P value 0.7513 using Fisher"s exact test.

Inference: In group 1, there were 12 males (57.14%) and 9 females (42.85%). Group 2 had 14 males (66.66%) and 7 females (33.33%). Thus distribution of sex in both groups were comparable.

Table 3. Comparison Of Weight Between Two Groups

	N	Mean ± SD	SE of mean	P value
Group 1	21	68.10±11.41	2.490	0.1304
Group 2	21	62.71±11.17	2.437	

Inference:- Weight was comparable between two groups. The mean weight for Group 1 was 68.10±11.41 and for Group 2 was 62.71±11.17.

Table 4. Comparison Of Height Between Two Groups

	N	Mean ± SD	SE of mean	P value
Group 1	21	162.6± 8.727	1.904	0.6672
Group 2	21	163.7± 7.618	1.662	

Inference:- Height was comparable between two groups. The mean height for Group 1 was 162.6± 8.727and for Group 2 was 163.7± 7.618.

Table 5. Comparison of ASA Distribution Between Two Groups

	Group 1	Group 2
ASA 3	57.14	66.66
ASA 4	42.85	33.33

Comparison of sex distribution between two groups. The values are represented as percentages. P value 0.5359 using Fisher"s exact test.
In group 1, there were 8 patients belonging to ASA 3 (38.09%) and 10 patients belonging to ASA 4 (61.9%). Group 2 had 11 patients belonging to ASA 3 (52.38%) and 10 patients belonging to ASA 4 (47.67%).

Table 6. Comparison Of Baseline Heart Rate Between Two Groups

	N	Mean ± SD	SE of mean	P value
Group 1	21	77.14±10.64	2.321	0.2286
Group 2	21	73.48±8.687	1.896	

Baseline heart rate was comparable between two groups. The mean baseline heart rate for Group 1 was 77.14±10.64 and for Group 2 was 73.48±8.687.

Table 7. Comparison Of Baseline SBP Between Two Groups

	N	Mean ± SD	SE of mean	P value
Group 1	21	132.1± 21.25	4.636	0.4299
Group 2	21	127.8± 12.88	2.811	

Inference:- Baseline SBP was comparable between two groups. The mean baseline SBP for Group 1 was 132.1± 21.25 and for Group 2 was 127.8± 12.88.

Table 8. Comparison Of Baseline DBP Between Two Groups

	N	Mean ± SD	SE of mean	P value
Group 1	21	79.52± 10.24	2.234	0.1573
Group 2	21	74.86± 10.74	2.344	

Inference:- Baseline DBP was comparable between two groups. The mean baseline DBP for Group 1 79.52± 10.24 was and for Group 2 was 74.86± 10.74.

Table 9. Comparison Of Baseline MAP Between Two Groups

	N	Mean ± SD	SE of mean	P value
Group 1	21	97.06± 13.19	2.877	0.2239
Group 2	21	92.51± 10.55	2.302	

Inference:- Baseline MAP was comparable between two groups. The mean baseline MAP for Group 1 was 97.06 ± 13.19 and for Group 2 was 92.51 ± 10.55.

Table 10. Comparison Of Time Of Extubation Between Two Groups

	N	Mean ± SD	SE of mean	P value
Group 1	21	296.0± 22.45	4.899	0.0451
Group 2	21	283.3± 16.53	3.608	

Inference:- There is statistically significant difference in time of extubation between two groups ($P < 0.05$). Time of extubation was lower in the group receiving demedetomidineketamine compared to groups receiving fentanyl-midazolam.

Table 11. Comparison Of Time Of Weaning Between Two Groups

	N	Mean ± SD	SE of mean	P value
Group 1	21	234.5± 27.38	5.975	0.1008
Group 2	21	222.9± 15.86	3.460	

Inference:- There is no significant difference in time of weaning between the two groups ($P > 0.05$). Time of weaning was comparable between two groups. The mean time of weaning for Group 1 was 234.5± 27.38 and for Group 2 was 222.9± 15.86.

Table 12. Comparison Of Duration Of ICU Stay Between Two Groups

	N	Mean ± SD	SE of mean	P value
Group 1	21	44.67± 2.106	0.4595	0.0968
Group 2	21	43.71± 1.454	0.3173	

Inference:- There is no significant difference in duration of ICU stay between the two groups ($P > 0.05$). Duration of ICU stay was comparable between two groups. The mean time duration of ICU stay for Group 1 was 44.67± 2.106 and for Group 2 was 43.71± 1.454.

Table 13. Comparison Of Intragroup Heart Rate In Group 1

Tukey's multiple comparisons test	Mean Diff	95% CI of diff	Adjusted P value
HR 0 min vs. HR 10 min	1.381	-1.226 to 3.988	0.5684
HR 0 min vs. HR 30 min	1.952	-1.268 to 5.173	0.4274
HR 0 min vs. HR 1 hour	2.286	-0.9106 to 5.482	0.2605
HR 0 min vs. HR 2 hour	-4.714	-9.362 to 0.06652	0.0456
HR 0 min vs. HR 4 hour	-7.238	-12.19 to -2.283	0.0021

Table 13: Comparison of intragroup heart rate in group 1 comparing pre-sedation heart rate to heart rate at different intervals after initiation of infusions.

Table 14. Comparison Of Intragroup Heart Rate In Group 2

Tukey's multiple comparisons test	Mean Diff	95% CI of diff	Adjusted P value
HR 0 min vs. HR 10 min	4.333	3.484 to 5.183	<0.0001
HR 0 min vs. HR 30 min	5.571	4.075 to 7.067	<0.0001
HR 0 min vs. HR 1 hour	7.048	5.585 to 8.510	<0.0001
HR 0 min vs. HR 2 hour	3.238	1.147 to 5.329	0.0011
HR 0 min vs. HR 4 hour	-0.2857	-2.287 to 1.716	0.9974

Table 14: Comparison of intragroup heart rate in group 2 comparing presedation heart rate to heart rate at different intervals after initiation of infusions.

Table 15. Comparison Of Heart Rates Between The Two Groups At Various Time Intervals During The Study

	0 minutes	10 minutes	30 minutes	1 hour	2 hour	4 hour
Group 1 Mean ±SD	82.90 ± 7.962	81.52 ± 7.277	80.95 ± 7.940	80.62 ± 9.019	87.62 ± 10.65	90.14 ± 11.44
Group 2 Mean ±SD	78.90 ± 6.090	74.57 ± 6.161	73.33 ± 6.240	71.86 ± 5.859	75.67 ± 5.713	79.19 ± 5.036
P value	0.0754	0.0018	0.0014	0.0007	<0.0001	0.0004

Inference:- Pre sedation heart rate was comparable between both the groups.

There is statistically significant difference in heart rate between the two groups at 10 minutes, 30 minutes, 1 hour, 2 hour and 4 hour ($P < 0.05$). Heart rate was lower in the group receiving dexmedetomidine-ketamine (group 2) as compared to the group receiving fentanylmidazolam (group 1) at various time intervals.

Table 16. Comparison Of Intragroup MAP In Group 1

Tukey's multiple comparisons test	Mean Diff	95% CI of diff	Adjusted P value
MAP 0 min vs. MAP 10 min	2.286	-2.015 to 6.586	0.5650
MAP 0 min vs. MAP 30 min	4.476	-1.600 to 10.55	0.2336
MAP 0 min vs. MAP 1 hour	5.381	-1.507 to 12.27	0.1848
MAP 0 min vs. MAP 2 hour	1.667	-7.259 to 10.59	0.9908
MAP 0 min vs. MAP 4 hour	-0.3810	-9.819 to 9.057	>0.9999

Table 16: Comparison of intragroup MAP in group 1 comparing presedation MAP to MAP at different intervals after initiation of infusions.

Table 17. Comparison Of Intragroup MAP In Group 2

Tukey's multiple comparisons test	Mean Diff	95% CI of diff	Adjusted P value
MAP 0 min vs. MAP 10 min	4.286	1.002 to 7.569	0.0063
MAP 0 min vs. MAP 30 min	6.190	2.152 to 10.23	0.0013
MAP 0 min vs. MAP 1 hour	7.000	3.442 to 10.56	<0.0001
MAP 0 min vs. MAP 2 hour	5.143	2.556 to 7.730	<0.0001
MAP 0 min vs. MAP 4 hour	2.667	0.2873 to 5.046	0.0225

Table 17: Comparison of intragroup MAP in group 2 comparing presedation MAP to MAP at different intervals after initiation of infusions.

Table 18. Comparison Of MAP Between The Two Groups At Various Time Intervals During The Study

	0 minutes	10 minutes	30 minutes	1 hour	2 hour	4 hour
Group 1 Mean ±SD	92.00 ± 10.73	89.71 ± 9.166	87.52 ± 9.781	86.62 ± 8.623	90.33 ± 11.72	92.38 ± 11.89
Group 2 Mean ±SD	86.33 ± 4.487	82.05 ± 3.626	80.14 ± 4.016	79.33 ± 3.759	81.19 ± 4.320	83.67 ± 3.183
P value	0.0342	0.0014	0.0036	0.0014	0.0025	0.0036

($P < 0.05$). The MAP in Dexmedetomidine-Ketamine group (group 2) was lower than the MAP in Fentanyl-Midazolam group (group 1) at all the time intervals.

Inference: There is a statistically significant difference in MAP between the two groups at 0 minutes, 10 minutes, 30 minutes, 1 hour, 2 hour and 4 hour ($P < 0.05$). The MAP in Dexmedetomidine-Ketamine group (group 2) was lower than the MAP in Fentanyl-Midazolam group (group 1) at all the time intervals.

Table 19. Comparison Of Intragroup RSS In Group 1

Tukey's multiple comparisons test	Mean Diff	95% CI of diff	Adjusted P value
RSS 0 min vs. RSS 10 min	-0.9048	-1.274 to -0.5351	<0.0001
RSS 0 min vs. RSS 30 min	-1.000	-1.376 to -0.6243	<0.0001
RSS 0 min vs. RSS 1 hour	-0.6667	-1.168 to -0.1657	0.0053
RSS 0 min vs. RSS 2 hour	0.9524	0.3593 to 1.545	0.0008
RSS 0 min vs. RSS 4 hour	2.571	1.900 to 3.242	<0.0001

Table 20. Comparison Of Intragroup RSS In Group 2

Tukey's multiple comparisons test	Mean Diff	95% CI of diff	Adjusted P value
RSS 0 min vs. RSS 10 min	-0.6667	-1.118 to -0.2151	0.0019
RSS 0 min vs. RSS 30 min	-0.5714	-1.127 to -0.01540	0.0418
RSS 0 min vs. RSS 1 hour	-0.1429	-0.8385 to 0.5528	0.9859
RSS 0 min vs. RSS 2 hour	1.286	0.4417 to 2.130	0.0014
RSS 0 min vs. RSS 4 hour	3.143	2.482 to 3.804	<0.0001

Table 21. Comparison Of RSS Between The Two Groups At Various Time Intervals During The Study

	0 minutes	10 minutes	30 minutes	1 hour	2 hour	4 hour
Group 1 Mean ±SD	4.619 ± 0.8646	5.524 ± 0.6796	5.619 ± 0.5896	5.286 ± 0.7171	3.667 ± 1.017	2.048 ± 0.7400
Group 2 Mean ±SD	5.333 ± 0.6583	6.000 ± 0.000	5.905 ± 0.3008	5.476 ± 0.6016	4.048 ± 0.8646	2.190 ± 0.5118
P value	0.0046	0.0044	0.0572	0.3568	0.1985	0.4716

Inference: There is a statistically significant difference in RSS between the two groups at 10 minutes ($P < 0.05$).

The RSS in Dexmedetomidine-Ketamine group (group 2) was higher than the RSS in Fentanyl-Midazolam group (group 1) at 30 minutes, 1 hour, 2 hour, 4 hour. However, it was not statistically significant.

Table 22. Multivariate Analysis

Term	Coef	SE Coef	T-Value	P-Value	VIF
Age	0.308	0.548	0.56	0.579	1.19
Weight	0.326	0.489	0.67	0.509	1.42
Ejection Fraction (%)	-0.75	1.06	-0.71	0.482	1.36
Total dose of Vecuronium(mg)	1.31	1.14	1.16	0.256	1.48
ASA grading	-3.1	11.0	-0.28	0.778	1.39
Diabetes Mellitus	8.5	11.3	0.75	0.456	1.06
Blood transfusions	4.6	17.7	0.26	0.795	1.25

RESULTS

Our study consisted of fourty two patients. Patients were allocated non randomized based on convenience method. For induction and maintenance of anaesthesia patients in both the groups were administered similar supplements of analgesics, relaxants or adjuvant. Patients in both the groups required almost similar volume for induction and maintenance of anaesthesia evincing a similar pharmacokinetic profile. After the procedure was done. Patient was shifted to Intensive Thoracic care unit with ET tube insitu connected to bains circuit with Oxygen of 10L/min. In ITU patient was connected to Mechanical Ventilator. FM group(group 1) of patients was sedated using Fentanyl 1mcg/kg/hr + Midazolam 0.02mg/kg/hr infusion for 1 hour through two separate infusion pumps. DK group(group 2) of patients was sedated using Ketamine 0.25mg/kg IV bolus + Dexmedetomidine 0.3mcg/kg IV bolus through a burette set over 5 minutes followed by Ketamine 0.25mg/kg/hr + Dexmedetomidine 0.3mcg/kg/hr infusion for 1 hour through two separate infusion pumps.

We evaluated our patients for the time of extubation, time of weaning, duration of ICU stay and mean arterial pressure, heart Rate from the baseline. We measured the patient"s heart rate and mean arterial blood pressure pre sedation and at 10,30 minutes, 1,2,4 hours.

Assessment of sedation level was conducted using Ramsay Sedation Scale. [If awake, Ramsay 1 – anxious, agitated, or restless; Ramsay 2 – cooperative, oriented, tranquil; and Ramsay 3 – responsive to commands only. Moreover, if asleep, Ramsay 4 – brisk response to light glabellar tap or loud auditory stimulus; Ramsay 5 – sluggish response to light glabellar tap or loud auditory stimulus; and Ramsay 6 – no response to light glabellar tap or loud auditory stimulus.] The time of weaning from mechanical ventilation, time of extubation and duration of ICU stay were noted.

Patients were evenly distributed for age, sex, weight and height in both the groups to eliminate the effects of patient characteristics on the results (Tables 1, 2, 3, 4). The distribution of patients whose Ejection fraction is lower than 60% were comparable among the two groups. The amount of Etomidate used, the duration of surgery and the total dose of muscle relaxant were comparable between the two groups as mentioned earlier.

We restricted our study group to ASA 3 and ASA 4 and most of them belonged to 5th and 6th decade of life. Confounding element was eliminated by equal distribution of ASA-PS status among the two groups (Table 5).

We analysed the results of our study with appropriate statistical tests. Firstly, the mean of time of extubation was compared among the two groups (Table 10). There was a significant difference in the meantime of extubation ($P = 0.0451$). The difference of means within the groups was compared in subsequent analysis. The means of time of extubation was significantly higher in the F-M group (283.3min) as compared to D-K group(296min). This indicates a decreased time of extubation in D-K group. The time of weaning and duration of ICU stay between the two groups were not significant ($P = 0.1008$ and $P = 0.0968$). This indicates that there was not any significant differences between the means in the groups in regards to time of weaning and duration of ICU stay.

The mean heart rate at various intervals of two different groups were compared. There was a significant difference in the means for heart rate in both the groups. The difference of means within the groups were

compared in subsequent analysis. In Group 1 the mean of heart rate at 10 min, 30 min and 1 hour was lower than baseline but was not significant. Heart rate was significantly higher than baseline at 2 and 4 hours ($P < 0.05$). In group 2 the mean heart rate was significantly lower at 10 min, 30 min, 1 hour and 2 hour than the mean heart rate of baseline. At 4 hour the heart rate was not significant. When comparing group 1 and group 2 at 0min there was no statistically significant difference ($P = 0.075$). However at 10min, 30 min, 1hour, 2 hour, 4 hour mean heart rate on group 2 was significantly lower than group 1 ($p < 0.05$).

The mean MAP at various intervals of two groups were compared. There was a significant difference in the means for MAP in both the groups. The difference of means within the groups were compared in subsequent analysis. In Group 1 the mean MAP at various time intervals were not significant as compared to the baseline ($P>0.05$). In group 2 the mean MAP at various time intervals were significantly lower as compared to baseline ($P<0.05$). When comparing group 1 and group 2, the mean MAP at various time intervals was significantly lower in group 2 than group 1 ($p<0.05$).

The mean RSS at various intervals of two groups were compared. The difference of means within the groups were compared in subsequent analysis. In both the groups the mean RSS was significantly higher at 10min, 30min and 1 hour ($P < 0.05$) while it was significantly lower at 2 hour and 4 hour as compared to mean baseline. When comparing group 1 and group 2, the mean RSS at 10 min and 30 min were significantly higher in Group 1, whereas 1 hour, 2 hour and 4 hour there was no statistically significant differences.

The correlation study revealed the factors that could influence the decrease in time of extubation and changes in Heart rate and MAP. Various variables like ASA grading, blood loss, presence of diabetes mellitus, total dose of muscle relaxant, ejection fraction and patient demographics were correlated using Pearson˝s correlation. A P value of < 0.1 was considered for significance.

We performed a multivariate regression analysis. We eliminated a variable each time to achieve a better fitting model and found that there is no association between any of the above mentioned variables and patient demographics ($P>0.1$).

Of the 21 patients in each group, 20 patients did not show any side effects in group 1, nor did 21 patients of group 2. One patient in group 1 developed hypotension post operatively and required ionotropic support for a brief period. No mortality was observed.

DISCUSSION

Prolonged mechanical ventilation after surgery is one of the leading causes of post-operative complications and deaths. The type of sedative used during mechanical ventilation can impact the duration that the patient requires ventilator support[9,10].When selecting a sedative agent, key considerations include the drug's speed of onset, potential side effects, and how quickly cognitive function returns after discontinuing the medication.

Using shorter-acting sedatives and opioid medications tends to allow earlier extubation from the ventilator. This can decrease pain, anxiety, cardiac stress from the sympathetic nervous system, and allow earlier mobilization of the patient. Getting patients off the ventilator sooner may facilitate faster discharge from the intensive care unit and hospital, reducing overall healthcare costs. Prolonged ventilation increases the risk of complications like ventilator-associated pneumonia, ventilator dependance, muscle wasting, stress ulcers, lung injury.

We compared the effects of Fentanyl-Midazolam versus Dexmeditomidine-Ketamine on their efficacy and safety post operatively in Intensive Thoracic Unit.

To our knowledge no other study directly compared Fentanyl-Midazolam to Dexmeditomidine-Ketamine for sedation post CABG. Numerous research studies have investigated the impacts of combining these sedative agents in pediatric and adult patients undergoing various procedures besides coronary artery bypass graft (CABG) surgery.

In our study we found that patients who received Dexmeditomidine-Ketamine combination for sedation were able to wean earlier from ventilator and had shorter duration of mechanical ventilation as compared to patients who received fentanyl-midazolam combination. Both sedation regimens significantly impacted heart rate over time compared to baseline. However, the effects diverged between the groups. Group FM exhibited a delayed increase in heart rate post-treatment. Conversely, Group DK demonstrated an immediate reduction in heart rate that remained significantly lower than baseline up until the 2-hour mark. While starting heart rates were comparable, Group DK sedation resulted in significantly lower heart rates compared to Group FM across various time intervals. Group DK regimen providedbetter heart rate control in the initial postoperative period, which could benefit hemodynamic stability. The later heart rate elevations seen in both groupsmay reflect wearing off of the sedative effects.

Mean arterial blood pressure (MAP) compared to baseline levels in GroupFM, there were no significant changes in MAP over the time intervals assessed. However, Group DK demonstrated a significant reduction in MAP from baseline across all time points measured. When directly comparing the groups, MAP was significantly lower in Group DK relative to Group FM at each time interval. Group DK, produced a more pronounced hypotensive response.

Both sedation regimens resulted in deeper sedation levels initially, as evidenced by significantly higher Ramsay Sedation Scale (RSS) scores compared to baseline. However, Group DKexhibited more profound sedation earlier on. Overall, while both regimens provided adequate sedation initially, Group DKproduced a more intensive early sedation response that equilibrated with Group FMlater on. The similar later time points indicate comparable timing for sedative offset between the two combination approaches.

The results obtained in this study is consistent with the results of the study James et al who examined the impact of different sedation strategies on early extubation after cardiac surgery. Their analysis compared outcomes between patients who received propofol-based sedation versus those given a dexmedetomidine-based regimen[11].The researchers found that the group sedated with dexmedetomidine experienced shorter times to extubation and shorter intensive care unit lengths of stay compared to the propofol group. However in our study we found no difference in the length of ICU stay.

In a study comparing sedation regimens for prolonged mechanical ventilation, Stephan et al evaluated dexmedetomidine against midazolam and propofol. Their findings suggested dexmedetomidine may be a favorable option for long-term sedation in intensive care unit (ICU) patients, as it was associated with a shorter duration of mechanical ventilation compared to midazolam. Patients receiving dexmedetomidine also experienced a reduced time to extubation versus both the midazolam and propofol groups. However, the choice of sedative did not significantly impact the overall length of ICU stay which is consistent with the result of our study[12].

In a study by Triltsch et al. examining dexmedetomidine for sedation in postoperative ventilated patients, they compared a dexmedetomidine group to a placebo control group. Their resultsindicated that use of dexmedetomidine was associated with a higher incidence of bradycardia in this patient population[13].

Additionally, research by Herr et al investigated sedation with dexmedetomidine versus propofol in 300 intensive care unit patientsfollowing coronary artery bypass graft surgery. Their findings revealed that dexmedetomidine produced a more pronounced reduction in blood pressure compared to propofol, with 36% of dexmedetomidine patients experiencing decreased blood pressure versus 24%in the propofol group[14,15].

These studies highlight some potential hemodynamic effects, namely bradycardia and hypotension risks, which is counteracted by the side effects of Ketamine thereby making it an ideal combination. Our study shows a markedly lower heart rate and mean arterial pressure in the DK group as compared to FM group which is in accordance to the above mentioned studies.

Dexmedetomidine can cause side effects such as bradycardia hypotension, and xerostomia. In contrast, ketamine is associated with side effects like hypertension, tachycardia, and increased secretions.

Combining these two drugs during sedation may help counteract some of their opposing side effect profiles. Additionally, ketamine is a potent analgesic and does not depress respiratory function.

Limitation Of My Study:

- Sample size was too small to apply to the entire population.
- Single-center study: The results are from a single healthcare facility, which may limit the generalizability of the findings to other settings or patient populations
- Different anaesthetists conducted the cases and administration of drug was monitored by different observers hence may cause discrepancy.
- The study used a low dose of drugs used for sedation and the results may differ with different doses. Further investigation is required to evaluate the impact with higher doses.
- Surgical factors were not included in the study

CONCLUSION

The dexmedetomidine-ketamine combination provided faster extubation compared to fentanyl-midazolam after CABG surgery, along with more favorable hemodynamic effects in terms of lower heart rate and mean arterial pressure.

However, both regimens achieved adequate sedation levels, with similar times to weaning from mechanical ventilation and ICU discharge.

The study suggests that dexmedetomidine-ketamine may be a viable alternative regimen for post-operative sedation in this setting, offering potential advantages in facilitating earlier extubation and maintaining hemodynamic stability, without compromising sedation quality or overall ICU course.

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