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INCIDENCE OF DELIRIUM WITH DEXMEDETOMIDINE COMPARED WITH FENTANYL BASED THERAPY IN POSTOPERATIVE CARDIAC SURGICAL PATIENTS: A RANDOMIZED CONTROLLED SINGLE BLINDED STUDY

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ABSTRACT

Background: Postoperative Delirium represents complication in cardiac surgery, associated with increased morbidity and mortality. This study compared the efficacy of dexmedetomidine versus fentanyl-based therapy on clinical outcomes in postoperative cardiac surgical patients.

Methods: This study design was a single blinded Randomized Control Trial was conducted in tertiary hospitals in IMS and SUM between January 2023 to January 2025. Patients were randomized into two groups i.e., Dexmedetomidine (DEX) and fentanyl-based therapy in cardiac surgery patient. The primary endpoint was delirium incidence and severity, assessed 12-hourly for 7 days via CAM-ICU. Secondary outcomes included pain (CPOT/Wong-Baker), sedation (RASS), extubation time, and hemodynamic stability. Analysis was performed using SPSS v27, with significance set at $p < 0.05$.

Results: One hundred fifty patients were randomized (n=75 per group) with no significant differences in age, weight, or gender. While delirium incidence was similar initially, Dexmedetomidine showed significantly lower mean delirium scores from day 5 to day 7 ($p < 0.05$) compared to Fentanyl. Additionally, Dexmedetomidine demonstrated significantly better sedation (RASS) and analgesia (CPOT) scores from 12 to 48 hours ($p < 0.001$). Furthermore, Dexmedetomidine group achieved significantly earlier extubation (17.54 ± 2.59 vs. 18.4 ± 3.16 hours; $p = 0.03$), lower incidences of tachyarrhythmias, and reduced rescue analgesia requirements. Hemodynamic parameters remained stable across both cohorts.

Conclusions: Postoperative dexmedetomidine significantly reduced delirium severity, improves sedation quality, and provided superior analgesia compared to fentanyl. Dexmedetomidine is a more effective postoperative sedative-analgesic than fentanyl, supports modern cardiac surgical protocols to improve clinical outcomes in high-risk populations.

KEYWORDS: Postoperative Delirium, Dexmedetomidine, Cardiac Surgery, Fentanyl, CAM-ICU

INTRODUCTION

Postoperative delirium is one of the most common neurocognitive complications after cardiac surgery and remains a major challenge in perioperative and intensive care practice. It is characterized by an acute disturbance in attention, awareness, and cognition, typically with a fluctuating course, and is associated with prolonged ICU stay, delayed recovery, higher morbidity, and increased healthcare costs [1,2]. However, the incidence of postoperative delirium after cardiac surgery is reported to be substantial, particularly in older adults and in patients exposed to prolonged cardiopulmonary bypass, major operative stress, or deep postoperative sedation. Several predisposing and precipitating factors contribute to its development, including advanced age, pre-existing cognitive impairment, neurologic vulnerability, anesthesia exposure, pain, hypoxia, infection, and postoperative hemodynamic instability [3-6]. In patients undergoing on-pump cardiac surgery, the inflammatory burden and cerebral perfusion changes associated with cardiopulmonary bypass further increase the risk of neurocognitive dysfunction [7-10].

Although there is a strong association between inadequate pain control and risk of postoperative delirium, the drugs used to alleviate pain, particularly some opioids known to promote both Delirium and cognition loss [11]. Delirium is a clinical syndrome that usually develops in elderly [12,13]. It is characterized by an alteration of attention, consciousness, and cognition, with reduced ability to focus, or shift attention [14].

The pathophysiology of delirium is multifactorial and incompletely understood. In cardiac surgery, systemic

inflammation, ischemia-reperfusion injury, hypothermia, non-pulsatile flow, and neuroinflammatory mediator release may disrupt blood-brain barrier integrity and alter neuronal signaling. The release of inflammatory mediators such as interleukin-6 and C-reactive protein may contribute to cerebral edema and central nervous system dysfunction. Prolonged cardiopulmonary bypass time is also considered an important contributor, with longer bypass exposure linked to a higher risk of delirium [15].

Notably, cardiac surgery frequently involves the use of an intraoperative cardiopulmonary bypass (CPB), which may contribute to the mechanisms responsible for Postoperative Delirium. The etiology of neurocognitive disorders after CPB is multifactorial, and results from a combination of preoperative, intraoperative, and postoperative insults, along with established patient risk factors. Preoperative risk stratification is essential to the management of postoperative neurocognitive complications.

Intraoperatively, certain factors have been proposed to increase or predict the risk of post-operative neurocognitive disorders. These include the CPB time, surgical complexity, and use of a cerebral oximetry or Bi Spectral Index (BIS). Postoperatively, non-pharmacological interventions such as reorientation, good sleep hygiene, early mobility, visual and hearing optimization, adequate nutrition, and cognitive exercise have been shown to reduce rates of postoperative delirium [16].

Dexmedetomidine is highly selective potent alpha 2 adrenergic receptor agonist, it provides sedation with modest analgesia and anti-delirium effects with minimal respiratory depression, with lower cardiovascular complications in high-risk surgeries and has shown Neuro protective effects· It has anxiolytic, analgesic and anti-inflammatory properties, and may modulate the stress response to illness [17]. Dexmedetomidine has also been shown to have organ-protective effects (neuroprotection, cardio protection and renoprotection) in non-cardiac and cardiac surgery [18]. Excessive norepinephrine release, perhaps in response to infection or inflammation in critically ill adults, is part of a cascade of events hypothesized to lead to neuronal damage and the development of delirium. Reduction in this neurotransmitter release through dexmedetomidine administration may prevent or limit the risk for delirium development [19]. Excitatory amino acid (glutamate) toxicity, gamma-aminobutyric acid (GABA) agonism, and acetylcholine deficiency have also been implicated in the development of delirium. Dexmedetomidine therefore may also be beneficial for delirium prevention through decreasing glutamate release and its lack of GABA receptor modulation or cholinergic receptor activity when compared to other commonly used sedatives [20].

Fentanyl, a potent opioid, is traditionally used for pain management in cardiac surgical patients, but its side effects, including respiratory depression and potential for neurotoxicity, may contribute to the development of delirium. Opioids based therapy offers hemodynamic stability and decreased intraoperative stress response and they have adverse effects such as nausea, vomiting, drowsiness and respiratory depression and have protracted refractory period after infusion is stopped [21]. The present study performed to show weather incidence of delirium is less with dexmedetomidine when compared to fentanyl in people undergoing major cardiac surgeries.

MATERIALS AND METHODS

The study design was a single blinded Randomized Control Trial which was conducted in the Department of Anesthesiology, Pain, Palliative and Critical Care, IMS and SUM Hospital, Bhubaneswar, India, from January 2023 to January 2025. The study included 150 of both the sexes patients aged 18-80 years scheduled for on-pump cardiac surgery. Ethical clearance was obtained from the Institutional Ethical Committee of IMS and SUM Hospital, Bhubaneswar. Informed consent was taken from all study participants before the study. Confidentiality was ensured at all stages. Participants were informed about their right to withdraw consent at any point in time. They were guaranteed strict privacy and confidentiality.

Patients were randomized using a computer-generated random number table, and allocation concealment was achieved using opaque sealed envelopes. The study was single blinded. Group F received fentanyl infusion at 1 mcg/kg/hr, while Group D received dexmedetomidine infusion at 0.5 mcg/kg/hr for 10 hours postoperatively in the ICU.

INCLUSION CRITERIA

The inclusion criteria for this study consist of adult patients between the ages of 18 and 80 years who are scheduled to undergo on-pump cardiac surgery.

EXCLUSION CRITERIA

The exclusion criteria for the study encompass several clinical and physiological factors to ensure patient safety and data integrity. Patients will be excluded if they present with severe congestive heart failure, defined by an ejection fraction of less than 40%, or if they have pre-existing liver or renal dysfunction. Neurological conditions, such as a history of cerebrovascular accidents (CVA), schizophrenia, or the current use of antipsychotic medications, also disqualify a candidate. Additionally, patients are ineligible if they exhibit preoperative hypotension, a baseline heart rate below 55 beats per minute, or have a pacemaker in situ. The study further excludes individuals undergoing reoperative procedures, those with known hypersensitivity to opioids, and any case where a patient or legal guardian refuses to provide informed consent.

Preoperative cognitive evaluation was performed using the Mini-Mental State Examination and the clock drawing test. Patients unable to perform these assessments were excluded. All patients were preoperatively assessed and standard routine investigations were completed.

Intraoperative management included standard anesthesia, preoxygenation, induction with thiopentone, neuromuscular blockade with rocuronium, maintenance with isoflurane in air-oxygen mixture, invasive hemodynamic monitoring, central venous access, and transesophageal echocardiography as appropriate. Cardiopulmonary bypass was instituted after systemic heparinization and standard surgical procedures were

completed.
Postoperatively, delirium was assessed using CAM-ICU at 12-hour intervals for 7 days. Delirium severity was categorized as no delirium, mild to moderate delirium, and severe delirium according to the scoring system used in this study. Sedation was monitored using the Richmond Agitation-Sedation Scale, and pain was assessed using CPOT in intubated patients and the Wong-Baker Faces scale in extubated patients. Mean arterial pressure and heart rate were recorded at serial time points up to 72 hours, and rescue analgesia was given when pain thresholds were exceeded.

Statistical Analysis

Statistical analysis was performed using SPSS version 27. Continuous variables were analyzed using the unpaired t-test, and categorical variables using the chi-square test, with $p < 0.05$ considered statistically significant.

RESULTS

A total of 150 postoperative cardiac surgery patients were included, with 75 in the fentanyl group and 75 in the dexmedetomidine group. The baseline demographic variables, including age, sex, weight, and duration of surgery, were comparable between the two groups and showed no statistically significant difference. The mean age was 48.26 ± 18.56 years in the fentanyl group and 47.36 ± 19.33 years in the dexmedetomidine group, while the majority of patients in both groups were male (Table 1). The mean duration of surgery was also similar, at 8.07 ± 1.03 hours in the fentanyl group and 7.39 ± 0.93 hours in the dexmedetomidine group.
The mean age of the patients is almost similar with Group-F Patients having a mean age of 48.26±18.56 years and group D patients having a mean age of 47.36±19.33. The difference was found to be statistically insignificant (p >0.05).

Table 1. Age wise distribution

	Group-F Mean±SD	Group-D Mean±SD	p-value
Age	48.26±18.56	47.36±19.33	0.385

(p value >0.05), not significant.
As age is the independent risk factor for delirium. Severity of delirium is more in the age group of 70-80 years of age in both the group, where severe delirium is noted in 10 patients (Table 2; Figure 1).

Table 2. Age wise distribution of delirium

Age(years)	Mild	Moderate	Severe
18-30	11	6	2
30-50	7	8	5
50-60	8	10	6
60-70	4	5	9
70-80	2	14	10

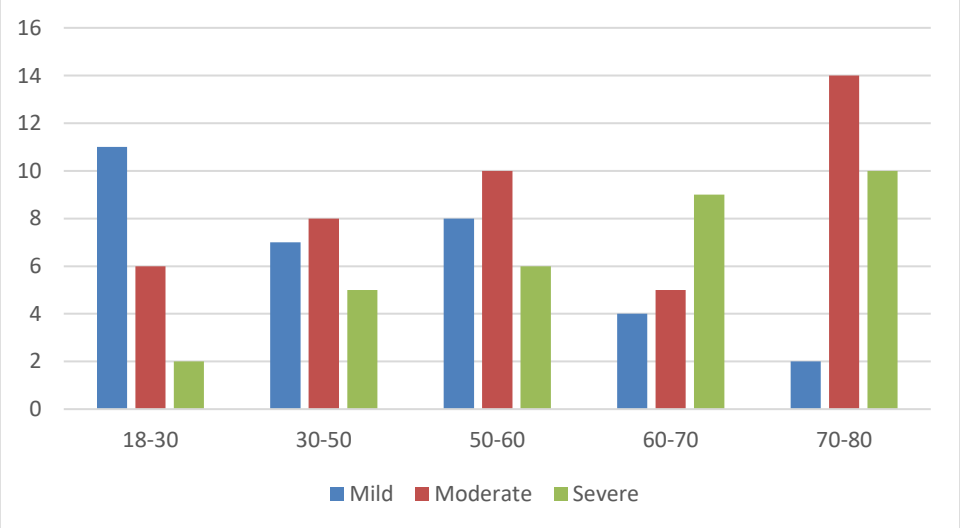


Figure 1: Age-wise distribution of delirium severity levels among the study population.

Gender

Most of them are males in both the group with 62%. Males in group F is 62.6 % and in group D is 61.3%. Percentage of Females in both the groups were 38%. Females in group F is 37.3% and in group D is 38.6 % (Table 3)

Table 3. Gender wise distribution.

	Group-F	Group-D
Gender (female/male)	28/47	29/46

Weight

The mean weight of the patients is almost similar with Group-F Patients having a mean weight of 58.14 ±18.56 kgs and group D patients having a mean weight of 59.01±12.37. The difference was found to be statistically insignificant (p >0.05) (Table 4).

Table 4. Weight wise distribution

	Group-F Mean±SD	Group-D Mean±SD	p value
Weight	58.14 ±18.56	59.01±12.37	0.336

Mean duration of surgery

Mean duration of surgery in group F was 7.59±1.02 hours and mean duration of surgery in group D is 7.39 ± 0.93, it is noted that the mean duration of surgery is same for fentanyl group and Dexmedetomidine. This difference was found to be statistically insignificant (p >0.05). Total 34 patients in both the groups had prolonged duration of surgery. Out of those 20 people were affected with severe delirium (Table 5).

Table 5. Mean duration of surgery

Group-F Mean±SD		Group-D Mean±SD	p value
Mean duration of surgery in hours	8.07±1.03	7.39 ±0.93	0.0001

Mean arterial pressure

When mean arterial pressure were measured between two groups. It was observed that mean arterial pressures of baseline, before induction, after induction, before sternotomy, after sternotomy, before CPB and after CPB and before shifting to ICU did not vary significantly (Table 6).

Table 6. Comparison of Mean arterial pressure of both groups

MAP Group-F Mean±SD		Group-D Mean±SD	p value
Baseline	79.82±7.94	80.9±8.81	0.80
Before induction	80.36±8.30	80.34±8.86	0.49
After induction	84.04±8.90	81.92±10.51	0.44
Before sternotomy	82.69±8.30	81.98±8.06	0.29
After sternotomy	86.45±8.95	84.48±8.29	0.15
Before CPB	80.36±8.30	80.28±8.98	0.48
After CPB	84.40±8.98	83.13±10.09	0.18
Before shifting to ICU	85.92±10.14	81.05±8.80	0.32

Mean arterial pressure

When mean arterial pressure were measured between two groups. It was observed that mean arterial pressures of baseline, before induction, after induction, before sternotomy, after sternotomy, before CPB and after CPB and before shifting to ICU did not vary significantly (Table 7).

Table 7. Comparison of Mean arterial pressure of both groups

MAP	Group-F Mean±SD	Group-D Mean±SD	p value
Baseline	79.82±7.94	80.9±8.81	0.80
Before induction	80.36±8.30	80.34±8.86	0.49

After induction	84.04±8.90	81.92±10.51	0.44
Before sternotomy	82.69±8.30	81.98±8.06	0.29
After sternotomy	86.45±8.95	84.48±8.29	0.15
Before CPB	80.36±8.30	80.28±8.98	0.48
After CPB	84.40±8.98	83.13±10.09	0.18
Before shifting to ICU	85.92±10.14	81.05±8.80	0.32

Mean Heart rate:

When mean heart rate were measured between two groups. It was observed that mean heart rate of baseline, before induction, after induction, before sternotomy, after sternotomy, before CPB and after CPB and before shifting to icu did not vary significantly (Table 8).

Table 8. Mean heart rate between the both groups.

Mean heart rate	**Group-F Mean±SD**	**Group-D Mean±SD**	**p value Mean±SD**
Baseline	80.42±8.09	81.05±8.80	0.32
Before induction	80.37±8.20	81.04±9.29	0.49
After induction	85.12±9.60	83.01±10.09	0.30
Before sternotomy	82.72±8.30	82.02±8.09	0.29
After sternotomy	83.38±8.25	83.86±8.07	0.35
Before CPB	80.49±8.13	79.94±8.99	0.34
After CPB	85.46±9.40	83.64±10.91	0.46
Before shifting to ICU	86.58±10.35	87.02±10.04	0.39

Delirium

CAM-ICU 7 Delirium severity scale was recorded at 12 hrs interval for 7 days in both the groups. From 12- 96 hours (4th day in icu) the mean delirium values in group F were 0.88,1.33,1.36,1.6,1.77,2.48,2.78,3.13. Whereas in group D the mean delirium values were 0.68,1.2,1.24,1.52,1.73,2.44,2.76,3.10. The difference was found to be statistically insignificant ($p>0.05$).

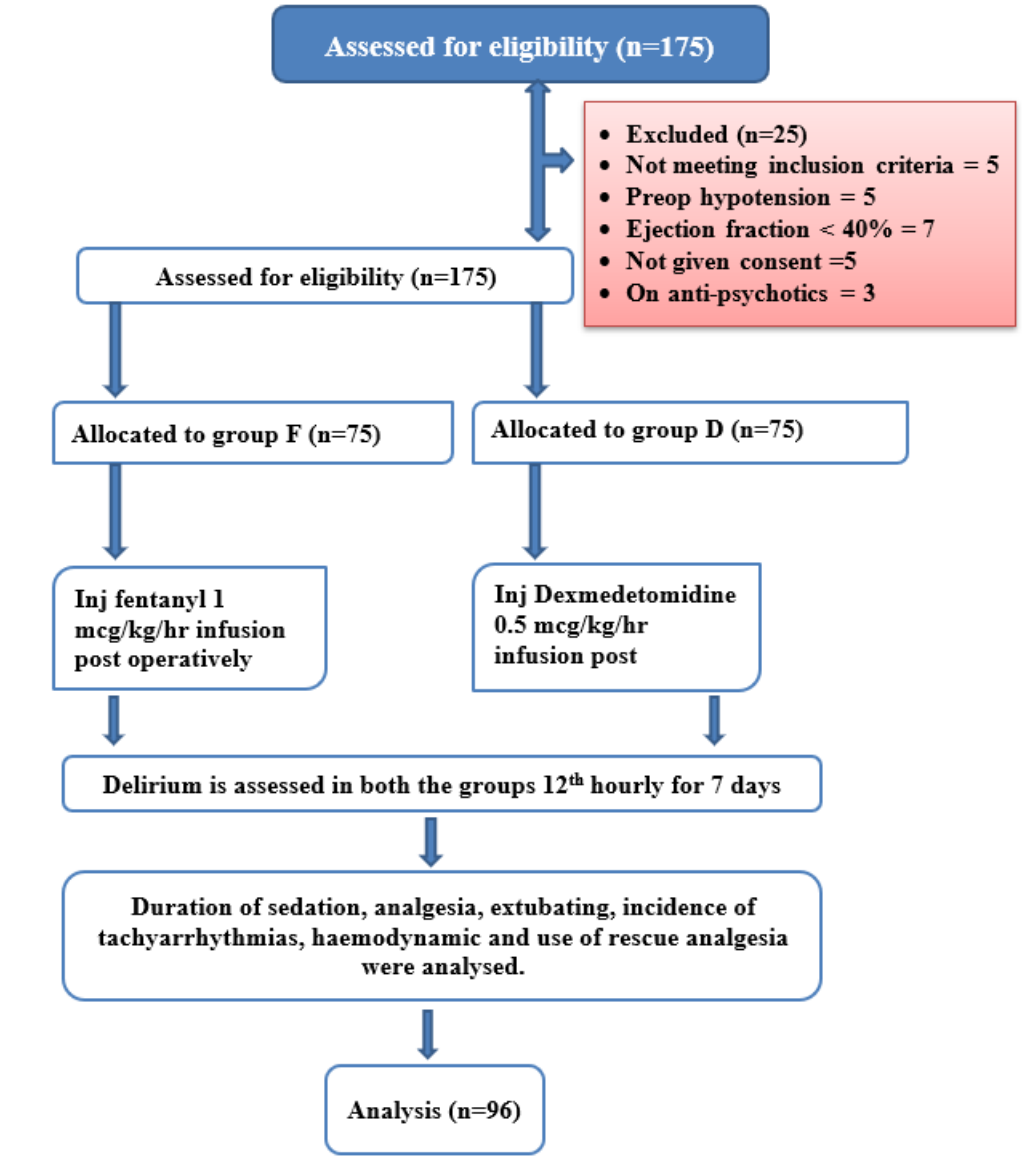
From 108 (5th day) - 168 hours (7th day) the mean delirium values in group F were 3.4,3.78,3.93,3.96,3.98,4.01. In group D the mean values in group D were 3.01,3.36,3.65,3.72,3.74,3.78. The difference was found to be statistically significant ($p<0.05$). In group F total 10 people were affected with mild delirium, 7 people were affected with moderate delirium and 22 people were affected with severe delirium.

In group D3 people were affected with mild delirium, 5 people were affected with moderate delirium and 10 people were affected with severe delirium (Table 9; Figure 2).

Table 9. Mean delirium in both the groups

Delirium in hours	**Group-F Mean±SD**	**Group-D Mean± SD**	**p value**
12	0.88±0.89	0.68±0.73	0.06
24	1.33±0.89	1.20±0.75	0.16
36	1.36±0.83	1.24±0.75	0.17
48	1.6±0.63	1.52±0.6	0.21
60	1.77±0.66	1.73±0.70	0.35
72	2.48±0.68	2.44±0.75	0.36
84	2.78±0.75	2.76±0.71	0.43
96	3.13±0.75	3.10±0.70	0.40
108	3.4±0.86	3.01±0.77	0.001
120	3.78±0.84	3.36±0.74	0.0001
132	3.93±0.97	3.65±0.76	0.02
144	3.96±0.96	3.72±0.76	0.04
156	3.98±0.90	3.74±0.75	0.03
168	4.01±0.90	3.78±0.70	0.04

RESULTS AND OBSERVATIONS



DISCUSSION

In the post-surgical Intensive Care Unit (ICU), optimizing delirium management, sedation, and analgesia is crucial for patients requiring mechanical ventilation following major cardiac surgery [22,23]. Effective sedation-analgesia regimens alleviate pain, mitigate anxiety, promote physiological sleep, and prevent psychomotor agitation. Controlling these factors prevents sudden surges in systemic or pulmonary vascular resistance, which can compromise myocardial oxygen balance and increase myocardial oxygen demand during recovery [24].

Postoperative delirium (POD) remains a critical neurocognitive complication after cardiac surgery, independently associated with prolonged intensive care stays, delayed functional recovery, and higher morbidity. Dexmedetomidine, known for its combined sedative and analgesic effects, which help reduce delirium and agitation, while also causing minimal respiratory depression and predictable cardiovascular responses, particularly when compared to traditional sedatives and opioids. Conversely, fentanyl is a potent synthetic 4-anilidopiperidine μ-opioid analgesic used for analgesic management in mechanically ventilated patients in the ICU. It is a synthetic opioid with a good profile, but undergoes hepatic metabolism, and thus accumulates in tissues following continuous infusion, resulting in prolonged drug effects [25].

Therefore, the present study evaluated whether the incidence and severity of delirium are reduced with dexmedetomidine compared to fentanyl in patients undergoing major cardiac surgeries. Demographic and baseline surgical parameters including weight and mean arterial pressure were statistically comparable between the cohorts, demonstrating effective randomization. The mean age was similar between the fentanyl group (48.26 ± 18.56 years) and the dexmedetomidine group (47.36 ± 19.33 years; P = 0.385). Notably, advanced age acted as an independent risk factor for delirium severity, with the highest concentration of severe delirium occurring within the 70-80 age. The higher prevalence of male patients matches cardiovascular epidemiological trends, as a majority of male patients had historical smoking and alcohol use, predisposing them to ischemic heart disease.

This demographic profile aligns with previous cardiac surgery literature by Yahya Shehabi, Ahmed Said Elgebaly, and Shio Priye [26,27,28]. Yahya shehabi et al., [26] in their study also reported similar demographic patterns of cardiac patients. Ahmed said Elgebaly et al., [26] in their study noted similar higher male patients compared to females and the average age was found to be similar in the present study. Shio priye et al., [28] in their study also reported the similar gender distribution and showed no significant differences between the two groups.

Furthermore, the mean surgical duration (8.07 hours for fentanyl, 7.39 hours for dexmedetomidine) was statistically insignificant, prolonged surgery operated as an independent risk factor for cognitive dysfunction, yielding a mean delirium duration of 3 days. This relationship is corroborated by Sandra Koster et al and Jan Bucerius et al study [29,30]. Sandra koster et al., reported similar relationship between mean duration of surgery and delirium [29]. The mean duration of delirium was found to be 2.5 days. Whereas, Jan Bucerius et al., reported as mean duration of surgery is independent risk factor for delirium, as they reported that higher the cardiopulmonary pump time higher is the incidence of delirium [30].

Regarding delirium kinetics, the overall incidence of early delirium (postoperative days 1 to 4) did not differ significantly between the two agents, with 12-hourly scores demonstrating statistical insignificance ($P > 0.05$; P-values ranging from 0.06 to 0.43). However, a major divergence occurred during the later postoperative period (days 5 to 7), where dexmedetomidine scores were significantly lower than fentanyl scores ($P < 0.05$; P-values ranging from 0.001 to 0.04). Ultimately, severe delirium was vastly overrepresented in the fentanyl cohort (22 patients) compared to the dexmedetomidine cohort (10 patients). This indicates that while dexmedetomidine does not prevent the initial onset of early delirium, it significantly limits late-stage delirium severity and overall duration, a finding that mirrors data by Yahya Shehabi, Tamer M Abdel Azeem, and Xue Li studies [26,31,32]. Yahya shehabi et al., compared the effect of Dexmedetomidine with morphine noted that Dexmedetomidine reduces the duration of delirium but not the incidence of delirium after cardiac surgery [26]. Tamer M Abdel Azeem et al., [31] reported Dexmedetomidine vs morphine and midazolam significant lower risk of delirium in Dexmedetomidine group compared to morphine and midazolam group in cardiac surgeries. Xue li et al., also observed that there is a decreased incidence of delirium in patients who received Dexmedetomidine in elder patients undergoing elective cardiac surgery [32].

Sedation depth and analgesic quality were evaluated using the Richmond Agitation-Sedation Scale, Critical-Care Pain Observation Tool, and Wong-Baker FACES scale. Patients in the dexmedetomidine cohort achieved a more stable, targeted level of sedation and lower pain scores ($P < 0.05$), which directly translated into a marked reduction in rescue analgesics (intravenous paracetamol and tramadol). This finding is supported by Tobias, showed that a maintenance infusion of dexmedetomidine (0.5µg/kg/h) reduced opioid requirements. While harish S [33] noted that dexmedetomidine offered weaker primary analgesic properties than pure fentanyl, she similarly observed higher rescue requirements in fentanyl cohorts. Our low pain scores are further aligning with studies by Shio Priye et al., [28] Eremenko et al., [34] Barletta et al., [35] and Ahmed Said Elgebaly et al., [27] reduced opioid requirements with dexmedetomidine compared to traditional regimens.

Successful fast-track extubation is a critical milestone signaling readiness for intensive care discharge. The fentanyl group experienced a statistically significant delay in time to extubation (18.40 ± 3.16 minutes) compared to the dexmedetomidine group (17.54 ± 2.59 minutes; $P < 0.05$). This was highlighted by the fact that 4 patients in the fentanyl group required reintubation on day 2 due to profound respiratory depression, delaying successful extubation until day 6. In contrast, only 2 patients in the dexmedetomidine group required reintubation on day 2, which was driven by psychomotor agitation rather than respiratory failure, and both were extubated by day 4. These weaning advantages match data by Noorizan Abd Aziz and Mui Ching Chue studies [36].

Overall, the findings of study demonstrate that dexmedetomidine does not alter the the initial incidence of early postoperative delirium compared to fentanyl. Furthermore, it provides clinically by reducing late-stage delirium severity, providing more stable conscious sedation with lower rescue analgesic requirements, and facilitating safer, earlier extubation without respiratory depression.

CONCLUSION

The finding of the study demonstrates that, the postoperative use of dexmedetomidine does not reduce the incidence of early delirium compared to fentanyl regimen. Dexmedetomidine significantly attenuates the delirium burden by shortening its duration and lowering later period delirium scores, while fostering a highly favorable recovery profile. Furthermore, dexmedetomidine facilitates earlier extubation and lowers tachyarrhythmia incidence without increasing the risk of hypotension, vasopressor requirements, or major hemodynamic compromise though bradycardia occurred more frequently than with fentanyl. Conversely, fentanyl was associated with delayed recovery and greater delirium severity. Overall, dexmedetomidine presents a valuable postoperative sedative-analgesic option with distinct clinically benefits. The larger multicenter studies with advanced cerebral monitoring and longer follow-up are needed to validate these outcomes and establish standardized dosing strategies.

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