

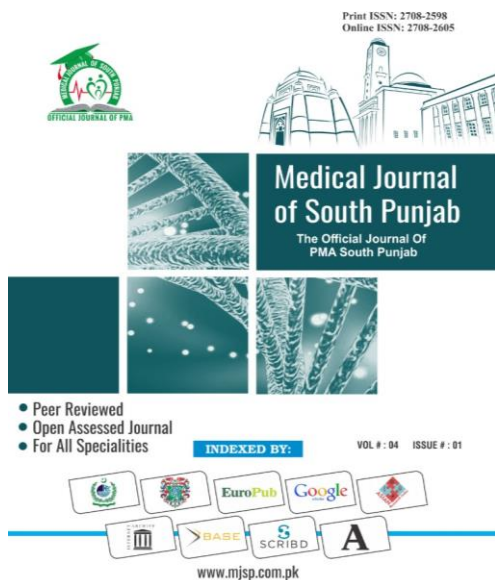
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Effects of Dexmedetomidine dosage on the short-term cognitive function of elderly patients undergoing cardiac surgery

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ABSTRACT

Objective: to explore how different infusion rates of perioperative dexmedetomidine (DEX) impacted short-term cognitive function post-surgery.

Methods: Study was conducted at department of cardiothoracic surgery Memon Medical Institute Hospital Karachi, Pakistan between January 2022 and November 2022. DEX infusion before extubation in post operative time was given until 1 hour and divided into two different doses. Low dose (group L) and high dose (group H). Patients were assigned in these groups by lottery method. Group L was given a low-rate DEX infusion of 0.1–0.5 µg/kg/h and Group H was given a high-rate DEX infusion of 0.5–0.9 µg/kg/h.

Results: The mean comparison between postoperative outcomes was shown in table. III. The mean MMSE (T_0) and MMSE (T_1) of the patients was 29.78 ± 3.96 and 25.82 ± 1.78 , respectively, ($p < 0.001$). The mean MMSE (T_1) and MMSE (T_2) of the patients was 25.82 ± 1.78 and 26.65 ± 1.81 , respectively, ($p = 0.015$). The mean MMSE (T_2) and MMSE (T_3) of the patients was 26.65 ± 1.81 and 28.55 ± 2.62 , respectively, ($p < 0.001$). The mean MMSE (T_3) and MMSE (T_4) of the patients was 28.55 ± 2.62 and 29.33 ± 2.93 , respectively, ($p = 0.109$).

Conclusion: DEX with infusion of low doses (0.1–0.5 µg/kg/h) is superior to high doses (0.5–0.9 µg/kg/h) in cognitive protection for older patients having age 60 years or above. Furthermore, opting for a low-dose (0.1–0.5 µg/kg/h) DEX infusion can help reduce the risk of bradycardia and hypotension during the perioperative period.

Keywords: Cognitive function, Dexmedetomidine, Dosage, Cardiac surgery, Elder patients

1. INTRODUCTION

Postoperative cognitive dysfunction (POCD) refers to a prevalent complication that often manifests within the timeframe of 1 to 3 months following a surgical procedure¹. Several factors significantly influence postoperative cognitive function. These encompass patient age, where older individuals tend to be more susceptible to cognitive impairments after surgery². Cerebral perfusion pressure, a critical determinant of brain oxygenation, plays a crucial role, as alterations in this pressure can impact cognitive performance post-surgery³.

Dexmedetomidine (DEX) is a pharmacological agent known for its high selectivity as an α_2 receptor agonist, and it exhibits a range of beneficial properties in medical settings^{4,5}. These include anti-inflammatory effects, sedation, analgesia, anxiolysis, modulation of sympathetic activity, and mild respiratory depression⁶. Additionally, DEX has been observed to have a protective impact on postoperative cognitive function, as well as effectiveness in preventing anesthesia-induced postoperative delirium⁸. Discrepancies can primarily be attributed to differences in several key factors such as the specific objects being compared (e.g., different patient populations or surgical techniques), the cognitive assessment tools employed (which can vary in sensitivity and specificity), and variations in the infusion dose of DEX administered during the perioperative period⁹. Mini-Mental State Examination (MMSE) is a commonly used assessment tool to evaluate cognitive function, with a focus on the MMSE score on postoperative day 2 as the primary index of study^{10,11}.

The findings from this study can directly influence clinical practice by

guiding anesthesiologists and surgeons in selecting the most appropriate dexmedetomidine dosage for elderly patients undergoing cardiac surgery. This can potentially reduce the incidence of POCD, improve patient outcomes, and enhance overall healthcare efficiency.

2. METHODOLOGY

Study was conducted at department of cardiothoracic surgery Memon Medical Institute Hospital Karachi, Pakistan between January 2022 and November 2022.

A total of 70 patients undergoing cardiac surgery either coronary artery bypass or valvular surgery, aged 60-75 years, and receiving a DEX infusion before extubation in post operative time was given until 1 hour and divided into two different doses were included in the study. Low dose (group L) and high dose (group H). Patients were assigned in these groups by lottery method. Group L was given a low-rate DEX infusion of 0.1–0.5 $\mu\text{g}/\text{kg}/\text{h}$ and Group H was given a high-rate DEX infusion of 0.5–0.9 $\mu\text{g}/\text{kg}/\text{h}$.

Exclusion criteria included preoperative disagreement, mental illness history, baseline MMSE score ≤ 20 , and ejection fraction $\leq 50\%$ post-admission. Withdrawal criteria comprised perioperative DEX use outside group parameters, second CSICU admission, incomplete postoperative data, data analysis failure, DEX infusion > 36 h, and III^o atrioventricular block during DEX infusion.

Demographics data include gender, age, and BMI, and study variables include duration of surgery, history of diabetes, hypertension, ejection fraction pre-operative, and duration of DEX infusion and MMSE score (preoperative and after surgery at day 2,7,14 and 28).

Data was analyzed by using SPSS version 27 and after test of significance p values ≤ 0.05 was taken as significant.

3. RESULTS

Seventy patients were included in this study. The study patients were equally divided into two groups as Group L and Group H. No difference was statistically significant in demographic, baseline and intraoperative characteristics among both the study groups, ($p>0.050$). (Table. I).

Postoperative primary outcomes in Group L and Group H were almost equal and statistically insignificant, ($p>0.050$). Whereas, according to secondary outcome, postoperative delirium was higher in Group L 7 (20.0%) than Group H 1 (2.9%), ($p=0.024$). Intraoperative hypotension was higher in Group H 10 (28.6%) than Group L 3 (8.6%), ($p=0.031$). Further, Intraoperative bradycardia was significantly higher in Group H 23 (65.7%) than Group L 4 (11.4%), ($p<0.001$). (Table. II).

The mean comparison between postoperative primary outcomes was shown in table. III. The mean MMSE(T₀) and MMSE(T₁) of the patients was 29.78±3.96 and 25.82±1.78, respectively, ($p<0.001$). The mean MMSE(T₁) and MMSE(T₂) of the patients was 25.82±1.78 and 26.65±1.81, respectively, ($p=0.015$). The mean MMSE(T₂) and MMSE(T₃) of the patients was 26.65±1.81 and 28.55±2.62, respectively, ($p<0.001$). The mean MMSE(T₃) and MMSE(T₄) of the patients was 28.55±2.62 and 29.33±2.93, respectively, ($p=0.109$). (Table. III).

Table. I
Demographic, baseline and intraoperative characteristics among the study groups

Characteristic	Group L 35 (50.0%)	Group H 35 (50.0%)	p- value
Age (years)	60.70±3.14	58.68±3.88	0.283
BMI (kg/m ²)	23.98±3.02	24.43±2.94	0.531
Gender			
Male	25 (71.4)	27 (77.1)	0.984
Female	10 (28.6)	8 (22.9)	
MMSE ₀	30.38±3.95	29.09±3.93	0.175
ASA			
III	1 (2.9)	6 (17.1)	0.056
IV	34 (97.1)	29 (82.9)	
Type of surgery			

Valve surgery	30 (85.7)	28 (80.0)	0.526
Aortic root surgery	5 (14.3)	7 (20.0)	
EF (%)	66.34±3.05	65.68±3.56	0.411
CAS ≥ 50%	1 (2.9)	2 (5.7)	0.555
Smoking	9 (25.7)	10 (28.6)	0.788
Hypertension	18 (51.4)	17 (48.6)	0.811
Diabetes	7 (20.0)	6 (17.1)	0.759
CPB time (minutes)	125.37±3.54	125.08±3.55	0.738
Length of surgery (minutes)	273.68±3.59	272.85±3.50	0.333
Anaesthesia time (minutes)	328.15±3.15	329.11±3.74	0.245
DEX infusion time (hours)	20.11±1.72	20.14±1.85	0.947
N (%), Mean±S.D			

Table. II
Primary and secondary outcomes at postoperative among the study groups

Outcome	Group L 35 (50.0%)	Group H 35 (50.0%)	p- value
Primary outcomes			
MMSE(T ₁)	25.74±1.51	25.91±2.04	0.705
MMSE(T ₂)	26.98±1.87	26.33±1.72	0.141
MMSE(T ₃)	28.37±2.54	28.72±2.72	0.573
MMSE(T ₄)	29.69±2.82	28.97±3.03	0.308
Secondary outcomes			
Postoperative delirium	7 (20.0)	1 (2.9)	0.024
Intraoperative hypotension	3 (8.6)	10 (28.6)	0.031
Intraoperative bradycardia	4 (11.4)	23 (65.7)	<0.001
Hours of initial intubation	22.85±1.71	22.54±1.71	0.451
Myocardial infarction	2 (5.7)	1 (2.9)	0.555
Stroke	2 (5.7)	1 (2.9)	0.555
CSICU stay(hours)	36.11±3.98	35.28±5.09	0.442
Hospital days (days)	26.14±3.46	26.25±3.16	0.886
Hospital mortality	2 (5.7)	1 (2.9)	0.555
N (%), Mean±S.D			

Table. III
Comparison of primary outcomes at postoperative among the study groups

Comparison		p-value
MMSE(T ₀)	MMSE(T ₁)	<0.001
29.78±3.96	25.82±1.78	
MMSE(T ₁)	MMSE(T ₂)	0.015
25.82±1.78	26.65±1.81	
MMSE(T ₂)	MMSE(T ₃)	<0.001
26.65±1.81	28.55±2.62	

MMSE(T ₃)	MMSE(T ₄)	
28.55±2.62	29.33±2.93	0.109
Mean±S.D		

4. DISCUSSION

The mean MMSE (T₀) and MMSE (T₁) of the patients was 29.78±3.96 and 25.82±1.78, respectively, (p<0.001). But MMSE score was almost equal postoperatively among the groups. Zhang et al¹². conducted a study on elderly patients undergoing laparoscopic colorectal cancer surgery, dividing them into control, D1, D2, and D3 groups receiving varying doses of DEX. The high dose (0.8 µg/kg/h) of DEX showed better neuroprotective effects compared to the low dose (0.20 µg/kg/h), possibly due to differing intervention durations.

Gottesman et al¹³ documented in their study that intraoperative hypotension could lead to an increase in early cognitive dysfunction, thereby reducing the neuroprotective advantages observed in the high-dose group on postoperative Day 2. In this study intraoperative hypotension was observed 8.6% in low dose group and 28.6% in high dose group.

In Ebert et al¹⁴ study, DEX plasma concentrations between 0 and 0.7 ng/mL showed an anti-sympathetic effect. This effect increased with higher DEX infusion doses. However, other outcomes like time to initial intubation, instances of myocardial infarction, stroke, CSICU stay duration, and hospital mortality did not differ significantly between the groups. Fang et al¹⁵ study revealed that patients in Group L had higher MMSE scores (26.0 [24.0, 27.0]) compared to those in Group H (24.5 [22.0, 26.0]), with a p-value of 0.046, and although there were no significant differences in scores between the groups at later time points, Group H

showed a greater incidence of hypotension and bradycardia in comparison to Group L.

Shaefi et al¹⁶ and Saczynski et al.¹⁷ conducted studies that revealed a significant finding regarding the Mini-Mental State Examination (MMSE) scores on postoperative Day 2. They observed that this day marked the lowest point in MMSE scores following surgery, with a minimum clinically significant difference of 2 points. In a pre-test involving 12 patients who received low-dose infusion, the mean MMSE score on postoperative Day 2 was 24.4 ± 2.6, indicating the average cognitive performance at this critical juncture in the recovery process.

Duan and colleagues¹⁸ conducted a meta-analysis, as outlined in their study referenced as, where they examined the optimal strategy for managing delirium as the primary endpoint. Their findings suggested that an effective approach could include administering a loading dose within the range of 0 to 0.5 µg/kg, followed by a maintenance dose of 0.2 µg/kg/h. This strategy aimed to address delirium effectively while considering the dosage thresholds for optimal management.

Fu et al¹⁹ reported that neither group experienced instances of myocardial infarction, stroke, or hospital death. Group H demonstrated significant reductions (T₁ vs. T₀, p < 0.001) alongside cognitive recovery stabilization beyond the early postoperative phase. Conversely, Group L experienced a considerable drop in MMSE scores after surgery.

Goveia et al²⁰ found that administering Dexmedetomidine reduced the likelihood of postoperative cognitive and behavioral dysfunction by at least 43% in adult patients undergoing general anesthesia for non-cardiac surgery.

5. CONCLUSION

DEX with infusion of low doses (0.1–0.5 µg/kg/h) is superior to high doses (0.5–0.9 µg/kg/h) in cognitive protection for older patients having age 60 years or above. Furthermore, opting for a low-dose (0.1–0.5 µg/kg/h) DEX infusion can help reduce the risk of bradycardia and hypotension during the perioperative period.

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