

Effect of Peri-Operative Dexmedetomidine on Incidence of Delirium in Elderly Patients After Cardiac Surgery

Peri-Operative
Dexmedetomidine
on Incidence of
Delirium

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ABSTRACT

Objective: The aim of this study was to compare the frequency of delirium in patients of elective cardiac surgery treated peri operatively with dexmedetomidine with those treated with midazolam.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of cardiac surgery, Punjab Institute of Cardiology, Lahore, Pakistan from July, 2020 till December, 2020.

Materials and Methods: Dexmedetomidine was given to half of the patients included in the study and other drug was taken as a controlled drug, Midazolam. The objective of this study was to compare the frequency of delirium in patients of elective cardiac surgery treated with peri operatively with dexmedetomidine with those treated with midazolam prei-operatively. Delirium was assessed using the scale - MMSE Scoring scale. Mini-Mental State Examination (MMSE) Score is of total 30 score. Patients were asked some questions in the form of an interview and 1 mark was given for each correct answer. Any patient with a score of less than 24 was labeled as having a cognitive impairment or delirium.

Results: The comparison of frequency of delirium in patients of cardiac surgery treated with perioperative dexmedetomidine vs midazolam was done, 8.57% (n=2) in Dexmedetomidine group and 22.86% (n=8) in midazolam group were found with delirium, p value was 0.04.

Conclusion: Delirium is a stressful complication observed in the post-operative period. With the use of dexmedetomidine along with the induction of general anesthesia, the chances of post-operative delirium can be reduced. This trial should be done on a larger scale documenting the effects of DEX on all the parameters monitored during the general anesthesia.

Key Words: Peri-Operative Dexmedetomidine, Incidence of Delirium, Elderly Patients, Cardiac Surgery

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INTRODUCTION

Apart from the other complications of surgery done under general anesthesia, some of the complications are related to the drugs used by the anesthetist for the induction and maintenance of anesthesia. Among these complications, post-operative delirium (POD) is an acute disorder of the central nervous system with disturbed conscious level and change in the cognition and perception.

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It is a common complaint of elderly patients in the initial days of post-operative period, mostly patients of cardiac and thoracic surgeries. The exact pattern of changes in the CNS leading to the cognitive impairment and post operative delirium (POD) is still not clear.¹

The incidence of POD in the old age patients ranges from 10% to 50% varying mostly with age. It negatively affects the overall quality of life (QOL) after the surgery along with long-term outcomes, mortality, cognitive disorders, stay inside the hospital.^{1,2}

Prevention of POD in elderly patients is now considered as a part of successful surgical outcome. Among various other drugs used in the prevention of POD, dexmedetomidine is now recommended because of its neuro-protective effect, still trials are under way to reach a decision and results of previous studies on various anti-psychotics and sedatives show inconsistent results.^{3,4}

Dexmedetomidine, an alpha-2selective adrenergic agonist, with its opioid-sparing property, decrease in the anesthetic dose required and neuroprotective effects, is now commonly used by consultant anesthetists in cardiac and thoracic surgeries.⁵ It is also

a used as a sedative drug the high risk units. Many studies have shown its significant role in the prevention of POD after cardiac as well and non-cardiac surgeries.⁶ Even than some studies have concluded with opposite results, like Deiner et al⁷ showed that dexmedetomidine had no significant advantage in the reduction of incidence of POD.

To date very limited local studies are available comparing the role of dexmedetomidine versus placebo or propofol or midazolam in the prevention of POD. As there is inconsistent results of trials done previously and controversy regarding the effect of dexmedetomidine on the incidence of POD, controlled trials should be done in our local population determining the frequency of POD after treatment with dexmedetomidine and comparing this frequency with other sedatives commonly used like midazolam.

MATERIALS AND METHODS

This study was conducted in the department of cardiac surgery and anesthesia, Punjab Institute of cardiology. In this randomized controlled trial patients of elective cardiac surgery were enrolled and divided into two groups. One of the sedative drugs used before the start of surgery was dexmedetomidine which was given to half of the patients included in the study. Other drug was taken as a controlled drug often used pre-operatively, Midazolam.

The objective of this study was to compare the frequency of delirium in patients of elective cardiac surgery treated with perioperatively with dexmedetomidine with those treated with midazolam pre-operatively.

Data collection for this study was done from July, 2020 till December, 2020 in the Punjab Institute of Cardiology. The study was approved by the clinical research ethics Committee of the Punjab Institute of Cardiology (PIC).

Each of the patients included, was explained about the procedure of the data collection and detail and purpose of the medicines used and a written informed consent was taken individually. Adult and elderly patients of age 55 to 75 years old scheduled for elective cardiac surgery, like coronary artery bypass graft surgery CABG, valve surgery, or combined surgery with cardiopulmonary bypass were enrolled into the study.

Patients with ASA class I and II were included and those of ASA class III and IV were not included in the study. All those patients with history of kind of psychiatric illness, those with difficulty in communicating with the primary investigator before the surgery and those already diagnosed with cognitive disorder (on history taking) were not included in the data collection process for this study. Any patient admitted for cardiac surgery but had preoperative sick sinus syndrome, significant fall in heart rate (heart rate less than 50); or with 2nd-degree or more severe

atrioventricular heart block without pacemaker or those who had any signs of liver or kidney failure were also removed from the study. Those patients who couldn't communicate due to visual, hearing, language difficulty and those who had history of head trauma were also excluded from the study.

Sampling was done through non probability consecutive sampling technique. Sample size 70 was calculated using the WHO sample size calculator with expected percentage of patients developing Delirium in dex group of 6.52%¹⁰ and in the midazolam group of 21.74%¹⁰ taking the power of the test of 80% and level of significance of 5%. 35 patients were randomly assigned to group 1 and 35 were randomly divided into group 2.

In order to remove bias, neither the patients were aware of the type of drug they were given nor were the person administering the drug was aware of the drug. One of the drugs was labeled as A (DEX) and other was labeled as B (MID).

Along with the other drugs to induce general anesthesia, patients in the group 1 were given dexmedetomidine infusion in the theater with a dose of 0.7 µg/kg/h and was later continued into the high dependency unit at a dose of 0.4 µg/kg/h.

Delirium was assessed using the scale - MMSE Scoring scale. Mini-Mental State Examination (MMSE) Score is of total 30 score. Patients were asked some questions in the form of an interview and 1 mark was given for each correct answer. Any patient with a score of less than 24 was labeled as having a cognitive impairment or delirium.

Electrocardiogram – ECG, blood pressure, heart rate were monitored during the whole procedure. Patients in the second group were given IV injection of Midazolam (0.05 µg/(kg.h) in the theater and then intravenous injection 0.02-0.08 µg/(kg.h) to maintain the anesthesia. After the procedure analgesic drugs were given and all types of narcotic drugs were stopped.

Cognitive impairment post-operatively was accessed using the Mini-Mental State Evaluation (MMSE) scoring. MMSE was accessed in the pre-operative room and later just after the surgery at 6 hours, 24 hours, 48 hours and 72 hours in the post operative period.

Data was enter in excel and SPSS data analyzing software (SPSS-23.0) and analyzed to calculate frequency and percentages of categorical data and mean with standard deviation for continuous data. The frequency of delirium in the post op period was documented and compared with the two groups using chi square test. Data was stratified for age and gender, post-stratified chi square test was applied to see the effect of these variables on the outcome variable. P<0.05 was taken significant.

RESULTS

In this randomized controlled study, patients of old age group admitted for elective cardiac surgeries were enrolled to determine the effect of dexmedetomidine on the incidence of POD. Half of patients in our study were given dexmedetomidine and half of the patients were given midazolam. Patients were randomly assigned in one of the two groups in order to prevent bias. A total of 70 cases (35 in each group) fulfilling the selection criteria were enrolled to compare the frequency of delirium patients of cardiac surgery treated with perioperative dexmedetomidine vs Placebo (midazolam).

In our study, majority of the cases i.e. 74.29%(n=26) in Dexmedetomidine group and 68.57%(n=24) in midazolam group were between 55-65 years of age whereas 25.71%(n=9) in Dexmedetomidine group and 31.43%(n=11) in midazolam group were between 66-75 years of age, mean age was 59.64 ± 12.47 years. (Table 1). Gender distribution shows 54.29% (n=19) in Dexmedetomidine group and 57.14%(n=20) were male cases and 45.71%(n=16) in Dexmedetomidine and 42.86%(n=15) in placebo group were females. After 24 hours, Mean MMSE scores in Dexmedetomidine group was 27.84 ± 6.87 and in midazolam group it was calculated as 23.67 ± 11.43 . (Table 2). The comparison of frequency of delirium patients of cardiac surgery treated with perioperative dexmedetomidine vs midazolam was done and illustrated in Table No. 3, where 8.57%(n=2) in Dexmedetomidine group and 22.86%(n=8) in midazolam group were found with delirium, p value was 0.04.

Table No. 1: Age Distribution (n=70)

Age(in years)	Dexmedetomidine group (n=35)		Midazolam group (n=35)	
	No. of patients	%	No. of patients	%
55-65	26	74.29	24	68.57
66-75	9	25.71	11	31.43
Total	35	100	35	100

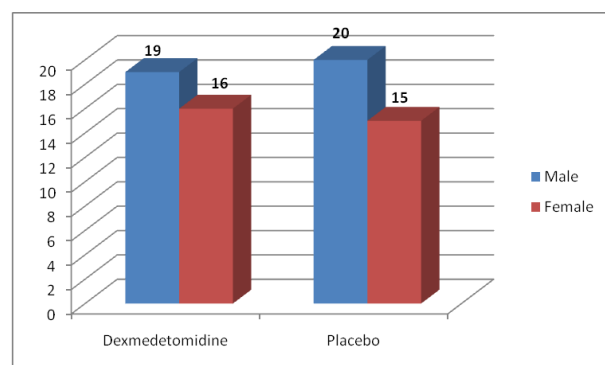


Figure No. 1: showing the Gender Distribution of patients included in our study

Table No. 2: Mean Mmse Scores (n=70)

MMSE Scores	Dexmedetomidine group (n=35)		Midazolam group (n=35)	
	Mean	SD	Mean	SD
	27.84	6.87	23.67	11.43

Table No. 3: Comparison of frequency of delirium patients of cardiac surgery treated with perioperative dexmedetomidine vs midazolam. (n=70)

Delirium	Dexmedetomidine group (n=35)		Midazolam group (n=35)	
	No. of patients	%	No. of patients	%
Yes	2	8.57	8	22.86
No	32	91.43	27	77.14
Total	35	100	35	100

P value=0.04

DISCUSSION

Postoperative delirium (POD) is one of the major complications seen in post-operative period among the old age patients of cardiac surgery. The incidence of POD varies among various populations and age groups, with reported peak incidence of upto 50% in old age group patients of cardiac surgery. As it is a very stressful condition for the patients and their families with disorientation and sudden loss of cognition, leading to prolonged hospital stay and rise in the cost of treatment, its prevention is necessary for the treating surgeon and anesthetist.⁸

Dexmedetomidine is a potent sedative, used previously in the post-op period as sedative following prolonged surgeries including cardiac and thoracic surgeries. Studies have proven that its use peri-operatively in the theatre showed significant reduction in the dose of anesthetic drug and morphine-sparing effect.⁹

In our study, patients of old age group admitted for elective cardiac surgeries were enrolled to determine the effect of dexmedetomidine on the incidence of POD. Half of patients in our study were given dexmedetomidine and half of the patients were given midazolam. Patients were randomly assigned in one of the two groups in order to prevent bias. The comparison of frequency of delirium patients of cardiac surgery treated with perioperative dexmedetomidine vs midazolam was done; 8.57%(n=2) in Dexmedetomidine group and 22.86%(n=8) in midazolam group were found to have delirium, p value was 0.04.

A randomized controlled trial similar to our trial was done by Yu D, et al. They recorded the incidence of delirium in the post-operative period after administration of DEX in the theatre. They reported that the time of recovery from general anesthesia, extubation time and awakening time, time of onset of POD, and total duration of POD, all these parameters

were shorter and better in the group treated with DEX as compared to midazolam. POD was seen in only 6.52% patients in the treatment group and its incidence was around 26% in the midazolam group ($P < 0.05$). Patients were evaluated using the Mini-Mental State Evaluation (MMSE) scores to diagnose POD.¹⁰ This was close to the results seen in our study.

In a similar study, Su X, et al collected data for 2 years and included around seven hundred patients, half of these were given dexmedetomidine and half were given some placebo. The percentage of patients who had POD was significantly less in the first group as compared to the placebo group. (9% vs 23%). They also studied the possible complications that can develop with the use of dexmedetomidine. Data showed that percentage of patients with hypertension and tachycardia during the surgery was also less in the trial group compared to placebo (10% vs 18% and 7% vs 14% patients, respectively), p value was also significant. Percentage of patients with hypotension and bradycardia was not significantly different between the two groups.¹¹ In our study, incidence of POD was almost similar to this reported, but we didn't collect the data related to heart rate changes and blood pressure changes.

Another recent study showed that POD was seen in around 40% patients treated with propofol as compared to 26% patients treated with dexmedetomidine. Along with the incidence of POD, patients who were given dexmedetomidine showed a delay in the onset and total duration of POD as compared to control group patients. Data analysis should that the stay in the ICU and overall hospital stay was not significantly different between the two groups.¹²

Likhvantsev VV, et al also reported a significant difference in the incidence of POD after dexmedetomidine treatment as compared to placebo (7.1% vs 18.8%; $p < 0.05$). Data regarding duration of stay in the high risk unit and total stay in the hospital was also reduced with the use of dexmedetomidine. Mean stay in the ICU was 18 hours in the dexmedetomidine group and 22 hours in the control group; $p < 0.05$; similarly, mean stay in the hospital was 17 days vs 19 days in dex vs control group, $p < 0.05$. They concluded that Dex if given during and after the general anesthesia for heart surgery showed a significant reduction in the rate of postoperative delirium and intensive care unit and hospital lengths of stay.¹³ In our study, we didn't collect data regarding the hospital stay and stay in the ICU, but the incidence of POD was similar.

Different other trials have been done to comparing Dex with other drugs. Djaiani G, et al¹⁴ reported the incidence of POD in Dex vs propofol of 17.5% and 31.5%, respectively, and proved that Dex can delay the onset and total duration of POD. Few studies also compared the incidence of atrial fibrillation during and after cardiac surgery with the use of Dex vs placebo.

The incidence of AF was reduced but was not statistically significant (30% vs 34%).

Some studies have reported an increase in the episodes of bradycardia with the administration of Dex.^{15,16} Serious adverse effects were seen in around 5% patients with the use of Dex during cardiac surgery, including bradycardia and fall in BP, pulmonary embolism, and deep venous thrombosis.¹⁷

Dexmedetomidine can be very effective in preventing the postoperative cognitive dysfunction and POD, especially in the old age group of cardiac surgery. It can improve the postoperative awakening time, decrease the chances of delirium, delay the onset and total duration of POD, thus decreasing the overall stay in the ICU and in the hospital, decaying cost of treatment.

CONCLUSION

Delirium is a stressful complication observed in the post-operative period. With the use of dexmedetomidine along with the induction of general anesthesia, the chances of post-operative delirium can be reduced. This trial should be done on a larger scale documenting the effects of DEX on all the parameters monitored during the general anesthesia.

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