Original Article

Dexmedetomidine for Heart Arrhythmia Prevention in Coronary Artery Bypass Surgery Patients

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ABSTRACT

Objective: The aim of this study was to compare the incidence of various types of cardiac arrhythmias between the two groups of CABG cardiac surgery treated peri operatively with dexmedetomidine with those treated with placebo in the department of cardiac surgery, Punjab Institute of Cardiology, Lahore, Pakistan.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of Cardiac Surgery and Anesthesia, Punjab Institute of Cardiology, Lahore from January 2020 to June 2020.

Materials and Methods: Patients of elective cardiac surgery were enrolled and divided into two groups. As per the inclusion criteria step in the research proposal all the patients undergoing off-pump CABG surgery of ASA class II and III, with age of 35 to 75 years having ejection fraction (EF) of >35% were enrolled. Patients in the trial group or DEX group was given 0.5 mcg/kg/h of dexmedetomidine during the induction process and later on an infusion was started at a dose of 0.5 mcg/kg/h till the completion of the surgery even till the shifting of the patient in the High risk units.The frequency of atrial fibrillation and other types of arrhythmias 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: A total of 60 cases (30 in each group) fulfilling the selection criteria were enrolled to compare the incidence of various types of cardiac arrhythmias between the two groups of CABG cardiac surgery treated peri-operatively with dexmedetomidine with those treated with placebo. Patients treated with DEX had an overall lower incidence of various types of arrhythmias. Most common arrhythmia was ventricular tachycardia and premature ventricular contractions.

Conclusion: With the use of dexmedetomidine as a sedative and adjuvant of general anesthesia drugs, the incidence of various tachyarrhythmia is decreased during cardiac surgery and in the post-operative period; but the decrease in the incidence was not statistically significant for all types of arrhythmias.

Key Words: DEX, dexmedetomidine, tachyarrhythmia,atrial fibrillation, Anesthesia, Cardiac surgery

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INTRODUCTION

In the past few years, the outcomes of cardiac surgeries have improved a lot due to significant advancements in the field of diagnostics, anesthesia and postoperative ICU care.[1] Still complications can occur varying from case to case depending upon the expertise of the surgeons and co-morbidities in the patients.

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Among various lethal morbidities and sometimes complications of cardiac surgery is the incidence of heart arrhythmias. Its incidence varies from 15 to 50%, and mostly commonly seen after the coronary artery bypass grafting surgery (CABG).[2]

Changes in the levels of epinephrine and nor-epinephrine while operating on the heart after surgical stimulation lead to significant Hemodynamic disruption and other changes in the body. This hemodynamic disruption leads to disturbance in the myocardial oxygen supply and demand ending up into ischemia with rise in the morbidity.[3] With the development of arrhythmias during or after the surgery can lead to significant rise in hospital stay and cost of the treatment.[4,5]

Many drug trials have been done to prevent heart arrhythmias and the hemodynamic disturbances during the heart surgeries, but still no specific treatment strategy have been recommended for routine use. One of these drugs is dexmedetomidine. It is short-acting

alpha-2 stimulator which can decrease the norepinephrine level in the body. With the fall in the level of nor-epi chances of development of tachycardia, hypertension, delirium are reduced. Even with the peri-operative treatment with DEX, need of analgesic is reduced.[6,7]

Prevoius studies have shown that dexmedetomidine treatment can prevent cardiac arrhythmias but the effect was statistically significant in most of the studies.[8,9,10] A meta-analysis concluded that DEXcan effectively decrease the incidence of atrial fibrillation at the cost of hypotension.[1]

Till today limited local studies are available comparing the effect of DEX with any other drug or placebo on the incidence of various heart arrhythmias. As there is inconsistent results of trials done previously and controversy regarding the effect of dexmedetomidine, controlled trials should be done in our local tertiary care hospitals.

MATERIALS AND METHODS

This study was conducted in the department of cardiac surgery and anesthesia, Punjab Institute of cardiology from January 2020 to June 2020. In this randomized controlled trial patients of elective cardiac surgery were enrolled and divided into two groups. As per the inclusion criteria step in the research proposal all the patients undergoing off-pump CABG surgery of ASA class II and III, with age of 35 to 75 years having ejection fraction (EF) of >35% were enrolled for the randomized controlled trial.

Any patient previously diagnosed with any kind of cardiac arrhythmias or any type of heart block, or those with any previous heart surgery or history of any valvular cardiac disease were not enrolled in the study. All patients diagnosed to have a large sized left atrium or enlarged heart size (cardiomegaly) was also excluded.

Non-probability consecutive sampling was done in this randomized controlled trial. The patients were either allocated in the DEX group or the control group. Allocation process was random and the anesthetist administering the drug was unaware of the allocated group of the patient and which trial drug will be given to a particular patient.

Induction process involved the administration of standard dosage of midazolam, atracurium and propofol. Patients in the trial group or DEX group was given 0.5 mcg/kg/h of dexmedetomidine during the induction process and later on an infusion was started at a dose of 0.5 mcg/kg/h till the completion of the surgery even till the shifting of the patient in the High risk units.

All the patients in the control group were administered with equal amount of infusion of normal saline as placebo. All the patients were monitored as per the protocols of the anesthesia and cardiac surgery. Regular medication was used for the maintenance of anesthesia were continued as protocol.

In order to control the blood pressure which may fall with the administration of dexmedetomidine, mean arterial pressure- MAP was monitored if a fall of >30% is observed during the surgery, fluid therapy was done and later dexmedetomidine infusion was reduced to 50%, along with the inotropic support. With the revival of MAP to its baseline level, dex infusion was also slowly increased to its previous rate. Similarly, if any patient developed raised blood pressure (change in the MAP of > 30%), an infusion of nitroglycerin was started.

Variables recorded include gender, age, ventricular ejection fraction, platelets, hemoglobin and INR as part of the checklist to meet the inclusion and exclusion criteria. All patients were given general anesthesia with standard protocols. All patients had off-pump CABG surgery by consultant cardiovascular surgeon.

The objective of this study was to compare the incidence of various types of cardiac arrhythmias between the two groups of CABG cardiac surgery treated peri operatively with dexmedetomidine with those treated with placebo in the department of cardiac surgery, Punjab Institute of Cardiology, Lahore, Pakistan.

Data collection for this study was done from Aug, 2020 till Jan, 2021 in the Punjab Institute of Cardiology. The study was approved by the clinical research ethics Committee of the Punjab Institute of Cardiology (PIC).

All the patients enrolled were explained about the procedure of data collection and purpose of the medicines used. A written informed consent was taken individually from each patient in the presence of their family members to use the data collected for the purpose of research.

Sampling was done through non probability consecutive sampling technique. Sample size 60 was calculated using the WHO sample size calculator with expected percentage of patients developing atrial fibrillation in dex group of 7.8% and in the controlled group of 26.3% taking the power of the test of 80% and level of significance of 5%. 30 patients were randomly assigned to group 1 and 30 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 (placebo).

At baseline i.e. just before the induction of anesthesia, MAP and heart rate – HR was noted. Readings were taken again after laryngoscopy, then after sternotomy, later while handling distal and proximal grafts. MAP and HR were again documented at the closure of the sternum and lastly in the ICU.

Epinephrine was used in case of significant fall in the MAP and atroprine was given for significantfall in the

HR. Continuous monitoring of the heart was done with ECG to pick any arrhythmias. These include premature atrial contraction – PAC, premature ventricular contractions – PVC, ventricular fibrillation - VF, atrial fibrillation - AF, ventricular tachycardia– VT were recorded from the start of induction to ICU admission.
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 atrial fibrillation and other types of arrhythmias 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 trial conducted in the department of cardiac surgery, Punjab Institute of cardiology, a total of 60 cases (30 in each group) fulfilling the selection criteria were enrolled to compare the incidence of various types of cardiac arrhythmias between the two groups of CABG cardiac surgery treated peri-operatively with dexmedetomidine with those treated with placebo in the department of cardiac surgery. Table no. 1 shows the distribution of the age of the patients included in our study. Table no. 2 shows the distribution of gender among the patients enrolled.

Table No. 1: Age Distribution (n=60)

Age(in years)	Dexmedetomidine group (n=30)		Control group (n=30)	
	No. of patients	%	No. of patients	%
35-50	11	36.67	14	46.67
51-75	19	63.33	16	53.33
Total	30	100	30	100

Table No. 2: Gender Distribution (n=60)

Gender	Dexmedetomidine group (n=30)		Control group (n=30)	
	No. of patients	%	No. of patients	%
Male	16	53.33	18	60
Female	14	46.67	12	40
Total	30	100	30	100

Table No. 3: Comparison of various types of cardiac arrhythmias in both groups (n=60)

Variables	DEX group(n=30)		Control group(n=30)		P value
	No. of patients	%	No. of patients	%	
PAC	5	16.67	17	56.67	0.001
VF	2	6.67	3	10	0.64
AF	3	10	8	26.67	0.09
VT	6	20	24	80	<0.00001
PVC	7	23.33	24	80	0.00001

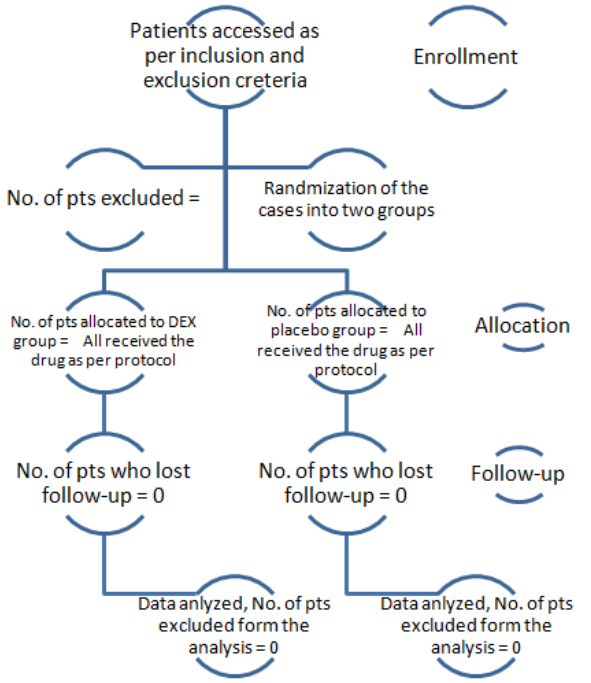

Figure No.1; CONSORT diagram showing the flow of participants through each stage of a randomized trial

Table no. 3 shows the frequency of various types of cardiac arrhythmias that was recorded during the monitoring of heart rhythm during CABG and after surgery in the stay in the ICU. Patients treated with DEX had an overall lower incidence of various types of arrhythmias. Most common arrhythmia was ventricular tachycardia and premature ventricular contractions.

DISCUSSION

Dexmedetomidine is a potent sedative drug and a short acting alpha-2 agonist. Some controlled trial have shown that its peri-operative administration can significantly reduce the chances of development cardiac arrhythmias, delirium, post-op anxiety and hypertension, along with its morphine-sparing effect.11
Many international studies have compared the incidence of atrial fibrillation during and after cardiac surgery with the use of DEXagainst some other drugs or placebo. Some of these studies showed a statistically significant reduction while most of them were non-significant. Some studies reported a significant association bradycardia among the patients administered with Dex.[12,13] Apart from bradycardia some other serious side effects were reported in around 5% of the patients treated with Dex during cardiac surgery. These include fall in BP, pulmonary embolism, and deep venous thrombosis.[14,15]
As DEX can lead to anti-anxiety and sedation without disturbing the respiration of the patients, it can be used in patients undergoing heart surgery. In this study, dexmedetomidine was administered and monitoring of

all the parameters was done throughout the CABG to detect any type of heart arrhythmias. The frequency of various types of heart arrhythmias was compared between the two groups: one treated with DEX and other treated with placebo. DEX treatment followed by continuous follow-up was done to see the role of DEX in the prevention of cardiac arrhythmias including pre-mature atrial contractions, pre-mature ventricular contractions, ventricular tachycardias, atrial fibrillation and other changes in the cardiac rhythm.[16]

Soltani G, et al reported that with the use of dexmedetomidine during cardiac surgery can decrease the incidence of atrial fibrillation in around 90% cases. Patients in DEX group also had a lower mean MAP and HR as compared to that in the control group at points during the surgery and during the stay in the ICU. Data analysis showed the incidence of various cardiac arrhythmias in DEX and placebo group as: PAC (55% vs. 15.7%), PVC (81% vs. 21%), AF (26% vs. 8%), VT (21% vs. 2.6%) $p<0.05$.16 Liu et al. also reported in a similar study that dexmedetomidine decreased the incidence of AF by 18%.[4]

Some studies have shown opposite results. In a larger study, patients of cardiac surgery were monitored for various adverse effects. Among the total patients enrolled in the study, 23.8% developed AF. Around 400 patients were treated with DEX and 400 patients were given a placebo drug. Data analysis showed that AF developed in 30% of the patients in the DEX group and 34% in placebo group. Of the total number of patients included in each group, 5% in the DEX group while 2% of the placebo group, had serious side events. They concluded that clinicians and anesthetists should not reply on the DEX should not be infused to reduce atrial fibrillation or delirium in patients having cardiac surgery.[17] Similarly, Zhu Z, et alanalyzed data from 9 studies with total around 1300 patients. Data analysis showed that DEX group was not significantly linked to decrease in the AF development as compared to the control group.[18]

Yared JP, et al concluded that incidence of AF was 41% in the patients treated with placebo and 30% in the DEX group. It was seen after data analysis of inflammatory markers produced during and after the surgery, that DEX reduced the release of these inflammatory markers.[19]

Turan A, et al reported after collecting data of 765 cardiac surgery patients treated with DEX as a sedative in the post-op period. Patients in the DEX group showed small percentage of atrial arrhythmias.[20]

In another study, cardiac surgeries were performed and DEX was administered in the immediate postoperative period. Data was compared with that of the control group showed that, group of patients who received DEX had much less incidence of tachyarrhythmias (29% versus 38%;$P<0.05$).[21]

As there is controversy in the data regarding the role of dexmedetomidine as compared to other drugs or placebo in altering the incidence of various cardiac arrhythmias, further trials should be done. However many other studies have shown significant decrease in the incidence of heart arrhythmias, specially the incidence of atrial fibrillation.

CONCLUSION

With the use of dexmedetomidine as a sedative and adjuvant of general anesthesia drugs, the incidence of various tachyarrhythmia is decreased during cardiac surgery and in the post-operative period; but the decrease in the incidence was not statistically significant for all types of arrhythmias.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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