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Evaluation of Efficacy of Intravenous Dexmedetomidinein Post-Operative Care of Cardiac Surgery Patients

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Abstract: ***Background: Cardiac surgery is associated with a high risk of cardiovascular and other complications that translate into increased mortality and healthcare costs. The hemodynamic stabilizing and sympatholytic effects of α-2 agonists can potentially reduce postoperative cardiovascular complications. This study was designed to evaluate the efficacy of Dexmedetomidine in cardiac surgery patients in post -operative period. Material & Methods: The present study was undertaken at a tertiary care hospital. 123 adult patients from either gender undergoing various cardiac surgical procedures were included and historical analysis from pooled data of various meta-analyses were then compared. Outcomes measured included mortality and postoperative major adverse cardio-cerebral events (stroke, coma, perioperative myocardial infarction, heart block, or cardiac arrest). Secondary outcomes included renal failure, sepsis, delirium, postoperative ventilation hours, length of hospital stay, and 30-day readmission. Results: Mean Length of stay (LOS) in ICCU was found to be 11.21 +/- SD 5.14 days with no incidence of 30 day re-admission. Mean ventilatory hours was found to be 15.28 +/- SD 5.45 Hrs with 3.3% incidence of post-operative delirium. There was no incidence of renal failure post operatively or requirement of post op dialysis. There were total 19 (15.4%) patients who developed peri-op Myocardial Infarction which was managed conservatively. There were total 16 (13%) patients who developed sepsis which were managed conservatively. There were total 12 mortality (9.75%) in the study group of which 11 (8.9%) occurred within 30 days of surgery in the same hospital admission whereas one occurred in out of hospital setting. Conclusion: Use of Intravenous Dexmedetomidine in the post-operative period of patients undergoing cardiac surgical procedures significantly reduces length of mechanical ventilation and incidence of delirium analysing historically with Meta analytic pooled data.***

Keywords: Dexmedetomidine, Stroke, Coma, Perioperative Myocardial Infarction, Heart Block, Cardiac Arrest, Renal Failure, Sepsis, Delirium, Postoperative Ventilation Hours, Length Of Hospital Stay, 30-Day Readmission

1. Introduction

Approximately 7 million invasive cardiovascular procedures are performed worldwide each year.[1]Currently, more than 67% of patients presenting for cardiac surgery are older with increased comorbidities. The major complication rates for valve and coronary artery bypass graft (CABG) procedures are as high as 30.1% in Society of Thoracic Surgeons (STS) reports.[2] Postoperative delirium, infection, acute renal failure, and major adverse cardio cerebral events (MACEs), which include permanent or transient stroke, coma, perioperative myocardial infarction (MI), heart block, and cardiac arrest, represent major postoperative complications.[3-4] These complications translate into increased mortality and prolonged hospital stays with increased expenditure. More than 50% of all perioperative complications are related to adverse cardiovascular events.[5]

Complications which are common include delirium, post-operative tachyarrhythmia and Acute Kidney Injury (AKI). Delirium is very common finding in older people admitted to hospital.[6-7]& the prevalence of delirium after cardiac surgery can vary from 20–50%, [8-9]Postoperative tachyarrhythmia remain a common complication after congenital cardiac surgery with an incidence between 25 and 50%[10,11] and finally AKI is a recognized complication of cardiovascular surgery and is the one associated with high mortality and costs-of-care[12].

Dexmedetomidine is a highly selective, shorter-acting intravenous α-2 agonist with a α-2 to alpha-1 selectivity ratio of 1600:1.[13] Studies evaluating the hemodynamic stabilizing and sympatholytic effects have shown that α-2 agonists can potentially reduce postoperative cardiovascular complications. Multiple studies have reported that Dexmedetomidine has a protective effect on specific organs, including the heart, brain, kidney, and lungs.[14] In addition, Dexmedetomidine has been shown to have anti-inflammatory properties, decreasing mortality and attenuating plasma cytokine concentrations in laboratory animals exposed to endotoxin in a dose-dependent fashion.[15]

The aim of the present study was to evaluate the potential impact of Dexmedetomidine on hemodynamic stability, arousability, congestive heart failure, myocardial ischemia, arrhythmia, stroke, delirium, infection, and acute renal failure during the postoperative period for patients undergoing cardiac surgery.

2. Material and Methods

The present studywas conducted in the department of Anaesthesiology & Critical care of a tertiary medical centre after getting approval of institutional research and ethical committee and approval from the university.it was a prospective study of two years duration and a total of 123 patients of either sex were included in the study.

Inclusion criteria included patients CABG or valve surgery/ combined with other procedures. Exclusion criteria included Patients undergoing emergency surgery, Off-pump surgery,Surgery requiring deep hypothermic circulatory arrest and Surgery involving the thoracic aorta

Anaesthesia Technique: Under strict aseptic precaution in Operation Theatre under local anaesthesia a wide bore peripheral IV cannula, Right Radial Artery Cannulation & Right Femoral Artery Cannulation was done to enable continuous hemodynamic monitoring. Patients were induced with Inj Etomidate (0.2mg/kg), Inj Fentanyl (3-5 µg/kg) & Rocuronium (0.8-1mg/kg). After induction of patients, central venous cannulation & pulmonary artery cannulation was done. Anaesthesia was maintained with Oxygen/air (50%) Sevoflurane (1-3%) &Inj Atracurium (0.5-1 mg/kg). After sternotomy & Heparinisation, CPB was established once ACT was ≥ 480 sec by cannulation of Ascending Aorta & Right Atrium.Base line ABG and ACT were done.

Preparation of solution: Inj Dexmedetomidine 2ml ampoule containing 100 µg/ml was diluted in 48 ml normal saline giving a concentration of 4 µg/ml in 50 ml syringe and it was thereafter installed in Fresenius Kabi Infusion pump.

Mode of administration: Post-operative Dexmedetomidine intravenous infusion (0.24 to 0.5 µg·kg−1·h−1) initiated without loading dose after cardio- pulmonary bypass before sternal closure titrated to conscious sedation and continued for <24 hours postoperatively till 15 minutes post-extubation in the ICU. The infusion rate of Dexmedetomidine was adjusted according to the manufacturer's package insert and in response to the patients' hemodynamic changes in response to stimulation.

Parameters observed: In hospital stay,30 day re-admission,Composite outcome of MACE(Permanent or transient stroke, Coma,Peri-operative Myocardial Infarction, Heart blocks, Cardiac arrest) Length of ventilation, Post-operative renal failure, Length of ICCU stay & Delirium

Statistical analysis : A historical analysis in which comprehensive literature search using multiple databases including EMBASE, MEDLINE, the Cochrane Library and Science Citation Index and PUBMED Central along with review of abstracts from select major cardiac surgical scientific meetings for unpublished studies was done, and then pooled data was compared with our institutional data.

3. Results

Demographic Profile

A total of 123 patients undergoing various cardiac surgical interventions were studied. The demographic profile of the patients in the study is as follows: (Table 1)

Table 1

Gender	No. of patients	%
Female	39	31.7
Male	84	68.3
Total	123	100.0

Age distribution The patients who participated in this study were in the age group 19 – 77 yrs. with mean age of 59.00 ± 10.70 yrs.(Table 2)

Table 2

Age in years	No. of patients	%
<30	3	2.4
30-40	6	4.9
41-50	8	6.5
51-60	44	35.8
61-70	51	41.5
>70	11	8.9
Total	123	100.0

Mean ± SD: 59.00±10.70 yrs.

Diagnosis of patients studied Table 3

Table 3

Diagnosis	Gender		Total
	Female	Male	
CAD	16(41%)	65(77.4%)	81(65.9%)
CAD+ valvular heart disease	0(0%)	5(6%)	5(4.1%)
ACHD	41(0.3%)	0(0%)	4(3.3%)
VHD	19(48.7%)	14(16.7%)	33(26.8%)
Total	39(100%)	84(100%)	123(100%)

Type of Surgical Interventions(Table 4)

Table 4

Surgery	Gender		Total
	Female	Male	
CABG	16(42.1%)	65(76.5%)	81(65.9%)
CABG + Valve	0(0%)	5(5.9%)	5(4.1%)
Other +CABG	0(0%)	0(0%)	0(0%)
Valve + other	22(57.9%)	15(17.6%)	37(30.1%)
Total	38(100%)	85(100%)	123(100%)

Length of stay and Length of hospital stay: Length of stay (LOS) is defined as admission to Intensive cardiac care unit day before the surgery as per institutional protocol till discharge and length of hospital stay (LOHS) defined as admission to hospital in medical ward for evaluation and work up prior to surgery till the discharge. (Table 5)

Table 5

Variables	Total (n=123)
LOS (DAYS)	
1-2	4(3.3%)
3-5	4(3.3%)
6-10	56(45.5%)
10-20	54(43.9%)
>20	5(4.1%)
LOHS (DAYS)	
1-2	0(0%)
3-5	2(1.6%)
6-10	4(3.3%)
10-20	44(35.8%)
>20	73(59.3%)

LOS: MEAN 11.21 +/- SD 5.14LOHS: MEAN 27.65 +/- SD 19.46

Mean CPB time & Aortic cross clamp time All 123 subjects undergoing cardio vascular interventions were taken on cardio pulmonary bypass machine for conduction of surgeries and procedures. Mean CPB Time was found out to

be 136.41 +/- SD 55.18 Hrs. Mean Cross Clamp Time was found to be 80.43 +/- SD 28.14 Hrs. (Table 6)
Table 6

Variables	*Total (n=123)*
CPB time (min)	
• <60	3(2.4%)
• 60-120	45(36.6%)
• 120-180	55(44.7%)
• >180	20(16.3%)
Cross-clamp time (min)	
• <60	30(24.4%)
• 60-120	81(65.9%)
• 120-180	12(9.8%)
• >180	0(0%)

MEAN CPB TIME 136.41 +/- SD 55.18 Hrs
MEAN CROSS CLAMP TIME 80.43 +/- SD 28.14 HRS

IABP Usage: Out of 123 patients who underwent various cardiac surgical interventions IABP was used in total 4 (3.3%) patients. (Table7)

Table 7

IABP Used	Total
Yes	4(3.3%)
Total	123(100%)

Post op Ventilator hours
All patients undergoing cardiac surgical interventions were not extubated on the OT table but were transferred to the ICCU on 100% oxygen IPPV through the Bain's circuit and put on ventilator maintaining conscious sedation through Inj Dexmedetomidine infusion titrated to effect till the patients met extubation criteria.Mean ventilatory hrs was found to be 15.28 +/- SD 5.45 Hrs. (Table8)

Table 8

Ventilatory Hrs	Total
6-12	30(24.4%)
12-18	75(61%)
18-24	14(11.4%)
>24	1(0.8%)
Total	123(100%)

MEAN VENTILATORY HRS 15.28 +/- SD 5.45 HRS

Post op complications Total 19 patients of 123 (15.4%) developed Peri-op MI which had the highest complication rate. (Table 9)

Table 9

Complications	Total (n=123)
Heart block	3(2.4%)
Cardiac arrest	11(8.9%)
Stroke	0(0%)
Coma	0(0%)
Delirium	4(3.3%)
Sepsis	16(13%)
Post-op renal failure	0(0%)
Post-op dialysis	0(0%)
30 day re-admission	0(0%)
In hospital mortality	11(8.9%)
30 day mortality	11 (8.9%)

Mortality observed
Of 123 patients in the study population total mortality observed were 12 (9.75%) of which in hospital deaths were 11 which occurred within 30 days of admission to the hospital and 1 (0.81%) patient was declared dead after 30 days in the Accident and Emergency department after he had cardiac arrest out of hospital. (Table 10)

Table 10

Mortality	Total(n=123)
In hospital mortality	11(8.9%)
30 day mortality	11 (8.9%)
1 year mortality	1 (0.81%)

4. Discussion

At our institution as a protocol, all patients undergoing cardiac surgical interventions are put on Inj Dexmedetomidine for post op sedation administered through electrically operated infusion pump and titrated as per desired effect.

Multiple studies including a meta-analysis by Yi Yun Lin et al [16] which included 11 publications has confirmed the well-known fact of Dexmedetomidine causing bradycardia and hypotension. In our study we did not encounter such incidents as post facto it was realised that the patients were already on high Inotropic supports in the post-operative period in the ICCU which were gradually reduced till extubation and so was the rate of Dexmedetomidine reduction accordingly maintaining sedation goals of RASS -2 to -3 during ventilator supports to -1 to 0 prior to extubation and so, few incidents of bradycardia if occurred, could not be attributed solely to the use of the drug.

FuhaiJi et al[17] published a study in 2013 where a retrospective analysis was done in a single centre involving 1260 consecutive patients who underwent cardiac surgery from January 1, 2006, to December 31, 2011 evaluating perioperative use of Dexmedetomidine in outcome of cardiac surgeries. The study showed significant reduction of In-hospital mortality (1.23%) in the Dexmedetomidine group versus 4.59% in the non-Dexmedetomidine group (OR, 0.26; 95% CI, 0.11–0.60; P=0.008). Thirty-day mortality was 1.76% in the Dexmedetomidine group versus 5.12% in the non-Dexmedetomidine group (OR, 0.33; 95% CI, 0.16–0.67; P=0.002). Our study shows much higher In-hospital (8.9%) and Thirty- day (8.9%) mortality rates but on further analysis of patient profile it was also found that these patients had multiple co-morbidities which could have also attributed to the poor outcome.

5. Conclusion

From our study it can be concluded thatUse of Intravenous Dexmedetomidine in the post-operative period of patients undergoing cardiac surgical procedures significantly reduces length of mechanical ventilation&reduces the incidence of delirium analysing historically with Meta analytic pooled data.

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