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Comparison of Sevoflurane Plus Dexmedetomidine Infusion and Dexmedetomidine Infusion to Prevent Awareness During Cardiopulmonary Bypass Surgery

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ABSTRACT

Objective: To find out the frequency of intra-operative awareness and to compare the effect of Sevoflurane plus Dexmedetomidine with only Dexmedetomidine infusion in preventing awareness during cardiopulmonary bypass surgery.
Study Design: Quasi-experimental study.
Place and Duration of Study: Adult Cardiac Surgery and Anesthesiology department, Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi Pakistan, from May to Nov 2023.
Methodology: Eighty patients who underwent elective cardiac surgery (valvular and CABG) on Cardiopulmonary Bypass under general anesthesia irrespective of age and gender were recruited through non-probability consecutive sampling with non-random allocation of study participants. Patients were divided into S Group (Sevoflurane plus Dexmedetomidine Group) and D Group (Dexmedetomidine Group). Modified Brice questionnaire was used to assess awareness after 24 hours of surgery. Chi-square and t-test were applied to compare the study variables among study groups. p <0.05 was considered as statistically significant.
Results: A total of 80 patients, who underwent cardiac surgery were recruited. Out of which 40(50.0%) were included in S group and 40(50.0%) were included in D group. 67(83.7%) were males and 13(16.3%) were females. Mean age of the study participants was 59.98±6.85 years. Comparison of study groups showed that 4(10.0%) patients from group-D and 3(7.50%) patients of group-S experienced awareness during surgery (p=1.00). Mean Cardiopulmonary Bypass time was significantly different among study groups (p=0.02)
Conclusion: Patients in S-group experienced slightly less awareness as compared to the patients in D-group but the difference was not statistically significant concluding the fact that Dexmedetomidine is sufficient to avoid awareness during cardiopulmonary bypass for CABG surgery.

Keywords: Awareness, Cardiopulmonary bypass, Dexmedetomidine infusion, Sevoflurane.

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INTRODUCTION

Anesthesiologists and patients equally consider Awareness during General Anaesthesia (AGA) to be a significant concern.[1] Anesthesiologists use their clinical expertise to select the appropriate anaesthetic agents and dosage based on each patient's condition. This ensures that patients are free from pain and maintained at the optimal level of anaesthesia during surgery. Despite the ongoing endeavour, the issue of AGA remains unresolved, with several aspects remaining unexplained.[2] Studies have shown that older age, female gender, not using opiate analgesics, undergoing tracheal intubation, and experiencing peri-operative anxiety were identified as risk factors for AGA.[3,4] AGA may be linked to psychological difficulties such as nightmares, difficulty focusing, recurring memories, sleep disturbances, post-traumatic stress disorder (PTSD), sudden episodes of intense fear, impatience, and even a desire to delay medical treatment.[5] The primary cause of consciousness is the administration of neuromuscular blocking drugs in conjunction with mild anaesthesia.[1] According to research conducted in the United States and Europe, using structured interviews after surgery, it is reported that the occurrence of AGA is around 0.1-0.2%.[6] The prevalence of AGA is estimated to be between 0.1% and 0.2% in the general population, and between 1.5% and 23% in individuals undergoing coronary artery bypass grafting (CABG).[7] Hou *et al*., found that cardiac surgery is often associated with a higher incidence of AGA compared to other surgical procedures.[3] Cardiac procedures performed with Cardiopulmonary Bypass (CPB) may elevate the likelihood of consciousness during general anesthesia.[8]

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To prevent intraoperative awareness, a comprehensive strategy is necessary. This strategy should involve precise administration of drugs, vigilant monitoring of the patient for any movement or autonomic responses to surgical stimulation, avoiding excessive use of muscle relaxants, and using appropriate monitors to assess the depth of anaesthesia.[4] Empirical research has demonstrated that the implementation of bispectral index (BIS) monitoring and the use of targeted volatile anaesthetic gas delivery, along with the presence of alarmed anaesthetic gas monitors, can effectively decrease the occurrence of intraoperative awareness. During CPB, sedation is either provided by intravenous infusion or inhalational agent through heart lung machine.[8] A study conducted by Rashad *et al*., found that during CPB, awareness was lower in patients receiving propofol compared with those who did not receive it.[9]

Dexmedetomidine, an alpha-2 adrenergic agonist is relatively a new drug and found out to be equally effective as Propofol in preventing awareness.[10] Sevoflurane is widely used for anesthesia, it is fluorinated inhalational anesthetic that favors rapid emergence as compared to other inhalational agents.[1] In our setup, Dexmedetomidine plus Sevoflurane or only Dexmedetomidine is being used for sedation during CPB. Very limited international literature and none from our region is available comparing these two agents during CPB for preventing awareness. The purpose of the current study was to find out the frequency of awareness among adult cardiac surgery patients in our institution and to compare Dexmedetomidine plus Sevoflurane with only Dexmedetomidine infusion for intraoperative awareness during cardiopulmonary bypass period.

METHODOLOGY

This Quasi-experimental study was conducted at Adult Cardiac Surgery and Anesthesiology Department in Armed Forces Institute of Cardiology & National Institute of Heart Diseases, Rawalpindi from May to November 2023 after the formal approval from Institutional Ethical Review Board (IERB) (Ltr No. 9/2/R&D/2023/260).

Calculated sample size was n=73 with reference to 5% prevalence of intra-operative awareness in cardiac surgery patients in our setup[9], keeping 95% confidence level and 5% margin of error. We included a total of 80 patients, 40 patients in each group.

Inclusion Criteria: All patients who underwent elective cardiac surgery (valvular & CABG both) on cardiopulmonary bypass under general anesthesia irrespective of age and gender were included.

Exclusion Criteria: The study excluded patients who required prolonged post-operative ventilation for more than 12 hours, patients who needed to be re-opened under general anaesthesia due to persistent blood loss or tamponade, patients with difficult intubation, and patients who experienced post-operative delirium or psychosis and had a low Glasgow Coma Scale (GCS). This was done to eliminate any potential recall bias from the patients during the interview.

All consecutive patients following inclusion criteria and willing to participate were recruited in the study. Written informed consent was taken from subjects before participation in the study. A detailed history was taken from the patient or his/her attendant. Patients were divided into S-Group (Sevoflurane plus Dexmedetomidine Group) (n=40) and D-Group (Dexmedetomidine Group) (n=40) by non-probability consecutive sampling technique with non-random allocation of study participants. Standard anesthesia induction technique and management was done in both groups except sedation during CPB. S-group was given 2.0% volume of Sevoflurane and Dexmedetomidine at dose of 0.75 ug/kg/hr during CPB period. While Group-D received Dexmedetomidine at dose of 0.75 ug/kg/hr. Modified Brice questionnaire was used to assess awareness after 24 hours of surgery before shifting from ICU. Data was recorded by medical officer who was not involved in management of patient to exclude bias.

Data entry and analysis was performed by using Statistical Package for Social Sciences (SPSS) version 28.00. For continuous variables like age, CPB time and CX-time, mean±SD was calculated and for categorical variables like awareness and study groups, frequencies and percentages were calculated. For inferential statistics, Pearson's chi-square test and t-test were used to find association and mean differences of study variables. A *p*-value of <0.05 was considered significant.

RESULTS

A total of 80 patients who underwent cardiac surgery were recruited. Out of which, 40(50.0%) were included in S-group (Sevoflurane plus Dexmedetomidine Group) and 40(50.0%) were included in D-group (Dexmedetomidine Group). 67(83.7%) were males and 13(16.3%) were females. Mean age of the study participants was 59.98±6.85

years (Age range: 47-71 years). Mean CPB time was 83.43±7.62 minutes and mean cross-clamp (CX) time was 58.30±7.48 minutes as shown in Table-I.

Comparison of study groups showed that 4(10.0%) patients of group-D and 3(7.5%) patients of group-S had awareness during surgery (p=1.00). Statistically significant difference of CPB time was observed in patients with and without awareness (p=0.02) among the study groups, CPB time was found to be more prolonged (89.71±7.34 min) in AGA patients. However, no statistically significant findings were seen with respect to age (p=0.68) and cross-clamp time (p=0.12) as mentioned in Table-II.

Table-I: Demographic and Intra-Operative Parameters of the Study Participants (n=80)

Variables	Total=80 Mean±SD	GroupD(n=40) Mean±SD	Group-S(n=40) Mean±SD	p-value
Age (years)	59.98±6.85	59.47±7.07	60.50±6.67	0.50
CPB time (min)	83.43±7.62	83.70±8.76	83.17±6.39	0.76
Cross-clamp time (min)	58.30±7.48	58.60±7.74	58.00±7.28	0.72
Presence of Awareness during surgery (Frequency (%)	7(8.8%)	4(10.0%)	3(7.5%)	1.00

Table-II: Comparison of Awareness During General Anesthesia (AGA) Among Study Participants (n=80)

Study variables		Awareness		p-value
		Present (n=07) Frequency (%)	Absent (n=73) Frequency (%)	
Study Groups Frequency (%)	Group-D (n=40)	4(57.1%)	36(49.3%)	1.00
	Group-S (n=40)	3(42.9%)	37(50.7%)	
Age (years) (mean±SD)		61.00±6.68	59.89±6.90	0.68
CPB time (min) (mean±SD)		89.71±7.34	82.83±7.42	0.02
CXT (min) (mean±SD)		62.42±8.24	57.90±7.34	0.12

CPB: Cardiopulmonary bypass time; CXT: Cross-clamp time

DISCUSSION

Our study compared the effect of Dexmedetomidine plus Sevoflurane infusion with Dexmedetomidine infusion to prevent awareness during cardiopulmonary bypass surgery in 80 patients. 40(50.0%) patients included in S-group (Sevoflurane plus Dexmedetomidine Group) and 40(50.0%) patients included in D-group (Dexmedetomidine Group) had the mean age of 59.98±6.85 years. Our study reported awareness in 7(8.8%) patients. Comparison showed that 4(10.0%) patients of group-D and 3(7.5%) patients of group-S had awareness during surgery (p=1.00). Similar to our results, Vali *et al*., and Gupta *et al*., also reported no significance with demographic data (p>0.05).[8,11] In our study, we found that CPB time was more prolonged (89.71±7.34 min) in AGA patients and it was statistically significant (p=0.02). Contrary to our study, no significant mean difference of cardiopulmonary bypass time was reported 50.26±7.59 minutes (35 - 70) in a study conducted by Imantalab V. *et al*.[8]

Inadvertent awareness during GA can lead to intraoperative discomfort and result in subsequent mild to severe long-term effects such as flashbacks, nightmares, hyperarousal, or post-traumatic stress disorder. The proportion of patients experiencing AGA can vary by up to 200 folds in different studies.[5] Heggy *et al*., reported the AGA rate of one case out of 200 patients (1:200).[12] On contrary, out of 59 patients investigated by Celebioglu *et al*., 5(16.6%) provided a positive history of awareness.[13] Likewise a previous study by Rashad *et al*., conducted in a Pakistani population reported intra-operative awareness of 5%.[9] Similarly, Vali *et al*., investigated patients with AGA during cardiac surgery and reported 4.3% incidence.[8] The incidence of awareness reported by our study was 8.8%. Considering the regional/ geographical difference, population size, and reported incidence of intraoperative awareness by other researchers, it is reasonable to say that result is likely favorable. It is uncertain from these contradictory findings if the variations in occurrence were due to differences in patient demographics, anesthesia approach, clinical significance, or detection method.[12]

We assessed awareness after 24 hours of surgery. Rashad *et al*., also conducted interview after 24 to 72 hours following the procedure.[9] Vali *et al*., also interviewed the patients once i.e. during 3 - 6 days after surgery.[8] In contrast to our research, Anna and colleagues conducted two interviews, first in the ICU and other after one week. Nearly fifty percent of their cases were identified after the second interview. In

addition, the author presented a significant discovery: by doing a postoperative survey within 30 days following the operation, they were able to determine cases of AWR that were not previously recognized during their regular screening i.e. 1 day after the surgery. The identification of AWR is intricate and relies on the interview approach and the time of the interview. Reliably detecting every case of awareness is not possible. Other studies also affirm that a multi-time period evaluation is required to obtain sufficient identification of AWR.[6]

The level of awareness can be controlled by the drug concentration used; volatile inhaled anesthetics and proper use of these measures can decrease the incidence.[11] Furthermore, the choice of anaesthetic agents is dependent upon the patient's specific medical problems, co-morbidities, as well as the associated costs and drug availability, all of which are influential variables.[8] Frequent administration of sevoflurane sedation during CPB can potentially decrease the occurrence of consciousness.[9] It is reported in literature that dexmedetomidine facilitates enhanced patient alertness and responsiveness to verbal commands in sedation, hence facilitating improved monitoring and communication between healthcare practitioners and the patient.[10] Likewise, our data suggested that the presence of awareness was more in the dexmedetomidine group (4/40) as compared to the Sevoflurane group (3/40). In contrast to our findings, a study by Momeni *et al*., also reported the reduced awareness (6%) in dexmedetomidine group.[14] Ahmed *et al*., also concluded that dexmedetomidine can serve as a substitute sedative drug to prevent consciousness and memory in cardiac surgeries.[15] Chattopadhyay *et al*., utilised dexmetedomidine infusion as a preventive measure against awareness in a study involving 60 patients undergoing general anesthesia. Subjects were administered either propofol at a dose of 1 mg/Kg, followed by a continuous infusion at a rate of 50 mcg per Kg per minute, or dexmedetomidine at a dose of 1 mcg/kg, followed by a continuous infusion at a rate of 0.5 mcg/kg per hour. All of the patients had no memory of any event that occurred during the surgery. Nevertheless, extensive prospective investigations are required to validate these findings.[16] On contrary, in line with our data, a recent study by Harsoor *et al*., also observed the same findings i.e. dexmedetomidine induced arousable sedation.[17] Similarly, the results by Hu *et al*., indicated that sevoflurane were associated with a significantly reduced intra-operative awareness rate compared to the dexmedetomidine but the incidence of side effects was lower with dexmedetomidine.[18]

LIMITATIONS OF STUDY

Our study had a few limitations. It was a single-centered study with smaller sample size, patients were interviewed once after surgery and the long-term psychological detrimental effects were not assessed in compliance with AGA. Future research including randomized controlled trials and systematic reviews with larger sample size is required.

CONCLUSION

Patients in Dexmedetomidine plus Sevoflurane group experienced slightly less awareness as compared to Dexmedetomidine group but the difference was not statistically significant concluding that only Dexmedetomidine is sufficient to avoid awareness during cardiopulmonary bypass for CABG surgery.

Conflict of Interest: None

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Authors' Contribution:

Following authors have made substantial contributions to the manuscript:

MAA & WA: Concept, drafting the manuscript, data acquisition and analysis, approval of final version to be published

RM & SARAS: Study design, critical review, approval of final version to be published

IBM & MAM: Data interpretation, critical review, approval of final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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