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Original Research Article

Hemodynamic Response of Dexmedetomidine as an Adjuvant to Fentanyl in Patients Undergoing Valvular Heart Surgery: A Comparative Study

Manish Kumar Mourya[1], Rajbala[2], Anurag Gill[3], Roshan Lal Jajoriya[4], Indu Verma[5]

[1]Medical Officer, Department of Anesthesia, SMS Medical College & Hospital, Jaipur
[2]3rd year PG Resident, Department of Anesthesia, SMS Medical College & Hospital, Jaipur
[3]Senior Resident, Department of Anesthesia, SMS Medical College & Hospital, Jaipur
[4]Medical Officer, Department of Anesthesia, SMS Medical College & Hospital, Jaipur
[5]Senior Professor, Department of Anesthesia, SMS Medical College & Hospital, Jaipur

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Corresponding author: Dr Rajbala
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Abstract

Background: Rheumatic fever (RF) and rheumatic heart disease (RHD) pose significant health risks in developing countries and sporadically in developed economies. Echocardiographic studies highlight the burden of RHD, necessitating updated diagnostic guidelines. RHD, a non-suppurative manifestation of Group A streptococcal pharyngitis, remains a major cause of morbidity and mortality in developing nations, including India with an estimated 2.0 to 2.5 million affected individuals.

Methods: This study included adult patients undergoing cardiac surgeries for valve replacement. They were randomized into two groups: one receiving dexmedetomidine infusion and the other saline infusion. Preoperative assessments and baseline data collection were performed. General anesthesia was induced, and intraoperative hemodynamic monitoring was conducted. After surgery, renal function parameters were monitored in the ICU.

Results: The study evaluated the hemodynamic response of dexmedetomidine as an adjuvant to fentanyl in patients undergoing valvular heart surgery. Dexmedetomidine demonstrated significant effects on heart rate, blood pressure, and plasma catecholamine concentrations during emergence from general anesthesia. The combination of dexmedetomidine and fentanyl resulted in better hemodynamic stability compared to fentanyl alone.

Conclusion: In valvular heart surgery, adding dexmedetomidine to fentanyl improved hemodynamic stability. Dexmedetomidine positively affected heart rate, blood pressure, and plasma catecholamine levels, showing promise for perioperative management. Further research is needed to validate these findings and investigate long-term benefits and safety of dexmedetomidine in this setting.

Keywords: Rheumatic Fever, Rheumatic Heart Disease, Diagnostic Criteria.

Introduction

Rheumatic fever (RF) and rheumatic heart disease (RHD) continue to pose significant health risks in many developing countries, as well as sporadically in developed economies. Despite concerns about the adequacy of the diagnostic criteria, echocardiographic and Doppler studies have revealed a substantial burden of RHD, suggesting the need for updated diagnostic guidelines. RHD develops as a non-suppurative manifestation of Group A beta-hemolytic streptococcal (GAS) pharyngitis, which is widely accepted as an immunological disorder following GAS infection [1]. While developed countries have witnessed a decline in RF cases, RHD remains a prominent cause of morbidity and mortality in developing nations. In India alone, with a population of around 1.3 billion, the estimated prevalence of RHD is approximately 1.5-2 cases per 1000 individuals, indicating a substantial patient population of 2.0 to 2.5 million [2].

The severity of RF lies in its potential to cause cardiac damage, with carditis being a common clinical finding during the initial attack. Rheumatic carditis is characterized by pericardial, myocardial, and endocardial involvement, with pericarditis occurring in around 15% of cases [3]. The most significant permanent damage in RF is caused by rheumatic endocarditis, primarily affecting the cardiac valves. Mitral valve involvement is observed in 90 to 95% of cases, often accompanied by aortic valve disease in 20 to 25% of patients. In contrast, isolated aortic valve involvement is rare, while tricuspid valve and pulmonary valve involvement are even less common. Valvular lesions resulting from RHD include mitral stenosis (MS), mitral regurgitation (MR), aortic stenosis (AS), and aortic regurgitation (AR). MS and AS are the most frequently encountered valvular lesions in clinical settings [4].

In the context of valvular heart surgery, the anesthetic management of patients with MS focuses on controlling heart rate, ventricular preload, diminishing right and left ventricular contractile function, and addressing coexisting pulmonary hypertension. Tachycardia is poorly tolerated due to reduced diastolic filling time of the left ventricle, making it crucial to maintain sinus rhythm and avoid increased sympathetic activity [5]. Maintaining adequate preload and preventing increases in right heart pressures and pulmonary arterial pressures are essential to manage MS effectively. Dexmedetomidine, an α2 adrenergic agonist, is considered for maintaining a heart rate that allows sufficient time for left atrial and left ventricular filling, ensuring normal cardiac output and arterial blood pressure during anesthesia induction and maintenance for MS cases [6].

Dexmedetomidine exhibits highly specific α2 agonist properties and possesses anesthetic, analgesic, and sympatholytic effects. Its sympatholytic action is manifested by reductions in arterial blood pressure, heart rate, and norepinephrine release, making it a potential candidate for attenuating perioperative increases in blood pressure and heart rate [7] In our study, we aim to investigate the hemodynamic response of dexmedetomidine when used as an adjuvant to fentanyl in patients undergoing valvular heart surgeries. By examining the effects of dexmedetomidine on heart rate, blood pressure, and plasma catecholamine concentrations during emergence from general anesthesia, we can evaluate its potential benefits in optimizing hemodynamic stability in these patients [8].

Methods

Study Location: This study was conducted in department of anesthesia, cardiac surgery operation theatre, S.M.S. Medical College, Jaipur.

Study Design: A prospective, randomized, double blind, hospital based interventional study.

Study Period: After the approval of plan by research review board and institutional ethics committee till the completion of desired sample size.

Sample Size: A sample of 30 cases in each group was adequate at 95% confidence and 80% power to verify the expected minimum difference of 7(±14) in change in H.R. from baseline to 10 min. post induction in both groups. This sample size is adequate for all other study variable too.

Study Universe: Patients undergoing cardiac surgery under general anesthesia.

Blinding: The anaesthetist who gave anaesthesia was different from the anaesthetist who would observe the study variables.

Randomization: Sixty eligible cases were allocated into two study groups using sealed envelope method.

Study Groups: Patients were randomly allocated into 2 groups. (30 patients in each group).

Group A (n=30): patients received dexmedetomidine with fentanyl

Group B (n=30): patients received fentanyl with normal saline.

Eligibility criteria

Inclusion Criteria

1. ASA grade II and III Patients
2. Patients willing to give written informed consent.
3. Age between 18 to 50 years
4. Weight 40 to 70 kg. Exclusion Criteria
5. Patients not willing to participate in study.
6. Patients having known allergy to anaesthetic agents used in study.
7. Patients having coagulopathies.
8. Patients with unstable hemodynamics or sick patients.
9. patients with renal failure, congestive cardiac failure.
10. Patients with history of adrenal insufficiency, serious psychiatric, endocrine and neurological illness.

Procedure

This study was conducted in the Department Of Anaesthesia SMS Medical College in cardiac anaesthesia unit after obtaining permission from the institutional ethical committee and review board no. 167-(2)/MC/EC/2020. Adult patients from the age group 18 year to 50 years included who were undergoing cardiac surgeries for replacement of valve due valvular heart disease. valvular heart lesion included MS, AS, MR, AR etc. Patients Were randomized using opaque sealed envelopes. Opaque sealed envelopes were numbered serially. Envelopes were used for allocation, concealment. PAC was done a day before the surgery which included history and clinical assessment, which included airway assessment, routine blood investigations like CBC, HB, TLC, DLC, ESR, RFT, LFT, Platelet Count, Activated partial thromboplastin time(APTT), ECG, etc. Cardiac examination included history of easy fatigability, dyspnea, orthopnea, examination for signs of congestive heart failure (CHF) such as hepatomegaly, pedal edema, raised jugular venous pressure, basal crepts. Written informed consent was taken for the surgery under general anaesthesia. Patient‘s were kept fasting overnight as per the institutional protocol. On arrival in the operation theatre, fasting status, written informed consent and PAC were checked. Routine noninvasive monitors attached and baseline parameters i.e. heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), and SPO2 were noted. ECG & ETCO2 were attached to the patient. General assessment for mental status, weight, heart

were recorded. Demographic data including age, sex, weight, ASA grade, before premedication were recorded. IV line secured and IV fluids was started .Patients were oxygenated with 100% oxygen for 3 minutes both groups. Patients were induced with etomidate 0.3 mg/kg, fentanyl 2µg/kg + Rocuronium 0.9 mg/kg.

Hemodynamic data will collected just before intubation. Patients were intubated with appropriate size of endotracheal tube. After tracheal intubation an infusion of fentanyl 1µg/kg/hr were started in both groups using syringe pump. In Group A. Bolus of dexmedetomidine 0.5 µg /kg/hr in 100 ml saline were given in 10 min After that Another infusion of 0.5 µg /kg/hr of in 50 ml of saline were given via syringe pump. And in group B Bolus of 100 ml saline were given in 10 min After that another infusion of 50 ml of saline were given via syringe pump. Intra op heart rate systolic BP, diastolic BP, MAP, SPO2 were monitored.

All drugs and infusion were stopped when patient was taken on cardiopulmonary bypass except Dexmedetomidine infusion to access its effect on renal function After completion of surgery. Patient was shifted to cardiac surgery ICU. Renal function parameter monitoring from post-surgery day 1,2,3. Then statistical analysis result and conclusion analysis.

Results

Table 1: Comparison of HEART RATE (BEATS/MIN)

	Group A		Group B		Results
	Mean	SD	Mean	SD	
Baseline	84.00	11.58	81.37	4.50	0.250 (NS)
Post Induction	75.53	1.94	81.57	4.30	p<0.001 (S)
1 min	68.67	3.65	60.00	2.52	p<0.001 (S)
5 min	61.40	1.40	60.60	2.24	0.102 (NS)
10 min	66.93	1.64	63.80	2.12	p<0.001 (S)
20 min	70.73	2.99	75.53	2.91	p<0.001 (S)
30 min	75.67	2.23	75.60	1.99	0.903 (NS)

S = Significant ; NS = Non Significant

The results of the study showed that there were significant differences in heart rate between Group A (dexmedetomidine infusion) and Group B (saline infusion) at various time points. Post-induction, 1 minute, 10 minutes, and 20 minutes after induction, Group A had significantly lower heart rates compared to Group B (p<0.001). However, there were no significant differences in heart rate between the two groups at baseline, 5 minutes, and 30 minutes after induction.

Table 2: Comparison of SBP (in mmHg) among two groups.

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	126.67	8.13	122.47	21.40	0.319 (NS)
Post Induction	116.00	2.63	121.87	3.10	p<0.001 (S)
1 min	110.73	2.90	115.00	3.70	p<0.001 (S)
5 min	115.60	2.19	117.80	1.61	p<0.001 (S)
10 min	119.27	2.80	121.67	2.35	0.0006 (S)
20 min	120.60	5.49	123.07	4.81	0.069 (NS)
30 min	121.60	2.06	121.93	2.95	0.613 (NS)

S = Significant ; NS = Non Significant

The comparison of systolic blood pressure (SBP) between Group A (dexmedetomidine infusion) and Group B (saline infusion) revealed significant differences at post-induction, 1 minute, 5 minutes, and 10 minutes after induction, with Group A having lower SBP values than Group B ($p<0.001$). However, there were no significant differences in SBP between the two groups at baseline, 20 minutes, and 30 minutes after induction.

Table 3: Comparison of DBP (mmHg) among two groups

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	76.37	5.28	77.63	3.82	0.291 (NS)
Post Induction	73.40	3.33	74.13	3.44	0.404 (NS)
1 min	72.60	1.40	74.00	1.74	0.001 (S)
5 min	72.27	2.18	74.43	2.14	0.0002 (S)
10 min	73.47	2.22	77.40	2.21	p<0.001 (S)
20 min	70.90	8.65	74.60	2.69	0.029 (S)
30 min	75.40	2.04	75.03	2.17	0.503 (NS)

S = Significant ; NS = Non Significant

The comparison of diastolic blood pressure (DBP) between Group A (dexmedetomidine infusion) and Group B (saline infusion) showed significant differences at 1 minute, 5 minutes, 10 minutes, and 20 minutes after induction, with Group A having lower DBP values than Group B ($p<0.001$, $p=0.001$, $p=0.0002$, and $p=0.029$, respectively). However, there were no significant differences in DBP between the two groups at baseline, post-induction, and 30 minutes after induction.

Table 4: Comparison of MAP (mmHg) among two groups

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	96.47	5.80	95.28	7.62	0.65 (NS)
Post Induction	87.60	2.20	90.04	2.68	0.0002 (S)
1 min	85.31	0.87	87.67	1.38	p<0.001 (S)
5 min	86.71	1.95	88.89	1.59	p<0.001 (S)
10 min	88.73	1.98	92.16	1.65	p<0.001 (S)
20 min	87.47	6.22	90.76	2.43	0.009 (S)
30 min	90.80	1.66	90.67	2.18	0.790 (NS)

S = Significant ; NS = Non Significant

The comparison of mean arterial pressure (MAP) between Group A (dexmedetomidine infusion) and Group B (saline infusion) revealed significant differences at post-induction, 1 minute, 5 minutes, and 10 minutes after induction, with Group A having lower MAP values than Group B ($p=0.0002$, $p<0.001$, $p<0.001$, and $p<0.001$, respectively). Additionally, at 20 minutes after induction, there was a significant difference, with Group A having a higher MAP value than Group B ($p=0.009$). However, there were no significant differences in MAP between the two groups at baseline and 30 minutes after induction.

Discussion

This open-label randomized trial aimed to compare the hemodynamic response when using Dexmedetomidine as an adjuvant to fentanyl in patients with valvular heart

disease undergoing surgical replacement. The study included adult patients with stable cardiac function, similar indications for surgical repair, and managed in the same setting. The primary goal was to ensure the anesthetic technique alleviated pain, anxiety, and stress, which could lead to cardiorespiratory and hemodynamic compromise. This was achieved through pre-procedure counseling, accurate drug dosage calculation, appropriate pre-medication, and prevention of hypothermia during the procedure [9].

The study found that Group A, which received dexmedetomidine added to fentanyl, exhibited more stable heart rates compared to Group B, which received fentanyl alone. Dexmedetomidine was shown to maintain a controlled heart rate more effectively during the pre-bypass period. Additionally, Group A experienced lower and more stable blood pressure changes (systolic, diastolic, and mean arterial pressure) compared to Group B. During the induction of anesthesia and the pre-bypass stage of cardiac surgery, maintaining control over heart rate is crucial, especially for patients with tight mitral stenosis, as high pulmonary artery pressure can lead to pulmonary congestion and impaired gas exchange [10]. Dexmedetomidine, as an alpha-2 adrenoceptor agonist, acts on presynaptic and postsynaptic locations in the central nervous system. It inhibits norepinephrine release and pain signal propagation, leading to decreased sympathetic activity, heart rate, and blood pressure. The study aimed to test the efficacy of dexmedetomidine in this context [11].

The study demonstrated that dexmedetomidine, in combination with fentanyl, effectively controlled heart rate and blood pressure during the pre-bypass period. The drug's sedative and anxiolytic effects, along with its analgesic-sparing properties, contributed to its effectiveness. Dexmedetomidine has also been used in combination with other drugs in similar contexts. Tracheal intubation and surgical procedures can trigger stress responses, resulting in increased heart rate and blood pressure. Dexmedetomidine has been shown to activate alpha-2 receptors in the medullary dorsal motor neuron complex, reducing blood pressure. Different anesthetic regimens can induce varying degrees of stress response, leading to hemodynamic instability [11]. Dexmedetomidine can effectively inhibit stress responses, maintaining hemodynamic stability throughout the procedure. The demographic variables, including age, sex, weight, and height, were comparable between Group A and Group B, with no statistically significant differences observed [13].

Regarding hemodynamic variables, the study found that heart rate was significantly decreased and more stable in Group A (dexmedetomidine-fentanyl) compared to Group B (fentanyl-saline). Dexmedetomidine's action as an alpha-2 adrenoceptor agonist and its sedative, analgesic, and anti-anxiety effects contributed to these findings. Systolic blood pressure was significantly lower in Group A compared to Group B. Previous studies have shown that dexmedetomidine can effectively reduce heart rate and arterial blood pressure during surgery, supporting the findings of this study [14]. Diastolic blood pressure was also significantly decreased in Group A compared to Group B. Studies conducted on children and older patients with less complex cardiac defects have reported similar results, confirming the efficacy of dexmedetomidine in attenuating the hemodynamic response without adverse effects. Mean arterial pressure was significantly lower in Group A, consistent with findings from other studies that have reported lower mean arterial pressure in patients receiving dexmedetomidine anesthesia [15].

Regarding renal function, the study findings align with previous research that suggests the renal protective effect of dexmedetomidine in the post-bypass surgical repair, and were managed in the same setting. The objective was to assess whether the addition of Dexmedetomidine to fentanyl could maintain a controlled heart rate and stabilize blood pressure during the pre-bypass period more effectively than fentanyl alone [16]. The induction of anesthesia and the pre-bypass stage of cardiac surgery are critical, particularly for patients with tight mitral stenosis, as it is often associated with high pulmonary artery pressure and the potential for pulmonary congestion and impaired gas exchange. Therefore, controlling the heart rate during this stage is crucial to reduce pulmonary congestion, allow for coronary perfusion, improve myocardial oxygenation, and decrease the workload on the heart and oxygen demand [17]. Dexmedetomidine is an α2 adrenoceptor agonist that acts on both presynaptic and postsynaptic locations in the central nervous system. Its presynaptic activation inhibits the release of norepinephrine and blocks pain signals, while its postsynaptic activation, particularly in the locus coeruleus, inhibits sympathetic activity, reduces heart rate and blood pressure. Fentanyl, on the other hand, is commonly used in various cardiac surgeries at different doses [18].

The study found that the group receiving Dexmedetomidine along with fentanyl (Group A) demonstrated a more stable heart rate during the pre-bypass period compared to the group receiving fentanyl alone (Group B). The Dexmedetomidine-fentanyl group also showed lower and more stable blood pressure changes (systolic, diastolic, mean arterial pressure) than the fentanyl-only group. Several studies support the findings of this study. M. Khalil *et al*. conducted a study using Dexmedetomidine and propofol for sedation in patients undergoing transcatheter aortic valve implantation (TAVI) under local anesthesia [19]. They observed a significant reduction in heart rate in the Dexmedetomidine group compared to the propofol group. Another study by Zi Wang *et al*. showed that Dexmedetomidine anesthesia effectively maintained hemodynamic stability and reduced myocardial injury in patients undergoing heart valve replacement. Tracheal intubation and surgical procedures can trigger a stress response, leading to increased heart rate and blood pressure. Dexmedetomidine has been shown to activate α2 receptors in the medullary dorsal motor neuron complex, reducing blood pressure. Various anesthesia regimens can induce different degrees of stress response, resulting in increased secretion of glucagon, catecholamines, and norepinephrine, leading to hemodynamic instability [20]. Dexmedetomidine can inhibit these stress responses and maintain hemodynamic stability. It also has sedative and analgesic effects, inhibits the release of norepinephrine, reduces sympathetic nervous system activity, and regulates blood pressure during the recovery period [21].

The demographic variables such as age, sex, weight, and height were comparable between Group A and Group B, showing no significant difference. However, the hemodynamic variables demonstrated notable distinctions between the two groups. Heart rate was significantly decreased and more stable in Group A (Dexmedetomidine-fentanyl) compared to Group B (fentanyl-saline). Similarly, systolic blood pressure, diastolic blood pressure, and mean arterial pressure showed a significant decrease in Group A compared to Group B. Regarding the impact on renal function, studies have shown that Dexmedetomidine infusion in the post-bypass period can have a protective effect on kidney function. Mukhtar *et al*. reported a reduced incidence of acute kidney injury (AKI) and complications with the use

of post-bypass Dexmedetomidine infusion. Ji *et al*. also found that post-bypass infusion of Dexmedetomidine was associated with a reduced incidence of AKI and improved patient outcomes in cardiac surgery [22-26].

In conclusion, the addition of Dexmedetomidine to fentanyl during the pre-bypass period of cardiac surgery appears to have beneficial effects on heart rate and blood pressure stability. Dexmedetomidine's ability to reduce sympathetic activity, inhibit stress responses, and provide sedation and analgesia contributes to its positive impact on hemodynamic stability. The findings of this study align with previous research highlighting the advantages of Dexmedetomidine in maintaining hemodynamic control and improving patient outcomes. However, it is important to note that this study focused specifically on the pre-bypass period and its immediate effects. Further research is needed to explore the long-term effects and potential complications associated with the use of Dexmedetomidine in cardiac surgery. Additionally, factors such as dosage, infusion rates, and patient-specific considerations should be taken into account when implementing this approach [27,28].

Overall, the findings support the use of Dexmedetomidine as an adjunct to fentanyl during the pre-bypass period of cardiac surgery, with the potential to enhance hemodynamic stability and improve patient outcomes. This combination provides an effective strategy for managing patients with tight mitral stenosis or other conditions requiring careful control of heart rate and blood pressure during cardiac surgery.

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