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The Hemodynamic Effects of Ketamine in Coronary Artery Bypass Graft Surgery

Luay Badr Hasan[1*], Othman Ismat Abdulmajeed[2] and Sabah Noori Al-Saad[2]
[1]College of Medicine, Hawler Medical University, Head of Cardiac anesthesia, Erbil cardiac center, Erbil, Kurdistan Region, Iraq
[2]College of Medicine, University of Baghdad, Baghdad, Iraq
luay.badrhasan@yahoo.com

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Abstract

Coronary artery bypass graft (CABG) surgery represents roughly 500000 agent methodology for each year in the United States. In spite of the fact that there is incredible interest and advancement in contrasting options to CABG, this agent technique remains a suitable, showed treatment for a substantial number of patients. The point of our study was to watch the haemodynemic impact of ketamine amid pre and post acceptance of anesthesia for patient experiencing coronary artery bypass graft surgery. A forthcoming trial similar study done. The study included 56 patients requiring CABG surgery admitted to Erbil heart focus. The patients were arbitrarily partitioned into two practically identical gatherings. We utilized for acceptance of anesthesia to the primary gathering low measurement of Sodium thiopental 1mg/kg, while for the second gathering Ketamine 2mg/kg. With institutionalized measurements of Midazolam and Fentanyl Pavilone and 1 MAC Isoflorane. Circulatory strain, mean blood vessel weight and heart rate were recorded three times for every patient in both gatherings (1 minute pre enlistment, 1 moment and 5 minutes post acceptance). The study demonstrated that the ketamine amass haemodynemicly is more steady than Sodium thiopental group.

Keywords: CABG surgery, Cardiac anesthesia, Hemodynamic changes, Ketamine, Sodium thiopental.

Introduction

Coronary artery bypass graft (CABG) surgery represents roughly 500000 operatives techniques for every year in the United States. In spite of the fact that there is awesome interest and advancement in contrasting options to CABG, this operatives methodology remains a fitting, showed treatment for countless. Acceptance of anesthesia in patients with coronary illness is risky on the grounds that the disabled circulatory framework is less tolerant of depression. Each cardiac cycle consists of a period of relaxation (diastole) followed by ventricular contraction (systole). During diastole the ventricles are relaxed to allow filling. In systole the right and left ventricles contract, ejecting blood into the pulmonary and systemic circulations respectively.

The left ventricle pumps blood into the systemic dissemination through the aorta. The systemic vascular resistance (SVR) is 5–7 times more noteworthy than the pneumonic vascular resistance (PVR). The free mass of the LV and the interventricular septum shape the greater part of the bulk in the heart. A normal LV can develop intraventricular pressures up to 300 mmHg. Coronary perfusion to the LV occurs mainly in diastole. The right ventricle receives blood from the venaecavae and coronary circulation, and pumps it via the pulmonary vasculature into the LV[1]. Since PVR is a fraction of SVR, pulmonary arterial pressures are relatively low and the wall thickness of the right ventricle (RV) is much less than that of the LV.

The RV thus resembles a passive conduit rather than a pump. Coronary perfusion to the RV occurs continuously during systole and diastole. In spite of the anatomical differences, the mechanical behaviour of the RV and LV is very similar. Parasympathetic fibres fundamentally innervate the atria and directing tissues. Acetylcholine follows up on particular cardiovascular muscarinic receptors (M2) to create negative chronotropic, dromotropic, and inotropic impacts. Conversely, thoughtful filaments are all the more broadly disseminated all through the heart. Cardiovascular thoughtful filaments begin in the thoracic spinal rope (T1–T4) and go to the heart at first through the cervical ganglia (stellate) and after that as the cardiovascular nerves. Norepinephrine discharge causes positive chronotropic, dromotropic, and inotropic impacts fundamentally through enactment of 1-adrenergic receptors. 2-Adrenergic receptors are less in number and are discovered essentially in the atria; initiation builds heart rate and, to a lesser degree, contractility. 1-Adrenergic receptors have a positive inotropic effect2.Blood dependably streams, obviously, from zones of high weight to territories of low weight, with the exception of in specific circumstances when force briefly supports stream. The relationship between mean stream, mean weight, and resistance in the veins is practically equivalent to for the most part to the relationship between the present, electromotive power, and resistance in an electrical circuit communicated in Ohm's law:

Current (I) = Electromotive force (E) / Resistance (R)
Flow (F) = Pressure (P) / Resistance (R)

Flow in any portion of the vascular system is equal to the effective perfusion pressure in that portion divided by the resistance**.** The effective perfusion pressure is the mean intraluminal pressure at the arterial end minus the mean pressure at the venous end. The units of resistance (pressure divided by flow) are (dyne.s/cm^5). To avoid dealing with such complex units, resistance in the cardiovascular system is sometimes expressed in R units**,** which are obtained by dividing pressure in mm Hg by flow in mL/s. The continuous blood stream which flows is pulsatile in vast arteries on account of the heart's cyclic movement; when blood achieves the systemic vessels, stream is consistent (laminar). The mean weight in extensive courses, which is regularly around 95 mm Hg, falls about to zero in the expansive systemic veins that arrival blood to the heart. The biggest weight drop, almost half, is over the arterioles, which represent the larger part of SVR[3].

MAP is proportionate to the result of SVR x CO. This relationship depends on a similarity to Ohm's law as connected to the flow:

$$\mathrm{MAP} - \mathrm{CVP} \approx \mathrm{SVR} \times \mathrm{CO}$$

Since CVP is regularly little contrasted and MAP, the previous can more often than not be disregarded. From this relationship, it is promptly evident that hypotension is the aftereffect of a lessening in SVR, CO, or both: To keep up blood vessel circulatory strain, abatement in one must be repaid by an expansion in the other. Guide can be measured as the incorporated mean of the blood vessel weight waveform. Then again, MAP might be assessed by the accompanying equation:

$$\mathrm{MAP} = \text{Diastolic pressure} + \frac{\text{Pulse Pressure}}{3}$$

Where pressure of the pulse is the distinction amongst systolic and diastolic in the so called blood pressure. We can assume that Arterial pulse pressure is straightforwardly identified with stroke volume yet is conversely proportional to the consistence of the arterial tree. Hence, diminishes in pulse beat pressure might be because of a decline in stroke volume, an expansion in SVR, or both. The Arerial blood pressure is controlled by a progression of prompt, middle, and long haul alterations that include complex neural, humeral, and renal components[4]. Moment to-moment control of blood pressure is fundamentally the capacity of autonomic sensory system reflexes. Changes in blood pressure are detected both halfway (in hypothalamic and areas of the brain stem) and incidentally by particular sensors (baroreceptors). Diminishes in arterial blood pressure improves thoughtful tone, increment adrenal discharge of epinephrine, and stifle vagal movement. The subsequent systemic vasoconstriction, rise in heart rate, and improved cardiovascular contractility increment blood pressure. On the other hand, hypertension diminishes thoughtful surge and upgrades vagal tone[4].

Over the span of a couple of minutes, managed diminishes in arterial pressure together with upgraded thoughtful surge actuate the renin–angiotensin–aldosterone framework increment emission of arginine vasopressin (AVP), and change ordinary narrow liquid trade. The impacts of slower renal mechanisms get to be obvious inside hours of supported changes in blood arterial pressure. Accordingly, the kidneys change all out body sodium and water parity to reestablish blood pressure to ordinary. Hypotension brings about sodium (and water) maintenance, while hypertension for the most part builds sodium discharge in ordinary people. Cardiac output yields gives a measure of the best performance of the heart as a pump. It is defined as the volume of blood pumped by the LV (or RV) every moment, and is equivalent to the result of the SV and heart rate:

$$\mathrm{CO} = \mathrm{SV} \times \mathrm{HR}$$

Cardiac output averages 5.0 L/min in a resting 70 kg supine man. It can increase fivefold with strenuous exercise. Varieties in cardiovascular output can be created by changes in heart rate or stroke volume. Heart rate is controlled principally by the autonomic nervous system. The stroke volume is dictated by three fundamental components: preload, afterload, and contractility. Preload and afterload are highly sensitive to changes in metabolic requirements (whole-body oxygen consumption).

To compare patients of different body sizes, CO can be divided by the patient's body surface area to give a normalized parameter called the cardiac index (CI):

$$\mathrm{CI} = \mathrm{CO}/\,\mathrm{BSA}$$

The result of stroke volume (SV) and heart rate (HR) gives cardiovascular yield (CO).The factors determining CO can thus be divided into those affecting HR and those that determine SV. Overall control of CO is a combination of the mechanisms controlling SV and HR. Several factors determine SV. The three major determinants of SV are:

End-diastolic volume. Also the end-diastolic pressure of the ventricles is commonly used as representing the preload. Changes in preload are associated with changes in stroke volume, stroke work, and cardiac output. The relationship between the cardiac output and end-diastolic pressure is curvilinear (ventricular capacity curve). This is the declaration of Starling's law of the heart. The most imperative determinant of right ventricular preload is venous return. Without critical pulmonary or right ventricular brokenness, venous return is likewise the significant determinant of left ventricular preload5. How mightily the ventricle contracts amid systole to discharge blood, Cardiac yield is conversely identified with after load. left ventricular after load is typically compared clinically with SVR, which is ascertained by

$$\mathrm{SVR} = 80 \times \frac{\mathrm{MAP} - \mathrm{CVP}}{\mathrm{CO}}$$

The following equation: It is a poorly defined term describing

the intrinsic ability of a cardiac muscle fibre to do mechanical work. The heart rate (HR) is normally determined by the spontaneous depolarisation rate of the SA node pacemaker cells. The ordinary heart rate of 60–80 bpm is much slower than the characteristic rate of the denervated heart (110 bpm). This is because of the dominant parasympathetic tone in the intact cardiovascular system[6].

Coronary Circulation: Myocardial blood flow is 200 ml/min, or 4% of cardiovascular yield, for an organ weighing just 0.4% of body weight. Oxygen utilization of the heart is additionally high, 23 ml/min, or 9% of aggregate. This is for a justifiable reason: the heart is a pump that perfuses whatever remains of the body, its work is hard and it needs a steady vitality supply from oxygen consuming digestion system. The coronary supply routes are the first to get oxygenated blood from the aorta; their perfusion relies on upon the pressure slope created by the heart. There is for all intents and purposes no endocardial flow amid systole, while the flow in epicardium is kept up. Now and again of expanded interest for perfusion, e.g. tachycardia, hypertension, this locale is then not able to build flow further and along these lines it is more defenseless to ischemia. Analgesic operators discourage myocardial execution and oxygen utilization falls in accordance with decreased myocardial work. Coronary blood flow thusly is lessened. Myocardial ischaemia occurs when myocardial oxygen demand exceeds supply. In a diseased myocardium symptoms of ischaemia occur at a higher perfusion pressure, inside the lower limit of autoregulation. Cardiac performance (power) is the product of mean arterial blood pressure and cardiac output. Stroke volume is not easily accessed by bedside measurements. Thus the rate–pressure product remains a useful clinical tool when estimating myocardial oxygen demand, and therapeutic manoeuvres can be directed at optimizing myocardial performance to maintain oxygen flow to the systemic circulation (which requires adequate cardiac output and haemoglobin concentration) while not overloading the heart by excessive pressures and rates[7].

Unlike the brain, the heart cannot effectively increase its oxygen flow by increasing its perfusion pressure since the heart generates the pressure: myocardial oxygen consumption rises proportionately with myocardial work. The heart, therefore, regulates its perfusion only via changes in coronary artery resistance. Autoregulation maintains a constant blood flow in the coronary circulation within a wide range of pressures; 60–140 mmHg. It must be kept in mind that the aortic diastolic pressure is the coronary perfusion pressure. The sympathetic and parasympathetic nervous system affects the coronary vascular resistance, but this is modified by autoregulation. Myocardial ischaemia happens when myocardial oxygen request surpasses supply, or when coronary blood flow and oxygen flow fall underneath the min base required. Three variables are basically in charge of deciding myocardial oxygen utilization (MVO2): wall tension, contractility, and heart rate (HR). Myocardial wall tension is controlled by the relationship between ventricular sweep (r), ventricular pressure (P), and ventricular divider thickness (w) as indicated by Laplace's law: T=P/w. Increments in end-diastolic volume (EDV) (preload) will increment ventricular span and will decrease divider thickness if widening is serious. These progressions will expand wall tension. Increments in the impedance to ventricular discharge (afterload) will fundamentally increment ventricular pressure and increment divider strain. Concentric ventricular hypertrophy will expand wall thickness and lessen wall strain. Work done in the isovolumic period of ventricular compression is exceptionally vitality wasteful so the expansion in MVO2 actuated by an expansion in preload (volume work) is a great deal not as much as that prompted by an increment in after load (pressure work).

Contractility is the condition of myocardial execution (inotropy) free of preload and afterload. Expanding the contractile condition of the heart will build MVO2.Heart rate specifically influences myocardial oxygen parity. Tachycardia increments myocardial oxygen request and lessens supply by decreasing the time in diastole. Ischemia happens with tachycardia since supply per beat is deficient to take care of demand per beat.1 Adequate myocardial oxygen supply is reliant on conveyance of the suitable volume of oxygenated coronary blood flow. LV CPP falls with either a lessening in diastolic blood pressure (DBP) or an expansion in LV end-diastolic pressure. An ordinarily neglected reason for lessened CPP is bradycardia. Bradycardia energizes diastolic overflow from the proximal aorta and may bring about a wide heartbeat pressure and lessened DBP. Moreover, support of CO with bradycardia requires an expanded SV. The expanded SV happens principally by an expansion in left ventricular end-diastolic volume (LVEDV) and pressure. This further lessens CPP. The left ventricle gets most its perfusion amid diastole; hence, decreases in diastolic time are conceivably detrimental. Any obstacle to flow in a coronary vein brings about a pressure drop over the deterrent. Albeit myocardial ischemia causes serious coronary vasodilation. Taking after a 10 to 30 second coronary impediment[8].

Myocardial oxygen conveyance is the result of coronary blood flow and the oxygen substance of the moved blood. Iron deficiency lessens myocardial oxygen conveyance by decreasing the oxygen-conveying limit of blood.

Pharmacology: 2-1- Ketamine: Phencyclidine was the principal medication of its class to be utilized for anesthesia, however had unsuitable reactions. Ketamine (Ketalar) was orchestrated in 1962 by Stevens and was initially utilized as a part of people in 1965 by Corssen and Domino. Ketamine was discharged for clinical use in 1970 is still utilized as a part of different clinical settings. Ketamine contrasts from most different medications used to instigate anesthesia since it has a huge pain relieving impact. It for the most part does not discourage the cardiovascular and respiratory frameworks, but rather it possesses a portion of the unfavorable mental impacts

found with alternate phencyclidines. Ketamine consists of two stereoisomers, S (+) and R (-). The S (+) is more potent and is associated with fewer side effects[9].

It is supplied as an aqueous solution in several concentrations, Formulated as a weak acid with a pH between 3.5 and 5.5. Ketamine has a single chiral carbon atom. Is partially water soluble, and forms a white crystalline salt with a pK_a of 7.5. It has lipid solubility 5 to 10 times that of Sodium thiopental. Ketamine has various impacts all through the focal nervous framework, incorporating blocking polysynaptic reflexes in the spinal string and restraining excitatory neurotransmitter impacts in chose regions of the cerebrum. As opposed to the wretchedness of the reticular enacting framework incited by the barbiturates, ketamine practically "separates" the thalamus (which transfers tangible motivations from the reticular initiating framework to the cerebral cortex) from the limbic cortex (which is included with the attention to sensation). Albeit some mind neurons are restrained, others are tonically energized. Clinically, this condition of dissociative anesthesia causes the patient to seem cognizant (eg, educational, swallowing, muscle contracture) yet not able to process or react to tactile information. Ketamine has been shown to be a N-methyl-D-aspartate receptor (a subtype of the glutamate receptor) antagonist. Ketamine interacts with the 6, k and m opioid receptors. Also interacts weakly with the Q receptor (formerly classified as an opioid receptor). The potency of ketamine at the receptors is in the order M >*K*>Q >6.High doses of ketamine have a local anaesthetic action, and there is supportive evidence of fast sodium channel blockade. Ketamine also acts stereo selectively at muscarinic acetylcholine receptors. This action is likely to be antagonist, as ketamine produces anticholinergic effects such as bronchodilatation, delirium and a sympathomimetic action. Ketamine anaesthesia is antagonized by anticholinesterases. It is thought that ketamine may also have an effect on voltage-sensitive Ca^{2+} channels. Ketamine apply pain relieving activity in the early phases of arrangement of torment boosts. Along these lines, it might be valuable in prompting pre-emptive anesthesia and lessening of opiate utilization[10].

Methodology

A prospective experimental comparative study was done. The study included 56 patients requiring CABAG surgery admitted to Erbil heart focus, those patients having other cardiovascular issues or pulmonary hypertension were barred. The patients age ranged from (40 y) to (80 y), and mean age was (60 y). The study included (45) males and (11) females. After agreement and written informed consent was obtained from all the patients, randomly allocated 56 patients into two groups. We used for induction of anesthesia to the first group low dose of Sodium thiopental 1mg/kg while for the second group Ketamine 2mg/kg. With standerized doses of Midazolam, Fentanyl, Pavilone and 1 MAC Isoflorane for both groups. Noradrenaline and Dobutamine Triglycerodinitrate were used according to the need to insure hemodynamic stability for both groups after taking the readings. All patients continued their medications up to the day of surgery, after admission to the operating room, five lead electrocardiogram monitoring, wide bore canulation, pulse oximetry, capnograph, non-invasive blood pressure monitoring, was done before induction of anaesthesia. Induction started with 2-3 mg of Midazolam I.V after premedication with Ranitidine 150 mg I.V, Dexamethasone 8 mg I.V and pre oxygenation for five minutes. Then 10 Mg/Kg Fentanyl I.V, the induction agent according to the group, Pavilone 0,01mg/kg I.V. after complete relaxation, intubation with endotracheal tube was done. Femoral artery catheterization for arterial blood pressure monitoring and Internal Jagular vein catheterization for central venous pressure monitoring was done. Blood pressure, mean blood pressure (by non-invasive monitoring) and heart rate were recorded three times for each patient in both groups (1 minute pre induction, 1 minute and 5 minutes post induction).

The statistical analysis used to calculate the P value was ANOVA test. P value **< 0.001** is strongly significant, **< 0.05** moderately significant, while **> 0.05** is not significant[11].

Results and Discussion

Comparism of blood pressure: The study showed that there is more fluctuating mean of systolic and diastolic blood pressure readings in pre induction, post induction, and 5 minutes later for group A as compared to group B. This is well noted in Table-1.

Table-1
Comparison of blood pressure readings of both groups

Time of reading	Group A		Group B	
	Systolic	Diastolic	Systolic	Diastolic
Preinduction	162.3	88.3	131.9	76
Post 1	117.2	64.6	118.4	69.8
Post5	92.1	57.1	122.6	69.7
P value	< 0.001	< 0.05	< 0.05	> 0.05

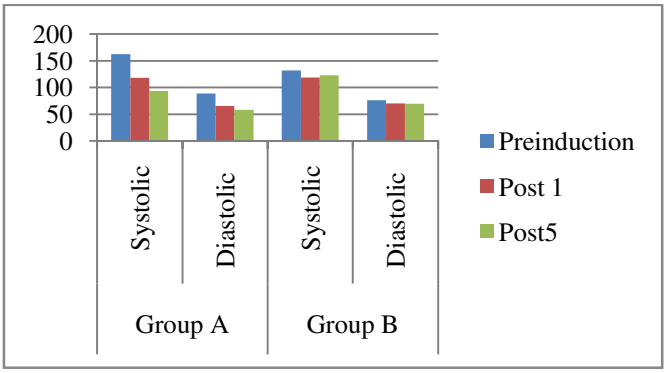

Figure-1
Comparison of blood pressure readings of both groups

Comparison of mean blood pressure: The mean of mean blood pressure readings for group A showing progressive decline in pre induction, post induction, and 5 minutes later (113.1, 82.9, 69.6) respectively compared to (94.6, 86, 87.3) for group B which revealed less obvious decline.

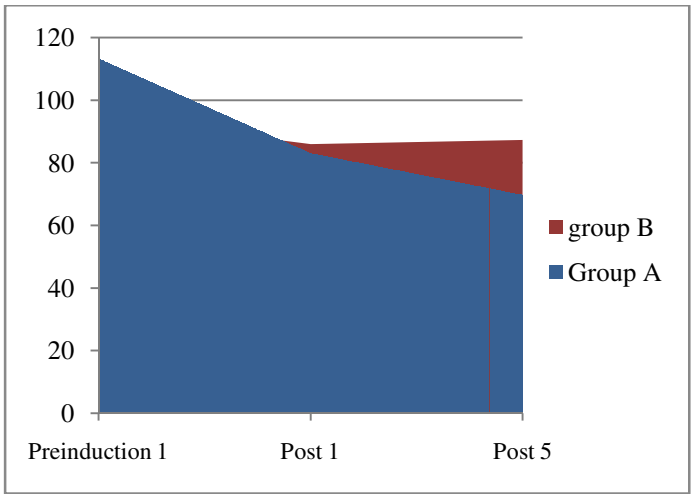

Figure-2
Comparison of mean blood pressure readings of both groups

Table-2
Comparison of mean blood pressure readings of both groups

Time of reading	Group A	group B
Preinduction 1	112.7	94.6
Post 1	82.1	86
Post 5	68.8	87.3
P value	< 0.001	< 0.05

Largest Mean BP difference: Although comparing blood pressure give a parameter for hemodynamic stability but it may give a false impression if taken separately without relating it to the baseline reading (pre induction). The largest difference in mean blood pressure reading compared to the pre induction reading was taken to estimate the hemodynamic stability for both groups as pure difference and as a percentage from the pre induction reading. The study reveals more fluctuating blood pressure for group A compared to more hemodynamically stable in group B as shown in Table-3.

Comparison of heart rate readings: In Table-4 we can notice that heart rate readings declined for group A from 82.2 beat/minute at pre induction to 74.3 post induction and 71.1 5 minutes later compared to a very little decline in group B (81.6, 79.4, 78.3) respectively.

Table-3
Comparison of Largest Mean BP difference and its percentile difference between the groups within 5 minutes

	Group A	Group B	P value
Biggest Mean BP difference	**46.4**	**9.4**	**< 0.001**
biggest Mean BP difference %	**40.4**	**9.53**	**< 0.001**

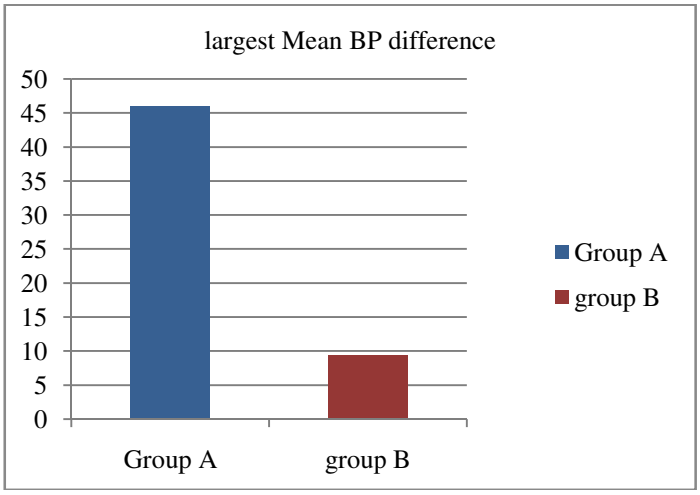

Figure-3
Comparison of Largest Mean BP difference and its percentile difference of between the groups within 5 minutes

Table-4
Comparison of heart rate readings of both groups

Time of reading	Group A	Group B
Pre induction 1	82.0	81.6
Post 1	74.1	79.4
Post 5	72.0	78.3
P value	< 0.05	> 0.05

Discussion: The general analgesic arrangement for a hypertensive patient is to keep up a proper stable blood pressure range. Patients with marginal hypertension might be dealt with as normotensive patients. Those with long-standing or ineffectively controlled hypertension, be that as it may, have changed autoregulation of cerebral blood flow; higher than ordinary mean blood pressures might be required to keep up satisfactory cerebral blood flow. Since most patients with long-standing hypertension are expected to have some component of CAD and heart hypertrophy, intemperate blood pressure heights are undesirable. Hypertension, especially in relationship with tachycardia, can accelerate or fuel myocardial ischemia, ventricular brokenness, or both. Blood vessel blood pressure

ought to by and large be kept inside 10–20% of preoperative levels[12].

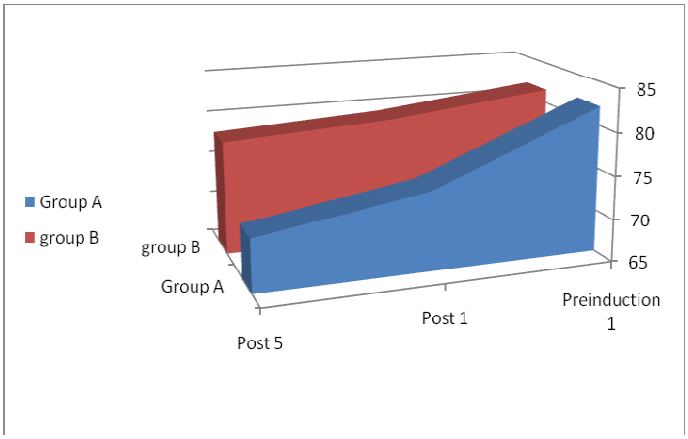

Figure-4
Comparison of heart rate readings of both groups

Comparison of blood pressure: The study showed statistically significant haemodynemic changes in the mean of systolic and diastolic blood pressure readings for group A, while ketamine group (B) showed no significant changes in the above readings. That's to say that the ketamine group had more stable blood pressure readings (Table-1).

Comparison of mean blood pressure: There was a significant decline in the successive readings of mean blood pressure for group A, while group B reveals less obvious decline.

Largest Mean BP difference: The study reveals more fluctuating blood pressure for group A compared to more hemo-dynamically stable in group B.

Comparison of heart rate readings: Group (A) showed significant declining heart rate in comparison to group (B).

The above parameters in this study was more stable in ketamine group than Sodium thiopental group, this is agreed with Hijazi Y. et al[12]. This is most probably due to sympathetic stimulation of ketamine. Although the use of ketamine should be avoided in patients with coronary artery disease, because it increase myocardial work. We are using midazolam and large dose of opioid this will apposite the ketamine sympathetic stimulation and giving more controlled and stable hemodynamic status.

Conclusion

The use of ketamine induction in coronary bypass surgery provides haemodynemic stability. We recommend to study this issue in a larger series with more parameters taken in consideration in a further studies. We recommend the use of ketamine because of its sympathetic stimulation that apposite the depressive effect of other anaesthatic drugs during induction and maintenance like midazolam and large dose of opioids and inhalational drugs. That using should be in precaution in case of sever hypertension or pulmonary hypertension. In order to adjust the dose of ketamine we recommend using less doses in further studies.

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