Research Article

Perioperative Use of Low Dose Dopamine Protects Against Renal Injury in Patients Undergoing on-Pump Coronary Artery Bypass Surgery

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Abstract

Objectives: To compare and determine the e ects of low dose dopamine in prevention of renal injury during cardiopulmonary bypass in patients undergoing isolated coronary artery bypass graft surgery.

Methods: Group I (n=25 patients) had mannitol 1g/Kg in the priming circuit and low dose dopamine (2 ug/Kg/min) was administered in perioperative period starting at induction of anesthesia and continued till postoperative day 3. Group-II (n=25 patients) also had mannitol 1g/Kg in the priming circuit but dopamine was not administered in the perioperative period. The groups were matched in terms of patient characteristics and preoperative creatinine levels. Highest postoperative creatinine level within 5 days was taken as marker of renal injury. Student's t-test was used to assess the significance of di erences in creatinine levels in two groups.

Results: There was a marginal increase in the postoperative creatinine level in group II patients, however this increase was statistically significant (p= 0.016).

Conclusion: We conclude that low dose of dopamine during perioperative period in patients undergoing coronary artery bypass surgery on cardiopulmonary bypass has a contributing factor in renal preservation.

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Introduction

Coronary Artery Bypass Surgery (CABG) is one of the most commonly performed surgery world over. CABG performed on cardiopulmonary bypass (CPB) has numerous e ects on many other organs of the body. These e ects are not physiological; rather they are graded as injury owing to non-physiological circulatory environment during CPB.[1] This entails a non-pulsatile flow, reduced body temperature, hemodilution, contact of blood with a large non-biological surface area and resultant activation of systemic inflammation. Truly speaking the body is under the state of a controlled shock during this period. Almost every organ is a ected to some degree with this alteration in physiology. There is a 30% reduction in the renal vascular flow during CPB.[2] The e ects of low dose dopamine are well documented, a dose of 2-4 ug/Kg/min acts through the DA1 and DA2 receptors in renal vasculature to increase renal blood flow.[3]

Mannitol another ingredient of CPB allows maintenance of glomerular capillary pressure and prevents tubular obstruction. It also prevents rise in plasma levels of hydrogen peroxide and other free oxygen radicals which contribute to the reperfusion injury.[4]

From the cardiac surgeons perspective although every

organ is important, yet kidneys presume a special importance. Crystalloid solutions are added to the priming volume of the oxygenator and tubing circuit. This extra crystalloid volume is then mixed with the entire circulating volume when cardiopulmonary bypass is initiated resulting in hemodilution.[1] It is the kidneys that are to remove this extra fluid after CPB. Moreover kidneys play an important role in hemodynamic tuning of the body by their role through elimination or conservation of circulating volume, maintaining electrolytes and acid-base balance as well as response of Rennin-Angiotensin system to varying systemic blood pressure. It is therefore natural for the cardiac surgeon to consider the preservation of renal function during the cardiac surgery. The factors influencing renal preservation like low perfusion pressure, vasoconstriction secondary to cooling and systemic inflammatory response are all un-avoidable. Measures have to be taken to contradict these deleterious e ects on renal function.[5]

Apart from maintaining the perfusion pressure, reducing the CPB time, maintaining good hematocrit and therefore oxygen delivery to the tissues, surgeons have been traditionally using low dose dopamine infusion to augment the renal perfusion and therefore protect its function.[6] This study was conducted to see if there is really a beneficial e ect of low dose dopamine on preserving renal function during on pump elective CABG cases.

Methods

We retrospectively examined the clinical records of patients in our department for patients undergoing isolated elective CABG with normal preoperative renal function, Ejection fraction (EF) > 40% and normal liver function. Patients taking ACE inhibitors, recent myocardial infarction or who had been given radio contrast in past 3 days were excluded from the study. Preoperative and postoperative creatinine till postoperative day 5 were noted and the highest value recorded was taken as the final postoperative creatinine and was used as an indicator of renal injury.

We formulated two groups of patients; group I (25 consecutive cases) in whom renal dose dopamine (2ug/Kg/min) was started at the induction of anesthesia and continued to postoperative day 3. Group II consisted of 25 consecutive patients in whom renal dose dopamine was not used. All patients were followed for serum creatinine till postoperative day 5 and the highest value noticed was considered as an indicator of renal injury.

All patients were operated on CPB, the circuit was primed using ringer's lactate (30 ml/Kg) + unfractionated heparin (1 mg/Kg) + mannitol 20% (1g /Kg). Hematocrit was maintained from 25-30% and temperature was cooled to 32C. Hemodynamic monitoring was done using invasive arterial line as well as CVP monitoring. A mean arterial pressure of 65 to 100 mm Hg was maintained while not on CPB, and any decrease was managed by giving bolus of IV fluid or 1-3 ug/kg/min of epinephrine infusion. Mean arterial pressure during CPB was maintained around 50mm Hg, and using Phenylepherine or altering flows to manage any decrease in pressures.

Statistical analysis was done using Statistical Package for Social Sciences (SPSS V 15.0) for windows. Continuous variables were expressed as means ± SD and using Student-t test for significance. The results were evaluated for 95% Confidence interval with a p value of < 0.05 as significant.

Results

Demographic characteristics of the patients in two groups are summarized in table 1. There was no significant di erence in the two groups. There were total of 50 patients in the study, 25 in each group. There were 37 males (19 in Group 1, 18 in Group 2) and 13 female (6 in Group 1 and 7 in Group 2) patients. Mean age was 56.36 ± 5.6 Vs 56.6 ± 5.9 p=0.570 in group 1 and 2 respectively. Both groups were balanced in terms of height, weight, cardiopulmonary bypass time, cross clamp time and preoperative creatinine levels (Table -1).

Postoperative highest creatinine level in group 1 was 1.384 mg/dl ±0.179 Vs 1.536 ± 0.265 (p=0.016). This finding was significant that there was a decreased rise in postoperative creatinine in patients with perioperative dopamine infusion. The lesser degree of creatinine rise in group 1 indicates better renal preservation with dopamine infusion (Fig 1).

Table 1: *Demographic Characteristics of Groups*

Parameter	Group 1 N=25	Group 2 N=25	P value (< 0.05 is significant)
Males	19	18	
Females	6	7	
Age (years)	56.36 ± 5.6	56.6 ± 5.9	0.570
Height (Cm)	169.64 ± 9.2	169.6 ± 9.8	0.972
Weight (Kg)	76.44 ± 7.84	75.84 ± 7.89	0.417
CPB Time (Min)	87.72 ± 14.06	87.64 ± 13.27	0.94
Cross Clamp Time	65.48 ±13.08	65.88 ±12.87	0.717
Pre-operative Createnine	1.032 ± 0.18	1.04 ± 0.17	0.746

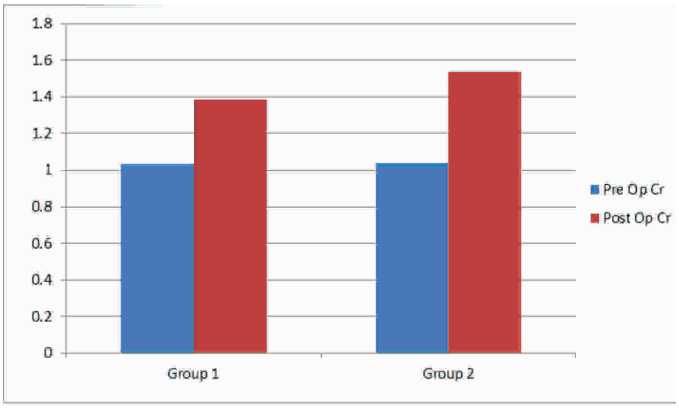

Fig 1: *Distribution of Pre-operative and Post-operative Creatinine among groups*

Discussion

Acute kidney injury after CABG is associated with increased morbidity and mortality. Therefore strategies to prevent it are very important. Preservation of renal function during cardiac surgical procedures has many facets. It is not a single variable mediated process that can be manipulated. Various researchers have identified a myriad of factors influencing renal preservation. The most significant and most commonly addressed however is the perioperative low cardiac output resulting in inadequate supply of blood to the renal parenchyma.[2] Kidney is metabolically very active organ and has very high demand for blood supply. This large blood supply on the one hand is required for optimal clearance of toxic and waste supplies from the blood and therefore production of urine, on the other hand the adequate blood supply is necessary for the optimal functioning of the renal parenchymal cells.

CPB is associated with many physiological changes that result in altered flow patterns in di erent organs. More specifically CPB related factors are cross clamp time, total cardiopulmonary bypass time and production of free radicals.[7] It was further observed in one study that the total CPB time > 70 min is associated with significant renal injury.[8] In our study both groups had total bypass time more than 80 min. Non Pulsatile nature of flow is also a contributing factor.[9] Despite flow rates almost similar to the normal cardiac output, there is marked fall in systemic vascu-lar resistance, which results in reduced hemodynamic pressures. Some vascular beds get vasoconstriction while others get vasodilatation, these results in non-uniform blood flow.[10] CPB is associated with purposeful hemodilution and systemic hypothermia. Hemodilution below 25% has shown significantly reduced oxygen delivery to cells and hypothermia causes vasospasm as well as increased blood viscosity.[11] Reduced temperature also increases a nity of oxygen binding to hemoglobin and thus reduced o -loading of oxygen from hemoglobin in the targeted tissues[(12)]. Several methods have been proposed to reduce renal injury during this period, a good perfusion pressure during CPB, optimum hemodilution and utilizing pulsatile flow are most commonly favored.[13]

Dopamine is a catecholamine produced in the body. It has a number of physiological e ects including behavior, movement, nerve conduction, blood pressure and electrolyte movements.[18] Renal dopamine receptors DA1 and DA2 cause natriuresis and vasodilatation.[14] Low dose dopamine has been shown convincingly to dilate the renal vasculature and therefore increase the renal perfusion.[15] Higher doses result in vasoconstriction and therefore the vasodilator e ect is lost. Starting low dose dopamine before CPB pre-dilates the renal vasculature and prepares for the altered flow dynamics that are going to happen with initiation of CPB. The improved blood flow in this manner tends to preserve the renal parenchyma and therefore its function.

N-Acetylecysteine is an alternate drug that may prevent renal injury due to its anti-inflammatory and anti-oxidant e ects. While the e ect of dopamine is only to increase the renal blood flow, it does not counteract many other mechanisms involved in renal injury. Omer Faruk et al. has shown that N-acetyl-

ecysteine gives better renal preservation in patients with pre-operative renal dysfunction undergoing CABG than low dose dopamine.[16]

Although role of low dose dopamine in the context of renal preservation is controversial, it is still one of the most commonly used prophylactic measure to reduce renal dysfunction. Several controlled trials have shown improvement in renal parameters with dopamine.[17] Lassining et al did not show an improvement in renal fuction after low dose dopamine.[18]

This study although has small study population, but it has shown that there is marginal but significant e ect on renal preservation when low dose dopamine was started preoperatively and carried out during the entire operative and early postoperative period. Woo et al. have also shown similar protective e ect of dopamine on renal preservation.[19] Narin EB and Oztekin have also suggested that pharmacological manipulation including dopamine infusion can significantly influence renal protection after CABG.[20] Stallwood has however shown that acute renal injury after CABG is an independent e ect of cardiopulmonary bypass and not influenced by perioperative dopamine.[21] Gatot et al conducted a double blind placebo controlled study on CABG patients with or without renal dose dopamine and studied the e ect on renal function. They also concluded that prophylactic administration of low dose dopamine prevents renal dysfunction and provides a better stable postoperative course.[22]

Conclusion

We conclude convincingly that dopamine infusion at a rate of 2ug/Kg/min during cardiopulmonary bypass was an e ective strategy to preserve the renal function and avoid pump related kidney injury. This study is limited by small sample size and certainly contains influence of other confounding factors a ecting renal preservation. More studies in this context are needed to identify which patient populations are more likely to benefit.

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References

1. O'Neal JB, Shaw AD, Billings FT. Acute kidney injury following cardiac surgery: current understanding and future directions. Critical care. 2016; 20(1): 187.
2. Toller W, Heringlake M, Guarracino F, Algotsson L, Alvarez J, Argyriadou H, et al. Preoperative and perioperative use of levosimendan in cardiac surgery: European expert opinion. Int J Cardiol.. 2015;184: 323-36.
3. Okusa MD, Davenport A. Reading between the (guide) lines—the KDIGO practice guideline on acute kidney injury in the individual patient. Kidney Int. 2014;85(1):39-48.
4. Thiele RH, Isbell JM, Rosner MH. AKI associated with cardiac surgery. Clin J Am Soc Nephrol.. 2015; 10(3):500-14.
5. Niu Z-Z, Wu S-M, Sun W-Y, Hou W-M, Chi Y-F. Perioperative levosimendan therapy is associated with a lower incidence of acute kidney injury after cardiac surgery: a meta-analysis. J Cardiovasc Pharmacol. 2014;63(2):107-12.
6. Vives M, Wijeysundera D, Marczin N, Monedero P, Rao V. Cardiac surgery-associated acute kidney injury. Interact Cardiovasc Thorac Surg. 2014; 18(5): 637-45.
7. Osawa EA, Rhodes A, Landoni G, Galas FR, Fukushima JT, Park CH, et al. E ect of perioperative goal-directed hemodynamic resuscitation therapy on outcomes following cardiac surgery: a randomized clinical trial and systematic review. Critical care medicine. 2016;44(4):724-33.
8. Wang Y, Bellomo R. Cardiac surgery-associated acute kidney injury: risk factors, pathophysiology and treatment. Nat Rev Nephrol. 2017;13(11):697.
9. Hu myer JL, Groves DS. Pulmonary complications of cardiopulmonary bypass. Best Pract Res Clin Anaesthesiol. . 2015;29(2):163-75.
10. Ortega-Loubon C, Fernández-Molina M, Carrascal-Hinojal Y, Fulquet-Carreras E. Cardiac surgery-associated acute kidney injury. Ann Card Anaesth. 2016;19(4):687.
11. Vanmassenhove J, Kielstein J, Jörres A, Van Biesen W. Management of patients at risk of acute kidney injury. The lancet. 2017;389(10084):2139-51.
12. Ball L, Costantino F, Pelosi P. Postoperative complications of patients undergoing cardiac surgery. Curr Opin Crit Care. 2016;22(4):386-92.
13. Zangrillo A, Alvaro G, Pisano A, Guarracino F, Lobreglio R, Bradic N, et al. A randomized controlled trial of levosimendan to reduce mortality in high-risk cardiac surgery patients (CHEETAH): Rationale and design. Am J Cardiol.. 2016;177:66-73.
14. Weisbord SD, Palevsky PM. Design of clinical trials

in acute kidney injury: lessons from the past and future directions. InSeminars in nephrology 2016 Jan 1; 36, (1): 42-52).

15. Lomivorotov VV, Efremov SM, Pokushalov EA, Karaskov AM. New-onset atrial fibrillation after cardiac surgery: pathophysiology, prophylaxis, and treatment.. J Cardiothorac Vasc Anesth 2016; 30(1): 200-16.
16. Di Tomasso N, Monaco F, Landoni G. Renal protection in cardiovascular surgery.Research. 2016; 44:5-9.
17. Ga ney AM, Sladen RN. Acute kidney injury in cardiac surgery. Current Opinion in Anesthesiology. 2015 Feb 1;28(1):50-9.
18. Pilarczyk K, Boening A, Jakob H, Langebartels G, Markewitz A, Haake N, et al. Preoperative intra-aortic counterpulsation in high-risk patients undergoing cardiac surgery: a meta-analysis of randomized controlled trials. European Journal of Cardio-Thoracic Surgery. 2015;49(1):5-17.
19. Xu J, Jiang W, Fang Y, Teng J, Ding X. Management of cardiac surgery-associated acute kidney injury. Acute Kidney Injury-From Diagnosis to Care: Karger Publishers; 2016;187(1): 42-131.
20. Ding W, Ji Q, Wei Q, Shi Y, Ma R, Wang C. Prophylactic application of an intra-aortic balloon pump in high-risk patients undergoing o -pump coronary artery bypass grafting. Cardiology. 2015;131(2):109-15.
21. Jakobsen CJ. High thoracic epidural in cardiac anesthesia: a review. InSeminars in cardiothoracic and vascular anesthesia 2015;19(1). 38-48 .
22. Pang X-Y, Fang C-C, Chen Y-Y, Liu K, Song G-M. E ects of ulinastatin on perioperative inflammatory response and pulmonary function in cardiopulmonary bypass patients. American journal of therapeutics. 2016;23(6):1680-9.