

A STUDY TO ASSESS THE EFFECTIVENESS OF REMOTE ISCHEMIC PRECONDITIONING IN PREVENTING CONTRAST INDUCED ACUTE KIDNEY INJURY IN PATIENTS WITH ST ELEVATION MYOCARDIAL INFARCTION UNDERGOING CORONARY ANGIOGRAM

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ABSTRACT

BACKGROUND

Acute kidney injury following administration of iodinated contrast (CI-AKI) has been referred to as contrast induced nephropathy (CIN). Ischemic preconditioning (IPC), transient brief episodes of ischemia before a subsequent prolonged ischemia/reperfusion injury, has been shown to reduce the extent of organ damage. Several studies have demonstrated the tissue-protective effects of remote ischemic preconditioning (RIPC) in various target organs, including the kidneys. The aim of this study is to assess if remote ischemic preconditioning reduces the incidence of contrast induced AKI in patients with STEMI undergoing coronary angiogram.

MATERIALS AND METHODS

The study was conducted in 100 patients (50 cases and 50 control) who were undergoing coronary angiogram (CAG) following acute ST elevation myocardial infarction in Govt. Rajaji Medical College, Madurai. Test group underwent RIPC (Remote Ischemic preconditioning) and control group underwent sham preconditioning prior to procedure whereas both test and control groups received normal saline infusion- 1 ml/kg/hr, beginning 12 hours before CAG till 12 hours after coronary angiogram (CAG). Both groups were followed with serial renal function tests for next 72 hrs after CAG.

RESULTS

Of the 50 patients in the control group, 18 developed CI-AKI and of the 50 patients in the test group 8 developed CI-AKI (36% vs. 16%). This shows that RIPC was associated with a lower incidence of CI-AKI and the difference was statistically significant. (p=0.040).

CONCLUSION

Not only was the incidence of CI-AKI lower in the RIPC group, the mean rise in serum creatinine was also lower which would further decrease the duration of hospital stay and short-term mortality. Thus, RIPC can serve as a cost-efficient tool in the lowering of occurrence of CI-AKI in patients undergoing contrast imaging.

KEYWORDS

Contrast Induced Nephropathy, Remote Ischemic Preconditioning, Renal Tubular Cell Injury.

HOW TO CITE THIS ARTICLE: Mohamed P, Thomas A, Bagialakshmi G. A study to assess the effectiveness of remote ischemic preconditioning in preventing contrast induced acute kidney injury in patients with st elevation myocardial infarction undergoing coronary angiogram. J. Evid. Based Med. Healthc. 2019; 6(9), 680-683. DOI: 10.18410/jebmh/2019/142

BACKGROUND

Acute kidney injury following administration of iodinated contrast (CI-AKI) has been referred to as contrast induced nephropathy (CIN). The pathophysiological processes involve renal vasoconstriction and medullary hypoxia, direct renal tubular toxicity and generation of reactive oxygen species leading to tubular cell injury. Risk factors for

development of CI -AKI include renal impairment, High-osmolal contrast media, Diabetes mellitus, large contrast volume, absolute intravascular volume depletion, multiple sequential procedures, intra-arterial administration, concomitant nephrotoxic medication use.

Preventive Measures for CI-AKI

- 1) The use of less nephrotoxic contrast agents;
- 2) The use of pharmacologic agents to counteract the nephrotoxic effects of contrast media.
- 3) The administration of intravenous fluids to expand the intravascular space and enhance diuresis.

Ischemic preconditioning (IPC), transient brief episodes of ischemia before a subsequent prolonged ischemia/reperfusion injury, has been shown to reduce the extent of organ damage. IPC can be induced locally when the

Financial or Other, Competing Interest: None.

Submission 15-02-2019, Peer Review 21-02-2019,

Acceptance 28-02-2019, Published 02-03-2019.

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DOI: 10.18410/jebmh/2019/142



preconditioning stimulus is applied to the same organ or tissue incurring the ischemic injury. Remote ischemic preconditioning (RIPC) is defined as transient brief episodes of ischemia at a remote site before a subsequent prolonged ischemia/reperfusion injury of the target organ.

Aim of The Study

To assess if remote ischemic preconditioning reduces the incidence of contrast induced AKI in patients with STEMI undergoing coronary angiogram.

Study Population

This study was conducted among 100 randomly selected patients who were admitted in Govt. Rajaji Medical college hospital, Madurai with acute ST elevation Myocardial Infarction.

Inclusion

Age >18 years, Both sexes.

1. Patients diagnosed with ST elevation myocardial infarction.
2. Patients with normal baseline RFT.

Exclusion Criteria

- Inability to give informed consent.
- Patients with Chronic kidney disease.
- Patients with Acute kidney injury.
- Patients with cardiogenic shock.

MATERIALS AND METHODS

Patients were divided into two groups (test and control). Those in the test group will undergo CAG after undergoing RIPC by three cycles of ischemia/ reperfusion of the upper arm achieved by 5-minute cuff inflation at 50 mm Hg above SBP followed by 5 minutes of complete cuff deflation. Sham conditioning was done by inflating the blood pressure cuff to 20 mm above diastolic BP for 5 minutes followed by deflation for 5 minutes for a total of 3 cycles. Both sets of Patients were hydrated with normal saline infusion- 1 ml/kg/hr beginning 12 hours before CAG till 12 hours after CAG. Necessary haematological, biochemical and radiological investigations were performed, and serum creatinine were serially monitored over next 72 hours

Design of Study

Prospective, single-blind, randomized, sham-controlled parallel-group study.

Period of Study

February 2017 to August 2017.

Ethical Clearance

The study was approved by Government Rajaji Hospital Ethical committee. Informed written consent was obtained before enrolling subjects to the study.

RESULTS

Of the 50 patients in the control group, 18 developed CI-AKI and of the 50 patients in the test group 8 developed CI-AKI (36% vs. 16%). This shows that RIPC was associated with a lower incidence of CI-AKI and the difference was statistically significant. (p=0.040). Not only was the incidence of CI-AKI lower in the RIPC group, but the mean rise in creatinine was lower as well. The mean rise in creatinine in the control group was 0.534 mg/dl and in the test group was 0.178 mg/dl.

In the control group, 10 of the 26 male patients (38.5%) and 8 of the 24 female patients (33.3%) developed CI-AKI. This was statistically nonsignificant (p – 0.934), showing sex was not a risk factor for developing CI-AKI.

Of the 32 diabetic patients in the control group, 12 developed CI-AKI whereas 6 of the 18 non-diabetics developed CI-AKI. This was not statistically significant (37.5% vs. 33.33%; p=0.99). Seven of the 10 patients with RBS >300 developed CI-AKI while 11 of the 40 patients with RBS <300 developed CI-AKI. This was statistically significant (70% vs. 27.5%; p= 0.024).

Ten of the thirty hypertensive patients (33.3%) and eight of the twenty non-hypertensive patients (40%) developed CI-AKI. The association between CI-AKI and systemic hypertension was found to be statistically nonsignificant. (p=0.857).

Thirteen of thirty-five patients with dyslipidaemia (37.14%) and five of fifteen (33.3%) patients without dyslipidaemia developed CI-AKI. The association between dyslipidaemia and CI-AKI was found to be statistically nonsignificant. (p= 0.949)

Ten out of twenty-one smokers and eight of 29 non-smokers developed CIAKI. The association between smoking and CI-AKI was found to be statistically non-significant. (47.61% vs. 27.58%; p=0.247).

Seven out of twenty-four patients with LAD occlusion and eleven out of twenty-six patients with non-LAD occlusion developed CI-AKI. This association between culprit artery and CI-AKI was statistically non-significant (29.16% vs 42.3%; p=0.501).

	Yes	No	Significance
Male	38.46%	33.33%	P>0.05
Age>50	37.53%	34.61%	P>0.05
Sys. Htn	33.33%	40%	P>0.05
RBS<300	37.5%	33.3%	P>0.05
RBS>300	70%	27.5%	P<0.05
Dyslipidaemia	37.13%	33.3%	P>0.05
Smoking	47.1%	27.5%	P>0.05

Table 1

Control (50)	No. of Cases
CI-AKI	18
Normal	32

Table 2

Test (50)	No. of Cases
CI-AKI	8
Normal	42

Table 3

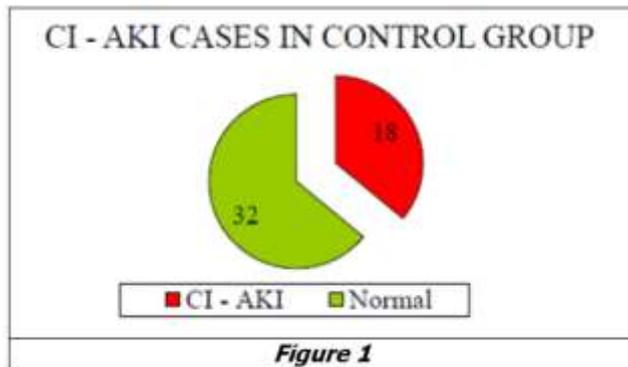


Figure 1

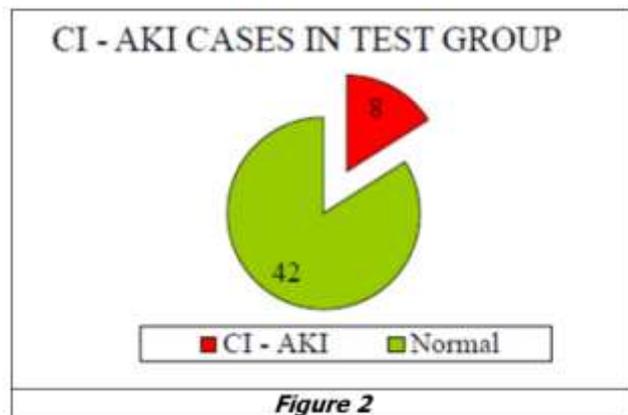


Figure 2

DISCUSSION

Based on the study, the mean age of the study population is 47.4 years. Controls were age and sex matched. According to this study, RIPC decreased the incidence of CI-AKI in patients with ST elevation myocardial infarction undergoing coronary angiogram and this decrease in incidence was statistically significant.

A similar study done by Yamanaka et al.¹ also showed lower incidence of CI-AKI with RIPC in STEMI patients undergoing CAG. The incidence of CI-AKI was 10% in the test group and 36% in the control group which is similar to the results of our study. The sample sizes too were similar. The above study demonstrated a decrease in the peak CK-MB levels and lower incidence of sustained ventricular tachycardia post PCI in RIPC group. These characteristics were not assessed in our study.

The Ren Pro trial, by Fikret Er et al,² also highlighted the efficacy of RIPC in patients with impaired renal function undergoing CAG. The incidence of CI-AKI was 40% in the control group and 12% in the RIPC group. This outcome is again comparable with the results of our study. This shows that RIPC was effective in decreasing the incidence of CI-AKI even in patients with high risk of developing CI-AKI. Patients with pre-existing renal impairment were excluded from our study.

The most common pathophysiological concept of CI-AKI is the induction of renal ischemic injury, possibly caused by iodinated contrast medium-induced reduction in renal blood

flow and oxygen free radical-mediated direct tubular toxicity. Other underlying mechanism for pathological changes in CI-AKI include contrast medium-induced natriuresis and diuresis, which activate the tubuloglomerular feedback response with subsequent vasoconstriction of the glomerular afferent arterioles, causing a decrease in glomerular filtration rate.

Another study by Zagidullin NS et al³ has also showed that RIPC decreases CI-AKI. In this study, CI-AKI occurred in 28% of control group and only 3.8% of test group patients. However, the total sample size was only 51 which is much smaller than our study population.

On the contrary, the RIPCIN trial by T. P Menting et al,⁴ showed no significant effect of RIPC in preventing CI-AKI. Two patients each from the control and RIPC groups developed CI-AKI. However, a subgroup analysis showed a significantly reduced change in serum creatinine in patients with high MEHRAN risk score in RIPC group compared to control group. Sub-analyses of our study showed that factors like age, sex, diabetes mellitus, hypertension, dyslipidaemia and smoking had no association with the incidence of CIAKI. The study by Yamanaka et al had found a significant association between CI-AKI and having LAD as the culprit artery.

Interestingly, our study failed to demonstrate any such association. Identity of the culprit artery was not a risk factor for developing CI-AKI. It is clear that this finding requires larger and more clinical trials before a valid deduction can be made.

Postoperative AKI is a recognized cause of significant postoperative morbidity and mortality. Several factors, including uniform definition of AKI, a predictable injury setting, and high incidence of AKI, are needed to study the role of any intervention in the prevention of AKI.⁵

CONCLUSION

Radiocontrast-induced nephropathy (RCIN) is a major complication of intravascular radiocontrast administration. Renal tubular cell apoptosis is a feature of RCIN,^{6,7,8} which is related to hypertonicity of contrast agents. Until now, there is no effective prophylactic drug regimen to prevent CI-AKI. Despite its potential clinical significance, the precise pathophysiological mechanisms of the action of RIPC on CI-AKI have not yet been elucidated. Some studies have shown fall in CK-MB levels with RIPC in post myocardial infarction setting and this is worth further study.

Limitations of The Study

Small sample size. The study did not include patients who were at a high risk for developing CI-AKI. i.e. Patients with pre-existing CKD and AKI. Mehran risk assessment scoring system was not used- it would have helped in determining which group of patients would have benefitted more with RIPC.

Acknowledgement

We would like to acknowledge The Dean, Madurai Medical College, for his administrative support; HOD, Department of

Medicine, Madurai Medical College; HOD, Department of Cardiology, Madurai Medical College; HOD, Department of Biochemistry, Madurai Medical College for their support. We would also like to acknowledge the subjects who took part in the study.

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