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Original Research Paper

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IMPACT OF ISCHEMIC PRECONDITIONING IN PREVENTION OF CONTRAST INDUCED NEPHROPATHY

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ABSTRACT

Contrast-medium-induced acute kidney injury is associated with substantial mortality and morbidity in patients undergoing coronary angiography. The underlying mechanism is partially attributed to ischemic kidney injury. Remote ischemic preconditioning (rIPC) is a non-pharmacological mechanism that may decrease the incidence of contrast-induced nephropathy (CIN) in high-risk patients. This prospective randomized controlled study evaluated the efficacy of remote ischemic preconditioning in preventing contrast-induced acute kidney injury. Seventy patients with impaired renal function (serum creatinine >1.4 mg/dL or eGFR <60 mL/min/1.73 m2) undergoing elective coronary angiography were randomized to standard care (n=35) or standard care plus ischemic preconditioning (n=35). The primary endpoint was the incidence of contrast-medium-induced kidney injury at 48 hours post-procedure. Results demonstrated that contrast-medium-induced acute kidney injury occurred in 23 patients (32.9%): 16 (47%) in the control group and 7 (20%) in the rIPC group (P<0.005). No major adverse events were associated with remote ischemic preconditioning. Remote ischemic preconditioning before contrast medium administration significantly prevents contrast medium-induced acute kidney injury in high-risk patients, offering a simple, non-pharmacological, cost-free intervention with potential for widespread clinical application.

KEYWORDS :

INTRODUCTION

Contrast-induced nephropathy (CIN) is a complication of coronary procedures and is associated with unfavorable outcomes, including major cardiovascular events, prolonged hospitalization, and even early death in certain individuals. An important risk factor for the incidence of CIN is chronic kidney disease (CKD). Pre-existing renal dysfunction with estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m2 is one of the most important predictors of contrast-induced acute kidney injury (CI-AKI), and its level correlates positively with the incidence of CI-AKI.

Other risk factors include diabetes mellitus, hypovolemia, administration of large amounts of contrast medium, and use of drugs that interfere with the regulation of renal perfusion. Remote ischemic preconditioning can offer a non-pharmacological mechanism for decreasing the incidence of CIN. The role of ischemic preconditioning to reduce the incidence of CI-AKI is not fully understood. In this prospective, randomized, controlled study, we hypothesized that ischemic preconditioning applied prior to coronary interventional procedures may be beneficial in the prevention of CIN in patients at high risk.

Ischemic Preconditioning: Background and Mechanisms

Ischemic preconditioning (IPC), which consists of transient brief episodes of ischemia before a subsequent prolonged ischemia/reperfusion injury, has been shown to reduce the extent of organ damage. The concept of IPC was introduced in 1986 by Murry et al., who first described the cardioprotective effect of multiple brief ischemic episodes before subsequent sustained ischemic insult in dogs with myocardial infarction. IPC can be induced locally when the preconditioning stimulus is applied to the same organ or tissue incurring the ischemic injury.

Remote IPC (rIPC) extends this protection to distant tissues. rIPC was first demonstrated in cardiac tissue in which brief episodes of myocardial ischemia and reperfusion applied to one vascular territory reduced the infarct size of the adjacent tissue that had not undergone any preconditioning. Subsequent studies showed that brief ischemia induced in nontarget tissue, most commonly in the limb or arm, confers protection at a remote site such as the brain, lung, kidney, intestine, or skeletal muscle. Due to their high energy demand and complex microvascular network, kidneys are one of the major organs of interest for clinical application of rIPC.

MATERIALS AND METHODS

Study Design and Patient Population: This study was conducted as a hospital-based observational study where written informed consent was obtained from 70 patients undergoing coronary angiography with eGFR <60 mL/min/1.73 m2 who were admitted to A.J. Institute of Medical Sciences and Research Centre and met pre-defined inclusion and exclusion criteria. The study was initiated after obtaining clearance from the institution's ethical committee.

Inclusion Criteria

Patients aged 18 years or older, presenting with angina pectoris and renal impairment with elevated serum creatinine >1.4 mg/dL or reduced estimated GFR <60 mL/min/1.73 m2. Both genders were included.

Exclusion Criteria

Patients without any renal impairment or chronic renal failure patients undergoing hemodialysis.

Intervention Protocol

Patients were randomized in 1:1 ratio to standard care with (n=35) or without ischemic preconditioning (n=35). All patients received standard care including oral N-acetylcysteine 600mg twice daily and intravenous saline infusion (0.9%) 12 hours before to 12 hours after coronary angiography. Remote ischemic preconditioning was performed by four cycles of alternating 5-minute inflation and 5-minute deflation of a standard upper arm blood pressure cuff to individual's systolic blood pressure plus 50 mmHg to induce transient and repetitive arm ischemia and reperfusion. The procedure was completed less than 45 minutes before coronary angiography.

Measurements

Serum creatinine and eGFR were estimated at baseline, 24 hours after contrast exposure, and 48 hours after contrast

exposure. The primary endpoint was the incidence of contrast-medium-induced kidney injury, defined as an increase in serum creatinine ≥25% or ≥0.5 mg/dL above the baseline at 48 hours after contrast-medium exposure.

Statistical Analysis

The collected data was analyzed using IBM SPSS Statistics software version 23.0. Descriptive statistics including frequency analysis and percentage analysis were used for categorical variables, and mean and standard deviation were used for continuous variables. To find significance in categorical data, chi-square test and Fisher's exact test were used. A probability value of 0.05 was considered as the significant level.

RESULTS

Parameter	IPC Group	Control Group(n=35)
CIN incidence	7 (20%)	16 (45.7%)
P-value	0.022	0.022

Baseline Characteristics: A total of 70 patients (mean age 71.6±5.8 years; 76% men, 24% women) were included. The study population showed high prevalence of cardiovascular risk factors: hypertension in 82.9%, diabetes mellitus in 74.3%, dyslipidemia in 67.1%, prior coronary angiography in 60%, and smoking in 18.6%.

Primary Endpoint: Contrast medium-induced nephropathy occurred in 23 patients (32.9%). Specifically, 7 (20%) cases occurred in the ischemic preconditioning group and 16 (45.7%) in the control group, demonstrating a statistically significant difference (p=0.022).

Serum Creatinine Changes: Serum creatinine measurements at baseline were similar between groups (IPC: 1.526±0.131 mg/dL vs. control: 1.544±0.121 mg/dL, p=0.546). At 24 hours post-contrast, levels remained comparable (IPC: 1.586±0.097 mg/dL vs. control: 1.594±0.124 mg/dL, p=0.748). However, at 48 hours after contrast exposure, a statistically significant difference emerged (IPC: 1.869±0.203 mg/dL vs. control: 2.011±0.223 mg/dL, p=0.007).

DISCUSSION

There is currently no effective prophylactic regimen available to prevent contrast-induced acute kidney injury (CI-AKI), a frequent and life-threatening complication after cardiac catheterization. Therefore, novel treatment strategies are required to decrease CI-AKI incidence and to improve clinical outcomes in these patients. This study demonstrates that remote ischemic preconditioning, induced by intermittent upper-arm ischemia before an invasive coronary procedure, dramatically reduces the incidence of contrast medium-induced nephropathy in patients with chronic kidney disease and high risk for CI-AKI.

The results of this study are consistent with previous research. Er F et al. demonstrated a decrease in CI-AKI by rIPC (40% in control group versus 12% in rIPC group; P=0.002) in patients undergoing elective coronary angiography with impaired renal function. Similarly, Deftereos et al. found that remote ischemic postconditioning reduced the CI-AKI rate from 29.5% in controls to 12.4% in the intervention group (P=0.002). These findings support the growing body of evidence that rIPC is a promising intervention for high-risk patients.

The mechanisms underlying the protective effect of rIPC are multifactorial and involve complex signaling pathways. These include activation of neuronal and humoral communication pathways, key molecular mediators such as protein kinases and transcription factors, and anti-inflammatory and anti-apoptotic effects. The protective mechanisms converge on mitochondrial activation and the opening of ATP-dependent potassium channels, which limit oxidative stress and preserve cell viability during ischemic injury.

Overall evidence suggests that rIPC is particularly beneficial in patients at intermediate or high risk with renal impairment. The simplicity, cost-effectiveness, and safety of rIPC make it an attractive therapeutic option that requires no specialized equipment or pharmacological agents. The procedure can be performed in any clinical setting with a standard blood pressure cuff and takes only 20-40 minutes.

CONCLUSIONS

This study provides evidence that remote ischemic preconditioning, induced by intermittent upper-arm ischemia before coronary angiography, significantly reduces the incidence of contrast medium-induced nephropathy in high-risk patients with chronic kidney disease. The use of ischemic preconditioning may be a feasible and highly attractive therapeutic procedure. It is a simple, non-pharmacological, virtually cost-free intervention with no significant adverse events. Future larger multicenter trials are warranted to establish its clinical utility and to integrate it into standard care protocols for high-risk patients undergoing contrast-enhanced procedures. The findings from this research support the integration of remote ischemic preconditioning into routine clinical practice for patients at risk of developing contrast-induced acute kidney injury.

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