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Original Article

Prevention of contrast induced nephropathy by ischemic preconditioning in patients undergoing percutaneous coronary angiography

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ABSTRACT

Background: Contrast-induced nephropathy (CIN) is the acute deterioration of renal function after parenteral administration of radio contrast media in the absence of other causes. The true incidence of CIN varies because of differences among the published studies in the definition of CIN, the proportion of high-risk patients, the types of contrast media, and the use of preventive measures. Remote ischemic preconditioning (IPC) may offer a non-pharmacological prevention strategy for lowering CIN in patients undergoing coronary procedures. The assumption that IPC produces protective effects on tissues or organs by multiple brief cycles of ischemia and reperfusion applied to another remote tissue or organ.
Aim: To investigate the effect of ischemic preconditioning in prevention of CIN in patients with renal impairment undergoing percutaneous coronary angiography.
Results: In this study, 100 patients undergoing elective PCI with a base line creatinine clearance <60 ml/min were studied. Patients were divided into two equal groups (ischemic preconditioning group and control group). The incidence of CIN was markedly lower in ischemic preconditioning group 14% VS 38% in control group. The incidence of CIN difference as was found to be (24%). Amount of dye used, decreased LVEF and presence of a significant LAD lesion were significant risk factors for occurrence of CIN.
Conclusions: The current study showed that remote ischemic preconditioning plays an important role in prevention of CIN in patients undergoing PCI with renal impairment GFR < 60 ml/min. The amount of contrast, decreased LVEF, and presence of LAD significant lesion were significant risk factors for developing of CIN and these subgroups benefited from application of ischemic preconditioning.

1. 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.[1,2]

Chronic kidney disease (CKD) is an important risk factor for the incidence of CIN.[3] Pre-existing renal dysfunction with estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m ^{2} is the 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.[3,4] 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.[4]

Remote ischemic preconditioning can offer a non-pharmacological mechanisms aiming at decreasing the incidence of CIN in patients undergoing coronary interventions. It is postulated that ischemic preconditioning promotes protective effects on tissues or organs by multiple brief cycles of ischemia and reperfusion applied to another remote tissue or organ.[5–7]

The role of ischemic preconditioning to reduce the incidence of CI-AKI is not fully understood. In our prospective, randomized, sham-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.

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1.1. Aim of the work

To investigate the effect of ischemic preconditioning in the prevention of contrast induced nephropathy in patients with renal impairment undergoing percutaneous coronary angiography.

2. Patients and methods

One hundred patients with a calculated GFR of <60 ml/min/1.73 m^2 were included. They were patients presenting to the Cardiology department of Ain Shams University Hospitals to undergo elective percutaneous coronary intervention, from the period from April 2015 till October 2015.

One type of radio-contrast dye was used which was non-ionic, low-osmolar dye (ULTRAVIST®, Bayer Healthcare). The amount of the radio-contrast medium given was calculated in every case.

2.1. Exclusion criteria

1. Recent exposure to radiographic contrast.
2. Known allergy to radiographic contrast.
3. Chronic peritoneal or hemodialysis treatment.

These included patients were consecutively divided through 1:1 randomization into 2 groups after screening for eligibility criteria regardless of the base line serum creatinine:

Group 1: which consisted of 50 patients who will had PCI with ischemic preconditioning. with a proper hydration with 0.9% sodium chloride as infusion of 3 ml/kg for 1 h prior the procedure followed by an infusion of 1 ml/kg/h for 6 h after the procedure.

Group 2: which consisted of 50 patients who had PCI without ischemic preconditioning. with a proper hydration with 0.9% sodium chloride as infusion of 3 ml/kg for 1 h prior the procedure followed by an infusion of 1 ml/kg/h for 6 h after the procedure.

3. Methods

Patients were subjected to the following:

1. Proper history taking including:
   (a) Age & gender of the patient (for the purpose of calculation of the serum creatinine clearance by applying the Cockcroft-Gault formula (Estimated creatinine clearance equals {((140-age in years) × weight in kg)/(72 × serum creatinine in mg/dl)}. The result was multiplied by 0.8 in females.[8]
   (b) Associated risk factors such as diabetes mellitus, hypertension, dyslipidemia and smoking.
   (c) History of allergy to radiographic contrast.
2. Clinical examination:
   (a) General examination: including weight and height of patients.
   (b) Local cardiac examination.
3. Samples were withdrawn for measurement of serum creatinine prior to the procedure and 48 h after the procedure, whether inpatient or out-patient. Patients was considered to have contrast induced nephropathy if there was an absolute increase in serum creatinine levels by ≥0.5 mg/dL or a relative increase in serum creatinine by ≥25% from baseline, or a creatinine clearance decrease more than 50% over the baseline value (RIFLE classification).[9]
4. 4 A nonionic contrast agent used during the procedure.
5. Patients in group 1 had ischemic preconditioning by performing four cycles of alternating 5-min inflation and 5-min deflation of a standard upper-arm blood-pressure cuff to individuals' systolic blood pressure plus 50 mmHg to induce transient and repetitive arm ischemia and reperfusion. This was done in the waiting ward before the procedure while being hydrated, thus not causing delay. The time between last inflation cycle and CA start was less than 45 min.
6. Group 2 underwent coronary angiography, and had an upper arm blood pressure cuff placed but without ischemic preconditioning as a sham procedure.

3.1. Data management and analysis

Statistical analyses were performed by using SPSS system for Windows (version 20 Chicago, IL, USA), Continuous variables were presented as mean ± SD and categorical variables were expressed as percentages. Wilcoxon signed ranks test for comparing between results before and after PCI. The receiver operational characteristic (ROC) analyses was performed and best cut off value was determined and at that point sensitivity and specificity were determined, the results were considered significant when the p value was less than .05 (see Tables 1–4).

4. Results

Regarding creatinine at baseline, at follow up and percent of change, there was no significant difference between the both groups in baseline creatinine, but there was a significant difference in follow up creatinine p = (.013) in group 2 and highly significant difference in percentage of change p = (.007).

When looking at the occurrence of CIN, 7 patients of 50 with ischemic preconditioning (14%) developed CIN, while 19 patients in control group (38%) developed CIN with highly significant difference between both groups p = (.006).

Table 5 shows that, after adjustment to all factors it was shown that amount of contrast, LVEF, Significant LAD and absence of preconditioning were independent factors for the occurrence CIN.

5. Discussion

Contrast induced nephropathy is not an infrequent complication following coronary diagnostic and interventional procedures. Moreover, it has been proven to be an independent predictor of one-year mortality in patients with ischemic heart disease. The incidence of contrast induced nephropathy varies substantially among several studies due to the lack of a uniform definition.[10] Rates of contrast induced nephropathy may occur in 50% of patients, depending on the presence of risk factors, such as chronic renal insufficiency and heart failure or diabetes mellitus.[1]

The exact mechanism of contrast nephropathy is not entirely comprehended and it may relate to alteration in renal hemodynamics, direct toxic effects on tubular renal epithelial cells, and damage by oxygen radicals.[11] The most common mechanism of CI-AKI is the induction of renal ischemia, possibly due to the iodinated contrast medium-induced reduction in renal blood flow as well as a surge in the oxygen free radical mediated direct tubular toxicity.[12] The underlying mechanism for pathological changes in CI-AKI consists of the contrast medium-induced natriuresis and diuresis, which activates the tubulu-glomerular feedback response with resultant vasoconstriction of the glomerular afferent arterioles producing a decrease in GFR.

There are limited effective prophylactic medications to prevent CI-AKI. Dopamine, mannitol, aminophylline, fenoldopam, captopril, furosemide, atrial natriuretic peptide, calcium channel block-

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