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ORIGINAL ARTICLE

Ischemic Postconditioning Before Percutaneous Coronary Intervention for Acute ST-Segment Elevation Myocardial Infarction Reduces Contrast-induced Nephropathy and Improves Long-term Prognosis

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Background and Aims. Contrast-induced nephropathy (CIN) after percutaneous coronary intervention (PCI) is one of the major adverse outcomes affecting the prognosis of patients with acute ST-segment elevation myocardial infarction (STEMI). Ischemic postconditioning prior to PCI (pre-PCI) in patients with STEMI is hypothesized to be protective against CIN after PCI.

Methods. A total of 251 patients with STEMI were randomized into two groups: ischemic postconditioning group (n = 123, age, 61.1 ± 12.5 years) who underwent ischemic postconditioning prior to PCI; control group (n = 128; age, 64.1 ± 12.1 years) who underwent only PCI. Ischemic postconditioning was administered by three cycles of deflation and inflation of the balloon (1-min ischemia and 1-min reperfusion) starting 1 min after infarct-related artery (IRA) opening. Diagnostic criterion for CIN was: increase in serum creatinine level by ≥0.5 mg/dL or by ≥25% increase from preoperative level within 48 h of surgery. All patients were followed for 1 year for incidence of major cardiovascular events (MACE).

Results. The incidence of postoperative CIN in the ischemic postconditioning group was 5.69% as compared to 14.06% in the control group (p <0.05). At one year, the MACE incidence in the ischemic postconditioning group was 7.32% as compared to 15.63% in the control group (p <0.05).

Conclusions. Pre-PCI ischemic postconditioning in STEMI patients significantly reduces the post-PCI incidence of CIN and improves long-term prognosis.

Key Words: Acute myocardial infarction, Ischemic postconditioning, Percutaneous coronary intervention, Contrast-induced nephropathy, Long term prognosis.

Introduction

Contrast-induced nephropathy (CIN) is a common complication associated with the use of contrast agents in patients undergoing percutaneous coronary intervention (PCI). The incidence of CIN has been reported as 2–3% (1). However, in patients with co-existing multiple risk factors such as renal impairment, diabetes mellitus, acute myocardial infarction (MI), congestive heart failure (CHF), or the use of a high dose of contrast agents, the incidence of CIN can be as high as 50% (1,2). Prevention and effective treatment of CIN is a key imperative owing to its association with prolonged length of hospital stay, increased risk of complications and high in-hospital mortality (3).

Strategies for reducing the incidence of CIN are not well developed. For instance, use of isotonic contrast agent was not found to be superior to low-osmolar contrast media. There was no difference in the occurrence of CIN when comparing iso-osmolar contrast media with low-osmolar contrast media (4). Further, early hydration therapy may

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reduce the incidence of CIN, but no apparent reduction in mortality has been observed (5). In addition, B-type natriuretic peptide (BNP) is known to reduce the incidence of CIN in patients with acute ST-segment elevation myocardial infarction (STEMI) with heart failure; however, its efficacy in STEMI patients without heart failure is yet to be evaluated (5–8). Finally, cysteine and statins have been shown to reduce the risk of CIN. However, most of these studies were small-scale, single-center preliminary trials; the efficacy of these interventions is yet to be definitively established (9,10).

The mechanisms underlying the pathogenesis of CIN are multifactorial, and the vascular, hemodynamic, and tubular factors contribute to its development. The well-accepted theory for development of CIN is the induction of renal ischemic injury, which is possibly caused by iodinated contrast medium-induced reduction in renal blood flow and oxygen free radical-mediated direct tubular toxicity (11). Other potential mechanisms for pathological changes in CIN include contrast medium-induced diuresis and natriuresis, which activate the tubuloglomerular feedback response with subsequent vasoconstriction of the glomerular afferent arterioles, causing a decrease in glomerular filtration rate (12). PCI is the mainstay of treatment for acute MI (including STEMI). However, PCI in STEMI patients is associated with a relatively high incidence of CIN. This phenomenon may be attributable to the following reasons: a) adequate hydration and assessment of renal function may not be possible in every case owing to the emergent nature of the condition; b) hypovolemia due to sweating and vomiting; c) the association of STEMI with large infarcts and poor cardiac function.

Reperfusion therapy, the primary treatment for STEMI patients, is a key priority in order to reduce the infarct size and improve prognosis. However, reperfusion therapy may be associated with myocardial ischemia-reperfusion injury, which may partially offset the clinical benefits of thrombolytic therapy or PCI (13).

Ischemic postconditioning refers to the repetitive cycles of very short duration of ischemia and reperfusion prior to continuous perfusion. Recent studies have shown that ischemic postconditioning protects a variety of organs including heart, brain and liver against ischemia-reperfusion injury (14–16). However, studies on the protective effect of ischemic postconditioning against kidney injury have largely been conducted in animal models such as rat (17,18) and rabbit (19).

Recent studies reported that remote ischemic preconditioning in the upper limb had a renoprotective effect in patients with STEMI and non-STEMI after PCI (20); however, the findings remain controversial (21–23). In this study we investigated the protective effect of ischemic postconditioning against CIN in STEMI patients undergoing PCI.

Materials and Methods

Ethics Statement

This study was approved by the ethics committee of The Third Central Hospital of Tian Jin. The study protocols were in compliance with the ethical guidelines of the Declaration of Helsinki. All subjects provided informed consent.

Subjects

This study was a prospective randomized, single-blind controlled trial. A total of 251 patients with STEMI who were admitted to the Tianjin Third Central Hospital Heart Center between January 2012 and June 2014 were randomly divided into two groups prior to PCI: ischemic postconditioning group and control group. Patients in the ischemic postconditioning group ($n = 123$) received ischemic postconditioning prior to PCI; control group ($n = 128$) received only PCI treatment. Written informed consent was obtained from all patients prior to their enrollment in the study.

Inclusion Criteria

Inclusion criteria were STEMI patients age ≥18 years, time elapsed since onset of symptoms <12 h, treated with direct PCI, presence of shock within 36 h after AMI or cardiogenic shock within 18 h of AMI, and TIMI grade 0 for the infarct-related artery (IRA) blood flow as determined on coronary angiography.

Exclusion Criteria

Patients meeting the following criteria were excluded: TIMI grade 1–3 for IRA as determined on coronary angiography, existing reverse collateral blood supply to the distal end of IRA, old myocardial infarction, history of prior PCI or coronary artery bypass graft, coagulation abnormalities, any acute or chronic infection, and presence of malignancy.

Ischemic Postconditioning Treatment

Preoperatively, all patients received chewable aspirin (300 mg), clopidogrel (600 mg), and heparin (70–100 U/kg body weight) via arterial sheath titrated to maintain the activated clotting time between 250 and 300 s. IRA intervention was performed. Based on the characteristics of the lesion, the decision on whether or not to use thrombus aspiration catheter, platelet membrane glycoprotein IIb/IIIa receptor antagonist (tirofiban), and the number and type of stent implanted was guided by the characteristics of the lesion. In the control group, standard coronary angiography (CAG) with stent implantation was performed. In ischemic postconditioning group, within 1 min of starting IRA interference, a low pressure reperfusion/stop irrigation method was used for ischemic postconditioning. After three rounds of ischemic postconditioning (reocclusion 60 s → reperfusion 60 s → reocclusion