The Egyptian Heart Journal (2015) 67, 315–323

HOSTED BY

ELSEVIER

Egyptian Society of Cardiology

The Egyptian Heart Journal

www.elsevier.com/locate/ehj
www.sciencedirect.com

ORIGINAL ARTICLE

Cardio- and reno-protective effect of remote ischemic preconditioning in patients undergoing percutaneous coronary intervention. A prospective, non-randomized controlled trial

Ayman K.M. Hassan [a,*], **Hamdy Shams-Eddin** [a], **Mona H.M. Abdel-Rahim** [b], **Heba A. Abd El-Hafeez** [c], **Sadat Edroos** [d]

[a] *Department of Cardiology, Faculty of Medicine, Assiut University, Egypt*
[b] *Department of Microbiology and Immunology, Faculty of Medicine, Assiut University, Egypt*
[c] *Department of Clinical Pathology, Faculty of Medicine, Assiut University, Egypt*
[d] *Department of Cardiology, Princess Alexandra Hospital, Harlow, Essex, United Kingdom*

Received 19 June 2015; accepted 16 August 2015
Available online 7 September 2015

KEYWORDS

Remote ischemic preconditioning;
Elective percutaneous coronary intervention;
Contrast induced nephropathy;
PCI-related myocardial infarction

Abstract *Objectives:* This study assessed the cardio- and renoprotective effect of remote ischemic Preconditioning (PreC) in patients undergoing percutaneous coronary intervention (PCI).
Background: Myocyte necrosis and contrast induced nephropathy (CIN) occur frequently in PCI and are associated with subsequent cardiovascular events. Methods: Two hundred consecutive patients undergoing elective PCI with normal baseline troponin-I (cTnI) values were recruited. Subjects were systematically allocated into 2 groups: 100 patients received PreC (created by three 5 min inflations of a blood pressure cuff to 200 mmHg around the upper arm, separated by 5 min intervals of reperfusion) <2 h before the PCI procedure, and control group ($n = 100$).
Results: The incidence of PCI-related myocardial infarction (MI 4a) at 24 h after PCI was lower in the PreC group compared with control group (41% vs 64%, $P = 0.02$). Subjects who received PreC had significant trend toward lower incidence of CIN at 72 h after contrast exposure (4 vs. 11, $P = 0.05$) and less chest pain during stent implantation compared to control group. At 3 months, the major adverse event rate was lower in the PreC group (6 vs. 14 events; $P = 0.04$).
Conclusions: The use of PreC < 2 h before PCI, reduces the incidence of PCI-related MI 4a, tends to decrease the incidence of CIN and improves ischemic symptoms in patients undergoing elective PCI. The observed cardio- and renoprotection appears to confer sustained benefit on reduced major

* Corresponding author at: Cardiovascular Medicine, Assiut University, Assiut 71526, Egypt. Tel.: +20 88 2413006, mobile: +20 1094438055; fax: +20 88 2333327.
E-mail address: ayman.hassan@aun.edu.eg (A.K.M. Hassan).

Peer review under responsibility of Egyptian Society of Cardiology.

http://dx.doi.org/10.1016/j.ehj.2015.08.001

adverse events at 3 month follow-up beyond what is seen with judicious pre- and post-hydration (ClinicalTrials.gov identifier: NCT02313441).

1. Introduction

The first serendipitous description of ischemic Preconditioning in 1986 found that intermittent and short-lived non-lethal organ ischemia prior to significant ischemia–reperfusion (I–R) induced a potent form of endogenous protection in the recipient organ.[1] Remote ischemic 'pre-conditioning' and 'post-conditioning' are now well-established mechanisms of cytoprotection against ischemia–reperfusion injury, triggered by intermittent Preceding ischemia prior to [remote Preconditioning, PreC[2,3]] or after [remote post-conditioning, PostC[4,5]] the index injury. This has been reflected in preliminary clinical trials that demonstrate significant cardio- and renoprotection in various settings.[6–10]

The implementation of PreC in clinical practice has been difficult as it requires an intervention which must be implemented before the onset of ischemia. Organ ischemia might be predicted in medical interventions, such as percutaneous coronary intervention (PCI) or cardiac surgery. PreC applies brief controlled episodes of intermittent ischemia in peripheral musculature of the arms or legs to evoke the signal of remote conditioning using a simple and ubiquitous blood pressure cuff, providing a means of safely applying this protection in these patients without perceived side effects.[11]

Elective PCI is frequently associated with elevation of cardiac troponin I (cTnI) and contrast induced nephropathy (CIN).[12–14] Type 4a myocardial infarction (MI) related to PCI is defined as cTnI elevation 5 times > 99th centile of the upper reference limit.[15] PCI-related troponin elevation of this magnitude and CIN correlates with a significant increase in major adverse events (MAE).[15] Micro-embolization of plaque debris and side branch occlusion during PCI procedure[16] and cardiac reperfusion injury,[17] have been proposed as the most likely causes of PCI-related MI, with prognostic relevance.[12]

This single-center prospective non-randomized controlled trial aimed to assess the cardio- and renoprotective effect of remote PreC after elective PCI.

2. Methods

2.1. Identification and recruitment of patients

We performed a prospective non-randomized parallel group comparison at the catheterization laboratory of Assiut University Hospitals (AUH).

Patients between 18 and 80 years of age, scheduled to undergo an elective PCI and able to give an informed consent were eligible for enrollment in the study (Fig. 1, Table 1). Elective PCI was defined as any coronary revascularization in a low-risk, hemodynamically stable patient who presents to the facility for a planned PCI or for a coronary angiogram followed by ad hoc PCI. Exclusion criteria were as follows: (1) emergency PCI; (2) baseline troponin value $\geqslant$0.04 ng/mL; (3) nicorandil or glibenclamide use; (4) those who could not give informed consent; and (5) patients with severe renal impairment or on regular dialysis as described in detail previously.[18]

2.2. Study groups and protocol

Consecutive patients undergoing elective PCI between September 2013 and May 2014, were invited to participate in the study during their attendance at a routine preadmission clinic. Eligible patients, after obtaining informed consent, were systematically allocated to the PreC treatment group or the control group according to our daily based allocation technique (Fig. 1). 259 patients were screened for eligibility. Of the 259 patients screened, 18 were on nicorandil, 20 were on glibenclamide, and 11 had incomplete data. These 49 were excluded from this analysis, leaving 210 participants for systematic allocation, 10 of whom were dropped out of the study (Fig. 1). PreC was successfully provided to 100 participants without complication. Demographic and clinical details showed no difference between control and PreC groups (Table 1).

2.3. Pre- and post-procedural hydration protocols

Patients were hydrated with intravenous saline infusion as prophylaxis against contrast induced nephropathy (CIN) [3–4 mL/kg/h 4 h before and after intervention and encouraged to drink lots of water after PCI (except those with left ventricular dysfunction or sever kidney disease, who underwent hydration with 1 mL/kg/h for 12 h before and after PCI)] as described in detail previously.[19,20]

2.4. Assignment method

Participants were allocated to the treatment group by a day-dependent method of allocation. The analysis was blinded as all outcome measures were recorded by an independent researcher without prior knowledge of the study allocation of the participants. The study protocol was approved by the ethical committee of Assiut faculty of medicine (IRB no: IRB00008718 at 23 June 2013). A written informed consent was obtained from all participants. The consent form was designed with an explanation on the purpose and conduction of this research project. The study identification number at ClinicalTrials.gov.is NCT02313441.

2.5. Sample size power calculation

The sample size was determined on the basis of the primary outcome, post-PCI cTnI at 24 h. PreC was estimated to reduce the prevalence of PCI-induced cTnI release by 15% as described in detail previously.[18] A power calculation ($\alpha = 0.05$; $\beta = 0.2$; statistical power = 80%) estimated a sample size of 100 patients per group would be needed. Hence 200