Mashhad University of Medical Sciences (MUMS)

Reviews in Clinical Medicine

Clinical Research Development Center Ghaem Hospital

Nicorandil in patients with acute coronary syndrome and stable angina undergoing Percutaneous Coronary Intervention: literature review

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ARTICLE INFO

Article type
Review article

Article history
Received: 23 Mar 2014
Revised: 4 May 2014
Accepted: 8 May 2014

Keywords
Nicorandil
Myocardial infarction (MI)
Percutaneous coronary intervention (PCI)
Stable angina
Unstable angina

ABSTRACT

Percutaneous coronary intervention is an option for the treatment of coronary artery disease such as acute coronary syndrome and stable angina.Acute coronary syndrome has two groups including acute myocardial infarction and unstable angina. Periprocedural myocardial infarction is a frequent and prognostically important complication of percutaneous coronary intervention and can be easily monitored by measuring myocardial enzymes. Coronary microvascular dysfunction in patients undergoing primary percutaneous coronary intervention for the treatment of ST-segment elevation myocardial infarction is associated with poor prognosis. Even after recanalization, reperfusion injury often occurs including no-reflow or slow-flow in which sufficient myocardial blood flow cannot be obtained and results in a poor outcome of cardiac function in the long term.

Nicorandil is the opener of the adenosine triphosphate-sensitive potassium channel and is known to have an antiarrhythmic effect and myocardial protective functions such as reduction of the coronary microvascular resistance by relaxing the smooth muscles of blood vessesl and preconditioning.In this literature review, we evaluate articles about acute coronary syndrome and stable angina undergoing PCI.

Please cite this paper as:
Partovi N, Falsoleiman H. Nicorandil in patients with acute coronary syndrome and stable angina undergoing Percutaneous Coronary Intervention: literature review. Rev Clin Med. 2015;2 (1):42-44.

Introduction

We performed a literature review of articles comparing treatment with nicorandil in acute coronary syndrome (ACS) and stable angina in patients undergoing percutaneous coronary intervention (PCI).

Hideki Ishii et al. evaluated 368 patients with first ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI) who were received 12 mg of nicorandil intravenously just before reperfusion.

There was significant difference in cardiovascular death and hospital admission for heart failure (HF) in nicorandil and placebo groups. Similar results were also obtained regarding angiographic parameters such as final achievement of TIMI (Thrombolysis in Myocardial Infarction) III grade and corrected TIMI frame count (TFC) after PCI. Nicorandil had significant effect on ST-segment resolution (50%) after PCI, maximum serum creatine kinase, and being free from reperfusion arrhythmias.

Nevertheless, there were no significant differences in all-cause mortality and need for re-PCI or coronary artery bypass grafting (CABG) in two groups (1) (Table1).

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Table 1. Comparison of clinical, laboratory, angiographic, and echocardiographic parameters in AMI patients undergoing PCI in nicorandil and control groups

Author Refrence	Ono H (6)	Noritoshi Ito (4)	Ju Han Kim (3)	Satoshi Ota (2)	Hideki Ishii (1)
Study population	58	60	200	92	368
Cardiovascular death	Decrease	-	-	-	Decrease in case group
All-cause mortality	_	-	-	-	No difference
Recurrent chest pain	_	-	-	Decrease	-
arrythmia	_	-	-	No difference	Decrease
Re- PCI	_	-	-	-	No difference
CABG	_	-	-	-	No difference
Worsening heart failure	Decrease	-	-	-	Decrease
ST resolusion	-	-	-	Increase	Increase
TFC	-	Decrease	-	Decrease	Decrease
TIMI grade	-	-	-	-	Increase
Slow flow	-	-	-	No difference	-
No-reflow	Decrease	-	-	No difference	-
CPK	-	Decrease	Decrease	-	Decrease
CKMB	-	Decrease	Decrease	-	Decrease
troponin	-	-	Decrease	-	-
LVEF	Increase	-	Increase	-	Increase
RWMA(regional wall motion abnormality)	-	-	Decrease	-	-

larization Trial (SMART) by Satoshi Ota et al. 92 patients with first AMI (acute myocardial infarction) were randomly assigned to 1 of 3 groups including intracoronary administration of nicorandil (group A), combined intravenous, and intracoronary administration of nicorandil (group B) and no nicorandil administration (group C). There were significant outcomes in reduction of chest pain in group B and significant ST resolution in group A and B rather than C. But there were no significant differences in reperfusion arrhythmia in three groups.

In angiographic data, there were significant differences in TIMI frame count in A and B rather than C but there were no significant differences in no-reflow and slow-flow in three groups (2) (Table1).

Ju Han Kim et al. evaluated 200 patients with unstable angina who did not require emergent PCI and were randomly assigned to 2 groups including intravenous isosorbide dinitrate (ISDN) and intravenous nicorandil. There was significant improvement in LV function, wall motion score index, and regional wall motion as well as less frequent complications in hospital and no-reflow phenomenon in nicorandil group.

There was low increase in myocardial enzymes including creatine phosphokinase (CPK), troponin I (TNI), and troponin T (TNT) in nicorandil group. They suggested a myocardial protective effect, which can be explained by nicorandil inhibiting myocardial damage during PCI (3) (Table2).

Noritoshi Ito et al. evaluated 60 patients with STEMI who received single intracoronary administration of nitroglycerin or nicorandil after primary PCI. There was significant reduction in serum CPK level. In angiographic data,

there was significant differences in index of microcirculatory resistance (IMR), myocardial blush grade, and angiographic TIMI frame count in nicorandil group (4) (Table1).

Seung-Ju Kim et al. reported 213 patients with stable or unstable angina who were scheduled for non-urgent PCI for de-novo coronary lesions and were randomized into group 1 (control), group 2 (adenosine), group 3 (nicorandil) and group 4 (adenosine-nicorandil combination). There were no significant differences in the incidence of post-procedural myocardial necrosis among the four groups (5) (Table2).

Ono H et al. examined 58 patients with AMI who were randomized into control and nicorandil pretreatment groups. There were significant differences in urinary 8-epi-PGF2alpha excretion.

Table 2. Comparison of clinical, laboratory, and echocardiographic parameters in patients with stable and unstable angina undergoing PCI in nicorandil and control groups.

Author Refrence	Jongmin Hwang (8)	Tsuyoshi Isono (7)	Seung-Ju Kim (5)
Study population	81	49	213
CPK	No difference	Decrease in case group	No difference
CKMB	No difference	Decrease	No difference
Troponin	No difference	Decrease	No difference
Myoglobin	No difference	Decrease	No difference
LVEF	-	Increase	-
RWMA	-	Decrease	-

Urinary 8-epi-PGF2alpha excretion as a marker of reactive oxygen species (ROS) formation increased 2-fold at 60 to 90 minutes after PCI in the control group, whereas it was unchanged after PCI in the nicorandil group. The incidence of no-reflow phenomenon was lower in the nicorandil group than in the control group. Left ventricular ejection fraction (LVEF) and cardiac index at 6 months were greater in the nicorandil group than in controls. Plasma brain natriuretic peptide level at 6 months was lower in the nicorandil group. Incidence of inhospital cardiac events and rehospitalization were lower in the nicorandil group than in controls (6) (Table1).

Tsuyoshi Isono et al. evaluated 49 patients undergoing elective PCI who were divided into two groups, nicorandil and control. There was significant suppression in myocardial enzyme levels (CPK, CKMB, TNI and myoglobin) in nicorandil group. Furthermore, regional left ventricular wall motion significantly improved at follow-up in the nicorandil compared to the control group (7) (Table2).

Jongmin Hwang et al. evaluated 81 patients with stable or unstable angina undergoing PCIs of the left anterior descending artery, randomly assigned to the nicorandil group or the control group. There were no significant differences in post-PCI peak creatine phosphokinase MB isoform (CKMB) and troponin I enzyme levels between two groups (8) (Table2).

Conclusion

There are more studies about MI than stable angina and it seems the effect of nicorandil is proven in MI patients; but we need more studies about stable angina.

Acknowledgement

We would like to thank Clinical Research Development Center of Ghaem Hospital for their assistant in this manuscript. This study was supported by a grant from the Vice Chancellor for Research of the Mashhad University of Medical Sciences for the research project as a medical student thesis with approval number of 910415.

Conflict of Interest

The authors declare no conflict of interest.

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