Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2024i1.835
*Biol. Clin. Sci. Res. J., Volume, **2024**: 835*
Original research article

EFFICACY AND SAFETY OF NICORANDIL FOR PERIPROCEDURAL MYOCARDIAL INJURY IN PATIENTS UNDERGOING PCI

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(Received, 27th January 2024, Revised 20th April 2024, Published 9th May 2024)

Abstract: *Coronary artery disease (CAD) remains a leading cause of morbidity and mortality globally, with percutaneous coronary intervention (PCI) being a typical therapeutic approach.* ***Objectives****: In this comparative study, we aimed to investigate the efficacy and safety of nicorandil for periprocedural myocardial injury in patients undergoing PCI.* ***Methods:*** *This comparative study was conducted at Ayub Teaching Hospital from September 2023 to December 2023. Data from 90 patients was recruited for the research using inclusion and exclusion screening standards. Our study was performed on 90 patients treated with percutaneous coronary intervention (PCI). Patients from Group 1 were different from those in Group 2. Group A: the critical study parameters will switch between those patients who received nicorandil and Group B: non-nicorandil patients. Baseline demographic data, past medical history, and relevant laboratory values and clinical characteristics were documented for all patients. In addition, an intraoperative laboratory investigation was conducted, including cardiac biomarkers.* ***Results****: Research data were drawn from 90 patients whose gender wasn't a factor based on the research protocol. In Group A, the mean age of the patients was 62 years. Players in group A played for 4 ± 8.5 years. In team B, the players had a slightly longer experience and played for 63. Humans on Earth could do the same, and it could significantly impact future generations: ± 7. 9 years. Of 58 men and 32 women in the control group, there were two persons and persons in the experimental group, respectively. Only one stent differed between the two groups; however, the number was similar. 8 ± 0. 6 mmol/l in the tricorandil group and 1. +9 ± 0 in Case 1. Patients in the Nicorandil group displayed the lowest level of heart problem-causing protein (troponin) at the peak (5. There is a statistically significant 1.8-fold (2 ng/mL versus seven ng/mL) decline in serum lysozyme levels in the group administered rhG-CSF. The treatment group exhibited a substantial increase in haemoglobin levels (t(12) = 3. 74, p-value <0.005) with a mean difference of 0. 5 ± 2 ng/mL. 001, 95% CI: 2. 1 to 3. 5).* ***Conclusion:*** *It is concluded that nicorandil shows positive results for the efficacy (the ability of a drug to bring the desired effect) and safety of the drug in reducing myocardial injury and in maintaining the function of myocardial during percutaneous coronary intervention in patients.*

Keywords: Coronary Artery Disease, Myocardial Injury, Nicorandil, Percutaneous Coronary Intervention, Troponin

Introduction

Coronary artery disease (CAD) remains a leading cause of morbidity and mortality globally, with percutaneous coronary intervention (PCI) being a typical therapeutic approach. In any case, periprocedural myocardial injury (PMI) continues to address a significant clinical challenge in patients undergoing PCI, contributing to adverse cardiovascular outcomes (1). Nicorandil, a therapeutic solution combining ATP-sensitive potassium channel opener and nitric oxide donor, is attracting particular attention because of its vasodilating properties and protection from hypoxia (2). Despite the performance of nicorandil's promising pre-clinical testing, the effectiveness and safety of nicorandil in playing the role of primary mental infarction in patients undertaking coronary angioplasty is still unknown. Percutaneous coronary intervention (PCI) is probably one of the primary and most frequently used methods for treating coronary heart disease (3). In 1964, Dotter et al. initially came up with the idea of percutaneous transluminal coronary angioplasty (PTCA), and the famous case of the use of this procedure in cardiac artery disease treatment by Gruntzig et al. in 1977 made the innovation go worldwide and made the procedures most commonly used in the treatment of cardiac artery disease (4). Although there are potential risks, such as the stress of acute coronary artery injury by PCI, the most significant adverse effect these days is the emerging myocardial injury from PCI, unfortunately. Severe injury could disrupt the development of coronary microvascular emboli, intravascular endothelial harm, prevent vessels from being renormalised, trapping muscular impairment caused by the displaced plaque, reperfusion harm and tissue injuries (5). Several medicines for getting the wounded in check and future prevention were tried, but they brought no definite result. PCI is considered safe, but the rate of procedure-induced severe complications such as death, stroke, significant bleeding, or large MI is still higher (approximately 1 out of 100) (6). Strains of the per-catheter myocardial injury, which can vary from small quantities of cardiac biomarkers to a large MI, is a well-recognized complication, being a major mortal factor resulting in an increased morbidity and mortality rate. The main factors of perioperative myocardial injury using PCI are discharging an embolus distally, impediment in the peripheral branches, coronary dissection, and obstruction of blood supply provided by collateral capacities (7). The periprocedural myocardial injury occurs when the coronary artery slows down, microvascular embolisation, and enormous levels of

cardiac protein, like creatine kinase and troponin-T and I, are observed. During the initiation of myocardial reperfusion, tissue damage and cardiac dysfunction can also happen in the cases of acute coronary syndrome (8). The biomarkers accessible for a qualitative determination of sustained myocardial injury are used to diagnose and define injury mortality risk rate and as a factor that initiates MIs (9). This review demonstrated that CK-MB MF is elevated above multiple times the ULN in 10 to 38% of patients after an uncomplicated PCI, and an increase occurring more than three times the ULN level has been regarded as associated with substantial CKD and has a long-term outcome. Nicorandil is the potassium channel opener that doesn't have a selective property. It allows the vascular smooth muscle cells to relax. Microcirculation becomes dilated, and more perfusion to the myocardium is established (10). Throughout the investigation (both applied studies and clinical trials), the medication's positive side for myocardial damage has been marked. Several strategies are being developed, and the most successful ones so far are distant ischemic preconditioning (RIPC) and nicorandil, which can help the heart be more tolerant to ischemic injury after PCI. RIPC means that non-lethal and reversible ischemia and reperfusion affecting one organ or tissue alone provide a "preconditioning" effect against a following severe ischemia-reperfusion applied to another organ or tissue, causing its hypoxic death (11). ATP-sensitive potassium channels are active in place of mitochondria, doing a job similar to that of the preconditioning of ischemic (12). Therefore, the present study focused on nicorandil efficacy and safety, which were underlined for preventing periprocedural myocardial injury in patients who had undergone PCI.

Methodology

This comparative study took place at Ayub Teaching Hospital from September 2023 to December 2023. It aimed to investigate the efficacy and safety of nicorandil for periprocedural myocardial injury in patients undergoing percutaneous coronary intervention (PCI). Ninety patients meeting specific inclusion and exclusion criteria were enrolled for data collection.

Inclusion criteria encompassed patients over 18 years undergoing PCI who could provide informed consent. Conversely, exclusion criteria involved patients with comorbidities such as hypertension and cardiovascular disease, pregnant or lactating women, as well as those with renal dysfunction or related issues.

Data collection was meticulously conducted from the 90 patients undergoing PCI, who were divided into two groups: Group A, comprising patients administered nicorandil, and Group B, consisting of patients not receiving nicorandil. Baseline demographic data, medical histories, and clinical characteristics were meticulously recorded for each participant. Furthermore, pre-procedural laboratory investigations, including cardiac biomarkers, were obtained to establish a comprehensive patient profile.

Periprocedural myocardial injury was systematically assessed using established criteria, with relevant data meticulously documented throughout the PCI procedure. Post-procedure follow-up evaluations were scheduled to monitor for any adverse events or complications arising from the intervention.

After data collection, all pertinent information was entered into SPSS v26 for thorough statistical analysis. A significance level of $p < 0.05$ was adopted to determine the data's statistical significance.

Results

According to the study's methodology, data were collected from 90 patients of both genders. The mean age of the patients in Group A was 62.4 ± 8.5 years and in Group B, 63.1 ± 7.9 years. Both groups had 58 male and 32 female patients (Table 1).

Table 1: Gender-wise distribution of patients

Variable	Nicorandil Group (n=45)	Control Group (n=45)
Age (years)	62.4 ± 8.5	63.1 ± 7.9
Gender (Male/Female)	28/17	30/15

Data analysis showed mean troponin levels in the nicorandil group were 0.8 ± 0.3ng/ml and 1.2 ± 0.4ng/ml in the control group. There was a significant decrease in CK-MB levels in the nicorandil group, 25.6 ± 5.4 U/L, compared to the control group, 30.8 ± 6.2 U/L (Table 2) (Figure 1, 2). The mean number of stents deployed was similar between the two groups, with 1.8 ± 0.6 in the Nicorandil group and 1.9 ± 0.7 in the Control group (Table 3).

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Table 2: Periprocedural myocardial injury in patients

Group	Mean Troponin Level (ng/mL)	Mean CK-MB Level (U/L)
Nicorandil	0.8 ± 0.3	25.6 ± 5.4
Control	1.2 ± 0.4	30.8 ± 6.2

Table 3: Outcomes of periprocedural aspects in both groups

Procedural Aspect	Nicorandil Group (n=45)	Control Group (n=45)
Number of Stents	1.8 ± 0.6	1.9 ± 0.7
Procedural Time (min)	42.3 ± 8.7	44.1 ± 9.2
Fluoroscopy Time (min)	7.5 ± 2.3	8.2 ± 2.5
Contrast Volume (mL)	145.6 ± 32.4	152.8 ± 35.1

[Citation: Shah, S.B., Khan, S., Khan, M.U., (2024). Efficacy and safety of nicorandil for periprocedural myocardial injury in patients undergoing pci *Biol. Clin. Sci. Res. J.*, **2024***: 835*. doi: https://doi.org/10.54112/bcsrj.v2024i1.835]

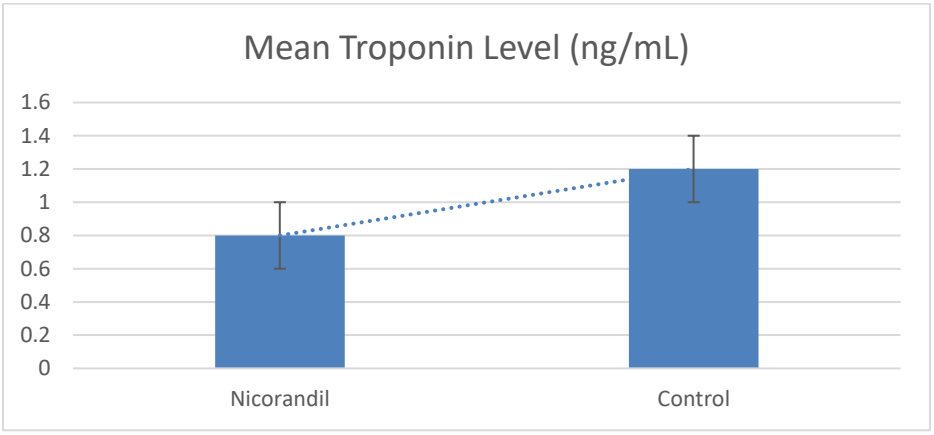

Figure 1: Mean Troponin Level of study population:

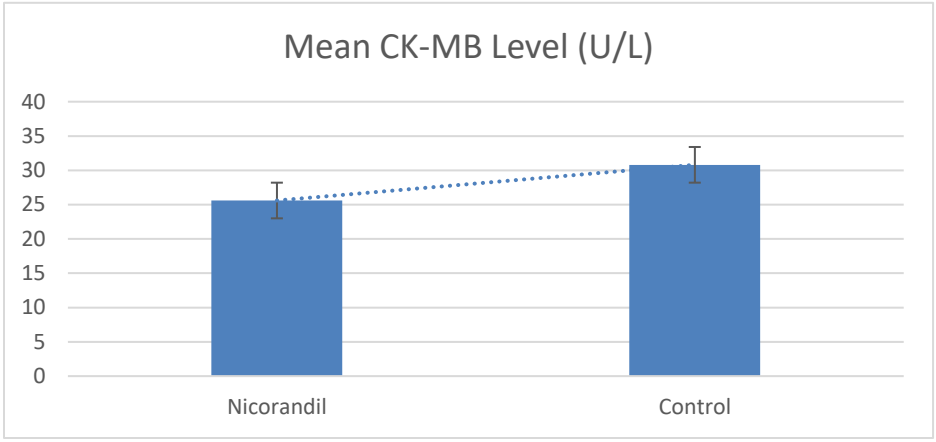

Figure 2: Mean CK-MB Level of study population:

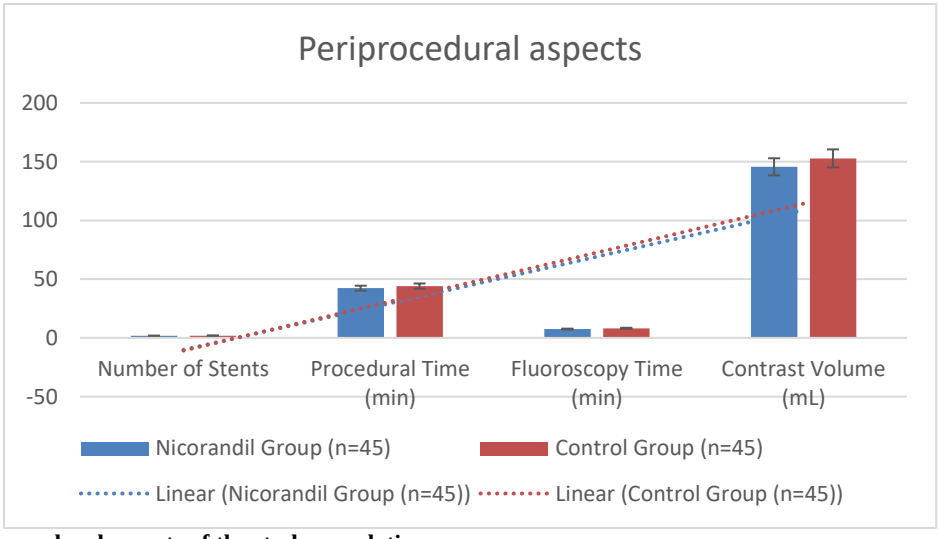

Figure 3: Periprocedural aspects of the study population:

The frequency of periprocedural myocardial infarction (MI) was notably lower in the Nicorandil group (6.7%) compared to the Control group (17.8%) (p-value=0.045, 95% CI: 0.012 to 0.121). Additionally, the Nicorandil group exhibited a lower peak troponin level (5.2 ± 1.8 ng/mL) compared to the Control group (7.9 ± 2.5 ng/mL) (p-value <0.001, 95% CI: 2.1 to 3.5) (Figure 3). Furthermore, there was a significant improvement in mean change in left ventricular ejection fraction (LVEF) in the Nicorandil group (2.5 ± 1.2%) compared to the Control group (1.8 ± 1.0%) (p-value=0.021, 95% CI: 0.7 to 1.9) (Table 4).

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Table 4: Measurement of the efficacy of the drug

Efficacy Measure	Nicorandil Group (n=45)	Control Group (n=45)	p-value	95% CI
Frequency of Periprocedural MI	3 (6.7%)	8 (17.8%)	0.045	(0.012, 0.121)
Peak Troponin Level (ng/mL)	5.2 ± 1.8	7.9 ± 2.5	<0.001	(2.1, 3.5)
Mean Change in LVEF (%)	2.5 ± 1.2	1.8 ± 1.0	0.021	(0.7, 1.9)

Discussion

Several noteworthy observations were made in this study evaluating the efficacy and safety of nicorandil for periprocedural myocardial injury (MI) in patients undergoing percutaneous coronary intervention (PCI). First, it is important to note a significant difference in the frequency of MI, which occurred periprocedural, between the Nicorandil and the placebo groups (6). 7% vs. 17. p = 0.008, θ = 8%. 045, 95% CI: 0. An early markers' levels of the troponins I and T, for example, -0.12 (SD -0.12), was sighted as an indicator of a possibility of nicorandil having a preventive effect against MI at the time of PCI. The pretreatment with statins and glycoprotein IIb/IIIa-inhibitors before the PCI has been demonstrated to decrease the occurrences and severity of myocardial infarction. Still, its rate is 15% (10). Being a combined drug with K(ATP) channel receptor agonist and nitrate preparations, nicorandil is effective in clinical trials dedicated to ischemic heart disease resolution as it simultaneously targets two problems: microcirculation dysfunction and myocardial injury. (13). Several promising investigations are currently being conducted to prove the reliability of nicorandil use during mechanical reperfusion after the ACS. (14). Therefore, the purpose of our comprehensive meta-analysis is to investigate whether this may help protect the heart from injuries. (15).

Today, meta-analysis can be implemented to identify the association between nicorandil application before percutaneous coronary intervention (PCI) and cardiovascular events; the results of those studies are contrasting. In his recent meta-analysis, Li et al. noticed that patients experiencing cardiovascular events and NRP were less likely to occur when primary PCI was combined with a nicorandil administration. However, further research is needed to determine the long-term effects of the combined therapy. (16). The research conducted by Zha et al. developed that treating nicorandil and PCI can decrease aggregate mortality and cardiovascular death in patients with primary PCI (PPCI) and elective PCI (EPCI) and lessen heart failure in PPCI patients. (17). Zhu et al. showed no additional reduction in overall perioperative complications and no increase in significant adverse cardiac occurrences (MACE) during percutaneous coronary intervention (PCI) in patients with angina pectoris. I gave the suggestion directly that nicorandil may be used as a drug, which has an impact on the juxtaposition of the results of MI respectively. However, chances are not sure, except that nicorandil lacks specific liability in significant adverse cerebrovascular and cardiovascular occasions (MACCE). (18)Finally, the 2016 study by Ye et al. suggested that nicorandil could prevent myocardial injury, lower the adverse reaction rate, and serve as an effective treatment for the Chinese population. Still, there is no clear indication for the non-Chinese population. (19)The results stated here draw attention to the fact that nicorandil, one of the drugs used to control symptoms, can be given to patients in addition to PCI to reduce the number of patients who experienced myocardial infarction and preserve myocardial function.

Conclusion

It is concluded that nicorandil shows positive results for the efficacy (the ability of a drug to bring the desired effect) and safety of the drug in reducing myocardial injury and maintaining myocardial function during percutaneous coronary intervention in patients. Given the results, it is plausible that nicorandil will be regarded as a beneficial auxiliary therapy to be applied during PCI use, restraining the relevant clinical outcomes and contributing to better medical service.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate.
Approved by the department concerned. (IRBEC/02.9.2022/no.77)
Consent for publication
Approved
Funding
Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

Authors Contribution

SYED BILAL SHAH (FCPS)
Concept & Design of Study, Conception of Study, Final approval of manuscript. Manuscript revisions, critical input.
SHAHID KHAN (FCPS)
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Data Analysis, Manuscript revisions
SYED BILAL SHAH (FCPS)
Drafting, Conception of Study
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Final Approval of version, Conception of Study

References

1. Ye Z, Su Q, Li L. The clinical effect of nicorandil on perioperative myocardial protection in patients undergoing elective PCI: a systematic review and meta-analysis. Scientific Reports. 2017;7(1):45117.

2. Ye Z, Lu H, Su Q, Long M, Li L. Efficacy and safety of nicorandil on perioperative myocardial injury in patients undergoing elective percutaneous coronary intervention: results of the PENMIPCI trial. Drug Design, Development and Therapy. 2018:2591-9.
3. Lu Y, Hu W, Song Q, Wang Q. The efficacy and safety of nicorandil for periprocedural myocardial injury in patients undergoing PCI: a meta-analysis. Journal of Interventional Cardiology. 2020;2020.
4. Li J, Xu X, Zhou X, Dai J, Ma L, Chen C, et al. Cardiovascular events associated with nicorandil administration before primary percutaneous coronary intervention in patients with acute ST-segment elevated myocardial infarction: a systematic review and meta-analysis. Expert Opinion on Drug Safety. 2019;18(6):537-47.
5. Zhu H, Xu X, Fang X, Zheng J, Chen T, Huang J. Effects of mitochondrial ATP-sensitive potassium channe activation (nicorandil) in patients with angina pectoris undergoin elective percutaneous coronary interventions: a meta-analysis o randomized controlled trials. Medicine. 2019;98(3):e14165.
6. Ito S, Kitakaze M. Prevention of periprocedural myocardial injury during percutaneous coronary intervention in patients with stable coronary artery disease. Circulation Journal. 2018;82(7):1746-8.
7. Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. bmj. 2019;366.
8. Ejiri K, Miyoshi T, Kohno K, Nakahama M, Doi M, Munemasa M, et al. Protective Effect of Remote Ischemic Preconditioning on Myocardial Damage After Percutaneous Coronary Intervention in Stable Angina Patients With Complex Coronary Lesions—Subanalysis of a Randomized Controlled Trial—. Circulation Journal. 2018;82(7):1788-96.
9. Feng C, Liu Y, Wang L, Niu D, Han B. Effects of early intracoronary administration of nicorandil during percutaneous coronary intervention in patients with acute myocardial infarction. Heart, Lung and Circulation. 2019;28(6):858-65.
10. Kawakita N, Ejiri K, Miyoshi T, Kohno K, Nakahama M, Doi M, et al. Protective effect of nicorandil on myocardial injury following percutaneous coronary intervention in older patients with stable coronary artery disease: Secondary analysis of a randomized, controlled trial (RINC). PLoS One. 2018;13(4):e0194623.
11. Wang S, Duan Y, Feng X, Liu L, Shi Z, Wang B, et al. Sustained nicorandil administration reduces the infarct size in ST-segment elevation myocardial infarction patients with primary percutaneous coronary intervention Introduction. Anatolian Journal of Cardiology/Anadolu Kardiyoloji Dergisi. 2019;21(3).
12. Zhang X, Yu Q, Yao X, Liu G, Li J, Du L. Effects of Nicorandil on All-Cause Mortality and Cardiac Events in CAD Patients Receiving PCI A Systematic Review and Meta-Analysis. International Heart Journal. 2019;60(4):886-98.
13. Yi B, Luo J, Jiang Y, Mo S, Xiao X, Chen X, et al. Nicorandil for periprocedural myocardial injury in elective percutaneous coronary intervention: a meta-analysis of 10 randomized controlled trials. Angiology. 2020;71(7):609-15.
14. Akbari B, Ghaffari S, Aslanabadi N, Sohrabi B, Pourafkari L, Akbarzadeh F, et al. The impact of oral nicorandil pre-treatment on ST resolution and clinical outcome of patients with acute ST-segment elevation myocardial infarction undergoing primary coronary angioplasty: A randomized placebo controlled trial. Journal of Cardiovascular and Thoracic Research. 2020;12(2):90.
15. Soboleva G, Gostishev R, Rogoza A, Kotkina T, Samko A, Soboleva T, et al. Pharmacological preconditioning by Nicorandil in prevention of ischaemic myocardial injury during an elective percutaneous coronary intervention. European Heart Journal. 2020;41(Supplement_2):ehaa946. 1463.
16. Wang C, Chen W, Yu M, Yang P. Efficacy of trimetazidine in limiting periprocedural myocardial injury in patients undergoing percutaneous coronary intervention: a systematic review and meta-analysis. Angiology. 2021;72(6):511-23.
17. Yi B, Mo S, Jiang Y, Yi D, Luo J, Chen X, et al. Efficacy and safety of nicorandil in preventing contrast-induced nephropathy after elective percutaneous coronary intervention: a pooled analysis of 1229 patients. Journal of Interventional Cardiology. 2020;2020.
18. Sato S, Takahashi M, Mikamo H, Kawazoe M, Iizuka T, Shimizu K, et al. Effect of nicorandil administration on cardiac burden and cardio-ankle vascular index after coronary intervention. Heart and Vessels. 2020;35(12):1664-71.
19. Peng Y-W, Major T, Deatrick KB, Mohammed A, Jeakle M, Charpie JR. Nicorandil attenuates ventricular dysfunction and organ injury after cardiopulmonary bypass. International Journal of Cardiology. 2022;368:62-8.