Tropical Journal of Pharmaceutical Research June 2023; 22 (6): 1327-1333
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v22i6.24

Original Research Article

Effect of pre-percutaneous coronary intervention ticagrelor administration on coronary reperfusion and short-term prognosis in patients with acute myocardial infarction

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Sent for review: 21 February 2023 *Revised accepted: 23 May 2023*

Abstract

Purpose: *To investigate the effect of ticagrelor administration prior to percutaneous coronary intervention (PCI) on coronary reperfusion and short-term prognosis in patients with acute myocardial infarction.*
Methods: *A total of 200 patients treated for acute myocardial infarction in The Second Affiliated Hospital of Qiqihar Medical College between May 2021 and October 2022 were assigned to receive either clopidogrel (control group) or ticagrelor (Ticagrelor group) before PCI, in a 1:1 ratio, with 100 patients in each group. Clinical indices, serum C-reactive protein (CRP), inhibition of platelet aggregation (IPA), lipid indices, coronary reperfusion, and short-term prognosis of the patients were analyzed to investigate the effectiveness of the pre-intervention.*
Results: *Patients receiving ticagrelor exhibited significantly lower levels of maximum platelet aggregation rate (MAR), P2Y12 reaction units (PRU), and left ventricular end-diastolic diameter (LVDD) and higher left ventricular ejection fraction (LVEF) than those given clopidogrel ($p < 0.01$). Also. patients administered pre-interventional ticagrelor administration exhibited significantly lower serum concentrations of total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) than those who received clopidogrel ($p < 0.01$), suggesting a better overall blood lipid profile for the former. Pre-PCI ticagrelor administration significantly mitigated inflammatory reactions more than clopidogrel, as evidenced by the reductions in serum CRP, cTnI, and CK-MB levels ($p < 0.01$). It further resulted in a lower risk of abnormal platelet aggregation than pre-interventional clopidogrel ($p < 0.01$).*
Conclusion: *Pre-interventional ticagrelor administration after the onset of acute myocardial infarction produces significant improvement in clinical indices and platelet indices, normalized blood lipid profiles, shortens coronary reperfusion, and enhances short-term prognosis of patients. Future randomized controlled trials with larger sample sizes and the use of more centers are required to validate the current results.*

Keywords: *Acute myocardial infarction, Ticagrelor, Coronary artery reperfusion, Short-term prognosis*

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INTRODUCTION

Acute myocardial infarction (AMI) refers to the necrosis of coronary vessels due to insufficient blood supply caused by infarction [1,2]. It is characterized by severe retrosternal pain, heart failure, and shock and may result in various complications that seriously compromise the quality of life of patients. Acute myocardial infarction is predominant in people over 40 years of age with a higher incidence in men than in women [3-5]. The management of AMI focuses on reducing myocardial infarction and improving left ventricular function by timely unblocking of occluded coronary arteries and restoring ischemic and hypoxic myocardial function [6].

Research has documented that the administration of ticagrelor prior to percutaneous coronary intervention (PCI) improves the clinical indices of patients. Ticagrelor, a novel antiplatelet agent, provides a rapid onset of action and is more effective in the treatment of myocardial infarction. The current study was performed to assess the effect of pre-interventional ticagrelor administration on coronary reperfusion and short-term prognosis in patients with acute myocardial infarction.

METHODS

Participants

A total of 200 patients treated for acute myocardial infarction in the Second Affiliated Hospital of Qiqihar Medical College between May 2021 and October 2022 were recruited using whole-group sampling and assigned to receive either pre-PCI clopidogrel (control group) or pre-PCI ticagrelor (Ticagrelor group), in a 1:1 ratio, with 100 patients in each group. This study was approved by the Ethics Committee of the Second Affiliated Hospital of Qiqihar Medical College (approval no. 09-290-221), and all participants provided written informed consent. Also, this study adhered to the guidelines of the Helsinki Declaration [7].

Inclusion and exclusion criteria

Inclusion criteria

Patients who met the clinical diagnostic criteria for AMI, met the relevant surgical indices for PCI and underwent surgery at the Second Affiliated Hospital of Qiqihar Medical College, aged < 80 years old, with first onset of AMI and a time-lapse before administration less than 12 h were included.

Exclusion criteria

Patients with abnormalities such as shock and coagulation, cerebrovascular and craniocerebral trauma, relevant surgical contraindications, or relevant diseases such as renal disease were excluded.

Treatments

The two groups of patients received percutaneous coronary intervention (PCI). Patients were given aspirin (300 mg) orally immediately after admission, followed by the administration of anti-ischemic and statin-related drugs before surgery. Patients with excessive thrombotic load were aspirated intraoperatively using a suction catheter manufactured by Medtronic, USA, followed by stent implantation.

Control group

Before and after PCI, the patients in the control group received 75 mg of clopidogrel, twice daily for a total of 6 months.

Ticagrelor group

Before and after PCI, the patients in Ticagrelor group received 90 mg of Ticagrelor twice daily for a total of 6 months.

Evaluation of parameters/indices

Clinical indices

The platelet aggregation rate (MAR) and P2Y12 reaction units (PRU) of both groups of patients were measured by the Aggran platelet aggregation meter (Helena, USA), using the optical turbidimetric method. Color Doppler ultrasonography was used to measure the left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVDD) of the patients.

Serum indicators

Before and 24 h after intervention, morning venous blood (5 mL) was collected from both groups and centrifuged for 15 min to obtain the serum. Serum C-reactive protein (CRP), cardiac troponin (cTnI), and creatine kinase-MB (CK-MB) concentrations were determined by immunoturbidimetric assay.

Blood lipid indices

Before and 24 h after the intervention, morning venous blood (3 ml) was collected to determine

levels of total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL).

Platelet indices

Maximum platelet aggregation rate (MPAR) was measured using a platelet aggregation analyzer. The inhibition of platelet aggregation (IPA) was calculated over four different periods before and after the drug administration in both groups.

Coronary artery reperfusion

Coronary reperfusion time, time from symptom to reperfusion, and time from drug administration to reperfusion, were analyzed in both groups.

Short-term prognosis

Patients were followed up for 1 month, and short-term prognostic effects after intervention with different drugs, including myocardial infarction, heart failure, dyspnea and bleeding, and in-stent thrombosis were determined.

Statistical analysis

Data obtained were analyzed using SPSS 22.0 statistical software, while GraphPad Prism 8 was used to plot the graphs. Measurement data are expressed as mean ± standard deviation (SD) and analyzed using *t*-test. Count data are expressed as the number of cases (%) and examined using chi-square test. Significant differences were established at $p < 0.05$.

RESULTS

Baseline patient profiles

The control group recruited 82 males and 18 females who were aged 42 - 80 (62.29 ± 1.38) years, with a height of 158 - 178 (167.74 ± 1.69) cm, and a BMI of 20 - 30 (23.53 ± 1.95) kg/m^2. There were 41 patients with an educational level of undergraduate or above and 59 cases with a junior college or below. Ticagrelor group recruited 83 males and 17 females who were aged 43 - 79 (63.56 ± 1.47) years, with a height of 159 - 180 (168.25 ± 1.72) cm, a BMI of 20 - 31 (24.09 ± 1.37) kg/m^2. There were 40 cases with an educational level of undergraduate or above and 60 cases with a junior college or below. The two groups were well-balanced in terms of baseline profiles ($p > 0.05$) (Table 1).

Clinical indices

Patients receiving ticagrelor exhibited significantly lower levels of maximum platelet aggregation rate (MAR), P2Y12 reaction units (PRU), and left ventricular end-diastolic diameter (LVDD) and higher left ventricular ejection fraction (LVEF) than those with clopidogrel ($p < 0.01$) (Table 2).

Blood lipids

Patients with pre-interventional ticagrelor administration exhibited significantly lower serum concentrations of TC, TG, LDL, and HDL than those with clopidogrel ($p < 0.01$), suggesting a better overall blood lipid profile (Figure 1).

Table 1: Baseline patient profiles (mean ± SD, n = 100)

Parameter	Item	Control group	Ticagrelor group	t/x^2
Sex	Male	82	83	2.341
	Female	18	17	
Age (year)	Range	42-80	43-79	4.587
	mean±SD	62.29±1.38	63.56±1.47	
Height (cm)	Range	158-178	159-180	8.365
	mean±SD	167.74±1.69	168.25±1.72	
BMI (kg/m^2)	Range	20-30	20-31	4.109
	mean±SD	23.53±1.95	24.09±1.37	
Education level	Undergraduate or above	41	40	1.274
	Junior college or below	59	60	

Table 2: Clinical indices (mean ± SD, n = 30)

Group	MAR (%)	PRU (h)	LVEF (%)	LVDD (mm)
Control	70.21±4.37	195.14±7.36	57.76±2.14	47.82±2.04
Ticagrelor	51.16±4.01	178.52±5.45	62.39±2.96	41.33±1.89
t	6.476	12.947	5.613	3.891
P-value	<0.001	<0.001	<0.001	<0.001

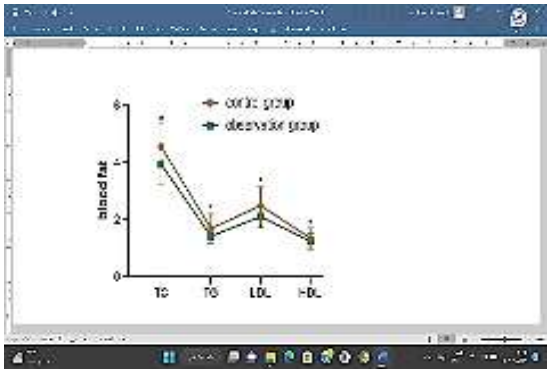

Figure 1: Blood lipids (mean ± SD). Note: *P < 0.01 when compared with Ticagrelor group

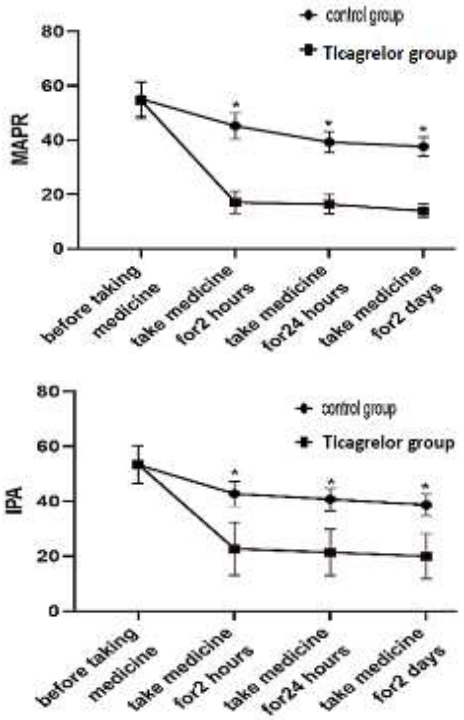

Figure 2: Neuroendocrine levels (mean ± SD). *P < 0.01 when compared with Ticagrelor group

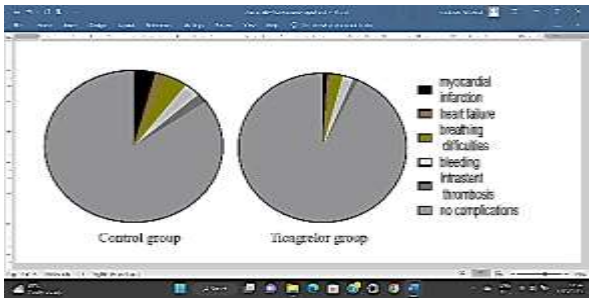

Figure 3: Incidence of complications in patients after ticagrelor versus clopidogrel administration

Serum CRP, cTnI, and CK-MB

Pre-PCI ticagrelor administration significantly mitigated inflammatory reactions more than clopidogrel, as evidenced by the reductions in serum CRP, cTnI, and CK-MB levels in the studied patients (p < 0.01) (Table 3).

Neuroendocrine levels

Pre-PCI ticagrelor administration resulted in a lower risk of abnormal platelet aggregation than pre-interventional clopidogrel, evidenced by the lower MAPR and IPA (p < 0.01) (Figure 2).

Coronary artery reperfusion

Patients given ticagrelor experienced shorter coronary artery reperfusion time and time-lapse from administration to reperfusion than those given clopidogrel (p < 0.01; Table 4).

Short-term prognosis

A significantly lower incidence of complications in patients after ticagrelor administration than clopidogrel suggested more significant short-term prognosis benefits (p < 0.01) (Figure 3).

Table 3: Serum CRP, cTnI, and CK-MB (mean ± SD, n = 100)

Group	CRP (mg/L)	cTnI (μg/L)	CK-MB (ng/mL)
Control	26.82±3.59	0.27±0.07	267.02±59.26
Ticagrelor	23.47±3.14	0.15±0.05	223.04±51.37
T	3.564	1.013	2.597
p-value	<0.001	<0.001	<0.001

Table 4: Coronary artery reperfusion (mean ± SD, n = 100)

Group	Coronary artery reperfusion time (h)	Onset of symptoms of reperfusion (h)	Time-lapse from administration to reperfusion (h)
Control	80.82±3.48	4.32±1.07	2.02±1.26
Ticagrelor	65.47±3.14	4.03±1.15	1.04±1.03
T	2.364	1.254	2.427
P-value	<0.001	<0.001	<0.001

DISCUSSION

According to Cardiovascular Health and Diseases in China 2021, there were about 330 million cardiovascular patients in China, and about 1 million of the patients suffer from acute myocardial infarction every year [8,9]. It has been reported that the mortality of AMI as high as 30 % can be reduced by 20 % if timely medical intervention is provided [10]. Clopidogrel and ticagrelor are currently the drugs of choice in the clinical treatment of AMI. Clopidogrel is a precursor-type antiplatelet drug that binds to cytochrome P450-related enzymes and attenuates the receptor activity of adenosine diphosphate p2y12 [11].

Ticagrelor is a newly developed antiplatelet agent, and its activation is independent of the hepatic CYP450. It allows direct antagonism of the p2y12 receptor and binds to fibrinogen to provide antiplatelet aggregation and inhibition of thrombosis [12,13]. It has been shown that ticagrelor produces a significant antithrombotic advantage due to the progressive increase in the emergence of resistance to clopidogrel and the less-than-optimal antiplatelet effect. A study [14] demonstrated that ticagrelor was effective in improving clinical indicators and serum profiles of patients, and this result was consistent with the results of the current research. In the present study, Patients receiving ticagrelor exhibited significantly lower levels of MAR, PRU, and LVDD and higher LVEF than those with clopidogrel. Pre-PCI ticagrelor administration significantly mitigated inflammatory reactions more than clopidogrel, as evidenced by the reductions in serum CRP, cTnI, and CK-MB levels in the studied patients. Patients given ticagrelor experienced shorter coronary artery reperfusion time and time-lapse from administration to reperfusion than those given clopidogrel.

The high incidence of adverse effects in Chinese patients who receive clopidogrel is attributable to the absence of CYP2C19 in the functional gene in Asian populations, and a higher incidence of thrombosis has been observed in Asians than in American and European groups [15,16]. Geographical difference is another factor affecting the use of clopidogrel in patients with acute myocardial infarction. Ticagrelor is a novel oral receptor antagonist of P2Y12 that efficiently blocks platelet aggregation induced by ADP production without activation by CYP450 enzymes [17,18]. Hamilos *et al* [19] found lower lipid indices in patients administered with ticagrelor than in patients with clopidogrel.

In the present study, Patients given pre-interventional ticagrelor administration exhibited significantly lower serum concentrations of TC, TG, LDL, and HDL than those given clopidogrel, suggesting a better overall blood lipid profile. Pre-PCI ticagrelor administration resulted in a lower risk of abnormal platelet aggregation than pre-interventional clopidogrel, evidenced by the lower MAPR and IPA. The administration of clopidogrel is dependent on hepatic cytochrome P450 enzyme activity to exert its anti-platelet effect. The role of clopidogrel in clinical treatment is relatively limited because of individual differences in efficacy due to genetic polymorphisms and the development of tolerance in most patients due to long-term use.

The circulating metabolites of ticagrelor effectively inhibit platelet activity, with high stability and potency. This effect of ticagrelor combined with P2Y12 is reversible, and the platelet aggregation function is restorable within a short time after discontinuation of the drug. In the current study, a significantly lower incidence of complications in patients after ticagrelor administration than clopidogrel suggests more significant short-term prognosis benefits for AMI patients.

Limitations of the study

The preliminary nature of the study resulted in several clinical research issues that could not be addressed. The investigators were aware of the treatment regimen and patient assignment, which would bias the patient assessment. Due to the nature of the design, the sample size was small and the sample type was not sufficiently diverse, resulting in a possible risk of bias in the results. In addition, no follow-up was performed.

CONCLUSION

Pre-interventional ticagrelor administration after the onset of acute myocardial infarction produces significant improvement in clinical and platelet indices, normalized blood lipid profiles, shortened coronary reperfusion, and enhanced short-term prognosis of patients. Future randomized controlled trials with larger sample sizes and more trial centers are required to validate the current results.

DECLARATIONS

Acknowledgements

None provided.

Funding

This study was supported by Clinical Research Fund of Qiqihar Academy of Medical Sciences (no. QMSI2019L-18).

Ethical approval

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Qiqihar Medical College, China (approval no. 09-290-221),

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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