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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Short-term efficacy and safety of three different antiplatelet regimens in diabetic patients treated with primary percutaneous coronary intervention: a randomised study

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Abstract

Background and aim: This study aimed to investigate the efficacy and safety of dual and triple antiplatelet therapy (DAPT and TAPT) in patients with diabetes and acute ST segment elevation myocardial infarction (D-STEMI), who had undergone primary percutaneous coronary intervention (PCI).

Methods: We designed a phase IV, single-centre, randomised, double-blind, placebo-controlled study. The D-STEMI patients (n = 258) were randomly divided into three groups. Control group A (85 patients), was treated with aspirin and clopidogrel; group B (87 patients) received aspirin, clopidogrel, and tirofiban; and group C (86 patients) were treated with aspirin, ticagrelor, and tirofiban. Patients in all three groups received oral DAPT, and patients in groups B and C received intravenous tirofiban when primary PCI was performed.

Results: Compared to the findings in group A, the post-PCI Thrombolysis in Myocardial Infarction (TIMI) grade 3 blood flow in groups B and C increased significantly (TIMI grade 3 in groups A, B, C: 74%, 91%, and 98%, respectively; TIMI myocardial perfusion grade [TMPG] grade 3 in groups A, B, C: 59%, 86%, and 97%, respectively), and the incidence of major adverse cardiac events (MACE) decreased significantly ($p < 0.05$). Compared to the findings in group B, the rate of TMPG 3 in group C was significantly higher ($p < 0.05$) and the incidence of MACE was significantly lower ($p < 0.05$). Patients in group B exhibited minor bleeding; however, the incidence of mild to moderate bleeding in group C increased significantly ($p < 0.05$).

Conclusions: TAPT effectively improved the TIMI blood flow and TMPG and reduced the occurrence of MACE. Ticagrelor was more effective than clopidogrel in TAPT; however, when using the combination of aspirin, ticagrelor, and tirofiban, close monitoring is required for possible bleeding complications.

Key words: diabetes, acute myocardial infarction, primary percutaneous coronary intervention, antiplatelet, complication, bleeding

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INTRODUCTION

The acute occlusion of blood vessel lumen(s) caused by vascular endothelial injury and unstable plaque rupture, along with platelet activation, aggregation, and adhesion, is the pathological basis of acute myocardial infarction (AMI) [1], and restoring the forward blood flow in the infarction-related vessels as early, continuously, and fully as possible is the most important therapeutic principle. Percutaneous coronary intervention (PCI) is the most effective treatment method to reopen infarction-related arteries [2, 3].

Slow flow, no-reflow, and in-stent thrombosis are the primary reasons for major adverse cardiac events (MACE) during primary PCI [4, 5]. The incidence of slow flow, no-reflow, and thromboembolic events in patients with diabetes is signifi-

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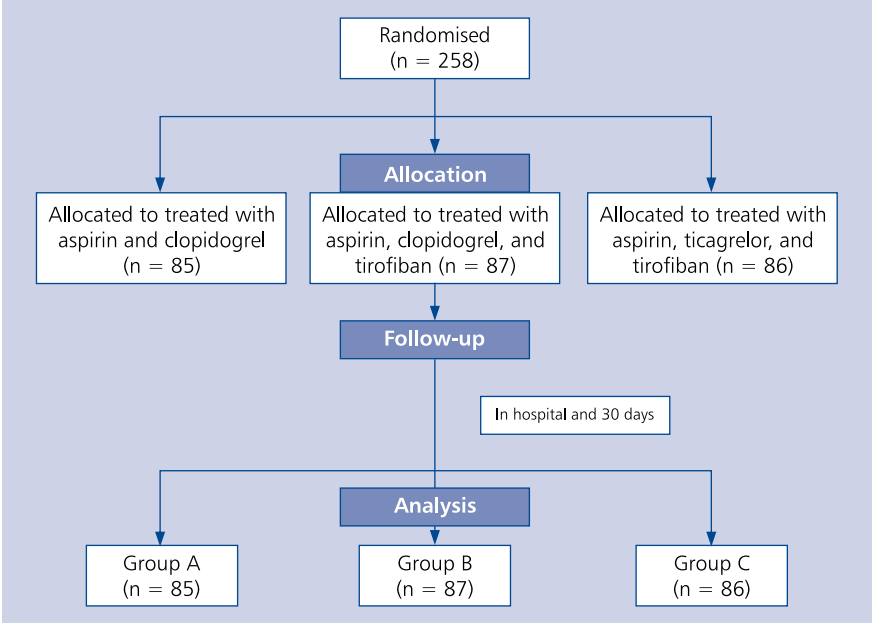

Figure 1. Flow diagram of the progress of the randomised trial of three groups.

cantly higher than that in patients without diabetes [5, 6]. Dual antiplatelet therapy (DAPT) with aspirin and P2Y12 receptor inhibitor(s), such as clopidogrel, prasugrel, and ticagrelor, is the primary treatment to prevent slow flow, no-reflow, and in-stent thrombosis [2]. However, DAPT-treated patients can still experience serious complications such as thrombosis; moreover, aspirin- and clopidogrel-resistance is one of the major causes of thrombosis [7]. The third-generation P2Y12 receptor inhibitor ticagrelor shows no gene polymorphic interference from CYP2C19 when used to inhibit platelets, and it is preferentially recommended by current guidelines due to its various characteristics, including fast onset of action and potent effect, dual inhibition, reversible binding, and coronary blood vessel expansion ability [2, 3]; however, slow flow, no-reflow, and thrombotic complications occur even in patients receiving DAPT with aspirin and ticagrelor. Combined treatment with glycoprotein (GP) IIb/IIIa receptor inhibitor(s) and DAPT can effectively reduce the occurrence of slow flow, no-reflow, and subacute thrombosis, and the rate of complications and MACE [6–8]; however, the combination of triple antiplatelet therapy (TAPT) drugs, particularly combinations containing ticagrelor, can increase the risk of bleeding. Balancing the risks of thromboembolic events and the possibility of bleeding complications is a crucial practical problem when treating ST-segment elevation myocardial infarction (STEMI) [9]. The present study aimed to investigate the short-term efficacy and safety of the combination of DAPT and tirofiban for patients with diabetes and STEMI (D-STEMI), who had been treated with primary PCI.

METHODS

Subjects

We designed a phase IV, single-centre, randomised, double-blind, placebo-controlled study. A total of 258 patients with diabetes who had STEMI underwent primary PCI in the cardiac care unit of our hospital from January 2012 to December 2015. The patients were selected and randomly divided into three groups by using a random number table method. Group A (85 patients, 54 men and 28 women; mean age, 58.6 ± 6.1 years) was the control group and received DAPT comprising aspirin and clopidogrel. Group B (87 patients, 57 men and 26 women; mean age, 57.5 ± 7.9 years) was administered TAPT consisting of aspirin, clopidogrel, and tirofiban. Group C (86 patients, 57 men and 29 women; mean age, 59.1 ± 9.8 years) received TAPT comprising aspirin, ticagrelor, and tirofiban (Fig. 1). The duration of follow-up was 30 days. The patients were followed up by telephone or in person in the outpatient department.

The diagnostic criteria for STEMI were based on the "PCI Guidelines" issued by the ACCF/AHA/SCAI in 2011 [9]. The diagnostic criteria for diabetes were based on those issued by the American Diabetes Association [10]. Patient inclusion criteria were as follows: 1) admission within 12 h from the onset of STEMI, 2) with confirmed diabetes, 3) consent to the implementation of primary PCI, and 4) no previous thrombolytic therapy. The exclusion criteria were as follows: 1) onset of STEMI longer than 12 h before admission; 2) clinical history, symptoms, and signs suggesting a history of aortic dissection; 3) presence of severe hypertension (systolic

blood pressure > 180 mm Hg and/or diastolic blood pressure > 110 mm Hg); 4) previous post-thrombolysis remedial PCI; 5) a history of ischaemic stroke or any haemorrhagic stroke, major surgery, or severe physical trauma within the last 30 days or a history of intracranial haemorrhage or intracranial tumour, arteriovenous anomalies, or aneurysms; 6) severe liver and kidney dysfunction; 7) presence of active internal bleeding or a history of bleeding within 30 days; 8) AMI combined with cardiogenic shock or severe left ventricular dysfunction; or 9) AMI combined with acute pericarditis. This study's protocol was in accordance with the Declaration of Helsinki and was approved by the ethics committee of Zhengzhou People's Hospital.

Primary PCI

After the patients arrived at the emergency room, an 18--lead electrocardiogram (ECG) tracing was immediately performed, together with ECG monitoring and oxygen inhalation. Meanwhile, intravenous access was established, and related biochemical and conventional tests such as blood sugar, blood lipids, and myocardial injury markers were performed. After obtaining informed consent from the patients or their families, the patients were randomly assigned to the treatment groups: Groups A and B received 300 mg of oral aspirin (100 mg/tablet, Bayer Co., Germany) and 600 mg of oral clopidogrel (75 mg/tablet, Sanofi Aventis, USA), while group C received 300 mg of oral aspirin and 180 mg of oral ticagrelor (90 mg/tablet, AstraZeneca, USA).

The patients then underwent primary PCI. Coronary angiography was performed using iohexol injection (GE Healthcare, USA), with the Judkins technique and the trans-left and trans-right radial artery approach (246 cases) or the trans-right femoral artery approach (12 cases). Before coronary angiography, 3000 U of heparin was administered via the sheath, and once the primary diseased vessel was identified by angiography, the total amount of heparin was increased to 100 U/kg before performing primary PCI. When the catheter was guided into the coronary arterial opening, if a thrombus shadow was visible on angiography, a thrombus aspiration catheter was first used to suction the thrombus (number of thrombus aspirations: seven cases in group A, nine cases in group B, and six cases in group C); then, a guidewire was passed through the occlusive site of the primary diseased vessel. Patients in groups B and C then received an intracoronary injection of 10 μg/kg tirofiban for 3 min (tirofiban hydrochloride-sodium chloride injection: Xinweining; Wuhan Grandpharma Co. Ltd., China). Following the bolus injection, the drug was intravenously infused at 0.15 μg/kg/min for 48 h. Patients in group A did not receive tirofiban [5]. Repeat angiography was performed in all patients to evaluate the coronary blood flow status, followed by percutaneous transluminal coronary angioplasty (PTCA) and stent implantation or direct stenting according to the status of the lesion(s). Drug-eluting stents produced by Abbott (Xience Prime), Medtronic (Endeavor® Resolute), or Lepu Medical Co. (Partner) were used.

Postoperatively, all patients were sent to the cardiac care unit for monitoring for 48–72 h; meanwhile, the levels of blood glucose and myocardial injury markers, ECG, echocardiogram findings, and hepatorenal functions were reviewed. Patients in groups A and B were prescribed continued therapy with 100 mg/d aspirin and 75 mg/d clopidogrel, and those in group C were prescribed 100 mg/d aspirin and 90 mg/d ticagrelor twice a day for at least one year postoperatively. Other medications, such as statins, angiotensin-converting enzyme inhibitors, beta-receptor blockers, and antidiabetic drugs, were maintained. Primary PCI was only performed for the primary diseased vessel(s). Other non-primary diseased vessels needing treatment underwent elective secondary PCI from 7 to 14 days later.

Outcome indexes

Based on the results of coronary angiography, the lesion characteristics were analysed, and clinical data such as hospital stay, average time from first medical contact (FMC) to balloon dilation (FMC-BD [min]), and time from hospitalisation to balloon dilation (H-BD [min]) in the three groups were collected. Information about diseased coronary arteries, primary diseased vessel(s) treated with primary PCI, as well as the type, diameter, and length of the stents, was also collected. If there were more than two primary diseased vessels, and more than two stents were implanted, their diameters were recorded and the total stent length was calculated as the sum of lengths of these two stents; if two or more stents were connected in series, the overall length of the stents was the total length of these stents minus 3 mm. The stents implanted in elective secondary PCI for the non-primary diseased vessel(s) were not counted. The efficacy endpoint was short-term complications and the safety endpoint was bleeding. Other information obtained included data for elective re-PCI during hospitalisation, post-infarction angina pectoris (PIAP), reinfarction during hospitalisation, acute and subacute in-stent thrombosis, serious arrhythmia (newly appearing, hemodynamically unstable atrial fibrillation or atrial flutter; high-degree atrioventricular block; sustained ventricular tachycardia and ventricular fibrillation; but not including intra-PCI reperfusion arrhythmias), heart function in Killip class III or above, cardiogenic shock, 30-day mortality, and use of intra-aortic balloon counterpulsation (IABP). MACE were defined as the composite of cardiac death, reinfarction, in-stent thrombosis, post-PCI cardiogenic shock, and severe arrhythmias. The recorded side effects included severe bleeding (intracranial haemorrhage or gastrointestinal bleeding, haemoptysis-associated unstable circulation, haemoglobin decreased by ≥ 5 g/dL, or haematocrit decreased by ≥ 15%), moderate bleeding (amount of haemoptysis or haematemesis ≥ 100 mL/d, melena, and/or gross haematuria), and mild bleeding (amount of haemoptysis

Table 1. Comparison of general clinical data among the three groups

Item	Group A (85 cases)	Group B (87 cases)	Group C (86 cases)	P
Age [years]	58.6 ± 6.1	57.5 ± 7.9	59.1 ± 9.8	0.324
Gender: male/female	57/28	52/35	63/23	0.170
History of diabetes [years]	10.9 ± 8.7	12.1 ± 8.2	11.7 ± 9.8	0.521
Blood glucose [mmol/L]	12.7 ± 4.9	12.1 ± 3.7	13.9 ± 5.1	0.651
Glycosylated haemoglobin ratio (% HbA1C)	9.3 ± 2.2	10.1 ± 2.3	9.6 ± 2.9	0.128
Low-density lipoprotein cholesterol [mmol/L]	3.98 ± 0.3	4.02 ± 0.6	3.89 ± 0.7	0.326
History of smoking	42 (49%)	33 (38%)	37 (43%)	0.314
History of hypertension	47 (55%)	56 (64%)	44 (51%)	0.200
Serum creatinine [mmol/L]	89.6 ± 9.9	93.8 ± 12.7	95.3 ± 13.6	0.075
Pre-infarction angina	6 (7%)	14 (16%)	9 (10%)	0.166

or haematemesis < 100 mL/d, haematoma at the puncture site, skin ecchymosis, mucosal and gingival bleeding, or microscopic haematuria). The post-PCI infarction-related arterial Thrombolysis in Myocardial Infarction (TIMI) flow grade and TIMI myocardial perfusion grade (TMPG) were also recorded [11–13]. The judgment criteria for the TIMI flow grade and TMPG were the same as those used by Chesebro et al. [11] and Liu et al. [12], respectively. The judgment of TIMI blood flow and TMPG myocardial perfusion was made by three experts in senior positions, using a blinded method.

Statistical analysis

SPSS 16.0 software was used for all statistical analyses, and the results were expressed as $\bar{x} \pm s$. The χ^2 test for categorical variables and variance analysis for three independent samples, or the Wilcoxon-Mann-Whitney test for continuous variables, was used to compare baseline characteristics in patients who received DAPT and TAPT, procedural characteristics of PCI, and outcomes, with $p < 0.05$ considered statistically significant.

RESULTS

Clinical information

Comparisons of age, sex, history of diabetes, blood glucose, glycosylated haemoglobin ratio, low-density lipoprotein level, history of smoking, history of hypertension, serum creatinine concentration, and history of pre-infarction angina among the three groups showed no statistically significant differences ($p > 0.05$, Table 1).

Features of coronary artery disease

The number of lesions in three coronary arteries in groups B and C were significantly higher than in group A ($p < 0.05$), but no significant difference was observed when comparing the impact of left main stem disease on prognosis, the primary PCI-treated target vessels, or the types, diameters, or lengths of the stents implanted among the three groups ($p > 0.05$). Compared to the findings in group A, the TIMI grade 3 flow and TMPG 3 in groups B and C were significantly higher ($p < 0.05$); moreover, the rate of TMPG 3 in group C was significantly higher than that in group B ($p < 0.05$, Table 2).

Hospital stay, PCI features, and incidence rates of complications

Comparisons of FMC-BD, H-BD, cases with two or more stents implanted in primary PCI, and cases with elective secondary PCI during hospitalisation showed no statistically significant differences among the three groups ($p > 0.05$). Compared to the findings in group A, the average hospital stays in groups B and C were significantly shorter ($p < 0.05$), and the rates of reinfarction during hospitalisation, PIAP, severe arrhythmia, heart function in Killip class III or above, cardiogenic shock, and 30-day mortality were significantly reduced ($p < 0.05$). The number of cases with post-PCI IABP implantation were also significantly lower ($p < 0.05$) in groups B and C than in group A. Moreover, the rates of PIAP, severe arrhythmia, and heart function in Killip class III or above were significantly lower in group C than in group B ($p < 0.05$). One patient in group A had an acute in-stent thrombosis 8 h postoperatively, and one patient developed subacute thrombosis 37 h postoperatively. Both of these patients underwent secondary emergency PTCA to treat the thrombus formation. The patients in groups B and C experienced no thrombotic events. Eight cases in group A required IABP implantation: one patient had an acute left main stem occlusion with no right collateral circulation supply, and this patient died 2 h after the left main stem was reopened. Four patients had combined lesions of the left main stem plus three other vessels; they developed postoperative shock and died 27, 49, 68, and 73 h after IABP support. Further, three patients developed postoperative shock, recurrent ventricular tachycardia, and ventricular fibrillation under IABP support and subsequently died of malignant arrhythmias. In groups B and C, one patient each

Table 2. Comparison of the features of coronary artery diseases among the three groups

Features	Group A (85 cases)	Group B (87 cases)	Group C (86 cases)	P
Single-vessel disease	11 (13%)	9 (10%)	5 (6%)	0.023
Dual-vessel disease	28 (33%)	18 (21%)	18 (21%)	
Triple-vessel disease	46 (54%)	60 (69%)[a]	63 (73%)[a]	
Combined with left main stem disease	6 (7%)	6 (7%)	7 (8%)	0.836
Emergency PCI-treated target vessel:				0.325
Left anterior descending branch	43 (51%)	47 (54%)	51 (59%)	
Left circumflex artery	8 (9%)	6 (7%)	10 (12%)	
Right coronary artery	34 (40%)	34 (39%)	25 (29%)	
Species of the stent(s):				0.457
Xinence Prime	19 (23%)	25 (29%)	15 (17%)	
Endevour resolute	27 (31%)	23 (26%)	31 (36%)	
Partner	39 (46%)	29 (33%)	40 (47%)	
Stent diameter [mm]	2.87 ± 0.33	2.73 ± 0.29	2.82 ± 0.31	
Stent length [mm]	25.52 ± 3.77	29.06 ± 5.28	28.72 ± 4.29	
Preoperative TIMI:				0.244
Grade 0	79 (93%)	81 (93%)	83 (97%)	
Grade 1 to 2	6 (7%)	6 (7%)	3 (3%)	
Grade 3	0 (0%)	0 (0%)	0 (0%)	
Postoperative TIMI:				0.523
Grade 0	8 (9%)[c]	3 (3.45%)[c]	0 (0.00%)[c]	
Grade 1 to 2	14 (17%)	5 (5.75%)[a]	1 (1.16%)[a]	
Grade 3	65 (74%)[c]	79 (90.80%)[a, c]	85 (98.84%)[a, c]	
Preoperative TMPG:				0.621
0	84 (99%)	85 (98%)	86 (100%)	
1 to 2	1 (1%)	2 (2%)	0 (0%)	
3	0 (0%)	0 (0%)	0 (0%)	
Postoperative TMPG:				0.024
0	16 (19%)[d]	4 (5%)[a, d]	1 (1%)[a,d]	
1 to 2	19 (22%)[d]	8 (9%)[a, d]	2 (2%)[a]	
3	50 (59%)[d]	75 (86%)[a, d]	83 (97%)[a, b, d]	

Note: Compared to group A: [a]$p < 0.05$, Compared to group B: [b]$p < 0.05$, Intragroup comparison to the same preoperative TIMI grade: [c]$p < 0.05$, Intragroup comparison to the same preoperative TMPG: [d]$p < 0.05$; PCI — percutaneous coronary intervention; TIMI — Thrombolysis in Myocardial Infarction, TMPG — TIMI Myocardial Perfusion Grade

required IABP implantation; both patients were successfully discharged (Table 3).

Bleeding complications

The incidence of mild to moderate bleeding in group C was significantly higher than that in groups A and B; of the three cases of severe bleeding in group C, two patients experienced gastrointestinal bleeding. These patients were found to have a history of peptic ulcer. One patient developed massive haemoptysis 4 h after PCI, and the emergency laboratory assay revealed that the platelet count had dropped to 17.6×10^9/L; therefore, the use of tirofiban was immediately discontinued in this patient, and intravenous injection of prednisolone (40 mg/day) was initiated under close monitoring for blood sugar fluctuations. Five days later, the platelet count recovered to 62.7×10^9/L, and the bleeding stopped (Table 3).

DISCUSSION

In the present study, group C showed significantly improved post-procedure TIMI flow and TMPG compared to group B, indicating that ticagrelor was better than clopidogrel for reducing slow flow and no-flow in emergency PCI in D-STEMI patients. The possible reasons for this finding are as follows: (1) some patients do not respond to clopidogrel; and (2) more importantly, the time interval between DAPT on admission to vessel opening was relatively short, and the onset of action

Table 3. Comparison of hospital stay, percutaneous coronary intervention (PCI) features and incidence of complications among the three groups

Item	Group A (85 cases)	Group B (87 cases)	Group C (86 cases)	P
Average hospital stay [day]	11.2 ± 3.7	8.1 ± 2.1[a]	8.3 ± 2.9[a]	0.012
FMC-BD [min]	146 ± 53.7	159 ± 71.2	153 ± 69.8	0.542
H-BD [min]	93.7 ± 29.7	101.1 ± 47.9	99.6 ± 41.6	0.078
With two or more stents implanted	13 (15%)	19 (22%)	23 (26%)	0.186
Elective secondary PCI during hospitalisation	16 (19%)	25 (29%)	15 (17%)	0.145
IABP Implantation	8 (9%)	1 (1%)[a]	1 (1%)[a]	0.006
PIAP	18 (21%)	8 (9%)[a]	1 (1%)[a, b]	<0.001
Re-infarction	9 (11%)	1 (1%)[a]	0 (0%)[a]	<0.001
In-stent thrombosis	2 (2%)	0 (0%)	0 (0%)	0.107
Severe arrhythmias	21 (25%)	11 (13%)[a]	2 (2%)[a, b]	< 0.001
Heart function in Killip class III or above	20 (24%)	10 (11%)[a]	2 (2%)[a, b]	< 0.001
Post-PCI cardiogenic shock	8 (9%)	1 (1%)[a]	0 (0%)[a]	0.001
Hospital mortality	6 (7%)	1 (1%)[a]	0 (0%)[a]	0.007
Bleeding:				< 0.001
Severe bleeding	0 (0%)	0 (0%)	3 (3%)	
Moderate bleeding	1 (1%)	2 (2%)	12 (14%)[a, b]	
Mild bleeding	5 (6%)	10 (11%)	21 (24%)[a, b]	

Note: Compared to group A: [a]p < 0.05. Compared to group B: [b]p < 0.05; FMC-BD — time from first medical contact to balloon dilation; H-BD — time from hospitalisation to balloon dilation; IABP — intra-aortic balloon counterpulsation; PIAP — post-infarction angina pectoris

for clopidogrel is considerably long; thus, when the vessels were reopened during emergency PCI, the activated platelets had not been sufficiently suppressed; however, ticagrelor can directly and quickly exert its effects [14]. The platelet aggregation inhibition rate (IPA) can reach 41% after 30 min of administration of ticagrelor (reaching only 8% with clopidogrel). In addition, ticagrelor has other beneficial effects, such as increasing the blood concentration of adenosine and coronary blood flow. One PLATO study demonstrated [14] that compared to that of clopidogrel, the primary endpoint efficacy of ticagrelor (combined endpoint of cardiovascular death/myocardial infarction/stroke) was reduced by 16%, and the in-stent thrombosis and one-year cardiovascular mortality of the patients who received ticagrelor was significantly reduced. Therefore, it is suitable for adequate and rapid platelet inhibition and increasing the coronary blood flow in emergency situations.

In addition, the ratios of triple-vessel disease in groups B and C were significantly higher than those in group A. However, the additional administration of tirofiban during emergency PCI significantly reduced the average hospital stay, reinfarction during hospitalisation, PIAP, severe arrhythmia, heart failure, cardiogenic shock, and 30-day mortality. The IABP implantation ratio and the 30-day mortality in group A were significantly higher than those in groups B and C. Further, compared to those in group B, the incidences of PIAP, severe arrhythmia, and heart failure in group C significantly decreased. The two thrombotic events in group A occurred 8 h and 37 h postoperatively, respectively, while none of the patients in groups B and C experienced any thrombotic events.

This study shows that DAPT therapy plus the administration of the GP IIb/IIIa receptor inhibitor tirofiban in primary PCI for D-STEMI patients can shorten the average hospital stay and reduce the intra-hospital MACE complications, 30-day mortality, and post-PCI IABP usage, along with a tendency to reduce in-stent thrombosis. The combination of TAPT with ticagrelor was better than that with clopidogrel, further reducing the incidence of PIAP, severe cardiac arrhythmias, and heart failure. Despite randomisation, patients in group B and C had more advanced coronary artery disease as compared with those in group A. Surprisingly, this was not an obstacle, and patients in group B and C had better reperfusion on angiography. An intracoronary injection of tirofiban in patients in groups B and C may have played an important role.

GP IIb/IIIa receptor inhibitors act on a final unique pathway, competitively occupying the GP IIb/IIIa receptors and preventing the binding of fibrinogen with such receptors, thus quickly and almost completely inhibiting platelet aggregation [5, 15–19]. These agents can take effect 5 min after intravenous administration, and the 30-min IPA is greater than 93%; hence, the platelet inhibitory effects of these drugs are faster and more direct.

Bleeding complications have always been an issue of concern for cardiovascular physicians when using TAPT [15,

20–22], particularly in diabetic patients with AMI; in this study, patients in both groups A and B had no serious bleeding events, indicating that it is essential to monitor bleeding caused by the administration of GP IIb/IIIa receptor antagonists and ticagrelor, especially when these two agents are combined. Although the incidence among these three groups did not reach statistical significance, severe bleeding is a high-risk complication, and clinicians should closely monitor patients when combining these agents, and reduce the dose when necessary [23]. A possible bleeding history should be carefully evaluated, and clinical symptoms should be closely observed. Furthermore, timely blood tests should be performed. The risk factors for bleeding combined with the administration of GP IIb/IIIa receptor antagonists is potentially the main reason underlying this effect [22, 24]. With regard to differences in the efficacy and side effects when the second-generation P2Y12 receptor inhibitor clopidogrel and ticagrelor are combined with tirofiban [25], DiNicolantonio et al. [22] thought that although ticagrelor had a faster onset and more persistent antiplatelet effects than clopidogrel, it could significantly increase the occurrence of adverse events such as intracranial haemorrhage, haematuria, subcutaneous bleeding, and mucosal bleeding .

Limitations of the study

This study has certain limitations. The observation period was only 30 days, and long-term MACE events, revascularisation rates of target lesions and target vessels, and bleeding events were not observed during follow-up. We plan to further expand the sample size and observation time to continue to analyse and compare the impact of clopidogrel, ticagrelor, DAPT, and TAPT on the long-term prognosis of D-STEMI patients. Additionally, this study did not perform multiple linear regression analysis; hence, there may be residual confounding factors that were not adjusted for when the association between antiplatelet therapy and mortality/bleeding risk was estimated.

CONCLUSIONS

In conclusion, in primary PCI for D-STEMI patients, the administration of a combination of aspirin, ticagrelor, and tirofiban effectively reduced the occurrence of serious complications, but increased the risk of bleeding complications.

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Skuteczność i bezpieczeństwo stosowania trzech różnych schematów terapii przeciwpłytkowej u chorych na cukrzycę poddanych pierwotnej przezskórnej interwencji wieńcowej w obserwacji krótkoterminowej: badanie z randomizacją

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Streszczenie

Wstęp i cel: Badanie przeprowadzono w celu oceny skuteczności i bezpieczeństwa stosowania podwójnej i potrójnej terapii przeciwpłytkowej (DAPT/TAPT) u pacjentów z cukrzycą i ostrym zawałem serca z uniesieniem odcina ST (D-STEMI), których poddano pierwotnej przezskórnej interwencji wieńcowej (PCI).

Metody: Autorzy zaprojektowali jednoośrodkowe badanie IV fazy z grupą kontrolną i randomizacją, prowadzone metodą podwójnie ślepej próby. Chorzy z D-STEMI (n = 258) zostali przydzieleni losowo do trzech grup. W grupie A (grupa kontrolna; 85 chorych) podawano kwas acetylosalicylowy (ASA) i klopidogrel, w grupie B (87 chorych) — ASA, klopidogrel i tirofiban, a w grupie C (86 chorych) — ASA, tikagrelor i tirofiban. Chorzy we wszystkich trzech grupach stosowali doustną DAPT, a pacjentom w grupach B i C podawano dożylnie tirofiban, kiedy przeprowadzano PCI.

Wyniki: W porównaniu z wynikami uzyskanymi w grupie A, w grupach B i C stwierdzono istotne zwiększenie odsetka chorych, u których ocena przepływu w skali TIMI (*Thrombolysis in Myocardial Infarction*) po zabiegu PCI wynosiła 3 (ocena 3 w skali TIMI w grupach A, B i C: odpowiednio 74%, 91% i 98%; ocena 3 w skali TMPG [*TIMI Myocardial Perfusion Grade*] w grupach A, B i C: odpowiednio 59%, 86% i 97%), natomiast liczba poważnych sercowych zdarzeń niepożądanych (MACE) była istotnie mniejsza ($p < 0,05$). W grupie C odsetek osób z oceną 3 w skali TMPG był znamiennie wyższy ($p < 0,05$), a częstość MACE istotnie niższa ($p < 0,05$) niż w grupie B. U chorych w grupie B występowały drobne krwawienia, jednak częstość łagodnych do umiarkowanych krwawień była istotnie większa ($p < 0,05$).

Wnioski: Stosowanie TAPT skutecznie poprawiło przepływ w skali TIMI i TMPG oraz spowodowało zmniejszenie częstości występowania MACE. Tikagrelor był bardziej skuteczny niż klopidogrel w TAPT, jednak w przypadku stosowania tikagreloru lub tirofibanu w połączeniu z ASA konieczne jest ścisłe monitorowanie chorych pod względem możliwych powikłań krwotocznych.

Słowa kluczowe: cukrzyca, ostry zawał serca, pierwotna przezskórna interwencja wieńcowa, leki przeciwpłytkowe, powikłanie, krwawienie

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