Treatment of progressive ischemic stroke with low-dose eptifibatide: A retrospective case-control study

LONG LUO, JINSHENG LIN, YE DENG, ZHIGANG LI, YING YUAN and WEN ZHANG

Department of Neurology, Xiangtan Central Hospital, Xiangtan, Hunan 411100, P.R. China

Received June 9, 2022; Accepted November 2, 2022

DOI: 10.3892/etm.2022.11721

Abstract. Progressive ischemic stroke (PIS) is a therapeutic challenge in clinical practice. The present retrospective study aimed to investigate the safety and effectiveness of eptifibatide in the treatment of PIS. The present study enrolled patients with PIS admitted to Xiangtan Central Hospital (Xiangtan, China) between March 2020 and March 2021 with National Institutes of Health Stroke Scale (NIHSS) progression scores of ≥2 points during the initial 72 h. Patients were then divided into two groups according to their different anti-platelet treatment regimens. The control group was administered anti-platelet aggregation with aspirin 100 mg/day, or aspirin 100 mg/day in combination with clopidogrel 75 mg/day, whilst eptifibatide was administered in the eptifibatide group in addition to the treatment regimen used in the control group. Changes in NIHSS scores at the time of progression and 7 days after treatment (ΔNIHSS) were used to assess early neurological recovery, and there were no significant differences in ΔNIHSS and adverse reactions between the groups (P>0.05). Subgroup analysis was subsequently performed according to the type of blood vessel that was involved [large artery atherosclerosis (LAA) or small artery occlusion (SAO)]. For the SAO subgroup, the ΔNIHSS in the eptifibatide group was significantly superior to that of the control group (P=0.008), while for the LAA subgroup, there were no significant differences in ΔNIHSS between groups (P=0.334). The present retrospective study found that patients with PIS tolerated eptifibatide treatment well. Eptifibatide exerted different effects on patients with acute PIS involving different types of blood vessels compared with oral antiplatelet drugs. In addition, application of eptifibatide may lead to faster and earlier recovery in patients with SAO, but not in those with LAA. Low-dose eptifibatide is a safe and effective treatment option for patients with PIS caused by SAO.

Correspondence to: Mr. Long Luo or Professor Jinsheng Lin, Department of Neurology, Xiangtan Central Hospital, 120 Heping Road, Xiangtan, Hunan 411100, P.R. China
E-mail: luol01@126.com
E-mail: jslin@aliyun.com

Key words: antiplatelet drugs, eptifibatide, progressive stroke, treatment, glycoprotein IIb/IIIa inhibitor

Introduction

The deterioration of neurological deficits is a frequent complication in acute stroke (1). Early progressive ischemic stroke (PIS) tightly related to poor prognosis (2,3). The existence of this gradual deterioration implies that it should theoretically be possible to at least arrest or delay this process. To the best of our knowledge, there is as yet no unified international definition or diagnostic criteria for PIS. The main differences in the types of PIS lie in the definition of the time window of progression and the severity of disease progression (4-6). PIS is generally defined as an increase of ≥2 points according to the National Institutes of Health Stroke Scale (NIHSS) within 48 or 72 h of stroke onset (4,5). A small NIHSS change (e.g., ΔNIHSS ≥2) is particularly applicable to the definition of PIS in minor strokes (defined as admission NIHSS ≤5) (6). The mechanism underlying PIS remains unclear, for which there is no effective treatment methods (7). As a result, PIS represents a clinical challenge.

Patients with PIS have been extensively treated using high-dose heparin (1). However, this is discouraged by the current stroke guidelines, since scientific support for its efficacy is poor (1). Therefore, a clinical trial with another therapeutic drug operating through a different mechanism is desired. The final common pathway of platelet aggregation and subsequent thrombus formation is the activation of glycoprotein (GP) IIb/IIIa receptors (8). Currently available drugs for acute ischemic stroke and acute coronary syndrome are abciximab, tirofiban and eptifibatide, all three of which are administered by intravascular and exert potent, rapid anti-platelet aggregation effects (9). Abciximab binds irreversibly to receptors and the platelet recovery time is 24-48 h after the treatment, but results in a rather higher risk of bleeding (10). By contrast, tirofiban and eptifibatide bind to receptors in a reversible manner, with platelet recovery times of 4-8 and 2-4 h, respectively, and might be relatively safer. A previous study showed that eptifibatide had a higher GP IIb/IIIa receptor occupancy ratio compared with tirofiban, where the incidence of 30-day adverse cardiovascular events was also lower compared with that of tirofiban (11). A meta-analysis also previously showed that the safety of eptifibatide was slightly superior to tirofiban in patients with acute coronary syndrome (12).

It has been previously shown that platelet GP IIb/IIIa receptor inhibitors could be used for treating thrombosis

mediated by activated platelets (9,13). Previous literature reviews summarized that a number of exploratory studies have tested them either alone or in combination with intravenous thrombolysis or endovascular therapy as an alternative strategy for the management of acute ischemic stroke (9,13). In a single-center retrospective study, 25 patients with subcortical progressive stroke were found to be safely treated with eptifibatide (14). However, additional research on the efficacy of eptifibatide is required (14). For the study of tirofiban, another (GP) IIb/IIIa receptor inhibitor, Philipps *et al* (15) previously found that during the early stages of PIS, patients with small-vessel occlusions tended to exhibit superior responses to tirofiban compared with those by patients with large-vessel occlusions. Therefore, outcomes in patients with progressive stroke may be associated with the blood vessels that are involved.

The present report aimed to provide evidence regarding the safety and validity of a specific low-dose eptifibatide antiplatelet strategy for the treatment of PIS. In addition, another aim of the present study was to test whether the efficacy of eptifibatide in patients with PIS is related to vascular classification.

Patients and methods

Patients. A total of 74 patients [mean age, 64.3±11.4 years; 53 males (71.6%)] with clinically confirmed PIS were enrolled in Xiangtan Central Hospital (Xiangtan, China) between March 2020 and March 2021. PIS was diagnosed as the condition worsening by ≥2 points according to the NIHSS within 72 h after stroke onset (2). Inclusion criteria were the following: i) Diagnosis of stroke as per the criteria published in 2018 in the Chinese Guidelines on the Diagnosis and Treatment of Acute Ischemic Stroke (16); ii) aged 18-80 years; iii) first onset, new infarction on head MRI; and iv) stroke due to large artery atherosclerosis (LAA) or small artery occlusion (SAO). Exclusion criteria were as follows: i) Haemorrhagic infarction; ii) transient ischemic attack; iii) cardiac cerebral infarction; iv) cerebral infarction with unknown pathogenesis or other less common causes; v) received intravenous thrombolysis or endovascular treatment in the acute phase; vi) disturbance of blood coagulation, aberrant thrombocytopenia or neutropenia; vii) history of previous diagnosis of cancer, brain injury or surgery; viii) history of neurodegenerative disease or other central nervous system diseases; and ix) history of liver disease or another end-stage disease.

Patients were divided into the eptifibatide group (n=32) and the control group (n=42) according to the different treatment regimens they received. For the eptifibatide group, eptifibatide was given to patients as a bolus injection at a loading dose of 135 μg/kg at the time of stroke progression, followed by a maintenance dose of 0.75 μg/kg/min for 48 h. In addition, oral antiplatelet agents were also given 4 h before eptifibatide administration was stopped. Patients in the control group received oral antiplatelet medication. For the specific oral antiplatelet drug regimens, patients with mild ischemic stroke (NIHSS score=3) were given dual-antiplatelet medication (aspirin 100 mg/day + clopidogrel hydrochloride 75 mg/day) for 21 days (17), followed by aspirin 100 mg/day. By contrast, patients with symptomatic intracranial artery stenosis (stenosis rate, 70-99%) were treated with dual-antiplatelet therapy for 90 days (18,19), followed by aspirin 100 mg/day. Other patients were only given aspirin 100 mg/day. After discharge, patients were recommended to use this plan for a long time and regularly visit the clinic. According to the blood vessel involved, patients were then divided into the following two subgroups: The LAA subgroup and the SAO subgroup.

The present study was approved by the Xiangtan Central Hospital ethics committee (Xiangtan, China). All patients signed informed consent and all data were anonymized.

Data acquisition and outcomes. The patients' demographic data (age and sex), lesion location, hypertension, diabetes, hypercholesterinaemia, current smoking habit, drinking history, coronary heart disease, hyperhomocysteinemia, classification for ischemic stroke based on the Trial of ORG 10172 (20) in Acute Stroke Treatment and other complications were obtained. In addition, intracranial haemorrhage was evaluated by CT and MRI (the head CT or MR of the patients in the eptifibatide group was checked within 48 h after eptifibatide administration, and the head CT or MR of the patients in the control group was checked after treatment during hospitalization), whilst other related bleeding events were also recorded (if the patient's gastric juice occult blood or fecal occult blood was positive during hospitalization, it was judged as gastrointestinal bleeding; if the patient's electronic system recorded skin and mucous membrane bleeding during hospitalization, it was judged as ecchymosis). The NIHSS scores were used to evaluate the degree of neurological deficit. The NIHSS score was evaluated on admission, at the time of progression (the disease is the most serious within 72 h) and 7 days after treatment. The samples used in the present study were collected when the patients were hospitalized. All laboratory test results were obtained from the Laboratory Department and Radiology Department of Xiangtan Central Hospital. The basic information and condition assessment data were obtained from the electronic medical record system of the Neurology Department of Xiangtan Central Hospital.

Statistical analysis. Categorical data are shown as numbers and percentages (%), whereas continuous data are shown as the means ± standard deviation or median with interquartile range (IQR). The continuous and categorical variables were compared using a two-tailed independent samples t-test or Mann-Whitney U test and the χ^2 test or Fisher's exact test, respectively. SPSS version 26.0 software (IBM Corp.) was used for analyses. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Baseline characteristics and clinical course of eptifibatide and control group. The present retrospective study enrolled 74 participants, all patients received routine basic treatment, including routine nursing, oxygen inhalation, management of blood pressure and blood sugar, intensive lipid lowering, maintenance of water electrolyte balance and rehabilitation treatment. Among them, 32 patients received eptifibatide

Table I. Baseline clinical characteristics and clinical course of patients.

Characteristic	Eptifibatide group (n=32)	Control group (n=42)	P-value
Age, years[a]	64.0±2.2	65.7±1.9	0.549
Sex, n (%)			
Male	23 (71.9)	30 (71.4)	0.996
Female	9 (28.1)	12 (28.6)	
Lesion location, n (%)			0.877
Brainstem/cerebellum	13 (40.6)	13 (31.0)	
Basal ganglia	6 (18.8)	10 (23.8)	
Cortical and subcortical of MCA	9 (28.1)	11 (26.2)	
Cortical and subcortical of ACA	1 (3.1)	3 (7.1)	
Cortical and subcortical of PCA	3 (9.4)	5 (11.9)	
Involved vessel, n (%)			
Small artery occlusion	11 (34.4)	19 (45.2)	0.346
Large artery atherosclerosis	21 (65.6)	23 (54.8)	
Risk factors, n (%)			
Hypertension	26 (81.3)	33 (78.6)	0.776
Diabetes mellitus	8 (25.0)	16 (38.1)	0.233
Hypercholesterinemia	13 (40.6)	22 (52.4)	0.316
Current smoking	9 (28.1)	10 (23.8)	0.674
Drinking	9 (28.1)	6 (14.3)	0.142
Coronary heart disease	8 (25.0)	12 (28.6)	0.732
Hyperhomocysteinemia	3 (9.4)	7 (16.7)	0.572
Family history of stroke	2 (6.3)	4 (9.5)	0.693
Antiplatelet regimen, n (%)			0.715
Dual antiplatelet 21 days	5 (15.6)	4 (9.5)	
Dual antiplatelet 90 days	10 (31.3)	15 (35.7)	
Monoclonal antiplatelet	17 (53.1)	23 (54.8)	
Clinical course, points[b]			
NIHSS on admission	3.0 (1.0-5.8)	3.0 (1.8-5.0)	0.821
NIHSS at progression	7.5 (4.0-11.8)	6.0 (5.0-9.0)	0.588
ΔNIHSS improvement	2.0 (0.3-4.0)	1.5 (0.0-2.0)	0.053
NIHSS 7 days after treatment	4 (2.0-10.0)	5.0 (3.0-7.5)	0.425
Complications, n (%)			
Ecchymosis	2 (6.3)	2 (4.8)	1.000
Asymptomatic cerebral haemorrhage	1 (3.1)	1 (2.4)	1.000
Gastrointestinal haemorrhage	2 (6.3)	3 (7.1)	1.000

[a]Mean ± standard deviation. [b]Median (interquartile range). Student's unpaired t-test was used for continuous variables, whereas the non-parametric Mann-Whitney U test was used when the data did not conform to a normal distribution or if the variance was uneven. χ^2 or Fisher's exact test was used for categorical variables. MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; NIHSS, National Institutes of Health Stroke Scale; ΔNIHSS improvement, NIHSS at progression compared with 7 days after treatment; dual antiplatelet, aspirin 100 mg/day combined with clopidogrel hydrochloride 75 mg/day; monoclonal antiplatelet, aspirin 100 mg/day.

whereas 42 patients did not. At baseline, the mean age in the eptifibatide group was 64.0±2.2 years, where 23 (71.9%) of the patients were male. The mean age and number of male patients in the control group was 65.7±1.9 years and 30 (71.4%), respectively (Table I). The proportion of the vessels involved [LAA, 21 (65.6%) vs. 23 (54.8%) for the eptifibatide and control group, respectively] were generally similar (Table I). The median NIHSS score at progression was 7.5 (IQR, 4.0-11.8) in the eptifibatide group and 6.0 (IQR, 5.0-9.0) in the control group (Table I). Overall, baseline demographic and clinical features of the two groups were largely comparable (Table I). Changes in NIHSS scores (ΔNIHSS) between progression and 7 days after treatment were used to evaluate the degree of early neurological recovery. The median ΔNIHSS was 2.0 (IQR, 0.3-4.0) in the eptifibatide group and 1.5 (IQR, 0.0-2.0) in the control group. During hospitalization, the incidence rates of subcutaneous ecchymosis in the eptifibatide group and control group were 6.3 and 4.8%,

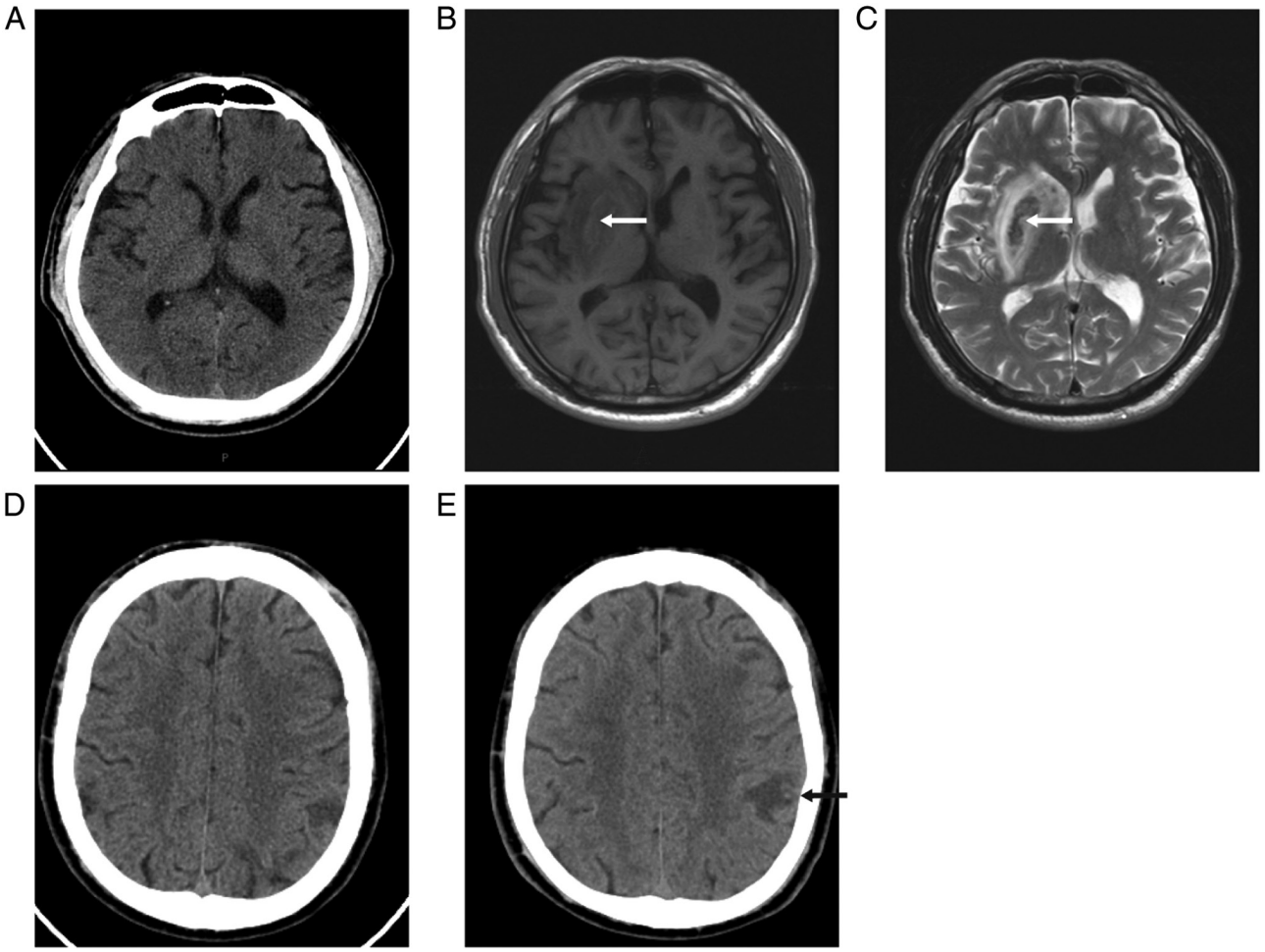

Figure 1. Representative CT and MRI images of two patients enrolled into the present study. A 64-year-old patient in the eptifibatide group. (A) Head CT at 13 h after progressive ischemic stroke onset (eptifibatide was administered at 17 h after onset). Head MRI (B) T1 and (C) T2 sequences on day 4 after onset showing patchy haemorrhagic areas (arrow). Head routine CT scans of a 70-year-old man in the control group on (D) day 2 and (E) day 5 after onset, with punctate haemorrhagic areas (arrow).

respectively. The rates of asymptomatic cerebral haemorrhage were 3.1 and 2.4%, respectively. The rates of gastrointestinal bleeding were 6.3 and 7.0%, respectively (Table I). Images of patients with asymptomatic intracerebral haemorrhage are shown in Fig. 1.

SAO subgroup analysis. There were 30 patients in the SAO subgroup, 11 patients were treated with eptifibatide whereas 19 patients were not. At baseline, in the eptifibatide group, the mean age was 64.1±15.7 years and 9 (81.8%) of the patients were male, whereas in the control group the mean age was 63.0±12.8 with 12 (63.2%) male patients (Table II). The median NIHSS score at progression was 7.0 (IQR, 5.0-10.0) in the eptifibatide group and 6.0 (IQR, 5.0-7.0) in the control group (Table II). Overall, the baseline demographic and clinical characteristics of the two groups were comparable (Table II). The median ΔNIHSS was 4.0 (IQR, 2.0-5.0) in the eptifibatide group, significantly higher than 2.0 (IQR, 1.0-3.0) in the control group (Table II).

LAA subgroup analysis. There were 44 patients in the LAA subgroup. In total, 21 patients were treated with eptifibatide whereas 23 patients were not. At baseline, in the eptifibatide group, the mean age was 63.9±10.9 years and 14 (66.7%) of the patients were male, whereas in the control group the mean age was 68.0±11.4 years with 18 (78.3%) male patients (Table III). The median NIHSS score at progression was 8.0 (IQR, 3.5-14.0) in the eptifibatide group and 7.0 (IQR, 5.0-12.0) in the control group (Table III). Overall, the baseline demographic and clinical characteristics of the two groups were also comparable with no significant differences (Table III). The median ΔNIHSS was 2.0 (IQR, 0.0-2.5) in the eptifibatide group and 1.0 (IQR, 0.0-2.0) in the control group (Table III).

Discussion

The selection of the eptifibatide dosage for the present study was based on limited evidence (14,21). To the best of our knowledge, there is currently no guideline or consensus for the treatment of PIS with eptifibatide. In a large Chinese clinical trial (ClinicalTrials.gov Identifier: NCT03844594) to determine the efficacy and safety of eptifibatide [Eptifibatide in Endovascular Treatment of Acute Ischemic Stroke (EPOCH) trial], intravenous or combined intra-catheter bolus treatment at a dose of 135-180 μg/kg

Table II. Subgroup analysis of patients with small artery occlusion.

Characteristic	Eptifibatide group (n=11)	Control group (n=19)	P-value
Age, years[a]	64.1±15.7	63.0±12.8	0.830
Sex, n (%)			0.508
Male	9 (81.8)	12 (63.2)	
Female	2 (18.2)	7 (36.8)	
Lesion location, n (%)			0.444
Brainstem/cerebellum	4 (36.4)	8 (42.1)	
Basal ganglia	4 (36.4)	6 (31.6)	
Cortical and Subcortical of MCA	3 (27.3)	2 (10.5)	
Cortical and Subcortical of ACA	0 (0.0)	3 (15.8)	
Cortical and Subcortical of PCA	0 (0.0)	0 (0.0)	
Risk factors, n (%)			
Hypertension	9 (81.8)	15 (78.9)	1.000
Diabetes mellitus	2 (18.2)	7 (36.8)	0.508
Hypercholesterinaemia	4 (36.4)	12 (63.2)	0.156
Current smoking	2 (18.2)	5 (26.3)	0.952
Drinking	4 (36.4)	3 (15.8)	0.403
Coronary heart disease	2 (18.2)	4 (21.1)	1.000
Hyperhomocysteinemia	0 (0.0)	2 (10.5)	0.520
Family history of stroke	1 (9.1)	0 (0.0)	0.367
Antiplatelet regimen, n (%)			0.520
Dual antiplatelet 21 days	0 (0.0)	2 (8.7)	
Dual antiplatelet 90 days	0 (0.0)	0 (0.0)	
Monoclonal antiplatelet	11 (100.0)	17 (89.5)	
Clinical course, points[b]			
NIHSS on admission	3.0 (2.0-7.0)	2.0 (1.0-3.0)	0.094
NIHSS at progression	7.0 (5.0-10.0)	6.0 (5.0-7.0)	0.171
ΔNIHSS improvement	4.0 (2.0-5.0)	2.0 (1.0-3.0)	0.008
NIHSS at 7 days after treatment	2.0 (2.0-5.0)	3.0 (2.0-5.0)	0.641

[a]Mean ± standard deviation. [b]Median (interquartile range). Student's unpaired t-test was used for continuous variables, whereas the non-parametric Mann-Whitney U test was used when the data did not conform to a normal distribution or the variance was uneven. χ^2 or Fisher's exact test was used for categorical variables. MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; NIHSS, National Institutes of Health Stroke Scale; ΔNIHSS improvement, NIHSS at progression compared with 7 days after treatment; dual antiplatelet, aspirin 100 mg/day combined with clopidogrel hydrochloride 75 mg/day; monoclonal antiplatelet, aspirin 100 mg/day.

administered over <5 min, followed by a maintenance dose of 0.75 to 2 μg/kg/min for 24 h (22). The results from this previous trial confirmed that this regimen was effective and safe (22). Considering that the process of platelet activation is consistent in patients with PIS and in patients treated with endovascular therapy, in addition to a previous report stating that eptifibatide has a high safety profile in PIS (14), the treatment protocol (135 μg/kg bolus followed by 0.75 μg/kg/min for 48 h) was used for the 32 patients in the present study.

In the present study, ΔNIHSS in the eptifibatide group was not significantly different compared with that in the control group. Further subgroup analysis revealed that in the eptifibatide group, the ΔNIHSS was significantly higher compared with that in the control group in patients with SAO, but not in patients with LAA. This suggests that treatment with eptifibatide could promote the early recovery of patients with PIS, specifically with SAO. Compared with previous studies using eptifibatide in patients with PIS, the present study established the control group as a reference and subgroup analyses were conducted according to different blood vessel types involved. The establishment of a control group can exclude other factors except the anti-platelet aggregation program. Subgroup analyses based on vascular type further helped to identify the population that can benefit the most from this treatment. The present study showed that eptifibatide may exert different effects on acute PIS caused by different types of vessels, where it appeared to significantly improve the early neurological deficits in patients with SAO.

Unlike SAO, early efficacy of eptifibatide in LAA could not be found in the present study and the reason for this remains unclear. SAO-associated stroke is known to be caused by small arterial hyalinosis, endothelial dysfunction and/or intracranial perforator atherosclerosis (23,24). SAO is a common cause of

Table III. Subgroup analysis of patients with large arteries atherosclerosis.

Characteristics	Eptifibatide group (n=21)	Control group (n=23)	P-value
Age, years[a]	63.9±10.9	68.0±11.4	0.231
Sex, n (%)			0.388
Male	14 (66.7)	18 (78.3)	
Female	7 (33.3)	5 (21.7)	
Lesion location, n (%)			0.481
Brainstem/cerebellum	9 (42.9)	5 (21.7)	
Basal ganglia	2 (9.5)	4 (17.4)	
Cortical and Subcortical of MCA	6 (28.6)	9 (39.1)	
Cortical and Subcortical of ACA	1 (4.8)	0 (0.0)	
Cortical and Subcortical of PCA	3 (14.3)	5 (21.7)	
Risk factors, n (%)			
Hypertension	17 (81.0)	18 (78.3)	1.000
Diabetes mellitus	6 (28.6)	9 (39.1)	0.460
Hypercholesterinaemia	9 (42.9)	10 (43.5)	0.967
Current Smoking	7 (33.3)	5 (21.7)	0.388
Drinking	5 (23.8)	3 (13.0)	0.594
Coronary heart disease	6 (28.6)	8 (34.8)	0.659
Hyperhomocysteinemia	3 (14.3)	5 (21.7)	0.803
Family history of stroke	1 (4.8)	4 (17.4)	0.348
Antiplatelet regimen, n (%)			0.342
Dual antiplatelet 21 days	5 (23.8)	2 (8.7)	
Dual antiplatelet 90 days	10 (47.6)	15 (65.2)	
Monoclonal antiplatelets	6 (28.6)	6 (26.1)	
Clinical course, points[b]			
NIHSS on admission	2.0 (1.0-5.0)	4.0 (2.0-8.0)	0.155
NIHSS at progression	8.0 (3.5-14.0)	7.0 (5.0-12.0)	0.934
ΔNIHSS improvement	2.0 (0.0-2.5)	1.0 (0.0-2.0)	0.334
NIHSS at 7 days after treatment	5.0 (2.0-12.5)	6.0 (3.0-11.0)	0.663

[a]Mean ± standard deviation. [b]Median (interquartile range). Student's unpaired t-test was used for continuous variables, whereas the non-parametric Mann-Whitney U test was used when the data did not conform to normal distribution or the variance was uneven. χ^2 or Fisher's exact test was used for categorical variables. MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; NIHSS, National Institutes of Health Stroke Scale; ΔNIHSS improvement, NIHSS at progression compared with 7 days after treatment; dual antiplatelet, aspirin 100 mg/day combined with clopidogrel hydrochloride 75 mg/day; monoclonal antiplatelet, aspirin 100 mg/day.

capsular warning syndrome (CWS), since CWS is most often due to small penetrating vessel hemodynamic disorder (25,26). A previous study on tirofiban showed that it could stop early symptomatic fluctuations and decrease the duration of functional impairments in patients with CWS compared with oral antiplatelet drugs (27). In addition, there is evidence that tirofiban is safe and efficacious in patients with ischemic stroke outside the thrombolytic therapy window compared with oral antiplatelet medications (28). This supports the likelihood of beneficial effects conferred by GP IIb/IIIa receptor antagonists for treatment during the early stages of ischemia episodes.

In the present retrospective study of 74 patients with PIS, the rates of complications, including ecchymosis, gastrointestinal bleeding and asymptomatic intracranial haemorrhage, did not differ between the eptifibatide and control group. In addition, no symptomatic intracranial haemorrhage occurred in either group. This suggests that the patients who received eptifibatide tolerated this drug well, consistent with a previous study (14).

There are several limitations in the present study. The possibility of selection bias cannot be excluded, since eptifibatide therapy was provided to the patients based on their preferences. Additionally, the sample size is relatively small, and the present study was a single-centre study in China. Due to the relatively high cost of eptifibatide, only a small proportion of individuals with PIS could afford this medication. With the reform of the national medical insurance policy, non-cerebral vascular interventional treatment using eptifibatide has become increasingly difficult. This has prevented the increase in sample size. In addition, methodological biases, such as the heterogeneity of individuals and potential drug interactions, may influence the efficacy of eptifibatide. Due to the difficulty in obtaining valid post-discharge assessments, long-term follow-up analysis was not performed in the present study.

In conclusion, the present study showed that eptifibatide treatment was well tolerated in patients with PIS. Furthermore, compared with oral antiplatelet regimen alone, adding eptifibatide promoted early recovery in patients with SAO but not in patients with LAA. Due to the limitations of the retrospective study design itself, more multi-center, randomized controlled trials are needed in the future to study the effect of eptifibatide on progressive stroke.

Acknowledgements

Not applicable.

Funding

The present study was supported by the Xiangtan Medical Association (grant no. 2021-xtyx-7).

Availability of data and materials

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

Authors' contributions

LL and JL designed the study. YD, ZL, YY and WZ collected the data. LL and JL confirm the authenticity of all the raw data. LL and YD analysed the data, and ZL, JL, YY and WZ helped perform the analysis, with constructive discussions. LL and JL wrote the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the Ethics Committee of Xiangtan Central Hospital (Xiangtan, China). All participants in this study provided written informed consent for the use of their samples and publication of their data.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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