Restoration of Normal Coronary Flow With Tirofiban by Intracoronary Administration for No-reflow Phenomenon After Stent Deployment

Teng-Yao Yang,1 MD, Shi-Tai Chang,1 MD, Chang-Ming Chung,1 MD, and Nye-Jan Cheng,2 MD

SUMMARY

No-reflow phenomenon is frequently observed during percutaneous coronary intervention in patients with acute coronary syndrome. It may jeopardize hemodynamic status or result in ischemic chest pain in these patients. Currently, there is no adequate solution for this problem. We report our experience with an acute coronary syndrome patient who developed no-reflow phenomenon associated with ST segment elevation and shock after percutaneous coronary balloon dilatation and stent deployment. Intracoronary administration of tirofiban immediately restored the coronary flow of the target vessel, and the disastrous condition reversed. Our experience suggests that intracoronary administration of tirofiban can be considered as an option in case of no-reflow phenomenon during percutaneous coronary intervention. (Int Heart J 2005; 46: 139-145)

Key words: No-reflow phenomenon, Percutaneous coronary intervention, Tirofiban

NO-REFLOW phenomenon was reported to occur in 2% of patients requiring coronary intervention.1) The incidence of this phenomenon may be as high as 29% in patients with acute myocardial infarction when myocardial contrast echocardiography is used for identifying the no-reflow zone.2) During percutaneous coronary intervention in patients with acute coronary syndrome, no-reflow phenomenon may jeopardize the hemodynamic status or result in ischemic chest pain in these patients.3) Microvasculature damage, tissue edema, intravascular plugging, and microemboli have been proposed to play an important role in this phenomenon. Intracoronary administration of verapamil1) or adenosine4) has been reported to be helpful in this situation. However, neither was shown to promptly and effectively restore the coronary flow. We present a patient with acute coronary syndrome who developed no-reflow phenomenon associated with ST segment elevation and shock after percutaneous coronary balloon dilatation and stent

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deployment. Intracoronary administration of tirofiban, a small-molecule platelet glycoprotein IIb/IIIa receptor inhibitor, immediately restored the flow and reversed the disastrous condition.

CASE REPORT

A 65-year-old male visited our hospital due to a non-ST elevation myocardial infarction that had occurred the previous day. The patient was admitted to the intensive care unit. Medications including heparin, aspirin, clopidogrel, propranolol, and isosorbide dinitrate were started. A coronary angiographic examination, which was done on the fourth hospital day, revealed a 90% stenosis at the distal left circumflex artery (LCX) and was associated with a TIMI-3 (thrombolysis in myocardial infarction grade 3) flow (Figure 1). There was no apparent thrombus in the coronary artery.

Percutaneous coronary intervention (PCI) for LCX was performed using a 6 Fr Vista Brite Tip JL4 guiding catheter (Cordis, Johnson and Johnson, Miami, FL) and an ATW wire (Cordis, Johnson and Johnson) via a transradial approach. The target LCX lesion was dilated using a Cross-sail 3.0 × 20 mm balloon (Guidant/Vascular Intervention, Temecula, CA) inflated to 8 bars for 30 seconds.

![Figure 1.](image)
After balloon dilatation, repeat coronary angiography disclosed an 85% residual stenosis with a distal TIMI-2 flow at the lesion.

Because of a suboptimal result after balloon dilatation, an ACS Multilink-Penta coronary stent (Guidant/Vascular Intervention), 3.0 × 13 mm, was deployed to the lesion at 10 bars for 20 seconds. Unfortunately, the subsequent coronary angiography showed no-reflow phenomenon distal to the lesion site (Figure 2). Because distal embolization was suspected, we attempted to inflate the balloon four times at 4-6 bars for 10-15 seconds sequentially from inside-the-stent to its distal segment.

However, the no-reflow phenomenon persisted despite our attempt to fragment the potential thrombus using balloon dilatation. An electrocardiogram (ECG) then showed ST-segment elevation. The systolic blood pressure began to decrease to 60 mmHg (Figure 3). Tirofiban 750 µg (10 µg / kg) was administered intracoronarily for 3-5 minutes through the guiding catheter. The ST-segment returned to the iso-electric level one to two minutes after administered of tirofiban, and the blood pressure returned to normal (Figure 3). Selective coronary angiography immediately after intracoronary administration of tirofiban showed a distal TIMI-3 flow, without identification of the thrombus (Figure 4).

Figure 2. Posterior-anterior projection with cranial angulation of selective left coronary (LCA) angiogram after stent deployment showed stagnation of the contrast agent, indicating no re-flow phenomenon (distal LCX delineated by arrows).
Figure 3. Electrocardiogram before PCI (left) and after stent deployment (center) showed elevated ST-segment during no-reflow phenomenon. The systemic blood pressure also dropped from 122/74 mmHg before PCI to 63/40 mmHg during the occurrence of no-reflow phenomenon. After tirofiban infusion (right), the ST-segment returned to the iso-electric level and the BP returned to 119/65 mmHg.

Figure 4. Posterior-anterior projection with cranial angulation (left, 4A) and right anterior oblique projection with caudal angulation (right, 4B) of selective left coronary angiogram after intracoronary administration of tirofiban showed restoration of TIMI 3 flow without residual thrombus at distal LCX.
This patient was transferred to the intensive care unit for further observation after the procedure. Intravenous tirofiban infusion after PCI was maintained at a rate of 0.15 µg/kg/min for 2 days. He was also treated with heparin, keeping adequate APTT for 3 days. We performed an immediate creatinine phosphokinase (CPK) iso-enzyme study and PCI follow-up studies at 8 and 16 hours, which revealed no MB isoform. This result was evidence of no myocardial injury during PCI. This patient was discharged without complications 4 days after PCI, and was followed at the outpatient clinic uneventfully.

**DISCUSSION**

Antegrade epicardial coronary flow may decrease or even disappear after balloon dilatation during percutaneous intervention, the so-called slow flow or no-reflow phenomenon. The proposed underlying pathophysiology of no-reflow phenomenon includes microvasculature damage, tissue edema, intravascular plugging by fibrin or platelets, leukocyte plugging, or oxygen free radical release. Microemboli released into the microvasculature during intervention or thrombolysis also play a very important role in acute myocardial infarction. Yet, the mechanism of this phenomenon is still not clear. No-reflow phenomenon may lead to acute myocardial infarction and result in in-hospital mortality. Intracoronary administration of verapamil, adenosine, nicorandil, papaverine, urokinase, or tissue-type plasminogen activator through the intravenous route has been attempted to treat no-reflow phenomenon. However, none was found to promptly and effectively restore the coronary flow.

Recently, administration of a platelet glycoprotein IIb/IIIa antagonist, abciximab, was reported to be able to enhance the fibrinolytic effect, change the thrombus architecture, and increase the coronary flow in vitro and platelet activation was considered an underlying mechanism in patients with an acute myocardial infarction. Using quantitative myocardial contrast echocardiographic study, tirofiban also improved microvascular flow and reduced the infarct area after coronary occlusion/reperfusion in open-chest dogs. This ex vivo observation was also evident clinically. For example, intracoronary administration of abciximab, a monoclonal antibody directed against the glycoprotein IIb/IIIa receptor, and tirofiban, a synthetic nonpeptide small-molecule platelet glycoprotein IIb/IIIa receptor inhibitor, were shown to be able to dissolve an intracoronary thrombus, although both are not thrombolytic agents. Glycoprotein IIb/IIIa antagonists were also reported to reduce major ischemic events in the PAPPORTrial and CADILLAC trial. However, they do not improve the percentage of patients achieving TIMI grade 3 flow after direct percutaneous coronary intervention. For
those patients with an angiogram suggestive of a high thrombus burden, a glycoprotein IIb/IIIa antagonist did not reduce the risk of slow flow or no-reflow.17)

In this single patient experience, tirofiban did restore the coronary blood flow promptly and effectively when no-reflow phenomenon occurred. Because tirofiban blocks the final common pathway of platelet aggregation and administration of tirofiban quickly resolved the no-reflow phenomenon, our experience is consistent with previous studies suggesting that platelets play a major role in no-reflow phenomenon.5)

Why did tirofiban restore the flow in our patient but not in previous studies?15-17) The most striking difference is our route of intracoronary administration rather than the intravenous administration used in previous studies. With venous administration, a long time is needed before the drug reaches the lesion, and thus, the drug could be metabolized, bound to protein, or diluted by the body pool. Only a limited amount of drug reaches the coronary artery and has an effect on the target lesion. Instead, intracoronary administration provides an instantaneous and high local drug concentration focused at the target lesion that effectively cleaves the thrombus.

**Conclusion:** Our experience in this patient showed that intracoronary administration of tirofiban may restore coronary flow in patients with acute coronary syndrome who have developed no-reflow phenomenon after percutaneous coronary balloon intervention. However, whether this option is effective will depend on the results of further studies.

**REFERENCES**


