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Review

Slow Blood Flow after Percutaneous Coronary Intervention in Patients with St-Segment Elevation Myocardial Infarction, Unstable Angina and Coronary Total Occlusion

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Abstract

The aims of treatment of ST-segment elevation myocardial infarctions are vessel recanalization and restore the normal coronary blood flow. The no-reflow or slow blood phenomenon is one of the common and critical occurrences after PCI in STEMI patients, unstable angina and coronary total occlusion in which myocardial reperfusion therapy does not restores the optimal level of blood flow. There are several predisposing factors of slow blood flow after PCI have been identified. Alprostadil have beneficial effects on fibrinolysis, vasodilatation and disaggregation. But the role of Alprostadil on coronary blood flow after PCI STEMI patients is remaining unclear. This review articles describes the risk factors, mechanism and management of slow blood flow or no-reflow phenomenon after PCI in patients having ST-Segments elevation myocardial infarctions.

Key words: No-Reflow Phenomenon, Acute Myocardial Infarction, Percutaneous Coronary Intervention, Angiography And Alprostadil.

1. Introduction

Acute myocardial infarction is a life threatening disease with high mortality. The main cause of acute myocardial infarction is the sudden occlusion of main coronary artery or its branch. Early reperfusion therapy is necessary to restores the normal blood flow, reduces the area of necrotic

myocardium and reduces the mortality (1-3). ST-segment elevation myocardial infarction (STEMI) is defined as combination of chest pain greater than 30 minute, ECG changing with ST-Segment elevation of greater than 2 mm in at least 2 precordial chest leads and greater than 1 mm in limb leads and increased levels of Troponin I or CKMB level higher than twice the upper limit of normal ranges. Primary percutaneous coronary intervention (PCI) is the reperfusion therapy used in treatment of ST-Segment elevation myocardial infarction, unstable angina and coronary total occlusion to prevent the progression of myocardial necrosis (3). However some patients have no reflow or slow blood flow in related blood vessel after emergency primary percutaneous coronary intervention with stent implantation (3-6).

1.1 ST-Segment Elevation Myocardial Infarction:

ST-segment elevation myocardial infarction is one of the most common diagnoses in hospital patients. More than half of the acute STEMI related death occurs before the individual reached the hospital. When patients with prolonged ischemic chest pain or chest discomfort at rest are first seen, the working clinical diagnosis is that they are suffers from acute coronary syndromes. The 12 lead electrocardiograms provide diagnosis and give decision pathways for management and help in differentiation of ST-Segment elevation myocardial infarction from those presenting without ST-segment elevation myocardial infarction. Serum cardiac biomarkers are obtained to differentiate unstable angina from non-ST-Segment elevation myocardial infarction (NSTEMI) and to assess the management of ST-segment elevation myocardial infarction.

Slow blood flow or no reflow blood phenomena is defined as no blood flow or slow blood flow in infracted related coronary artery after percutaneous coronary intervention (Stenting or balloon inflation), without angiographic evidence of mechanical vessel obstruction, resulting in no perfusion or hypoperfusion in myocardium (1,4,5,7,8). Slow blood flow or no reflow phenomenon is associated with poor left ventricular functions recovery and worse long term outcomes. The exact mechanism of slow blood flow or no reflow phenomenon after PCI is not established till now. Slow blood flow after percutaneous coronary intervention is a series complication in the treatment of ST-Elevation myocardial infarction, unstable angina and coronary total occlusion (5,9,10). The no reflow phenomenon after PCI is strong predictors of death extending up to 5 years, in patients with STEMI (11).

2. Risk factors of slow blood flow or no reflow phenomenon.

The patient with slow blood flow or no reflows phenomenon in infracted related blood vessel after emergency PCI in STEMI is related to genetically susceptibility and diabetes mellitus, smoking, Hypertension, Hyperlipidemia are unfavorable conditions for no reflow phenomenon **as shown in Table 1** (12-14). The inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) also play major role in restenosis after PCI (15-18). Other risk factors included high WBC count, thrombus grade, pain duration, maximal ST-changes, Left ventricular function, bifurcation and coronary anatomy. Incidences are higher in patients with high thromboembolic lesions (19, 20). There is also relationship between the onset time of acute myocardial infarction and slow blood flow phenomenon during surgery. The longer the onset of acute MI, there is a higher incidence slow blood flow or no reflow phenomenon.

3. Mechanism of slow blood flow or no reflow phenomenon.

The exact mechanism of slow blood flow or no reflow phenomenon is not understood but the main mechanism considered is myocardial ischemic injury, endothelial dysfunction, microvascular

spasm, microvascular dysfunction, myocardial reperfusion injury, distal coronary artery embolization and microcirculation injury (1, 5, 13, 21, 22).

Table 1: Risk factors of slow blood flow after PCI in patients with STEMI(1, 13, 14).

Following are the risk factors of slow blood flow after PCI in patients with STEMI:
1. Smoking.
2. Diabetes mellitus.
3. Age.
4. Systolic Blood pressure.
5. Local interleukin.
6. Hyperlipidemia.
7. Increased white blood cells count.
8. Pain duration.
9. Coronary anatomy.
10. LV function.

PCI: Percutaneous coronary intervention. STEMI: ST-Segment elevation myocardial infarction.
LV: Left ventricular.

Myocardial ischemia causes damage to vascular endothelium, adhesion of platelets and Neutrophil causes occlusion of the lumen, which aggravating microcirculatory disorders. After the myocardial reperfusion, there is increased production of oxygen free radical, calcium overload, and infiltration of acute inflammatory cells such as Neutrophil and activation of apoptotic signaling pathways, which aggravate ischemia (23, 24). Acute myocardial infarction patients undergo PCI, due to balloon expansion or stent implantation, intracoronary plagues rupture microparticles which lead to vascular obstruction in distal coronary artery (5). When the diameter of particles is less than 200 μm, which generally does not cause vascular obstruction and when the diameter of the particle is greater 200 μm, which causes severe microvascular obstruction. The thromboxane or Angiotensin released by plagues, which may lead to microcirculatory disorders (21, 25, 26). The culprits lesion in STEMI are composed of fragile tissue such as cholesterol, foam cells, thrombus and microcalcification (27), which causes distal embolization following stent implantation, resulting slow blood flow (28).

The shorter the pain duration, fresh clot in artery and fresh clot increase the occurrences of no-reflow phenomenon in acute MI patients after PCI (29-31). The high WBC counts will increase inflammation and aggregation of WBC in artery of myocardium, which causes no-reflow phenomenon (32). The increased clot volume causes higher thrombus grade, which increased the possibility of no-reflow phenomenon (33). So WBC counts and thrombus grade are most important predictive factors of developing no-reflow phenomenon (30, 32). The number of abnormal pathological Q-waves, larger infarct size and wall motion score are also most important predictive factors for developing no-reflow phenomenon (8, 11).

The cytokines, interleukin-6 (IL-6) is implicated in both proinflammatory and anti-inflammatory response in development of slow flow or no-reflow phenomenon (34). In chronic inflammatory condition such as idiopathic pulmonary fibrosis, bronchial asthma, arthritis, colitis, IL-6 play a proinflammatory role while in acute inflammation, its play role as anti-inflammatory (35). The inflammatory markers such as C-reactive protein and IL-6 play important role in occurrences of restenosis after PCI (15-18, 36). So the elevation of IL-6 is important indicators

of increased mortality rate in case of ST-Segment elevation of myocardial infarction, who undergoes PCI (36, 37).

In patients with percutaneous coronary intervention at greater than 3 hours onset of acute MI, having white thrombus are more likely to have no-reflow or slow blood flow after stent implantation than patients with red thrombus. This will predict, there is a slow blood flow or re-flow phenomenon after stent implantation.

4. Management of slow blood flow or no-reflow phenomenon after percutaneous coronary intervention:

In patients with hyperthrombotic lesions, to achieve complete recanalization of infracted coronary artery, pre-coronary administration of drugs such as glycoprotein IIb/IIIa receptors antagonist can be given for prevention of slow blood flow after PCI.

Medical treatment with sodium nitropruside (38), Nicorandil (39) nitroglycerin, Diltiazem and verapamil (38, 40)are effective in relaxing vascular smooth muscle, regulated endothelial function and preventing microvascular spasm as shown in table 2 (1, 38) and figure 1. These medicines lowered the blood pressure, among which verapamil and diltiazem causes malignant Atrioventricular blocks and significant bradycardia while nitropruside and nitroglycerin causes increase heart rate (1). Therefore the effectiveness for the intravenous infusion of these drugs after PCI is still controversial.

Prostaglandin E1 (PGE1) is widely used now a day in clinical practices due to its beneficial effects on fibrinolysis, vasodilatation and platelet disaggregation (1). Alprostadil is a kind of liposomal PGE1, which dilates the coronary arterioles (1) and prevent coronary restenosis (1). Alprostadil accumulates around the target lesion, which lead to mild cardiopulmonary side effects but Alprostadil will dilate the coronary arteries and improve the coronary circulation in STEMI is still controversial.

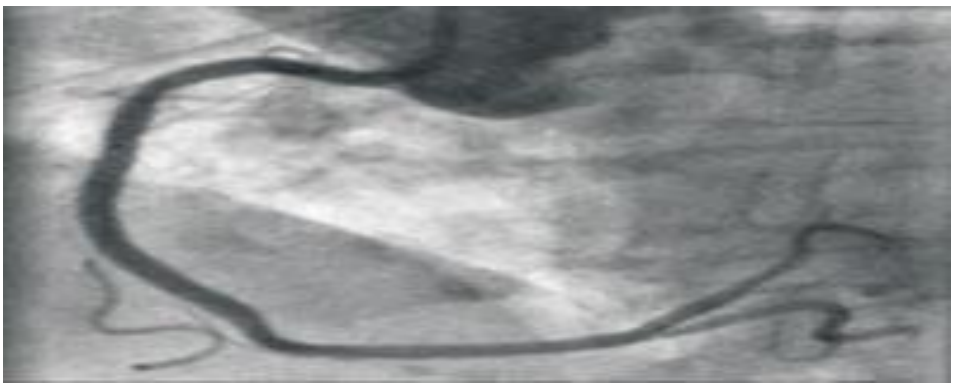

Figure 1. Slow blood flow improved after intracoronary injection of verapamil and nitroglycerin.

Table 2: Drugs used for prevention of slow blood flow after PCI in patients with STEMI (1, 38)

Following are the drugs used for prevention of slow blood flow after PCI in STEMI:

1. Verapamil.
2. Diltiazem.
3. Nitroglycerin.
4. Sodium nitropruside.
5. Alprostadil.
6. Nicorandil.

Mechanical technique such as thrombus aspiration and distal protection devices can be chosen to tackle thrombus in major coronaries arteries (1). An intracoronary drugs infusion technique is more commonly used for small vessel where thrombus is not visible (1). Thrombus aspiration during primary percutaneous coronary intervention show controversial result for the effectiveness of aspiration of thrombus (41-43).

A slow blood flow or no-reflow phenomenon is one of the major and common complications in STEMI, who undergoes percutaneous coronary intervention. The incidence of slow blood flow phenomenon is ranges from 5 % to 25 % (1). The no-reflow phenomenon, if not reversed, then causes high mortality and morbidity rate (44).

Slow blood flow or no re-flow phenomenon is strong predictors of major cardiac complications such as congestive heart failures, life threatening malignant arrhythmia (45, 46) and cardiac death after PCI in patients with STEMI thus induces higher in hospital mortality and poor long term prognosis (47).

5. Conclusion:

Slow blood flow is a common complication after percutaneous coronary intervention in patients with ST-Segment elevation myocardial infarction, unstable angina and coronary total occlusion and associated with poor outcomes. The slow blood flow or no-reflow phenomenon remains a significant challenge for STEMI and unstable angina patients. It is associated with poor prognosis. Time of acute myocardial infarction, WBC count, diabetes mellitus, and hypertension, characters of thrombus, thrombus grading, age, and ratio of stent diameters to vessel diameters are the strong predictive factors for developing slow blood flow or no-reflow phenomenon after percutaneous coronary intervention in patient with ST-segment elevation myocardial infarction. Although we have several device and drugs to treat slow blood flow phenomenon after PCI in STEMI patients. Alprostadil can be used for prevention of slow blood flow after PCI in patients with STEMI.

Abbreviations

ECG: Electrocardiogram.
STEMI: ST-Segment elevation myocardial infarction.
PCI: percutaneous coronary intervention.
MI: Myocardial infarction.
UA: Unstable angina.
IL-6: Interleukin-6.
CKMB: Creatine kinase-MB

Declarations

1) ***Consent to publication***
We declare that all authors agreed to publish the manuscript at this journal based on the signed Copyright Transfer Agreement and followed publication ethics.
2) ***Ethical approval and consent to participants***
Not applicable.
3) ***Disclosure of conflict of interests***
There authors have no Conflicts of interest to declare.
4) ***Funding***
None
5) ***Availability of data and material***
We declare that the data supporting the results reported in the article are available in the published article.
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7) Authors 'contribution

Authors contributed to this paper with the design (LNG and SY), literature search (LNG), revision (LNG and SY), editing (LNG) and final approval (LNG and SY).

8) Authors' biography

None

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