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**ABOUT COVER**

Editorial Board Member of *World Journal of Clinical Cases*, Moises Rodriguez-Gonzalez, MD, Adjunct Professor, Senior Researcher, Department of Pediatric Cardiology, Hospital Universitario Puerta del Mar, Cadiz 11009, Spain. doctormoisesrodriguez@gmail.com

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## Retrospective Study

**Sodium nitroprusside injection immediately before balloon inflation during percutaneous coronary intervention**

Yan Yu, Bao-Ping Yang

**ORCID number:** Yan Yu 0000-0002-2483-3141; Bao-Ping Yang 0000-0003-1359-9182.

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**Yan Yu, Bao-Ping Yang**, Department of Cardiovascular Medicine, Gansu Provincial Hospital of Traditional Chinese Medicine, Lanzhou 730050, Gansu Province, China

**Corresponding author:** Bao-Ping Yang, BSc, Associate Chief Physician, Department of Cardiovascular Medicine, Gansu Provincial Hospital of Traditional Chinese Medicine, No. 418 Guazhou Road, Qilihe District, Lanzhou 730050, Gansu Province, China. [ybp1788@163.com](mailto:ybp1788@163.com)

**Abstract****BACKGROUND**

No reflow or slow flow frequently occurs during percutaneous coronary intervention (PCI) and it is associated with adverse outcomes. Strategies should be undertaken to prevent its occurrence.

**AIM**

To observe whether conventional target intracoronary administration of sodium nitroprusside immediately before balloon inflation can reduce the incidence of no reflow and slow flow, which are defined as thrombolysis in myocardial infarction flow grade  $\leq$  II during PCI.

**METHODS**

A retrospective study was conducted in 740 patients with coronary artery disease admitted to Gansu Provincial Hospital of Traditional Chinese Medicine between January 2016 and October 2020. Among them, 360 patients receiving sodium nitroprusside immediately before balloon inflation during PCI were enrolled in an experimental group between January 2019 and October 2020 and 380 patients receiving sodium nitroprusside after incident no reflow and slow flow during PCI were enrolled in a control group between January 2016 and January 2019. The occurrence of no reflow and slow flow was compared between the two groups and left ventricular end-diastolic diameter (LVEDD) and left ventricular ejection fraction (LVEF) were detected 1 mo after the operation.

**RESULTS**

After treatment, the proportion of patients with thrombolysis in myocardial infarction flow grades 0 to II was lower in the experimental group than in the control group ( $P < 0.05$ ). At 1 mo after treatment, LVEDD was lower and LVEF was higher in the experimental group than in the control group ( $P < 0.05$ ). In terms of incidence of adverse cardiovascular events within 1 mo after treatment, in the experimental group, malignant arrhythmia occurred in three patients,

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intractable myocardial ischemia in three, congestive heart failure in four, and recurrent myocardial infarction in five; one patient died. In the control group, malignant arrhythmia occurred in eight patients, intractable myocardial ischemia in five, congestive heart failure in seven, and recurrent myocardial infarction in 14; two patients died. The incidence of adverse cardiovascular events was 4.4% in experimental group which was lower than that of the control group at 1 mo after operation (9.5%;  $P < 0.05$ ).

### CONCLUSION

Administration of sodium nitroprusside into target vessels immediately before balloon inflation can significantly reduce the incidence of no reflow and slow flow, improve LVEDD and LVEF, and reduce the incidence of adverse cardiovascular events in patients treated by PCI. It is worthy of clinical promotion.

**Key Words:** Sodium nitroprusside; No reflow; Slow blood flow; Coronary artery disease; Percutaneous coronary intervention

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**Core Tip:** The present study explored the effectiveness of coronary injection with nitroprusside, a commonly used vasodilator, as a pharmacological intervention strategy administered before balloon inflation for the prevention of no reflow or slow flow during percutaneous coronary intervention. The results showed that preventive use of sodium nitroprusside proved beneficial. It resulted in improved coronary blood flow and outcome of percutaneous coronary intervention.

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## INTRODUCTION

Coronary heart disease (CHD) is a common cardiac disease and percutaneous coronary intervention (PCI) is an effective therapy for CHD with a high success rate[1-3]. Postoperative remission determines outcomes and quality of life in patients with CHD. However, no obvious stenosis was reported in the affected vessels in 5% to 30% patients after revascularization in stenosis or occlusion of the coronary artery. However, angiographic results indicated that antegrade flow was decreased or lost. Coronary angiographic results indicated that thrombolysis in myocardial infarction (TIMI) flow grades 0 to II are classified as coronary slow flow or no re-flow[4-6]. Coronary slow flow or no re-flow may lead to microcirculation hypoperfusion, continuous myocardial ischemia, abnormal myocardial metabolism in cancer cells, poor prognosis, rise in mortality, reinfarction rate, reinfarction rate, and reoperation rate, cardiac insufficiency, ventricular dilatation, obvious reconstruction, and increased mortality[7]. Sodium nitroprusside is usually used for vascular relaxation in the coronary microcirculation of patients with CHD. Sodium nitroprusside releases NO into blood, which is then degraded into bradykinin and dilate microvascular vessels and improve myocardial perfusion[8]. Previous studies[9,10] showed that sodium nitroprusside can improve blood flow in patients with no reflow and slow flow undergoing reperfusion. The present study aimed to explore whether target intravascular sodium nitroprusside injection immediately before balloon inflation or preventive use of sodium nitroprusside can reduce the incidence of no reflow and slow flow during PCI.

## MATERIALS AND METHODS

### Research data

A retrospective study was conducted in 740 patients undergoing PCI at Gansu Provincial Hospital of Traditional Chinese Medicine between January 2016 and October 2020. Three hundred and sixty patients who were admitted to the hospital from January 2019 to October 2020 were included in an experimental group and 380 patients who were admitted to the hospital from January 2016 to January 2019 were included in a control group. Eligible participants included patients who ranged in age from 18 to 70 years, were diagnosed with CHD, or had a history of CHD with > 70% stenosis of the coronary artery on coronarography. Patients complicated with severe heart, lung, liver, and kidney dysfunction, severe diseases which caused psychological disorders or poor compliance, or other malignant cancer, and patients in poor physical condition and who are unable to tolerate surgery were excluded from the study. In the experimental group, 248 patients were male and 112 were female with average age of 32 to 68 ( $61.23 \pm 10.14$ ) years. Of them, 203 patients had a history of smoking and 157 were non-smokers. In terms of comorbidities, 187 patients had hypertension, 183 had hyperlipidemia, and 115 had a history of diabetes. For thrombolysis in myocardial infarction (TIMI) flow grade, 338 patients had TIMI grades 0 to II and 22 had TIMI grade III. Infarction occurred in the anterior descending branch in 119 patients, in the circumflex branch in 123, and in the right coronary artery in 127. The average lesion length was  $23.09 \pm 5.67$  mm. Balloon inflation was performed  $1.87 \pm 0.62$  times. The proportion of stenosis was  $83.69 \pm 7.21\%$ . In the control group, 261 patients were male and 119 were female. The average age was 31 to 69 ( $62.35 \pm 11.47$ ) years. Of them, 212 were smokers and 168 were non-smokers, 196 patients had hypertension, 188 had hyperlipidemia, and 121 had diabetes. With regards to TIMI flow grade, 345 patients had TIMI grades 0 to II and 35 had TIMI grade III. Infarction occurred in the anterior descending branch in 131 patients, in the circumflex branch in 128, and in the right coronary artery in 134. The average lesion length was  $22.96 \pm 6.12$  mm. Balloon inflation was performed  $1.87 \pm 0.62$  times. The proportion of stenosis was  $82.37 \pm 7.19\%$ . There was no significant difference in general information such as age, gender, or disease type between the two groups with high compatibility ( $P > 0.05$ ).

### Research methods

All patients received oral aspirin (Bayer Healthcare Co Ltd, Cat. No. J20130078) 300 mg and tegrello (AstraZeneca AB, Cat. No. J20130020) 180 mg before undergoing acute PCI in the catheter room. Arterial puncture was achieved through the radial artery or the femoral artery. Then, low molecular weight heparin calcium injection (Sanofi Winthrop Industrie, Cat. No. H20080481) 3000 IU was administered. The experimental group received target intravascular sodium nitroprusside injection 200  $\mu$ g immediately before balloon inflation (China Resources Double-Crane Pharmaceutical Co. Ltd., Cat. No. H11020635). The control group received sodium nitroprusside injection after no reflow and slow flow occurred during the operation.

### Measures

The outcomes of the study included the incidence of no reflow and slow flow during PCI which was assessed by two experienced interventional physicians 30 min after the treatment. The diagnostic criteria were TIMI grade for antegrade flow < II after PCI when no obvious stenosis was reported in the affected vessels[11]. Left cardiac function indexes were compared, including left ventricular end-diastolic dimension (LVEDD) and left ventricular ejection fraction (LVEF) at 1 mo after the operation. The incidence of adverse cardiac events was compared, including malignant arrhythmia, intractable myocardial ischemia, congestive heart failure, recurrent myocardial infarctions, and death at 1 mo after the operation.

### Statistical analysis

SPSS22.0 software was used for data processing. Quantitative data are expressed as the mean  $\pm$  SD. Qualitative data are expressed as percentages. Inter-group difference was compared using  $\chi^2$  test.  $P < 0.05$  represented that there was a significant difference.

## RESULTS

For posttreatment TIMI flow grade, the proportion of patients who had TIMI grades 0

to II was lower in the experimental group than in the control group, and the proportion of patients who had TIMI grade III was higher in the experimental group than in the control group ( $P < 0.05$ ; Table 1).

When comparing left ventricular function indices between the two groups, it was found that LVEDD was lower and LVEF was higher in the experimental group than in the control group ( $P < 0.05$ ; Table 2).

In terms of incidence of adverse cardiovascular events within 1 mo after treatment, in the experimental group, malignant arrhythmia occurred in three patients, intractable myocardial ischemia in three, congestive heart failure in four, and recurrent myocardial infarction in five; one patient died. In the control group, malignant arrhythmia occurred in eight patients, intractable myocardial ischemia in five, congestive heart failure in seven, and recurrent myocardial infarction in 14; two patients died. The incidence of adverse cardiovascular events was 4.4% in the experimental group, which was lower than that of the control group at 1 mo after operation (9.5%;  $P < 0.05$ ; Table 3).

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## DISCUSSION

PCI is one of the most used choices for the treatment of coronary heart disease. It opens blocked arteries, improves function of the heart, and protects cardiac muscle cells in a short time[12,13]. Sodium nitroprusside helps alleviate no reflow and slow flow during PCI, reduce myocardial microdamage, modulate local inflammatory response to protect cardiac muscle cells, improve heart function, cardiac ejection function, and outcomes, and reduce adverse cardiac events[14,15]. The present study explored whether preventive use of sodium nitroprusside or intravascular sodium nitroprusside injection immediately before balloon inflation can reduce no reflow and slow flow during PCI.

Coexisting diseases such as diabetes, hypertension, hyperlipemia, and multiple microangiopathic lesions are common in patients with coronary heart disease, leading to a high risk of no reflow and slow flow associated with PCI[16]. The occurrence of no reflow and slow flow may be attributed to distal microembolization of the coronary circulation, injury associated with microvascular reperfusion microvascular obstruction, and spasm[17,18]. Moreover, blood platelet and leukocyte levels, cell swelling in the myocardium, and stromal edema may cause no reflow and slow flow. Sodium nitroprusside as a vasodilator is used in patients experiencing no reflow and slow flow during PCI[19]. Sodium nitroprusside functions as an NO direct donor, releasing NO into the vascular vessels, which may result in significant dilation of arterioles and improvement of coronary microcirculation[20]. The present study found that target intravascular sodium nitroprusside injection immediately before balloon inflation can significantly reduce the incidence of no reflow and slow flow during PCI. This can be explained by timely use of sodium nitroprusside which can prevent reperfusion injury[21]. Meanwhile, target intravascular sodium nitroprusside injection immediately before balloon inflation over 1 mo can reduce LVEDD and increase LVEF, suggesting that sodium nitroprusside injection immediately before balloon inflation can improve outcomes and cardiac ejection function. This may be attributed to reduced time of reperfusion. Thus, it can effectively open vessels, relieve a blockage, and reduce reperfusion injury[22-24]. Furthermore, the current study revealed that target intravascular sodium nitroprusside injection immediately before balloon inflation can reduce the incidence of adverse cardiac events at 1 mo and improve long-term treatment effectiveness.

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## CONCLUSION

In summary, target intravascular sodium nitroprusside injection immediately before balloon inflation can reduce the incidence of no reflow and slow flow during PCI, significantly improving LVEDD and LVEF and reducing postoperative incidence of adverse cardiac events. Multi-center large sample studies are needed to further verify the findings of the study.

**Table 1 Posttreatment thrombolysis in myocardial infarction flow grade of diseased vessels, *n* (%)**

Group	<i>n</i>	TIMI	
		Grades 0 to II	Grade III
Experimental	360	28 (7.8)	332 (92.2)
Control	380	79 (20.8)	301 (79.2)
$\chi^2$ value		12.422	12.422
<i>P</i> value		0.001	0.001

TIMI: Thrombolysis in myocardial infarction.

**Table 2 Comparison of left ventricular function indices between the two groups**

Group	<i>n</i>	LVEDD (mm)	LVEF (%)
Experimental	360	54.21 ± 5.38	50.83 ± 8.38
Control	380	56.78 ± 4.90	47.56 ± 5.47
<i>t</i> value		6.329	7.542
<i>P</i> value		0.034	0.027

LVEDD: Left ventricular end-diastolic diameter; LVEF: Left ventricular ejection fraction.

**Table 3 Comparison of adverse cardiovascular events between the two groups at 1 mo after operation, *n* (%)**

Group	<i>n</i>	Malignant arrhythmia	Intractable myocardial ischemia	Congestive heart failure	Recurrent myocardial infarction	Death	Overall incidence
Experimental	360	3	3	4	5	1	16 (4.4)
Control	380	8	5	7	14	2	36 (9.5)
$\chi^2$ value							9.124
<i>P</i> value							0.001

## ARTICLE HIGHLIGHTS

### Research background

The incidence of no reflow or slow flow appears to be high in patients with coronary heart disease (CHD) undergoing percutaneous coronary intervention (PCI). This may lead to microvascular obstruction and endothelial disruption. Nipride has been proved effective in treating no reflow or slow flow.

### Research motivation

How does sodium nitroprusside benefit in the prevention of no reflow or slow flow? Does the time of administration affect the efficacy of sodium nitroprusside in the prevention of no reflow or slow flow?

### Research objectives

The present study was conducted to evaluate efficacy and usefulness of sodium nitroprusside administrated before balloon inflation in prevention of no reflow or slow flow.

### Research methods

Patients with CHD undergoing PCI were included. They were divided into two groups. The experimental group received sodium nitroprusside immediately before balloon inflation and the control group received sodium nitroprusside after no reflow or slow flow occurred during the PCI. The incidence of no reflow or slow flow was

compared between the two groups. Moreover, thrombolysis in myocardial infarction (TIMI) grade, cardiac function, and adverse events were also compared between the two groups.

### Research results

TIMI grade and cardiac function were better in the experimental group than in the control group. The incidence of adverse events was lower in the experimental group than in the control group.

### Research conclusions

Sodium nitroprusside administered immediately before balloon inflation is useful for the prevention of no reflow or slow flow during PCI.

### Research perspectives

Long-term, larger sample size and high-quality follow-up RCTs are needed for preventive use of sodium nitroprusside in patients with cardiac disease undergoing PCI.

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